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Iraqi Journal of Medical Sciences

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3. Chapter in book: Phillips, S.J., and Whisnant, J.P.: Hypertension and strock. In: Laragh, J.H., and Brenner, B.M. editors. Hypertension: Pathophysiology, diagnosis, and management. 2nd ed. NewYork: Raven Press; 1995. p. 465-78.

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رقم الإيداع في دار الكتب و الوثائق ببغداد ٧٠٩ لسنة ٢٠٠٠

EDITORIAL

IT IS THE TIME TO IMPROVE OUR TEACHING PROGRAMS

Fakher S. Al-Ani *MBChB, MSc, PhD*

Learning in general depends on essential prospects, or aims. These prospects determine the main frames of education programs and control the different schools that concerned with teaching processes. These prospects of learning processes could be one of the following:

- Learning is "to memorize special information"
- Learning is "Training of the mind to solve a problem"
- Learning is "Changing of the behavior to solve a problem"

The last prospect is the most acceptable one since it is the broadest meaning and covers the different aspects of the teaching processes (Gates). These learning processes should be continuous and need effort of training to reach the level that satisfy the subject and agree with his ambitions (Mursell). The learning processes are usually stimulated by either internal (privet) or external stimulus (Guilford).

Accordingly the aim of teaching
Is to change the behavior in solving special problems

To reach this goal (changing the behavior of the subjects and community) we need special teaching programs. These programs have been developed and progresses with the expansion and progresses of the knowledge in the different fields of life. So different programs of teaching were emerged to arm the subject with the specialized skillfulness toward the different aspects of sciences that are essential to build the developed societies.

Six years ago USA found that the teaching programs in Japan and Korea are better than their program. Accordingly, a wide scientific conference under the title of (Nationality in danger) was committed in the presence of governmental representatives to discus this problem. Since, they believe that; if the graduated students in these two countries are better educated than the American then after ten years America will be in danger.

This is true because developments of countries depend on how much their employers are educated. Teaching programs are the method and the tool by which we can introduce the knowledge to the mind and make them effective in changing the behavior of the individual and finally the behavior of the community, so improving teaching programs will improve the community and their performance.

Medical education programs:

Medical education through the different historical steps passes through different method of teaching. It is started as training program between the teachers and one or more of his students, that was at the time of Avicenna and Al-Razi. With the development of the community and medical knowledge, this type of training becomes insufficient. Later on medical schools were established following different rules and different specialties. Moreover; the new technologies, the computers, and the internet opens a wide field in the progress of medical teaching.

Medical teaching at the time being dose not depends on a personal effort, but on many factors including the personal, social, financial, and even the political factors. Not only that but the introduction of the different instruments in the new diagnostic and therapeutic fields of medicine, make at least a minimum degree of knowledge in other sciences like computer, physics, electronics as essential requirements for the new doctors.

Medical teaching programs in Iraq:

As in most of the countries, different teaching systems were used in the different medical schools in Iraq:

- Annual system
- Semester system
- Topic and quarter system
- Problem solving technique

In practice, these systems were taken as a core then they are changed according to the practical availability of their needs from personals and equipments.

Chairman of the Dept. Physiology, College of Medicine, Al-Nahrain University

Accordingly we can not compare which is better for our community due to the different factors included in the teaching programs starting from the score of the students passing through the standard of the college (equipment and staff) ending with the aim of that college.

In general although the standard of our graduated students seems to be good if not very good taking in consideration the results of competition when our student try to take their opportunity to get a job or to complete their studies outside the country especially in the developed countries, but during the past decade a very wide steps in the developments of new technique in medicine, little if any changes in our teaching programs were done. This made our student knowledge deficit in these fields.

I think it is the time to re-evaluate our teaching program to overcome the defect and improve the good things in our teaching.

EMBRYONIC STEM CELLS DIFFERENTIATE INTO NEURAL-LIKE CELLS *IN VITRO* AND *IN VIVO* AFTER INTRACEREBRAL TRANSPLANTATION

Mahmoud H. Hammash *MBChB, Ph.D.*[1] **Intissar N. Waheed** *B.Sc., Ph.D.*[2]

Abstract

Background: Pluripotent embryonic stem (ES) cells may provide a virtually unlimited donor source for transplantation, according to protocols that permit the *in vitro* generation of neural precursors from ES cells.

Objectives: To described conditions that induce differentiation of ES cells reliably and high efficiency into neural pathway.

Materials & Methods: Mouse ES cells obtained from cultured Blastocyst, were subcultured with addition of embryonic brain extract. The cells from these cultures as well as from cultured cells without addition of brain extract were transplanted into adult mice brain by injection using stereotaxic technique. Horse Raddish Peroxidase (HRP) was added to culture medium in the aim of labeling the transplanted stem cells, to enable the observation of transplanted location within the recipient brain.

Results: Results show that ES cells derived neural precursors have migrated for variable distances of different regions of the brain to replace damaged cells at the site of transplantation.

Conclusion: Thus, brain extract serves here as a source of neurotrophic factors for the induction of ES cells to neuronal pathway of differentiation, in which ES cell can serve as a valuable source of cell type-specific somatic precursors for neural transplantation. HRP histochemical marker was used for first time in culture medium for marking ES cells *in vitro* and *in vivo* to allow determination of the fate of the transplanted ES cells.

Key words: Embryonic stem (ES) cell/ neurogenesis/ neurotrophic factor / ES cell transplantation (cell transplant)

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Introduction

Embryonic stem (ES) cells, derive from the inner cell mass (ICM) of blastocyst-stage embryos are pluripotent, undifferentiated, immortal cells, capable of differentiating into derivatives of all three embryonic germ layers[1,2]. ES cells can be maintained *in vitro* in the undifferentiated state for periods of several months without loss of their developmental capacity, by coculturing with mitotically inactivated feeder cells, such as embryonic fibroblast[3,4] or with the addition of a differentiation inhibiting activity, {Leukaemia inhibitory factor (LIF)}[5,6].

In the past fifteen years, pluripotential ES-cell lines have been used extensively as amodel system to study aspects of gene expression and early embryonic development[6-8]. But recently, these self-renewing pluripotent ES cells (after induced to differentiate *in vitro*) may considered the bases of new cell replacement therapies[9].

To initiate differentiation of ES cells into specialized population need to change the growth conditions of the ES cells, in specific ways, such as by adding growth factors to the culture medium Of ES cells aggregate and embryoid bodies[9], or changing the chemical composition of the surface on which ES cells are growing[10], or to introduce foreign genes into the cells via transfiecion or by using cloning technology[11-13] and this directed derivation of ES cells is then vital to the ultimate use of such cells in the development of new therapies (in cell transplantation)[14-17].

The present study deals with how to direct the differentiation of these ES cells *in vitro* into neural pathway to be used *in vivo*, by grafting and transplanting ES cells into the injured area of mouse brain tissue and by using Horse raddish peroxidase (HRP) as a histochemical marker[18] to follow the fate of these transplanted cells.

Materials & Methods

Culture conditions

ES cells derived from the ICM of blastocyst-stage mouse embryo (Albino mice of strain:*Blab/C*) (Hammash of Waheed, 2003 in preparation)[4] were used in this study.

ES cells were maintained under 5% CO_2, 37^oC in minimum essential medium eagle modified (MEM) (Sigma) on mitotically inactive mouse

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embryonic fibroblast (feeder layer) supplemented with 20% new born bovine serum (NBBS) (Sigma).

To initiate differentiation, ES cells were dispersed with trypsin-EDTA 0.25% (w/v) powdered trypsin in 0.04% (w/v) Ethylene diamine tetra acetic acid (EDTA) in Calcium and Magnesium Free-Phasphate buffer saline (CMF-PBS) (PH 7.6) into single cell suspension, the later was cultivated without feeder layer or substrate attached layer, on non adhesive bacteriological petridish (to prevent attachment) with culture medium containing 20% NBBS, then incubated for few days, where they spontaneously form floating clusters of cells termed aggregates and simple embryoid bodies (EBs).

Induction of differentiation

As the aggregates and simple EBs were formed they were allowed to attach to the (0.01%) gelatin substrate coated tissue culture plate well and were left for 12 hr with MEM medium-plus 20% NBBS to form monolayer.

To initiate directed differentiation, the monolayer were plated in a defined medium (induction medium) that favor's the survival of ES cell-derived neural precursors and incubated for 10 days and this medium was changed every two days.

ES cells induction medium containing MEM medium plus 20% NBBS plus 25 µl/ml embryonic brain extract (prepared from 14-16 days mouse embryo following the general principles of embryo extract preparation as set by New[19] with some modification.

The directed differentiation pathway of these treated ES cells was evaluated after 10 days of incubation and as the cells form a monolayer.

a-*In vitro* differentiation:

Single cell suspension of these treated cells were prepared and passaged in the absence of feeder layer and cultured on gelatin substrate coated tissue culture plate and incubated for 2-5 days.

b-*In vivo*: Preparation of marking ES cells for transplantation:-

As a monolayer of directed and non directed (control group) ES cells was prepared, the medium was aspirated and change with MEM medium plus 20% NBBS plus 4% HRP-histochemical marker (Sigma), then incubated for 6 hours, washed for 5 times with CMF-PBS to remove the excess HRP. The cells dispersed into single cell suspension, centrifuged, then the cell number was determined at concentration of 20000 cells/ 10 µl of medium ready for transplantation.

Animals and transplantation procedure

Adult male mice (Albino mice: strain: *Balb/C*) were used as graft recipients. Mice were annaesthetized by inhalation of ether and placed in a stereotactic frame with tooth bar at +Z level, the rest of the body placed over thermoregulated operating table fixed at 37^{o}C. Midline incision starting 5 mm anterior to orbital level extending back to the occipital region.

3mm X 3mm craniotomy was done just lateral to the midline and 1mm anterior to the lambda. The above flap is elevated, dura opened exposing by this the superior parietal area of the brain.

A needle was introduced for 2.5-3 mm into the brain in a fixed direction of stereotactic frame, in order to produce limited damaged in a specific location.The damaged may be considered severe when over manipulation was done by the needle.

Injection of ES cells (for both directed and non directed) was done as follow: 5 µl Hamilton's syringe loaded with the ES cells (two times) was fixed to X-Y-Z coordinate of the stereotactic frame. The tip of the needle advanced in brain tissue to adepth of 2.5-3 mm from the cortical surface. The coordinate of site of injection were L+Z, P-10, +2.3 mm and the tip of the needle was fixed at these coordinate for 3 minute befor injection for proper settlement in brain parenchyma.

ES cells were injected at rate of 1µl/4 minutes with a total volume of 10µl which contain 20000 cells, and the needle was kept in its position for additional 5 minute after the completion of injection.

The syringe withdrawn and the skin closed with interrupted skin suture and the animal was allowed to recover and returned to its cage alone to be re-explored after 17-20 days[10].

Histochemical evaluation:- These studies were carried out into the brain tissue in order to follow-up the fate of these transplanted marked ES cells and as follow:-

After 17-20 days from transplantation, the whole brain was obtained and HRP marker was detected histochemically following fixation of the frozen sections (4 µ thickness) with 4% formaline for 10 minutes and histochemical

visualization of the HRP is achieved by incubating the fixed tissue sections in a medium containing the substrate (H_2O_2) and a 3,3-diaminobenzidine tetrahydrochloride (DAB)[20].

Results

In vitro and *in vivo* (in the transplantation study) we initiated and adopted this protocol which appeared more suitable to promote the differentiation of ES cells to the neuronal pathway, this protocol included three steps:

First step: ES cells were cultured in a non-adhesive dish, where they form floating clusters of cells, termed aggregates when these aggregate cultivated for 2-3 days in suspension they for simple EBs.

Second step: attached cultures were initiated by plating these aggregates with simple EBs onto gelatin coated dish to allow adherence.

Third step: these adhered (attached) cells was exposed to MEM medium plus serum plus embryonic brain extract, then cultivated in this condition without passage for 10 days.

The *in vitro* examination of this culture during this period, showed no differentiated ES cells as a neuronal-like cells in the monolayer of the culture.

Differentiation of directed ES cells

In vitro (after passaged) these cells were differentiated to neuronal-like cells as shown in (Figure 1).

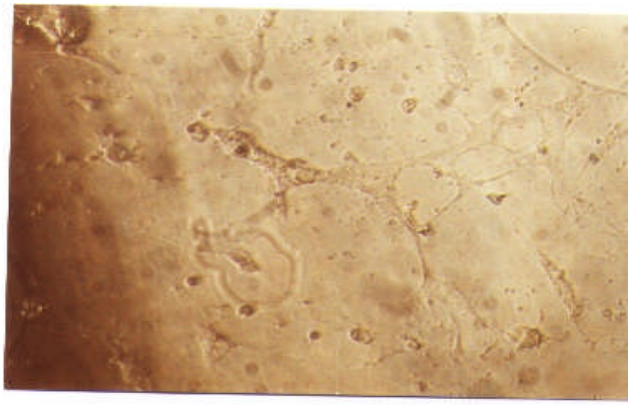

Figure 1: In vitro differentiation of ES cells to neural-like cells (living materail) x 100.8

The *in vivo*, grafting and transplanting of the ES cells into the adult mice brain, showed the following:

First: When there is severe damage in the brain tissue the transplanted cells settled in this damaged area then proliferate and differentiate enhancing the repair of damaged area.

Second: When there is no severe damaged carried in the brain tissue, some of the transplanted cells migrated away from the site of transplantation to different regions of the brain tissue, then proliferate and differentiate to cells of this brain tissue they migrated to it.

When these cells are transplanted via injection (without damage was carried, only the damaged of the site of injection) in the Hipocampus region (at the tip of dentate gyrus medial to the corn of Ammon layer (CA1), the transplanted cells migrated away from the site of injection to the gray matter of parietal lobule (sensory area) for distance of 1.5 mm surrounding the site of injection (Figures 2A & B) according to[21].

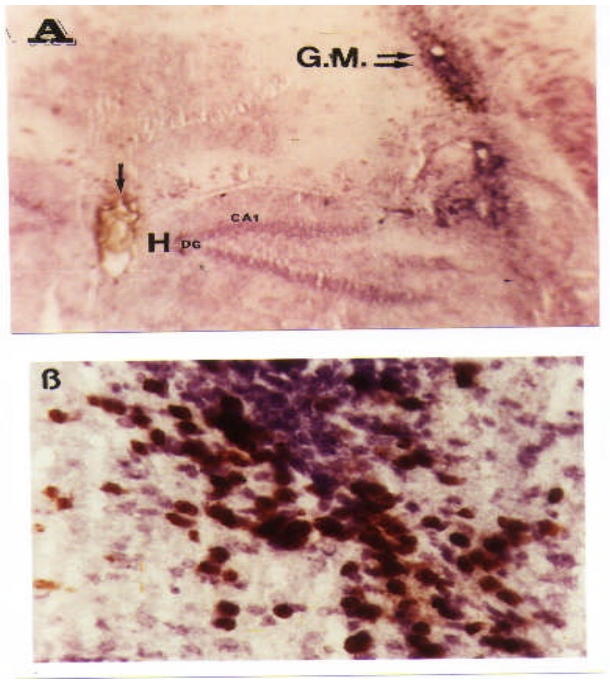

Figure 2: Transplantation of the (treated and marked) ES cells in the mouse brain. A: shows the site of injection (↓) Hipocampus region (H) at the tip of the dentate gyrus (DG), medial to the corn of Ammon layer (CA1) and the site of the fate migrating these cells (→) the Gray matter of parietal lobule (sensory area (GM) x 60. B: The higher magification of the site of fate migrating ES cells (HRP) marked ES cells brown in color. X 600

Cells transplanted into the damaged right superior parietal lobe showed the following possibites, as appeared in brain section:

A. Some of them are settled and diffused in damaged area (Figures 3A & B) and when the original brain cells and transplanted differentiated ES cells were examined under high magnification, showed similarity between

transplanted cells, and the host cells, in size and shape (Figures 4A & B).

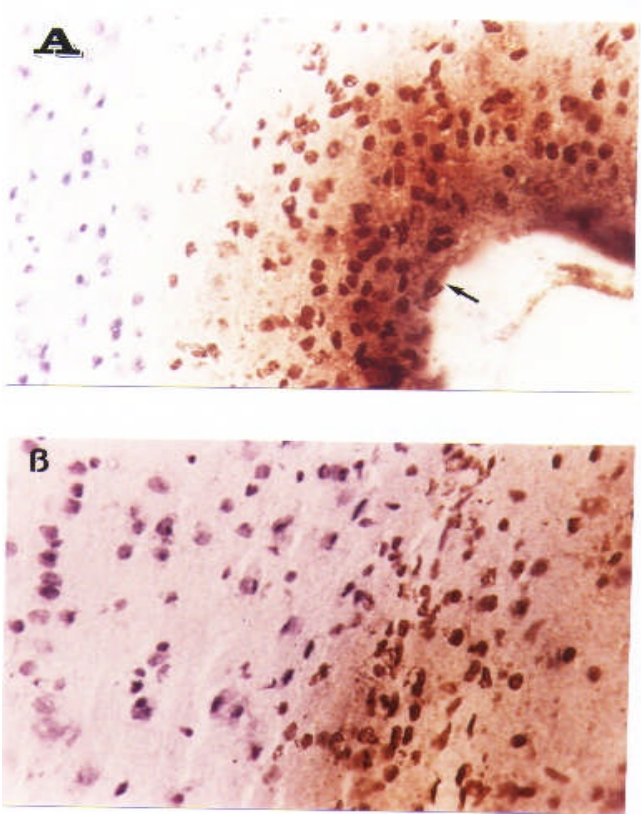

Figure 3: (A & B): Transplantation of the ES cells in the superior parietal lobe (Rt. Side) x 600.

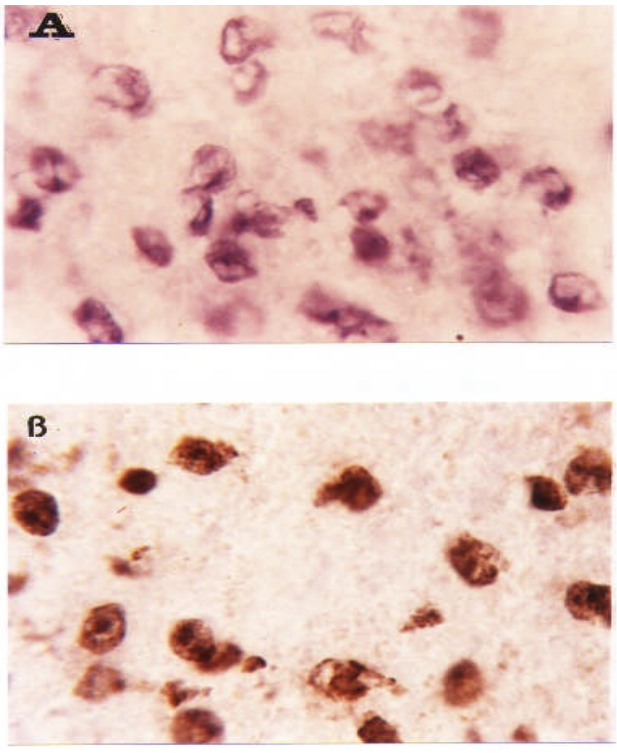

Figure 4A & B: By using higher magnification in order to compare between the original cells at the site of injection (A) and transplantd (treated and marked) ES cells (B). These pictures indicate the similarity between these cells. X 1500

B. Other transplanted cells migrated and were observed in the subcallosal area in the CA_3, Dentats Gyrus (DG), for distance 3-5 mm from the site of transplantation (Figure 5A) then proliferated and differentiated in this area (Figures 5B, C & D).

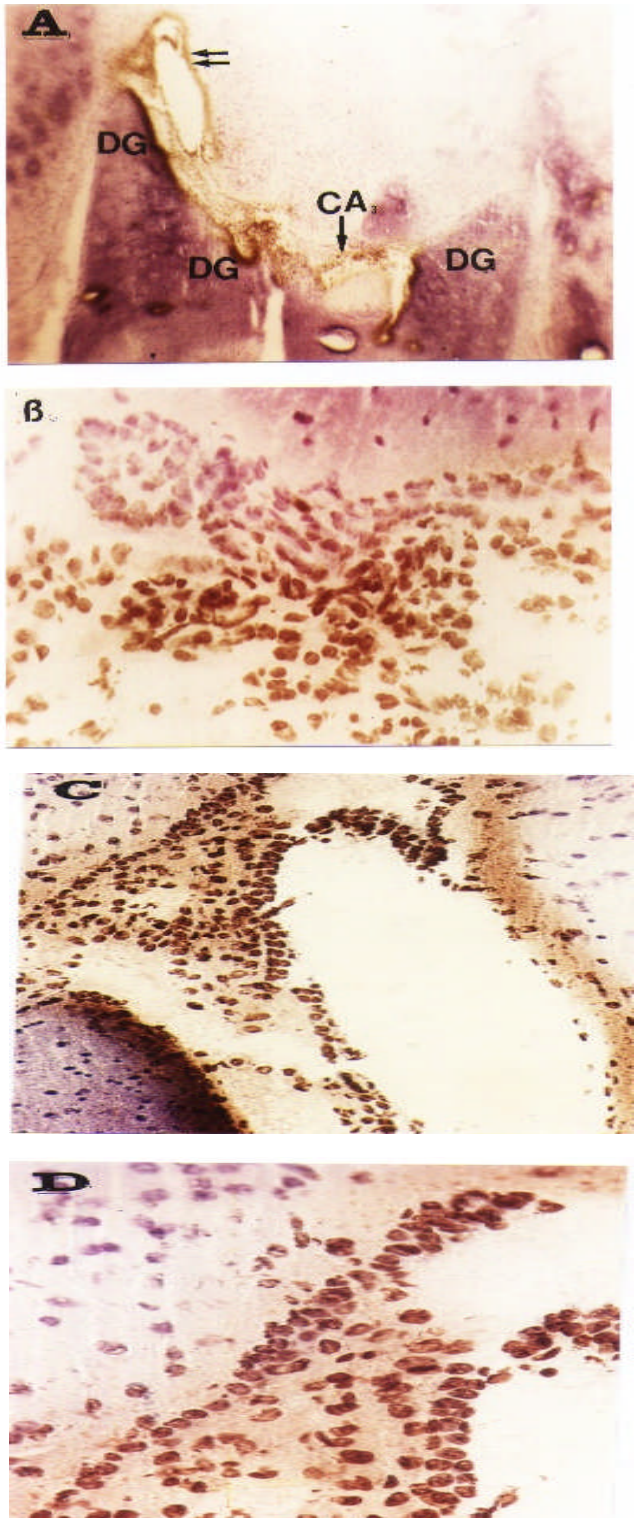

Figure 5 A: Migration of the transplanted (treated and marked) ES cells from superior parietal lobe (Rt. Side) to the subcallosal area in the corn Ammon (CA3), dentate gyrus (DG). X60 B: High magnification of area (▼) from figure A. x 600 C: High magnification of area (▶) from figure A. x 300 D: More higher magnification of figure C. x600.

C. Another group of transplanted cells migrated away from the site of transplantation and observed in the inferior parietal lobule of the right side for distance of 5.45 mm from the side of transplantation (Figure 6).

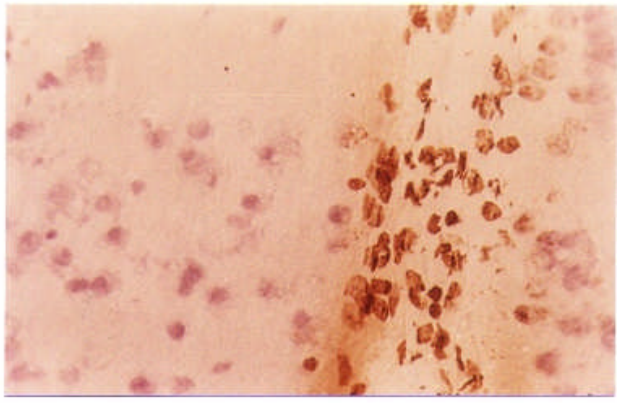

Figure 6: Migration of the transplanted (treated and marked) ES cells from the superior parietal lobe (Rt. Side) to the inferior parietal lobule of the Rt. Side. X600

D. Others migrated away from the superior parietal lobule to the inferior parietal lobule (or angular gyrus) of the left side for a distance of 6.5 mm from the site of transplantation (Figure 7A). They were setteld and has to proliferated and differentiated in to an isomorphous population of round to bipolar cells (Figure 7B).

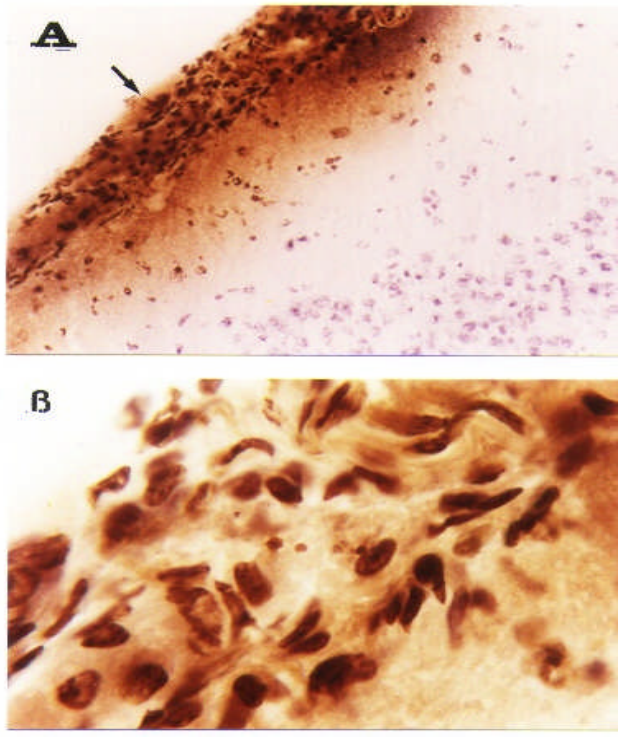

Figure 7 A: Migration of the transplanted (treated and marked) ES cells from the site of injection (superior parietal lobe) of the Rt. Side to the inferior parietal lobule (or angular gyrus) of the Lt. side and sattled, proliferate and differentiate in this area (↓). X150. B: shows an isomorphous population of round to bipolar (differentiate) transplanted ES cells. X 1500

Third: When cells were transplanted in the right parietal area after sever damage most of ES cells were restricted and settled in the damaged area and proliferated and differentiated replacing the damaged brain tissue (Figure 8).

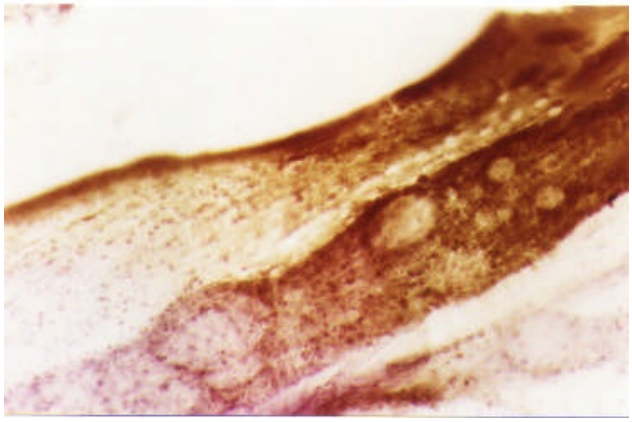

Figure 8: Transplantation of (treated and marked) ES cells in the parietal area after severe damage was carried in this area, note the repaire and healing of damaged tissue were carried by ES cells, which appeared as brown stained layer. X300

In all these three conditions of transplanted ES cells and after the end of the experiment, no signs of tumor growth or non-neural tissue in the transplanted recipients was noted.

Forth: Marked ES cells but not treated with embryonic brain extract were transplanted in the simillar location. They form a heterogeneous tissue inside the brain (Figure 9).

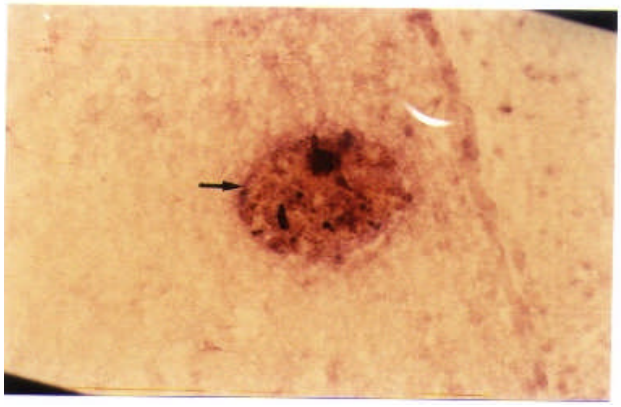

Figure 9: Transplantation of marked ES cells (non-treated with brain extract) (↓) in the mouse brain tissue, the piocture indicates that these cells did not differentiate and they form a heterogenous tissue inside the brain. X250

As described above these transplanted ES cells were tracked by prelabelling *in vitro* with histochemical marker HRP before transplantation and from the result of the present study, this marker can provide good information about events occuring within long period (for 17-20

days in this study) after transplantation. This marker appeared non deleterious or harm to the cells, because the cells survive and for long period after marking as shown in the result of transplantation.

Discussion

In the present study, part of a long term goal to develop cell transplantation therapy for specific diseases (that results from the destruction and/or dysfunction of a limited number of cell types) using ES cells as a source of pluripotent cells.

The use of ES cells to generate replacement tissue for treating neurological diseases is a major focus of researches on spinal cord injury, stroke, multiple sclerosis, and Parkinson's diseases, at which the concept of replacing destroyed or dysfunctional cells in the brain or spinal cord seems plausable[22,23].

ES cells have the ability to choose between prolonged self renewal and differentiation. This fate choice is highly regulated by intrinsic signals and the external microenvironment, the elements of which are being rapidly elucidated[24]. These cells will need to be differentiated or otherwise modified before they can be used clinically.

ES cells are theoretically capable of differentiating into any cell type *in vitro. T*he previous works have shown that they can be induced *in vitro* to become nural precorsers by using a number of protocols which depend on using compilation of several and different growth factors plus other compound and serum-free medium. *In vivo* neuronal histogenesis is regulated by neurotrophic factors, neuron-glia reactions, extracellular matrix molecules and sex steroid. Growth factors (such as fibroblast growth factors (FGF) have a broad survival and growth effect on cell culture from different regions of the embryonic brain and large amount of these growth factors are present in all regions of fetal brain suggesting an important role for these growth factors in early neurogenesis[9,16,25,26].

Results of this study has shown that mouse ES cells, cultured with addition of embryonic brain extract can develop neuronal- like cells in the culture, as observed morphologically.

In this, we substituted, the specified growth factors by embryonic brain extract, as a crude source of neurotrophic factors for directing the differentiation of ES cells to obtain neural precursors *in vitro* and to be used for transplantation *in vivo*.

For induction of ES cells differentiation to the neuronal pathway, we used protocol given above which is different from other protocols[9,10,25,27], that the induction is carried to the ES cells monolayer.

To evaluate the lasting differentiation of ES cells grown under this protocol, *in vivo*, immortalized cells were implanted into the brain and where they seem to be migrate broadly,as if they differentiated and replaced the depleted cells. These cells induced to differentiate into a mixed population of cells enriched with neuronal precursors. These results are in agreement with a study[28] (using combination of growth factors with serum-free medium) and implanted in the spinal cord of myelin-deficient rats depleted of endogenous oligodondroglia and with Benninger *et al*[29] who used several different media to assess the influence of serum and growth factors on the differentiation pattern of the intracerebrally transplanted EB. It appeared that ES cells are capable of differentiating into circumscribed transplants of central nervous system (CNS) tissue containing neuron.

Previous transplant studies involving ES cells-derived neural cells generated without brain extract treatment or growth factors or retinoic acid treatment[9] were complicated by the formation of heterogenous tissue, while in this study, embryonic brain extract may play a role in directing the differentiation of ES cells to the neural pathway.

The ellucidation mechanism of migration of transplanted ES cells, need further study.

FGF have been shown to be involved in stem cell migration and lineage commitment and have been implicated in self-renewal[30,31].

Definitive identification will require phenotypic markers that discriminate between different cell types or different states of a common cells. Once a stem cell divided and the born cells migrate to specific regions, it matures further until it reaches a site when it stops and become fully differentiated into a functioning cell. From our and other studies, neural cells can be derived from more primitive cells, including ES cells, but the major obstacle of identifying and discovering markers that define a stem cell is that the most primitive cells are probably in a

quiescent state and do not express many unique antigens. Thus, as with other fields like hematopoisis, a combination of positive and negative markers will be required to define the primitive stem cell[32], that is why we thought the use of HRP as a useful marker[18], because there is a great need for a simple marker that could be applied on cells in tissue culture. ES cells appeared to have the ability to take up this large molecule marker into inside due to the active phagocytosis nature of these cells as shown by scanning electron microscope study[4]. This marker is a protein that could be kept inside the cells for long period usually as granules, although these cells proliferated and migrated for several millimeters distance from the site of injection, The labeled cells are in most cases completely distinguished from other cells in tissue.

Conclusions

Using embryonic brain extract as a crude source of neurotrophic factors, for the first time, seems to direct the differentiation of these cells to neural precursors *in vitro* and vivo.

Pluripotent ES cells are of potential interest as a possible source for cell replacement therapies for the nervous system. These cells have been shown to proliferate, migrate and differentiate into neural cells after intracerebral transplantation by using mouse as an animal model of injury.

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ULTRA-HISTOCHEMICAL STUDY ON LEMMOCYTES IN RABBIT

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Abstract

Background: The biosynthesis of myelin in the peripheral nervous system of adult healthy male rabbits was studied utilizing the activity of NSE at EM level.

Materials & Methods: One centimeter length of sciatic nerve from each animal was obtained, fixed and processed for demonstration of NSEs activity using ANA as a substrate. The specimens were stained with uranyl acetate and lead citrate then examined with EM.

Results: There is high reactivity of NSEs in the layers of myelin that wrap the axoplasm and nuclear pore of Schwann cells. No reactivity can be demonstrated at the axoplasm itself or at the microtubules and microfilaments.

Conclusion: These findings hypothesize that NSEs may play a role in the processes of regeneration and regeneration processes.

Key words: Myelin, Non-specific Esterases, Alpha naphtyl Acetate.

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Introduction

Schwann cells or lemmocytes are non-excitable, supporting cells of the peripheral nervous system, they are associated with all peripheral nerve trunks and they form the capsular or satellite cells of the dorsal root and autonomic ganglia[1].

They are of neural crest origin, morphologically, Schwann cells are large, rounded with rather heterochromatic and ellipsoidal nucleus and of dense cytoplasm. Their cytoplasm is rich in mitochondria, microtubules & microfilaments, in addition to prominent lysosomes and a well-developed rough endoplasmic reticulum. A basement membrane is present at its external surface, except where this lies adjacent to a nerve cell process[2].

Functionally, Schwann cells are important for supplying energy and metabolites to the nerve cells. In addition embryonic growth of nerve cell processes and re-growth of axon after local injury was found only in the presence of Schwann cells[3], so these cells are also responsible for trophic function that maintain and preserve the ensheathed nerve cell processes. Schwann cells are also responsible for myelin production, thickness and internodal lengths, which are related to the axonal caliber that may be determined genetically[3]. Thus myelin sheath is important for preservation of energy that is utilized during conduction of nerve impulses and so enhanced conduction along myelinated nerve fibers.

The chemical composition of myelin is a protein lipid complex. The protein forms about thirty percent of adult human myelin; peripheral myelin protein contains a low molecular weight glycoprotein and two basic proteins[4].

Many enzymes were identified in Schwann cells that accompany myelin metabolism. Some of them like 2:3 Cyclic AMP, and 3-phosphohydrolase, are of unknown role[5]. While other enzymes like Lipoprotein lipase (triacylglycero-protein acylhydrolase, EC (3.1.1.34) which mediated hydrolysis of exogenous triacylglycerol was found to be an important source of free fatty acids for the schwann cell and may play a critical role in myelin biosynthesis in the peripheral nervous system[6]. Moreover, histochemical localization of the activities of other enzymes (like nonspecific cholinesterase, alkaline phosphatases, acid phosphatase, adenosine tri- and diphosphatases, adenylate cyclase, and dipeptidylpeptidase-IV) in the cutaneous sensory nerve formations, mainly sensory corpuscles, has been also reviewed[7].

In regard to the carboxylic ester hydrolases, there are three commonly designated esterases; these are carboxylesterase (EC 3.1.1.1), arylesterase (EC 3.1.1.2) and acetylesterase (EC 3.1.1.6). The identification of the non-specific esterases has been rested on their ability to hydrolyse synthetic ester substrate; however natural substrates have not been identified for most of the non-specific esterases (NSE), various metabolic roles are

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attributed to NSE in the nervous system. It seems that the normal role of esterases in metabolism is poorly understood and probably represents a wide variety of functions[8]. This point directed our mind to study the biosynthesis of myelin in the peripheral nervous system utilizing the activity of NSE at EM level

Materials & Methods

Adult male, healthy, New Zealand rabbits weighing 1-1.5 Kg were used in this study. The animal was sacrificed by sectioning of the great vessels in the neck under light chloroform anesthesia. Sciatic nerve was exposed after reflection of gluteus maxims muscle and 1 cm length of sciatic nerve was obtained (1 cm above the knee joint).

This tissue specimen was processed for demonstration of NSEs activity using an incubation medium prepared according to the simultaneous coupling methods of (Nachlas & Seligman, 1949)[9].

Small cubes of sciatic nerve (0.1 cm^3) were obtained with a surgical blade and were placed in a fixative solution for 2 hours at 4˚C. The fixative solution is composed of 2.5% glutaraldehyde buffered to pH 6.8 with 0.15M-phosphate buffer. Then the blocks were further minced into smaller pieces and washed (2-3) times with the same buffer prior to incubation.

The substrate (10mg of alpha naphthyl acetate; ANA), was dissolved in 0.5 ml of acetone. The dissolved substrate was added to 8.9 ml of 0.15 M phosphate buffer pH 6.3. Then 0.6 ml of freshly prepared hexazotized pararosaniline (Fluka) was added to the mixture. The minced tissues blocks then were incubated for 6 hours in this medium (Modified after Bozdech & Bainton, 1981)[10]. (The hexazotized pararosaniline was prepared by mixing equal volumes, 1ml of 4% pararosaniline in 2N HCl & 4% sodium nitrite newly made, and then the cloudy mixture was filtered with No.1 Whatman filter paper).

Post incubation, another fixation step was performed with 2.5% gluteraldehyde buffered pH 7.2 with phosphate buffer, then the tissue was fixed in 1% osmium tetraoxide and dehydrated in ethanol for embedding in araldite.

The semi-thin sections (0.5-1μm) were stained with 1% methylene blue for selecting the most adequate areas for farther processing. Ultra thin sections were obtained and doubly stained with uranyl acetate and lead citrate and examined by electron microscopy.

Results

Minced tissue block obtained from transverse section shows different diameters of axons (Figure 1).

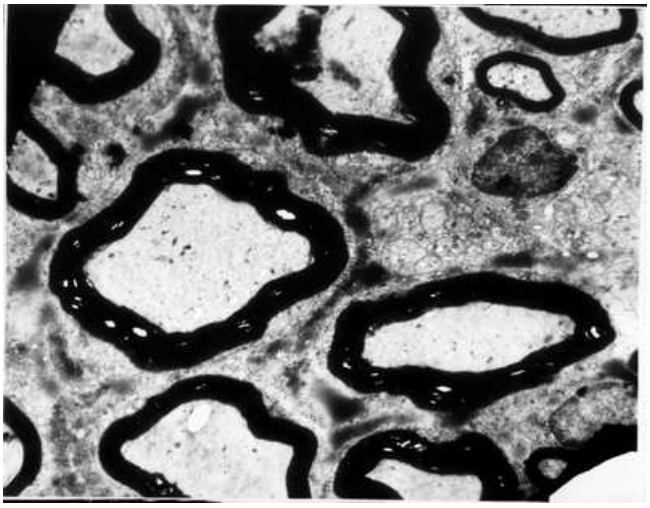

Figure 1: Cross section in the sciatic nerve treated with ANA prior to Ossmification x3000

However, this study was focused on the largest diameter one. (A-α skeletomotor) that belongs to the α-motoneurons. Ossmifications of the lipid content of the axons was perfect.

The method of processing and fixation and the preincubation fixation with a solution composed of 2.5% glutaraldehyde buffered to pH 6.8 with 0.15M phosphate buffer for 2 hours at 4˚C, was found to be very efficient in visualizing esterase enzyme reactivity with the using of ANA as a broad spectrum substrate. It shows perfect reactivity regarding the intensity of FRP (vide infra).

The reactivity was demonstrated in a form of deep stained granules in the axonal wall, in the layers of the myelin that warp the axoplasm. However; no reactivity can be demonstrated in the axoplasm (Figure 2), neither in the microtubules and microfilaments nor in the mitochondria

In the axonal wall two forms of reactivity could be encountered with regarding the intensity of FRP especially in the largest diameter axons (Figure 3).

In the same consequences the nucleus of Schwann cell shows two pattern of reactivity (Figures 4 A & B) precisely in the nuclear

membrane, nucleoleous nuclear pores & nucleoplasm, moreover a homogenized distribution of FRP was encountered within the nucleus (Figure 4 B).

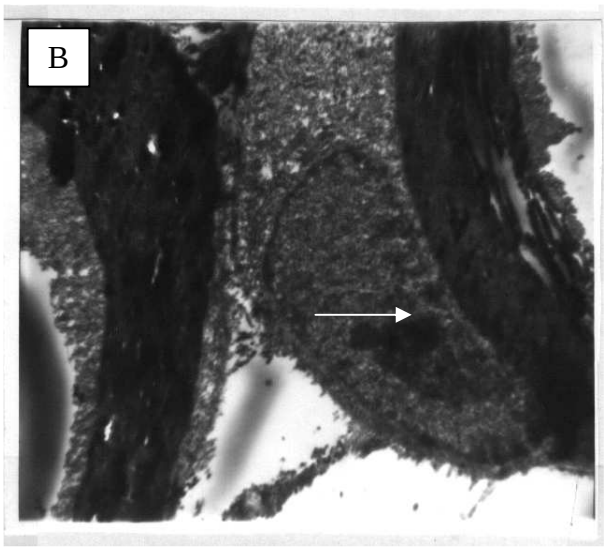

Figure 2: A: Schwann cell nucleus (arrow); nuclear pore x 18000 B: another form of reactivity in Schwann cell (arrow); nucleolus x 18000

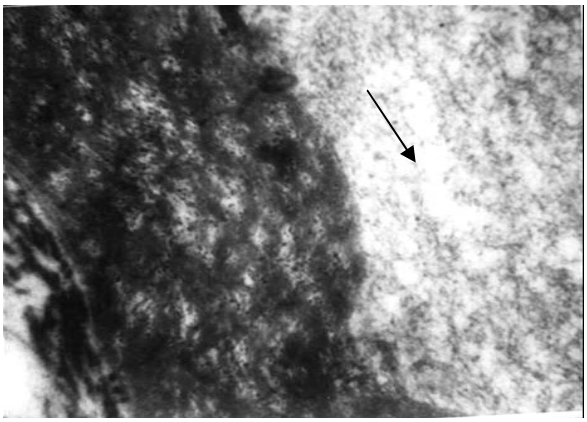

Figure 3: Axonal wall shows discrete granules of FRP. No reactivity could be detected in the axoplasm (arrow) x 31000

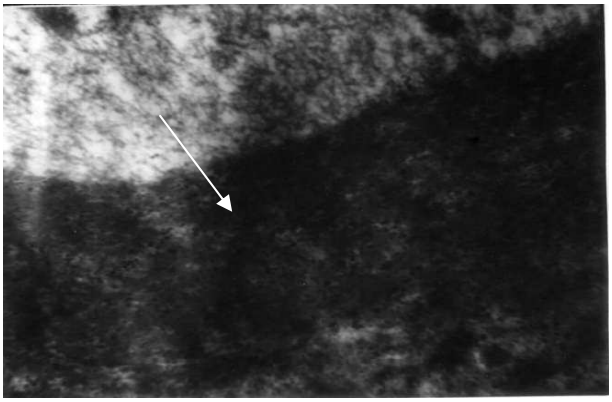

Figure 4: Axonal wall shows intense reactivity of FRP (arrow) x 31000

Discussion

Reactivity of ANAE was perfectly visualized in a form of granular appearance with the circumstances used, regarding different parameters of fixation, incubation media, and duration of incubation.

In the present study especial attention was paid on the pattern of reactivity in regard to the Schwann cells of the motor& sensory nerves and specifically in the largest diameter nerve fibers. Different reactivity can be encountered within the nucleus of Schwann, nucleoplasm & the myelin sheath.

Esterases have been found to be suitable marker enzymes for certain changes in the physiological state[11], as it reflects from their functions in the issue of synthesis and hydrolysis of lipid and lipoprotein[12].

Moreover; the high reactivity of the enzyme at the axoplasmic membrane and nuclear pore that we demonstrate at the nuclear pores of the Schwann hypothesized that they may play a role in intracellular transport[13,14].

Myelin is a lipoprotein so the identification of NSE in the Schwann cell may refer to their involvement in lipid metabolism. One of these NSE is A-esterase which is arylesterase (EC 3.1.1.2), that involved in the metabolism of free fatty acids primarily in the transesterification reaction between acids of long carbon chains and acetic acid, or acts as co-factor with lipase in hydrolysis of lipoproteins[15]. This confirmed other studies which showed that histochemistry for non-specific esterases were able to demonstrate the age-related development and maturation of myelin at the terminal Schwann cells[16].

Since the activity of non-specific cholinesterases persists in terminal Schwann cells for a long time

after loss of the sensory axons, this combined enzyme useful for experimental studies involving denervation and re-innervation of sensory nerve endings[7]. The finding of this study (Fig. 4 A, & B).shows two varieties of reaction fo the NSE, and this reflects two functional categories of Schwann cells.

Farther studies of histochemistry are needed to confirm the specific role of the esterases iso-enzyme in the Schwann cell at different circumstances, like variation in the activity of enzymes with aging and their relation to degenerative regenerative processes.

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THE ACTIVITY OF NA/K ATPASE IN EXPERIMENTAL NEPHROTIC SYNDROME

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Abstract

Background: Adriamycin nephropathy is a nonimmune-mediated rat model of proteinuric chronic glomerular disease, is induced by a single intravenous injection of doxorubicin hydrochloride into the tail vein. The development of edema and ascites in adriamycin induced nephrosis, due to sodium retention.

Objectives: to evaluate whether enhanced Na^+/K^+-ATPase activity in the kidneys is a general feature of experimental nephrotic syndromes and whether this enhanced activity is responsible for decreased urinary sodium excretion, and to study the role of zn^+ supplement on ATPase activity and the probable mechanism of its increment.

Materials & Methods: 12 rats were involved in this work. Control nephrotic (adriamycin 15mg/100g BW) given IV in rat-tail vein**.** The other group; rats received zinc chloride 0.2 mg^+/Kg in addition to Adriamycin (same dose), after 2 week animals were scarified. Blood sample were aspirated before and after administration of adriamycin. In all samples Na^+/K^+ATPase activity were estimated. Urine analysis (for proteinurea) was done using dipsticks.
Kidneys were homogenized for estimation of Na^+/K^+ATPase activity in tissue from all groups. Lastly kidneys were dissected and examined by light microscope and Electron microscope.

Results: Histopathological sections of rat kidneys treated with ADR show nephrotic changes. The activity of Na^+/K^+ ATPase was significantly increased in nephrotic rats ($p<.05$), and was further increased in nephrotic rats receiving zinc chloride ($p<0.01$). Sections examined by E/M confirmed the diagnosis of nephrosis and revealed apoptotic changes mainly in tubular epithelial cells of nephrotic rats.

Discussion: The activity Na^+/K^+-ATPase was increased in nephrotic rats; this may be attributed to mobilization of some ion channels from basolateral to apical membrane, further increase in enzyme activity after zinc chloride supplements; since the enzyme is a metalloenzyme and require Mg^{+2} and Zn^{+2} for its full activity.

Conclusion: there was a marked increase in Na^+/K^+ATPase activity found in adriamycine nephropathy and the activity was further elevated upon zinc chloride supplement.

Key words: Na+/K+-ATPase, adriamycin , nephrotic syndrome

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Introduction

The kidneys clean the blood by filtering out excess water and salt and waste products from food. Healthy kidneys keep protein in the blood, which helps the blood absorb water from tissues. But kidneys with damaged filters may let protein leak into the urine. As a result, not enough protein is left in the blood to soak up the water. The water then moves from the blood into body tissues and causes swelling. The most common form of the nephrotic syndrome in children is called minimal change disease[1]. Adriamycin nephropathy (AN) is a widely used nonimmune-mediated rat model of proteinuric chronic glomerular disease and is usually induced by a single intravenous injection of doxorubicin hydrochloride (DX) into the tail vein[2,3,4]. Nephrotic syndrome characterized by: High levels of protein in the urine, Low levels of protein in the blood, In addition to proteinuria and podocyte foot process effacement, development of edema and ascites are permanent features in the majority of models and diseases[3,4]. Marked decreases in urinary sodium excretion are common clinical observations in human minimal change disease[5], and decreases in the fractional excretion of sodium are observed in animal models such as puromycin aminonucleoside nephrosis PAN[6], adriamycin nephrosis[7], immune glomerulonephritis resulting from rabbit anti-rat serum[8]. The collecting duct is the site of final Na reabsorption according to Na balance requirement, and this reabsorption is achieved by Na^+/K^+ ATPase. Activation of local Na^+/K^+ ATPase in cortical collecting duct could be involved in Na retention with or without

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generalized activation of tubular ATPases in nephrotic syndrome[9]. Na^+/K^+ATPase are P-type translocases consists of two transmembrane protein the larger of which, catalytic subunit; exchange extracellular k against intrracellular Na or proton, at expense of ATP hydrolysis. ATPases utilizes 80% of renal metabolic energy. Na^+/K^+ATPase is the major factor in primary renal Na retention[10].

Therefore, to evaluate whether enhanced Na^+/K^+ATPase activity in the kidneys is a general feature of experimental nephrotic syndromes and whether this enhanced activity is responsible for decreased urinary sodium excretion. Finally to study the role of zinc chloride in activation and/or restoring the activity of the enzymes. For this purpose, Na^+/K^+ATPase activity was measured in kidneys and blood, perhaps to explain the probable mechanisms responsible for this increment in its activity in adriamycin nephrosis in rats.

Materials & Method

12 rats were involved in this work. Rats were stratified into control group (4rats) and experimental group (ADR-induced nephropathy group; 8 rats). Rats (Rattus norvegicus albinus) weight (308±9) gram aged 3 months. The control group receives zinc chloride on 3 successive days.

The experimental group was then divided into:

Control nephrotic group (ADR-induced nephropathy; adriamycin 15mg/100g body weight) given iv in rat tail vein, then animals were scarified after 2 weeks.

Blood samples; blood sample aspirated before and after administration of adriamycin, third blood sample before scarifying the animal. In all samples estimation of Na^+-K^+ATPase activity was performed according to Reddy et al[11].

Second group; rats received zinc chloride 0.2 mg/Kg for 3 successive days, then 2 days rest ,then animal receive Adriamycin (15mg/100g body weight) in rat tail vein, after 2 week animals were scarified.

Urine analysis to check protein in urine; checked by dipstick (med-testcombi 3A Macherey-Naglel).

Kidneys were homogenized for estimation of Na^+-K^+ATPase activity in tissue from all groups.

Also kidneys were dissected and examined by light microscope after staining with (H and E) stain, and were processed for Electron microscope study according to the method of Reynold[12].

Results

Nephrotic syndrome was diagnosed on bases of: Edema; especially puffiness of the eyes and weight increment, proteinuria (>3g/ L), which was significantly higher level compared with control groups ($P < 0.05$).

Histopathological examination of the kidneys of rats treated with ADR revealed focal areas of mesangial proliferation and mild tubulointerstitial inflammation. These results similar to those found by Ozen (2001)[13] and were diagnostic of nephrotic syndrome.

The activity of Na^+/K^+ATPase was significantly increased in blood and tissue of nephrotic rats ($p<0.05$), and was further increased significantly in nephrotic rats receiving zinc chloride ($p<0.01$) as shown in table 1.

Table 1: Activity of Na^+/K^+ ATPase in different groups of the study

	control/tissue	**nephrotic/tissue**	**nephrotic/tissue/ receiving zinc chloride**
Na/K-Atpase nmol/mg/min	97.6235 ± 10.4805	112.0758 ± 30.6908	206.9018 ± 37.63815
	Control/ blood	**nephrotic/blood**	**nephrotic/blood/ receiving zinc chloride**
Na/K-Atpase nmol/mg/min	38.34825 ± 5.627057	55.72275 ± 4.918427	121.6513 ± 9.651917

The sections of the kidneys were examined by electron microscope which confirmed our diagnosis of nephrosis and revealed apoptotic changes: In nephrotic rats tubular epithelial cells exhibit condensed and fragmented chromatin typical of apoptotic cell death while normal kidneys had 0.18±0.04 ($P<0.02$) apoptotic cell/HPF as compared with 2.76±0.2 ($P<0.001$) in edematous rats with end stage disease, apoptosis was mainly observed in tubules and only rare apoptotic cells observed in glomeruli from rat kidneys. The apoptotic changes in the kidneys of nephrotic rats are showing in figures 1 and 2.

Discussion

Polarized epithelial cells have characteristic cellular organization that include a surface plasma membrane organized into distinct apical

and basolateral domains within these surface membrane domains are enzymes, transporters, hormone receptors and lipids are localized in a polarized fashion. The alterations in vectorial transport function were related to the redistribution of surface membrane phospholipids and domain specific apical and basolateral membrane enzymes. i.e. redistribution of Na^+/K^+ATPase from basolateral to apical membrane in renal proximal tubular cells, was associated with reduced Na reabsorption secondary to Na^+/K^+ATPase pumping Na+ back to the urinary lumen. Reestablishment of surface membrane Na^+/K^+ATPase was essential for restoration of normal cellular Na+ transport[6]. In PAN nephrosis Na reabsorption in outer medullary collecting duct does not altered while an increased synthesis and membrane expression of Na^+/K^+ATPase in cortical collecting duct occurs. Moreover, an altered normal trafficking of intracellular Na^+/K^+ATPase unit to the basolateral has been documented[9]. In vivo micro puncture experiments have shown that the collecting duct is the site of sodium retention in the kidney of nephrotic rats[14] and this phenomenon is independent on proteinuria or the level of vassopressin[15]. Na^+/K^+ATPase activity is significantly enhanced in the cortical collecting ducts (CCD) of rats with PAN nephrosis, during a period with a positive sodium balance and this is independent on endogenous inhibitors suggesting primary a paracrine or cellular mechanism[16].

While recent literature data suggest that a primary impairment in sodium excretion is the basic abnormality in the pathogenesis of edema formation in the nephrotic syndrome, the activity of the enzyme was measured in blood and tissue of adriamycin induced nephrosis[17].

ATPases are metalloenzymes; required magnesium for their maximum activity, the effect of zn^+ on ATPase activity was examined. A significant increase in enzyme activity was observed in both control normal and adriamycin induced nephrosis. The enzyme activity measured in blood samples and renal tissue show increment in the activity in blood and renal tissue in the same manner. Faurkov demonstrate the effect of trace metal cadmium on Cl-ions and the closely related metals zn^+ and Ni were also able to activate the Cl^- secretion. Moreover zn^+ and Ni^+ completely prevent the inhibition process of some inhibitors for transport[18]. However basolateral Na^+/K^+ATPase of CCD which causes Na retention if the activity is elevated may affect some how the apical membrane ATPase as it was found that basolateral Cadmium (or zn^+, Ni^+) causes calcium mobilization and activation of apical membrane sensitive channel[18], i.e. mobilization of some ions from basolateral to apical membrane and activate ATPases.

In this work apoptotic process was increased in end stage disease and was ameliorated by addition of zn^+ (this was proved in our previous work), since zinc can inhibit apoptotic process by different mechanisms[19].

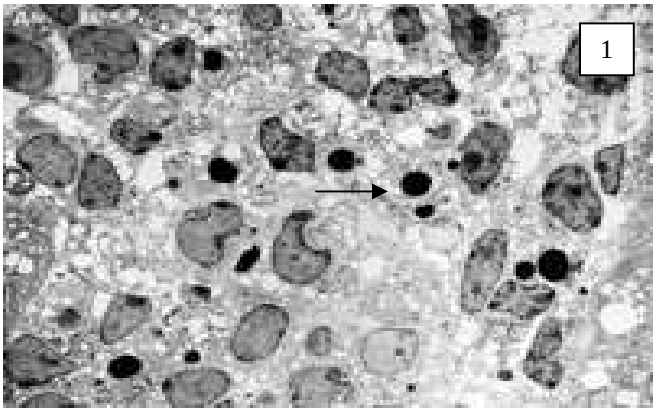
Zn^+ stimulate ATPase activity by inhibition of proteolysis, as zn^+ is well known caspase 3 inhibitor that regulate apoptotic process and hence protein proteolysis[20].

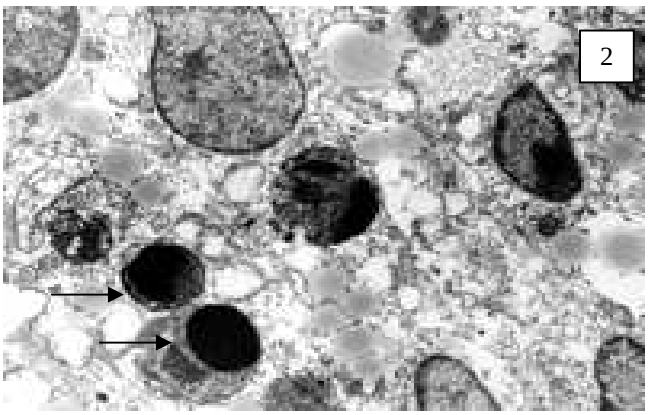
Marked increase in Na^+/K^+ATPase activity found (twofold) in nephrotic and further elevated upon zinc chloride supplement (another twofold), as nephrotic dysregulate distribution of transporter in CCD and elevated the number and size of basolateral ATPase to some extent that cause Na/water retention ,zinc will activate ATPase in both sites leading to another twofold increment. In puromycin aminonucleoside induced nephrosis (PAN), sodium retention originates in part from the collecting duct, and it is associated with increased Na^+/K^+ATPase activity lead to the formation of ascites and edema[9]. Cloning of four isoform of Na^+/K^+ and two of K^+/H^+ ATPases has provided a molecular bases to the heterogeneity of these ATPases beside its house keeping function, renal ATPases energizes most solute and water transport along whole nephrone. ATPases utilizes 80% of renal metabolic energy[10].

It was suggested that increase Na reabsorption associated with shift of Na^+/H^+ exchanger (NHE3) from an inactive pool to an active pool thus contributing to Na retention[21] i.e. dysregulation of Na^+/K^+ATPase in CCD is the major factor in primary renal Na retention in nephrotic syndrome. Water reabsorption and retention could be attributed to extensive down regulation of aquaporin and urea transporter expression this may represent an appropriate renal response to extra cellular volume expansion and may occur at expense of

decreased urinary concentrating and diluting capacity[22].

Conclusion: The activity of Na^+/K^+ATPase is increased due probably to mobilization and activation of some ion channels from basolateral to apical membrane.





Figures 1 and 2: E/M of the kidneys showing nuclear fragmentation chromatin condensation in centrifugal pattern (arrow) on nuclear envelop: 1: x 1600, 2: x 5000

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A COMPARATIVE CLINICAL STUDY OF TOPICAL FINASTERIDE AS A NEW THERAPY OF ACNE VULGARIS

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Abstract

Background: Androgen regulation of sebum production requires the local conversion of testosterone to dihydrotestosterone catalyzed by 5 alpha-reductase; thus, its competitive inhibitor, finasteride, might be beneficial for treatment of cutaneous hyperandrogenism conditions like acne vulgaris.

Objective: To evaluate the efficacy and tolerability of topical finasteride as a new therapy for acne vulgaris.

Subjects & Method: Sixty patients with mild to moderate acne were enrolled and randomly assigned to receive topical solution of either 0.01 % finasteride (n=30) or 1.5% clindamycin (n=30) two times a day for 3 months. Efficacy was assessed by determining the patients' number exhibiting improvement per each recovery percentage.

Results: The initial response to finasteride or clindamycin was elicited at 4.15 ± 0.15 and 3.56 ± 0.13 weeks respectively ($p>0.05$) whereas the maximum response required 8.2 ± 0.23 and 8 ± 0.14 weeks respectively ($p>0.05$). Acne remissions were detected at week 12 of therapy in 66.67 % of finasteride group versus 80% of clindamycin group ($p>0.05$). Both drugs were well tolerated and safe.

Conclusion: 0.01% finasteride solution applied twice daily for 12 weeks has clinical efficacy and safety profile comparable to a similar regime of 1.5% clindamycin solution in treatment of mild to moderate inflammatory acne vulgaris.

Keywords: Finasteride, Clindamycin, Acne Vulgaris

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Introduction

Acne vulgaris is a multifactorial disease of the pilosebaceous unit of the skin. It may have profound psychological sequelae. Depending upon the degree of follicular hyperkeratinization, sebum production, *Propionibacterium acnes* (*P. acnes)* growth, and inflammation, the microcomedo evolves into a non-inflammatory lesions [closed comedo (a whitehead), and an open comedo (a blackhead)] or an inflammatory lesions [pustule, papule, or nodule]. In addition, scarring and hyperpigmentation may occur[1,2].

Mild cases of comedonal acne may respond to a topical retinoid or benzoyl peroxide, while inflammatory lesions such as papules and pustules benefit from topical antibiotics including topical clindamycin. More severe inflammatory acne is treated with systemic antibiotics. Recalcitrant cases often require oral isotretinoin or hormonal manipulation[1,3-5].

Topical clindamycin is thought to reduce free fatty acid concentrations on the skin and to suppress the growth of *P. acnes*, an anaerobe found in sebaceous glands and follicles. P. acnes produce proteases, hyaluronidases, lipases, and chemotactic factors, all of which can produce inflammatory components or inflammation directly[4].

Androgenic stimulation of sebaceous glands is an important factor in development of acne[6]. Most patients with acne do not overproduce androgens. Instead, they likely have sebaceous glands that are locally hyper responsive to androgens[7]. Nevertheless, androgens play a more important role in female than in male acne at the hormonal and at the peripheral level in skin[8]. The level of dehydroepiandrosterone sulfate, an androgen of adrenal origin, was significantly higher in prepubertal girls with acne[9].

Hormonal therapy is an alternative to systemic isotretinoin in women with acne that is unresponsive to other methods of treatment. Minimums of 3-6 months of therapy are required prior to evaluation of the efficacy of hormonal therapies that includes estrogens (oral contraceptives) or oral anti-androgens (spironolactone, cimetidine, flutamide, and ketoconazole); these act at the peripheral receptor level to decrease sebum production[7].

Finasteride is a competitive inhibitor of Type II 5(alpha)-reductase; it produces a rapid and

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significant reduction in serum and tissue dihydrotestosterone (DHT) concentration. The turnover for the enzyme complex is slow ($t_{1/2}$ approximately 30 days for the Type II enzyme complex and 14 days for the Type I complex).

Type II 5(alpha)-reductase isozyme is responsible for two-thirds of circulating DHT. It is primarily found in prostate, seminal vesicles, epididymides, and hair follicles as well as liver.

Studies with finasteride had indicated that the hypothalamic-pituitary-testicular axis was not affected. However, mean circulating levels of testosterone and estradiol were increased by approximately 15% as compared to baseline, but these remained within the physiologic range. Finaseteride is indicated for treatment of benign prostatic hyperplasia and androgenic alopecia in men. Its adverse effects included breast tenderness and enlargement, as well as hypersensitivity reactions, including lip swelling and skin rash, has been reported. No drug interactions of clinical importance have been identified[10].

Aim of the Study:

Systemic and topical anti-microbials are effective in the treatment of inflammatory acne vulgaris; however, widespread use of these agents is becoming increasingly associated with the emergence of resistant pathogens indicating the need to develop strategies to minimize antibiotic use in acne therapy[11,12]; thus, this comparative clinical therapeutic trial aimed to evaluate the tolerability and clinical efficacy of topical finasteride as a new therapy for acne vulgaris in Iraqi patients.

Subjects & Methods

This prospective clinical study was performed on 60 patients with mild to moderate acne vulgaris among those attended the dermatologic consultation unit in Al-Kadhimiya Teaching Hospital. The study started in July 2001; patient admittance was completed in April 2002. The enrolled patients were randomly assigned into 2 treatment groups:

1. Topical finasteride group (n=30): Patients of this group received this tested drug at concentrations of 0.01 % as a thin film applied topically to the skin, twice daily to the affected areas; 70% ethanol was used as a vehicle in which finasteride was dissolved[10].

2. Topical clindamycin group (n=30): Patients of this group received a topical solution of 1.5% clindamycin phosphate, the routinely used topical antibacterial drug as a thin film applied topically to the skin, two times a day to the affected areas[4]; 70% ethanol was used as a vehicle in which clindamycin phosphate was dissolved[10].

The exclusive criteria included severe acne, pregnancy or a possibility of pregnancy, and cases of acne who were already receiving topical clindamycin or any type of hormonal therapy.

For each included patient, a detailed history was taken including: name, age, sex, residence, marital state, duration of acne, impact of the disease (whether disfigurement, occupational disability, psychological impact, or failure of previous treatment), aggravating factors (seasonal variation or stress), family history (regarding the acne), and previous anti-acne drug history.

Specific type of acne lesions whether non-inflammatory lesions [closed or open comedone] or an inflammatory lesions [pustule, papule, or nodule], or scarring and hyperpigmentation[1,2] were recorded at baseline (i.e., pre-treatment value) and then 4 weekly along the trial period of therapy which equal to 12 weeks.

Severity grades of inflammatory acne could be determined according the criteria shown in the table (1)[13].

Table 1: Severity grades of inflammatory acne[13]

Grade of severity	Factors that determine severity of inflammatory acne		
	Papules/pustules	Nodules	Additional factor
Mild	Few/several	0	Psychosocial circumstances
Moderate	Several/many	few/several	Occupational difficulties
Severe	Many/extensive	many	Inadequate therapeutic responsiveness

In each treatment group, the patients treated themselves twice daily for 3 months[14] to be seen at 4 weeks intervals during the follow up period (i.e., 12 weeks) in order to assess both clinical efficacy and tolerability (i.e., erythema, desquamation, dryness, itching, and burning[14,15] or any other noticeable side effects of the employed therapy).

According to Ersoy et al. (1996)[16], the efficacy of treatment in the present study was assessed by 4 weekly determination of number of the patients who exhibited drug-induced improvement per

each recovery percentage which was graded as follows: 0% (i.e., no improvement), < 25%, 25-50%, 50-75%, or 75-100%.

Staistical analaysis

Student paired t-test (for dependent data), student unpaired t-test (for independent data), or Chi- square (X^2) tests were used accordingly to assess whether the obtained differences could be accepted as insignificant (if P 0.05), significant (if 0.01 < P ≤ 0.05), or highly significant (if P ≤ 0.01)[17].

Results

With the aid of table 2, some characteristics of the 60 included acne cases are demonstrated. There was no significant difference (p>0.05) between the mean age of the 30 acne cases who received topical finasteride (22.0±0.7 years) (mean±S.E.M) and that of 30 acne cases who received topical clindamycin (21.33±0.8 years). The sex distribution pointed out that 20 (66.7 %) patients in each treatment group were females.

Table 2: Some characteristics of the included acne cases

Treatment group	No. of patients	Sex		Age (years)	
		Male	Female	mean±SEM*	range
Finasteride	30	10	20	22.0±0.7	15-30
Clindamycin	30	10	20	21.33±0.8	15-30

SEM = standard error of mean

Table 3, demonstrated the distribution of patients regarding aggravating factors (seasonal variation or stress) and family history of acne. Compared to clindamycin group, finasteride group significantly (P<0.05) had more patient with positive family history of acne whereas no significant difference (p>0.05) could be elicited regarding aggravating factors.

Furthermore, there were no significant differences (p>0.05) between the two treatment groups in respect of types of impact that induced by the acne vulgaris (Table 3).

When the included patients were distributed according their previous specific therapy of acne (Table 3), there were no significant differences (p>0.05) between the two treatment groups except in case of previous treatment with topical clindamycin where the difference was highly significant (p< 0.01).

Table 3: Distribution of patients regarding each of factors affecting acne presentation (&/or its severity), impact that induced by acne and their previous specific therapy

Parameters according to which the patients were distributed		No. of patients	
		Finasteride N = 30	Clindamycin N = 30
Factors affecting acne presentation &/or severity	Seasonal variation*	10	12
	Stress	16	15
	Family history	10[s]	8
Type of impact that induced by acne	Disfigurement	13	10
	Occupational disability	13	10
	Psychosocial impact	19	20
	Failure of previous treatment	11	7
Previous specific therapy of acne	**Topical**		
	Clindamycin	8[hs]	0
	Benzoyl peroxide	8	7
	Tretinoin	8	4
	Oral		
	Doxycyclin	3	5
	Tetracyclin	2	2
	Co-trimoxazol	1	1

* = increase severity during summer, S = significant difference (P<0.05) when compared with other group. hs = highly significant difference (P<0.01) when compared with other group.

According to sites of acne lesions (Table 4), no significant differences (p>0.05) could be elicited between the two treatment groups regardless the site itself, i.e., whether face, chest, or back.

Moreover, Patients presented with specific types of acne lesions whether non-inflammatory lesions [closed or open comedone] or an inflammatory lesions [pustule, papule, or nodule], or complications [scarring and hyperpigmentation] in a way that no significant differences (p>0.05) could be elicited between the two treatment groups (Table 4).

Besides, the differences between the two groups in respect of the grades of severity were found to be insignificant (p>0.05); the majority of patients presented with acne of moderate severity [24/30 (80%) patients in finasteride group Vs 22/30 (73%) patients in clindamycin group] whereas the remainders in each group had mild acne (Table 4).

Table 4: Distribution of patients regarding location and types of acne lesions and regarding grades of severity of acne

Parameters according to which the patients were distributed			No. of patients	
			Finasteride N = 30	Clindamycin N = 30
Location of acne lesions	Face		30	30
	Chest		10	7
	Back		10	7
Various types of acne lesions	Non-inflammatory	Comedones	15	18
	Inflammatory	Papules	30	30
		Postules	26	26
		Nodules &/or cysts	8	6
	Complicated	Atrophic scar	11	5
		Hyper-pigmentation	11	7
Severity grades of inflammatory acne lesions	Mild*		6	8
	Moderate**		24	22
	Severe***		0	0

Note: papules/pustules (*) = (+/++) (few/several) (**) = (++/+++) (several/many) (***) = (+++/++++) (many/extensive)
Nodules (*) = (0) (**) = (+/++) (***) = (+++)
Additional factors that determine severity:
(*) = Psychosocial circumstances, (**) = occupational difficulties, (***) = inadequate therapeutic responsiveness.

The initial response could be elicited at mean duration 4.15 ± 0.15 and 3.56 ± 0.13 weeks after commencement of topical therapy with either finasteride or clindamycin respectively; however, such difference was found to be insignificant ($p>0.05$). On the other hand, the maximum response required mean duration of 8.2 ± 0.23 and 8 ± 0.14 weeks of treatment by either finasteride or clindamycin respectively; this difference was also insignificant ($p>0.05$) (Figure1).

Finasteride reduced the sebum and skin greasiness within first 10 days whereas clindamycin could do so within first 2 weeks of therapy.

In this study, it was noticed that 0.01% Finasteride, like 1.5% clindamycin, had no effect on both whitehead and blackhead comedones and an only little effect on nodules; i.e., their effects particularly involved the papules and pustules.

Figures (2A, B, & C) illustrated the distribution of patients regarding their therapy-induced improvement per each recovery percentage throughout period of treatment with finasteride or clindamycin. Besides, tables (5A & B) outlined the significance of differences yielded from comparison of values of each follow-up interval with Pre-treatment (0 weeks) taking into account each recovery percentage within the same treatment group, i.e., finasteride (Table 5A) or clindamycin (Table 5B) accordingly. However, table (5C) revealed the results of comparison between finasteride and clindamycin groups.

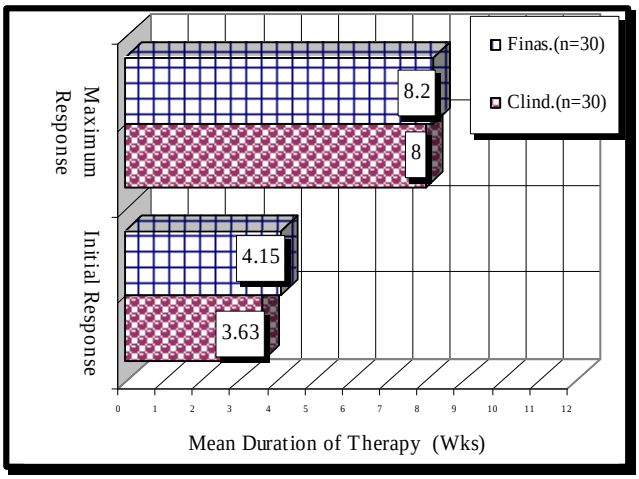
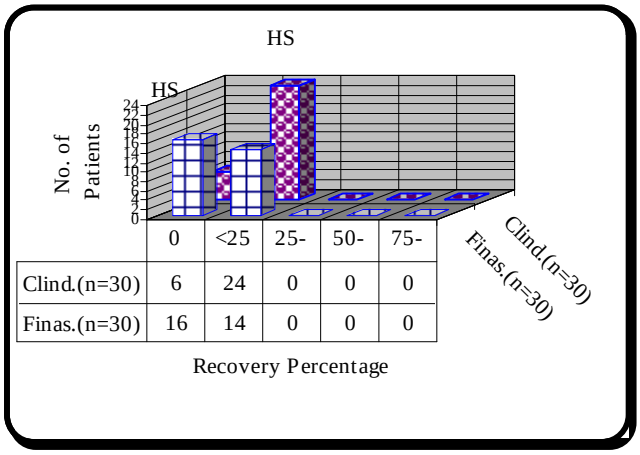
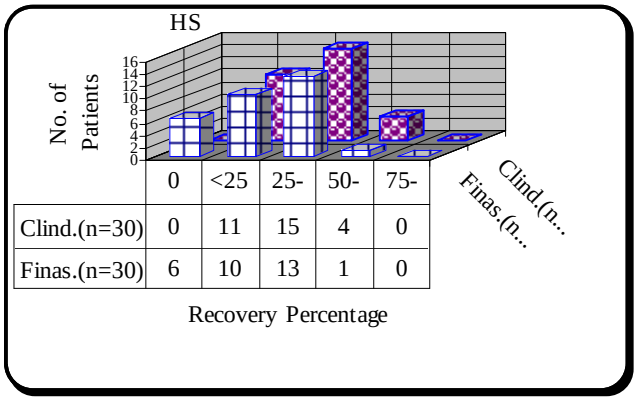


Figure 1: The mean duration (weeks) of therapy required for each group to show initial and maximum response



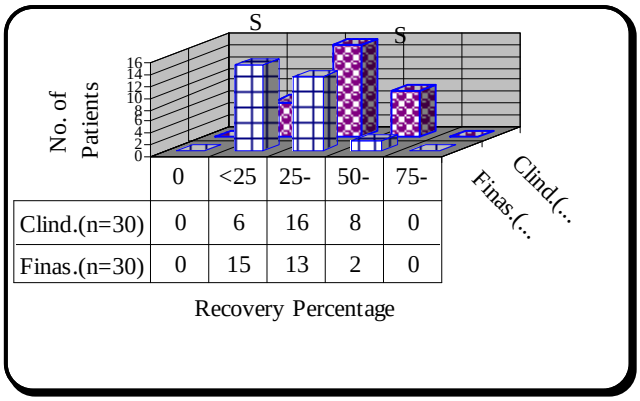
HS = highly significant difference (P<0.01) betweenthe two treated groups

Figure 2A: Distribution of patients with acne treated for 4 weeks with finasteride or clindamycin regarding their therapy-induced improvement per each recovery percentage



HS = highly significant difference (P<0.01) betweenthe two treated groups

Figure 2B: Distribution of patients with acne treated for 8 weeks with finasteride or clindamycin regarding their therapy-induced improvement per each recovery percentage



S = significant difference (P<0.05) between the two groups

Figure 2C: Distribution of patients with acne treated for 12 weeks with finasteride or clindamycin regarding their therapy-induced improvement per each recovery percentage

Table 5A: Significance of difference yielded from comparison with baseline values regarding number of patients exhibited finasteride-induced improvement per each recovery percentage

Recovery percentage	Follow up intervals (weeks of treatment)		
	4th	8th	12th
0%	HS* (baseline)$	HS (baseline)	HS (baseline)
<25%	HS (4th week)	HS (8th week)	HS (12th week)
25-50%	NS**	HS (8th week)	HS (12th week)
50-75%	NS	NS	NS

HS* = highly significant difference (P<0.01), NS** = no significant difference, $ the highest value belongs to those of follow up interval mentioned between brackets

Table 5B: Significance of difference yielded from comparison with baseline values regarding distribution of patients according to clindamycin-induced improvement per each recovery percentage

Recovery percentage	Follow up intervals (weeks of treatment)		
	4th	8th	12th
0%	HS* (baseline)$	HS (baseline)	HS (baseline)
<25%	HS (4th week)	HS (8th week)	HS (12th week)
25-50%	NS**	HS (8th week)	HS (12th week)
50-75%	NS	S (8th week)	HS (12th week)

HS* = highly significant difference (P<0.01), NS** = no significant difference, $ the highest value belongs to those of follow up interval mentioned between brackets

Table 5C: Significance of difference between finasteride and clindamycin groups regarding the distribution of patients according to their therapy-induced improvement per each recovery percentage

Recovery percentage	Follow up intervals (weeks of treatment)			
	0	4th	8th	12th
0%	NS*	HS*** (F)#	HS (F)	NS
<25%	NS	HS (C)$	NS	S** (F)
25-50%	NS	NS**	NS	NS
50-75%	NS	NS	NS	S (C)

0 = baseline (pre-treatment), NS* = no significant difference, S** significant difference (P<0.01), HS*** = highly significant difference (P≤0.01), (F)# = the highest value belongs to finasteride group, (C)$ = the highest value belongs to clindamyci group.

As it was shown in figures (3A & B) and based on the overall response of each patient individually, by the end of 12 weeks of therapy, acne remissions were found in 66.67 % of finasteride group (Figure 3A) and 80% of clindamycin group (Figure 3B).

The difference between the two treatment groups was found to be insignificant (p>0.05).

When the patients of each group were differentiated into mild and moderate cases, acne remissions were found in 100% of those with mild acne in either treatment group. However, acne remissions of those with moderate acne were found in 58.33% in finasteride group versus 72.73% in clindamycin group; however, such difference was also found to be insignificant (p>0.05).

Finally, both topical drugs were well tolerated along the trial period, i.e., 12 weeks, without noticeable side effects among the included patients in this prospective study.

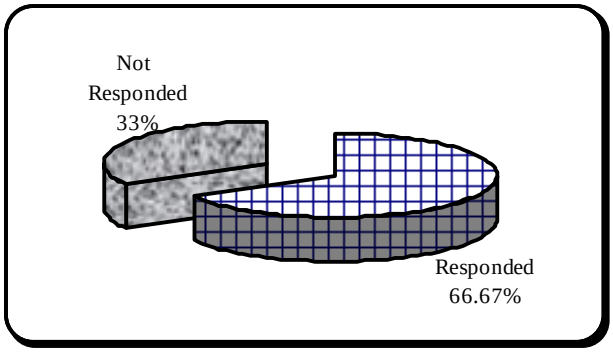


Figure 3A: The overall responses of patients with acne to 12 weeks of topical finasteride therapy

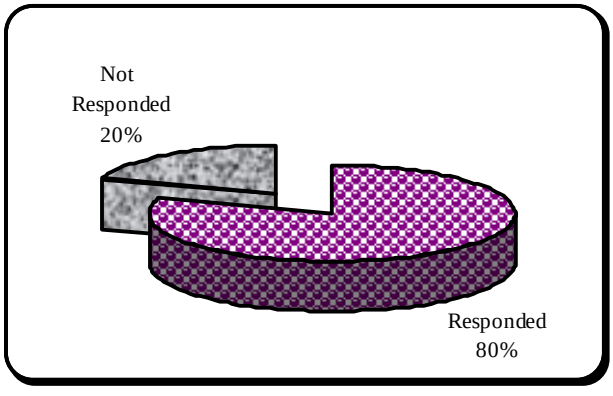


Figure 3B: The overall responses of patients with acne to 12 weeks of topical clindamycin therapy

Discussion

This prospective clinical study represents the first published work, at least in Iraq, which explores the role of finasteride as a new topical therapy for acne vulgaris.

Acne vulgaris is now recognized to be a disease that causes significant physical and emotional discomfort. Yet there is currently little consensus about the management of acne[18].

Androgens enhance lipogenesis, proliferation and terminal differentiation of human sebocytes by binding to nuclear androgen receptors[19]. The presence of 5 alpha-reductase in skin may indicate that the androgen regulation of sebaceous glands and sebum production requires the local conversion of testosterone to dihydrotestosterone[20]. Additionally, an exaggeration of this peripheral metabolism has been associated with acne in women[21].

Finasteride is the first available medication of a new class of drugs that is a competitive inhibitor of 5 alpha-reductase and therefore should be beneficial for medical treatment of cutaneous hyperandrogenism[22]. It has a 100-fold selectivity for the human Type II 5(alpha)-reductase over Type I isozyme (IC50=500 and 4.2 nM for Type I and II, respectively)[11].

Finasteride is freely soluble in lower alcohol solvents but is practically insoluble in water[10], in addition, alcohol aids in the removal of sebum from the surface of the skin[23]. Thus, we selected ethyl alcohol, the vehicle of clindamycin solution, to also be the vehicle used in preparation of fresh finasteride solution tested in this clinical trial.

Finasteride is contraindicated in women when they are or may potentially be pregnant. finasteride may cause abnormalities of the external genitalia of a male fetus of a pregnant woman who receives finasteride[10]. Thus, in the present study, the exclusive criteria included pregnancy or its possibility.

Both groups seemed comparable when the various factors which could affect the clinical presentation of acne were taken into account, i.e., in respect of patients' mean age, patients' gender distribution (with predominance of females), aggravating factors, types of impact that induced by acne, and previous specific therapy of acne. However, patients with positive family history of acne were significantly more in finasteride group. Besides, regarding history of previous treatment, a highly significant difference ($p< 0.01$) between the two treatment groups was obtained in case of previous treatment with topical clindamycin; this difference was expected after exclusion every patient who previously received clindamycin from involving within clindamycin group.

It was interesting to discover that both groups of patients were presented in a comparable way, i.e., regarding severity of inflammatory acne, sites and types of acne lesions.

Thus, it became clear that unexpectedly, the conditions of this clinical trial were offering a suitable and more or less fair opportunity to explore the actual role of the applied topical therapy.

The duration of therapy in either group was decided to be continued up to 12 weeks since it takes 8 weeks for a microcomedo to mature; thus, any therapy must be continued beyond this duration in order to assess efficacy[7].

As it was discovered in this study, 0.01% finasteride had earlier and more obvious anti-sebum effect than 1.5% clindamycin. This probably explained as a consequence of finasteride-induced inhibition of an essential step required for sebum production which is the local conversion of testosterone to dihydrotestosterone mediated by 5 alpha-reductase in skin[20].

Another interesting finding in this study was the similarity between finasteride and clindamycin regarding the types of acne lesions which were responsive to their effects; i.e., the inflammatory lesions and namely both papules and pustules.

Approximately 4 weeks of treatment with either drug were enough for the initial response to evolve. However, as it was demonstrated in this study, in order to achieve the maximum response, continued treatment with either drug for further 4 weeks was mandatory. Furthermore, the maximum response seemed valid since it could also be maintained throughout the rest period of this clinical trial.

Every 4 weeks assessment of numbers of patients who showed improvement per each recovery percentage appeared to follow a manner that warrant a high significant difference when compared to the relevant pre-treatment values. The exceptions probably confined to the recovery percentage 50-75% where the differences were insignificant along the trial period of treatment with finasteride.

At 12^{th} week of this clinical trial, finasteride treatment could increase the number of patients who showed improvement in recovery percentage (<25%) was significantly higher than

clindamycin did whereas the opposite was true regarding the recovery percentage (50-75%).

By the end of 12 weeks of topical therapy and based on the overall response of each patient individually, the number of patients who showed a valid response in finasteride group was comparable to that of clindamycin group regardless their grades of acne severity. Besides, all patients with mild acne in each group responded well; however, the non-responded patients were confined among those with moderate acne in each group. This probably pointed out the need for additive therapy since many times topical anti-acne therapy may be effective as maintenance therapy after initial control is achieved by combination of oral and topical therapy[24, 25].

Results of this study may represent an advanced step in accentuating the role of topical anti-androgen drugs in treatment of acne since topical 0.01% finasteride could achieve a comparable efficacy to that of topical 1.5% clindamycin whereas results of a previous study published by Erosy L. et.al. (1996)[16] revealed that topical 5% spironolactone, an anti-androgen drug, failed to do so and was less effective than topical 1.5% clindamycin.

The promising results obtained in this study counteract what was reported by Randall V.A. (1994)[26] who pointed out the availability of evidence that discounts the role of 5 alpha reductase II in sebaceous glands and acne.

Interestingly, treatment of 30 acne patients with topical finasteride solution (0.01%) for about 3 months seemed to maintain a good safety profile and lack any reported side effect from its oral use. This probably because of the too little dose of finasteride applied topically in this study compared to that of its oral use; thus, its amount reaching systemic circulation should be too little than that achievable from its oral use.

Conclusion

Finasteride solution 0.01% applied topically twice daily is as effective as the same regime of topical clindamycin solution 1.5% in the treatment of inflammatory mild-moderate acne vulgaris and has an excellent safety and tolerability profile.

Recommendations

1. Since finasteride seemed, from the present study, to have an excellent safety profile and because its efficacy might be a dose-related one so further comparative clinical studies with higher concentrations of topical finasteride solution are warrantable.
2. Clinical trials with combined therapy of topical finasteride solution with other anti-acne therapies appeared justified particularly for moderate-severe cases.
3. There is a need for studies that assess the effectiveness of topical finasteride solution in comparison to systemic hormones when the latter is indicated, for example, in treatment of acne of adult women happens when they are more than 20 years old and hadn't acne on their adolescence; this acne can be clinically classified as hypoestrogenic and hyperandrogenic[27].

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BRONCHIAL WASH IN THE DIAGNOSIS OF LUNG LESIONS

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Abstract

Objective: To correlate bronchial wash cytology with histology and bronchoscopic findings.

Methods: A total of 495 bronchial washing were reviewed and correlated with their bronchoscopic findings and histology.

Results: A clinical suspicion of lung tumor, hemoptysis, and pulmonary infiltration in chest X-ray were the most common indications for bronchial wash. Malignancy was found in 62.5% and positive Z.N. stain in 1.8% of wash cytology. The sensitivity of bronchial washing in malignant cell detection was 82%, increased to 95% when combined with brush and the overall accuracy of the procedure was 86%.

Conclusions: This study shows that bronchial wash is a useful procedure in diagnosing many chest diseases and that it has a high sensitivity and accuracy rate.

Key Words: Bronchoscopy, Wash, and Brush.

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Introduction

Bronchoscopy and bronchial wash were introduced by Ikeda in 1964. Since then bronchoscopy has become an important diagnostic and therapeutic tool for management of chest diseases[1,2]. Common indications of bronchoscopy and wash are chronic cough, hemoptysis, pulmonary infiltration, pleural effusion, unresolved pneumonia, tuberculosis, lung collapse and pulmonary mass[2-6]. In areas with high prevalence of pulmonary tuberculosis, bronchoscopy, bronchial wash and transbronchial lung biopsy are useful procedures in the diagnosis of pulmonary tuberculosis[2,5-7].

Several studies have shown that bronchoscopy and bronchial wash are safe procedures that carry very low mortality rate that range from 0% to 0.1%[2,7-10].

Materials & Methods

Four hundred and ninety five (495) Bronchial washings that were performed in the last two years (from March 2000 to March 2002), were reviewed in the Department of Pathology, College of Medicine, Al-Nahrin university, and the following data were analyzed; Age sex, indications, type of procedure carried out (wash, brush and biopsies) and bronchoscopic findings.

Bronchial wash: After centrifugation of bronchial washing each sample was smeared on 4 albuminized slides, 3 were placed immediately in 95% ethylalcohol for a minimum of 20 minutes and stained with H&E and the fourth air dried smear was stained with Z.N. Stain for Acid Fast Bacilli (AFB).

Bronchial brush: Smears of 73 bronchial brush were prepared after pouring each specimen in a petri dish, examining it against a blackboard, selecting any bloody, discolored, or solid particles, smeared on albuminized slides with a clean slide crushing the particles using a gentle pressure then placed immediately in 95% ethylalcohol for a minimum 20 minutes and stained with H&E.

In 86 cases the results of bronchial wash and brush were compared with histological lung biopsy (the latter was bronchoscopy biopsy, percutaneous needle biopsy or thoracotomy biopsy).

Statistical analysis: Chi square test was used as appropriate level of significance set to be <0.05 through analysis.

Results

A total of 495 bronchial washings were studied, male patients comprised 77.3% and the peak age was 61-70 years (32.3%).

The vast priorities (99%) of bronchial washings were carried out for diagnostic purposes. The most important indications for bronchoscopy in this study were pulmonary infiltration demonstrated in the chest X-ray, lung mass, hemoptysis and interstitial fibrosis in that order which constitute 93% of the total. Bronchial

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washings and brushing were carried out in 14.7% (73 patients). Biopsies were carried out in 86 patients (17.3%).

Cytology revealed malignancy in 297 cases (60%), (85.4% of them were male and only 14.6% were female), non-small cell lung carcinoma was found in 83.5% (248 patients), small cell lung carcinoma in 16.49% (49 patients).

Cytology of lung cancer was positive in 88% of cases with a bronchoscopy finding of fungating tumor mass, in 72% of stenosed bronchus, 28.6% unhealthy mucosa and in 8% of normal mucosa (Table-1).

Table 1: Correlation between Bronchoscopic Findings and Percent of Malignancy in Bronchial Wash

Bronchoscopic findings	Percent of positive malignancy in bronchial wash smears.
Fungating tumor like mass	88%
Narrow segment	72%
Unhealthy mucosa	28.6%
Normal Findings	8%

Table 2 shows the sensitivity and accuracy of bronchial wash cytology to be (82% and 86% respectively), Washing smears predict malignancy in 51 cases out of 62 cases proved malignant by biopsy. 11 cases were false negative (six of the cases proved to be squamous cell carcinoma by histology, four were small cell lung carcinoma and one was adenocarcinoma) and one case was false positive (proved to be pulmonary tuberculosis by histology.). The combination of wash and brush cytology raised the sensitivity rate to 95%. Tubercle bacilli were positive in 9 cases (1.8%). of bronchial wash using Z.N. stain.

Table2: Sensetivity and Accuracy of Bronchial Wash and Brush According to Lung Biopsies

	True +	True -	False +	False -	Total	Sensitivity	Accuracy
Bronch. wash	51	32	1	11	86	82%	86%
Wash & brush	70	0	0	3	73	95.8%	95.8%

Discussion

In Iraq bronchogenic carcinoma should be considered as a high priority problem with the need for expanded facilities for early detection, diagnosis and control and this should underline the provision of screening program that include radiographic, cytologic, and histologic methods to detect early stages of lung cancer and this is the most important step for reducing the disease mortality[1,2,5-8]. Data from Cancer Registry Center (1996) showed that lung cancer is the commonest tumor among male population[11].

The safety of bronchoscopy and the sensitivity of wash have been documented from different parts of the world[5-7]. In this study bronchial wash gave fairly good accuracy (86%) and the sensitivity was (82%). Brush increased the sensitivity of cytology to 95% when done with the wash. These figures are comparable to those reported in other studies (sensitivity ranged from 65% to 94%)[1,4,9-14]. Furthermore of the 9 patients, who were diagnosed as tuberculosis from wash smears stained by Z.N. stain, all had been proved by biopsy. Two cases proved to have both malignancy (squamous cell carcinoma) and tuberculosis, which is not remote possibility to have both pathologies together[5-7].

In conclusion bronchial wash and brush are useful procedures in diagnosing many lung diseases and it has a high sensitivity and accuracy rate.

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FINE NEEDLE CAPILLARY TECHNIQUE: IS ASPIRATION SUCTION NECESSARY? A STUDY OF 30 CASES AT VARIOUS PATHOLOGICAL LESIONS

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Abstract

Background: Fine needle capillary cytology (FNCC) or the non-aspiration technique is now gaining popularity as a diagnostic tool. Little has been published regarding the efficacy off the procedure in which the cellular material is most likely drawn by capillary action rather than by suction.

Objective: the aim of this study is to evaluate the value and reliability of (FNCC) technique done at various pathological sites.

Subjects & Methods: over 19-month period, 30 patients with various pathological lesions underwent fine needle capillary sampling, some with ultrasonic guidance. Smears were fixed in 95% ethyl alcohol and then stained by H&E stain and examined by the same cytopathologist. The technique was evaluated by an objective scoring system using five criteria. Cytological diagnosis was confirmed histologically.

Results: the mean age and sex distributions of all cases were evaluated. The ultimate histopathological diagnosis of all lesions revealed 21 malignant and 9 benign lesions. The average score per site regarding the assessment of (FNC) technique was adequate for diagnosis for all lesions submitted to this technique; the failure rate was zero by this technique.

Conclusion: by the application of an objective scoring system, (FNC) technique produces a comparable cellular yield and has similar diagnostic accuracy to (FNAC). On the other hand the former technique is less traumatic, produces less frequent bloody samples, and allows a more sensitive fingertip feeling of the lesion.

Key words: Aspiration cytology, fine needle cytology, fine needle capillary, non-aspiration cytology

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Introduction

Fine needle aspiration cytology is a rapid, reliable, accurate and safe procedure for the diagnosis of superficial and deep-seated mass lesions. Recently, fine needle sampling without aspiration has been introduced in certain centers[1,2].

Little has been published regarding the efficacy of this latter technique, which depends on the principle of capillary and may thus be called fine needle capillary (FNC) sampling technique.

The objective of this study is to evaluate and assess fine needle capillary sampling technique done at various pathological lesions.

Subjects & Methods

From January 2000 to July 2001, thirty patients with clinico-radiological diagnosis of various pathological lesions at different sites underwent (FNC) sampling technique, some under ultrasonic guidance, to study, evaluate and assess this technique in the diagnosis of such lesions. All patients were referred to Al-Khadhimiya Teaching Hospital; this technique was done at the radiology department using 20-21 gauge needles, the length of which ranged from 3.2 to 16 cm. For both superficial and deep-seated lesions, the technique was done by the same cytopatholgist using ultrasound guidance by an expert sonographer whenever needed. Smears were fixed immediately in 95% ethyl alcohol for at least 30 minutes then stained by hematoxylin and eosin (H & E) and examined by the same cytopathologist. Regarding the evaluation and assessment of this technique, five objective (criteria) parameters were applied for each sample and a point scoring system is predetermined as shown in table 1.

In the cytological smears examined there may be regional variation of the examined criterion e.g. cellularity within the same slide and thus the final score given for each criterion will represent the mean score. A score between (0 and 9) points was given to each fine needle capillary specimen

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on the basis of the five criteria tabulated in table 1.

Samples were classified to

1. Unsuitable for cytodiagnosis (0-2 points)
2. Adequate for cytodiagnosis (3-6 points)
3. Diagnostically superior (7-10 points).

The diagnosis was confirmed by histopathology.

Table 1: Methodology of point allocation (criteria and scoring system used)

Criteria	Quantitative description	Point score
1.cellularity(cellular yield)	Minimal or absent Sufficient for cytodiagnosis abundant (frequent cell clusters)	0 1 2
2. Degree of cellular degeneration and distortion(trauma)	Marked Moderate: diagnosis possible Minimal: diagnosis possible	0 1 2
3. Background blood or clot	Large amount (diagnosis not possible "obscured") Moderate amount (diagnosis possible) Minimal (diagnosis easy "clear background"	0 1 2
4. Architecture preservation (maintenance of appropriate cellular arrangement)	Non-diagnostic (minimal or absnt) Some preservation, flat sheets, syncytia or single cell patterns Excellent (diagnosis obvious)	0 1 2
5. Finger tip felling assessment	Poor Excellent	0 1

Results

The mean age and sex distribution of thirty cases studied is illustrated in table 2. Table 3 shows the results of FNC sampling of thirty cases from, various pathological sites. Table 4 shows the final histopathological diagnosis of the lesions submitted to FNC sampling technique and from this table we can notice that collectively there were 21 malignant lesions and 9 benign lesions. The average or mean score per site regarding the assessment of this technique was shown in table 5.

Table 2: Age and sex distribution of 30 cases with FNC sampling technique

Sample site	Sex		Mean age (years)
	Female	Male	
Liver	6	7	46±5
Breast	3	0	38±6
Thyroid	3	1	30±4
Kidney	2	3	54±5
Pancreas	1	2	64±5
Retroperitoneal	0	2	50±5

Table 3: Final histopathological diagnosis of all lesions submitted to FNC sampling

Location of lesion	No.	Benign lesion (including cystic lesion)	Malignant lesion
Liver	13	1	12
Breast	3	2	1
Thyroid	4	4	0
Kidney	5	2	3
pancreas	3	0	3
Retroperitoneal	2	0	2
Total	30	9	21

Table 4: Final histopathological diagnosis (biopsy diagnosis) for different lesions examined

Organ	No.	Final diagnosis
Liver	13	3 hepatocellular Ca. 9 metastatic Ca. 1 benign cyst
Breast	3	2 fibroadenoma 1 invasive ductal Ca.
Thyroid	4	multinodular goiter
Kidney	5	3 renal cell Ca. 2 simple renal cyst
Pancreas	3	adenocarcinoma
Retroperitoneal	2	soft tissue sarcoma

Table 5: The mean score per site regarding assessment of FNC technique

Site sampled	No.	Background of slides	Cellularity of samples	Degree of cellular degradation and trauma	Maintenance of cellular arrangement	Finger tip felling	Mean total score per site
Liver	13	0.87	1.02	1.94	0.48	1.0	Adequate
Breast	3	0.95	0.76	1.56	0.51	1.0	Adequate
Thyroid	4	0.48	1.87	1.88	0.43	1.0	Adequate
Kidney	5	0.71	1.54	1.73	0.49	1.0	Adequate
Pancreas	3	0.59	0.98	1.64	0.39	1.0	Adequate
Retroperitoneal	2	0.84	0.45	1.85	0.26	1.0	Adequate

- sufficient material was obtained in 30/30 (100%) of cases
- No inadequate sampling was obtained with the technique
- No evidence of complications was encountered in this technique

Table 5: The mean score per site regarding assessment of FNC technique

Thirty patients with different pathological lesions underwent cytological diagnosis using FNC sampling technique.

Table 2 shows mean age and sex distribution of 30 cases with different pathological lesions. Among these lesions sampled consisted of 13 liver masses (12 malignant, 3 primary hepatocellular carcinoma, 9 metastatic, one benign cystic lesion), 3 breast masses (two benign fibroadenoma, one invasive ductal carcinoma of breast), 4 thyroid lesions (all are of multinodular goiter), 5 kidney lesions (three primary renal cell carcinoma, two simple renal cysts), 3 pancreas (all proved to be adenocarcinoma), 2 retroperitoneal (both of soft tissue sarcoma), as shown in table 4.

Biopsies of all cases were subsequently received; histological results were all compatible with preceding cytological results.

All cytological smears were classified according to five basic criteria tabulated, using a predetermined point scoring system Table 1.

Table 5 shows average point scored for all 30 cases with different pathological lesions for each specific site using five basic cytological criteria.

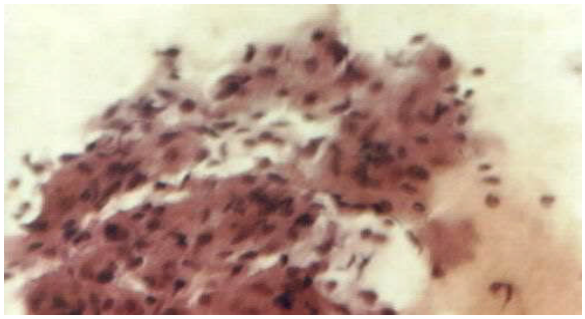

Figure 1: FNCC renal mass, renal cell carcinoma; notice abundant granular cytoplasm. H & E stain X 400.

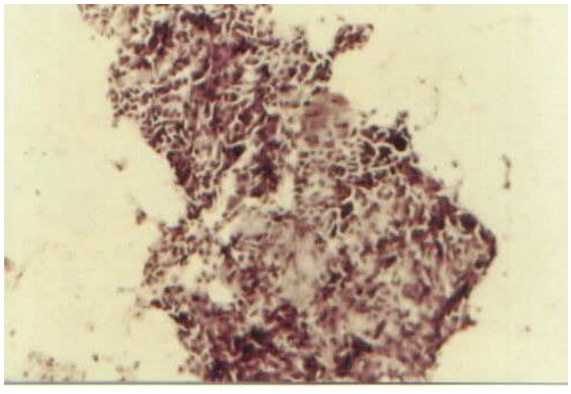

Figure 2: FNCC renal mass; angiomyolipoma, H & E stain X 200.

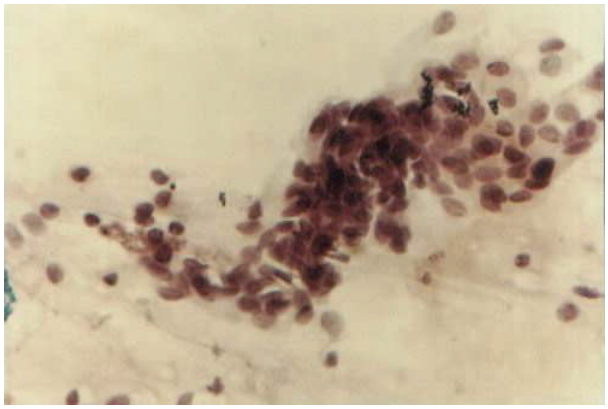

Figure 3: FNCC soft tissue mass, soft tissue sarcoma, H & E stain X 400. Notice adequacy of the sample.

Discussion

In 1930[3], Martin and Ellis first presented their results of tumor diagnosis by FNA technique; this report was followed by a second article in 1934[4]. In 1955 Frenzen et al[5] introduced a special aspiration syringe holder, described in detail in 1960 and 1967[6].

Since 1981, a new modified technique had been introduced, namely fine needle capillary sampling technique (fine needle without aspiration). The same procedure was also practiced by Briffod et al[7], since that time the technique become has gained popularity in different centers. It has been shown that by the application of an objective scoring system, the fine needle capillary sampling without aspiration produces a comparable cellular yield, and has a similar diagnostic accuracy to classic fine needle aspiration technique[8-10]. Also that FNC sampling technique permits a significant reduction in trauma to the tumoral and surrounding tissues, and that it reduces the amount of blood in the samples, particularly from vascular tumors. In addition, the direct contact with the needle allows a more sensitive fingertip feeling of the consistency of the tumor tissue during sampling.

This technique has certain disadvantages and as follows:

1. Relatively less Cellularity of the sample compared with classical needle aspiration that is in less cellular (fibrotic) lesions it is better to do fine needle aspiration cytology.
2. In cystic lesions, fine needle aspiration is the procedure of choice; it decreases the risk of spillage and loss of fluid contents that occurs from the open-ended needle used in fine needle capillary sampling to prevent direct

communication or contamination with the surrounding environment. Furthermore, fine needle aspiration enables drainage of enough material, in most cases, for biochemical, bacteriological as well as cytological studies. Additionally, fine needle aspiration may be therapeutic in cases of simple benign cystic lesions, which are often completely collapsed by aspiration with or without sclerotherapeutic agents.

3. It gives minimal maintenance of cellular arrangement compared with classic needle aspiration technique.

Conclusion

Each sampling technique has the advantages and disadvantages and to choose one of them, this is personal preference issue that is more suitable for him or herself. If only one needle pass is to be performed, to minimize patient discomfort or to reduce screening times, fine needle aspiration probably has a greater chance of producing a diagnosis than dose fine needle capillary sampling technique.

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WESTERGREN SEDIMENTATION RATE USING K_3EDTA

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Abstract

Background: The (ESR) measures the sedimentation rate of aggregated erythrocyte in plasma, the (ICSH) recommendation published in 1977 on measurement of the ESR was for a selected (routine) method based on that of Westergren.

Objectives: This study describes the use of K_3EDTA as an alternative anticoagulant to sodium citrate in measuring the ESR by the Westergren technique. We have therefore used this method to compare the results of ESR by both the classic and modified methods, in addition, to establish the normal limits for the modified method. And to assess the storage stability of whole blood preserved with K_3EDTA at 4^{o}C.

Subjects & methods: The erythrocyte sedimentation rate (ESR) values determined by the classic and the modified Westergren methods were recorded in 84 persons.

Results: There was no significant difference between the two methods using paired t-test (0.5>p>0.1), with a mean ESR in the classic method of 24.69 mm/hr, and 25.01 mm/hr in the modified Westergren method. Also the normal values of ESR using the modified method had been recorded in 74 apparently healthy persons, women tend to have a higher sedimentation rate values than men of comparable age. The storage stability of ESR of whole blood anticoagulant with K_3EDTA was determined; there was excellent storage stability up to 12 hours.

Conclusion: The modified method is an excellent method for measuring ESR using K_3EDTA anticoagulant, and it can be used in routine work because using the same anticoagulant used in routine hematological work. There was no significant difference between this method and the classic Westergren method.

Key Words: Westergren Sedimentation Rate, K_3EDTA

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Introduction

The erythrocyte sedimentation rate (ESR) test measures the sedimentation rate of aggregated erythrocytes in plasma. The international committee for standardization in hematology (ICSH) recommendation published in 1977 on measurement of the ESR was for a selected (routine) method based on that of Westergren method which proved a greater precision than the Wintrobe method[1-4]. Measurement of the ESR is frequently used non specific test which may indicate the presence of inflammation

The Westergren method for measuring the ESR has greater clinical precision than the Wintrobe method[1-4].

Measurement of the ESR is a frequently used non-specific test which may indicate the presence of inflammation or occult disease and confirm the presence of disease diagnosed by other means, or serve as a guide in following the course of a disease.

The ESR may be significantly increased suggesting an organic disease, when clinical and other laboratory findings are negative. Conversely, a normal ESR is reassuring in a patient believed to have no organic disease, although a normal ESR does not role out the presence of organic disease[5].

This study described the use of K3 EDTA as an alternative anticoagulant to sodium citrate in measuring the ESR by the Westergren technique following the exact procedure of the classic method.

Aim of the study:

This study is designed to:

1. Compare the results of ESR read by both the classic and modified methods.
2. Establishing the normal limits for the modified method.
3. Assessing the storage stability of whole blood preserved with K_3EDTA at 4^{o}C.

Patients & Methods

Prospectively, during the period from February 2001 to March 2002, the blood samples of 84 patients with different clinical disorders (42 males and 42 females, their ages range between 10-75 years) along with 74 apparently healthy individuals, no systemic illness, non pregnant and on no medications, utilized as control (37

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males and 37 females, their ages range between 10-73 years), were analyzed for ESR measurement by the classic and modified Westergren methods at the Hematological department of the Teaching Laboratories of College of Medicine, Al-Nahrain University.

Procedure

Classic Westergren method[4]

1. Four parts of venous whole blood is diluted with one part of 3.8% (W/V) of sodium citrate.
2. The sample is well mixed and blood drawn up into Westergren tube to 200 marks.
3. The tube is placed exactly vertical and left undisturbed for 60 minutes, free from vibration and away from direct sun light.
4. The height of plasma above the upper limit of the column of sediment cells is then read as the ESR.

The modified Westergren method[16]

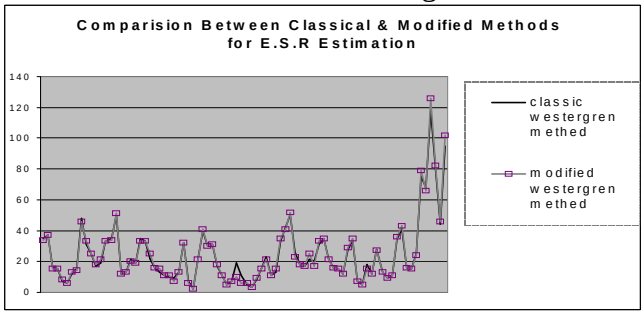
Its procedure and limitations are similar to the above method with the exception that, in this method 4 parts of the anticoagulated blood by 30% (W/V) K_3EDTA is diluted with 1 part of 0.85% (W/V) saline solution.

Statistical analysis

Using paired t-test for difference between means of paired samples. The values were expressed as means ± SD, when the P value (0.5>P>0.1), there is no significant difference between the two means.

Results

Listed in table 1 are E.S.R. values determined by means of the classic and the modified Westergren methods in 84 persons. There was no significant difference between the two methods (0.5>p>0.1). The mean E.S.R with the classic Westergren method is 24.69 mm/hr and the mean E.S.R. with the modified Westergren method is 25.01 mm/hr. The E.S.R. values range from 2mm/hr to 126mm/hr. when the ESR is greater than 25 mm/hr, the results by the modified method tends to be slightly higher than the classic method as shown in the figure.



No.	Classic westergren method	Modified westergren method	Differences d
1	**35**	34	-1
2	**37**	37	0
3	**16**	15	-1
4	**15**	15	0
5	**7**	8	+1
6	**6**	6	0
7	**12**	13	+1
8	**15**	14	-1
9	**48**	46	-2
10	**31**	33	+2
11	**25**	25	0
121	**17**	18	+1
3	**19**	21	+2
14	**33**	33	0
15	**35**	34	-1
16	**50**	51	+1
17	**12**	12	0
18	**13**	13	0
19	**21**	20	-1
20	**19**	19	0
21	**35**	33	-2
22	**33**	33	0
23	**22**	25	+3
24	**16**	16	0
25	**13**	15	+2
26	**11**	11	0
27	**10**	11	+1
28	**9**	7	-2
29	**13**	13	0
30	**32**	32	0
31	**7**	6	-1
32	**2**	2	0
33	**22**	21	-1
34	**40**	41	+1
35	**30**	30	0
36	**31**	31	0
37	**17**	18	+1
38	**11**	11	0
39	**5**	5	0
40	**7**	7	0
41	**19**	18	-1
42	**11**	10	-1
43	**5**	6	+1
44	**3**	3	0
45	**8**	9	+1
46	**15**	15	0
47	**23**	21	-2
48	**11**	11	0
49	**13**	15	+2
50	**33**	35	+2
51	**42**	41	-1
52	**50**	52	+2
53	**26**	23	-3
54	**18**	18	0
55	**17**	17	0
56	**21**	25	+4
57	**20**	17	-3
58	**31**	33	+2
59	**35**	35	0
60	**22**	21	-1
61	**16**	16	0
62	**15**	15	0
63	**12**	12	0
64	**27**	29	+2
65	**34**	35	+1
66	**7**	7	0
67	**5**	5	0
68	**18**	15	-3
69	**12**	12	0
70	**28**	27	-1
71	**13**	13	0
72	9	9	0

Table 1 ***(continued)***

No.	Classic westergren method	Modified westergren method	Differences d
73	11	11	0
74	35	36	+1
75	41	43	+2
76	16	16	0
77	15	15	0
78	25	24	-1
79	75	79	+4
80	68	66	-2
81	118	126	+8
82	80	82	+2
83	44	46	+2
84	95	102	+7
Mean	**24.69**	**25.01**	
S.D.	**20.003**	**20.945**	
P value > 0.1 N.S.			

Listed in table 2 are E.S.R. values for 37 apparently normal males and 37 apparently normal females. The results are ranked in order of age for both sexes. Females tend to have higher sedimentation values than males of comparable age, and the normal E.S.R. tends to increase slightly with age.

Table 2: Normal ESR values for 74 healthy individuals

Age (years)	Men mm/hr	Women mm/hr
18-30	6.8	10.3
31-40	8.6	11.6
41-50	10.8	13.0
51-60	12.0	18.5
> 60	14.1	19.7

Table 3 is a tabulation of E.S.R. values of 31 samples after storage for 0,8,12, and 16 hours at 4^{o}C. There is an excellent storage stability up to 12 hours and there is no significant difference between the mean ESR at 0,8,12 hours (0.5 >P> 0.1).

Table 3: Storage stability of the modified westergren E.S.R. at different temperatures in 31 samples

No.	Immediate mm/hr	8 hours mm/hr	12 hours mm/hr	16 hours mm/hr
1	2	3	2	2
2	3	5	5	4
3	4	4	5	6
4	4	5	4	6
5	4	6	7	5
6	6	5	4	6
7	6	5	6	5
8	6	7	8	4
9	7	8	8	8
10	9	10		10
11	10	10	10	9
12	10	10	11	9
13	11	10	12	10
14	12	14	15	13
15	12	14	14	5
16	14	14	16	16
17	26	26	28	21
18	26	25	28	21
19	30	32	34	23
20	31	34	39	32
21	31	31	31	20
22	35	36	38	30
23	50	47	50	46
24	65	67	68	60
25	68	70	75	51
26	70	70	68	48
27	70	70	70	68
28	77	79	83	78
29	83	81	85	79
30	101	98	105	95
31	103	107	118	92

Table 3 *(continued)*

Discussion

The excellent correlation between the results of classic and modified Westergren methods makes it unnecessary to have special tubes filled with 3.8 percent (w/v) of sodium citrate for collection and dilution. Dilution with saline solution in the laboratory rather than with sodium citrate at the time of collection will conserve patient's blood because the K_3EDTA tubes can be used for other hematology and chemistry tests[6-8]. Blood samples may be stored up to 12 hours at 4^{o}C before dilution with saline without significantly altering the ESR (table 3), which makes it possible for a busy laboratory to schedule its work. Moreover, EDTA is an ideal anticoagulant in that it has the least effect on blood cell morphology and does not interfere with electronic counting of red cells and leukocytes and platelets[1,2,9-14].

The result of this study of normal values (table 2) is in agreement with Hilder and Gunz[15]. These authors studied 603 healthy blood donors of varying age, using the classic Westergren method.

Dawson believed the normal range to be 0 to 10 mm. per hr. for men and 0 to 15 for women. Westergren originally believed the normal range to be 0 to 5 mm. per hr. for men and 0 to 10 for women, but he did not regard readings as abnormal until they exceed 10 mm/hr in men and 20 mm/hr in women.

Blood anticoagulated with tripottasium ethylenediamine tetraacetate monohydrate (K_3EDTA) and subsequently diluted with 0.85 percent (W/V) saline solution (4 parts of whole blood with one part of saline solution has been shown to yield an excellent ESR values compared to classic Westergren method. The samples remain stable up to 12 hour without affecting the rate of red cell sedimentation. Moreover, preserving blood in EDTA tubes will

preserve the samples for other haematologic and biochemical tests that patients may need avoiding repuncturing.

Conclusions

1. The modified method is an excellent method for measuring ESR using K_3EDTA anticoagulant.
2. This method can be used in routine work using the same anticoagulant (K_3EDTA) used in routine Hematological work.
3. There was no significant difference between this method and the classic Westergren method.

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THE VALUE OF RAPID STAINING ASSESSMENT AND TECHNIQUE EMPLOYED IN FINE NEEDLE ASPIRATION CYTOLOGY

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Abstract

Background: Fine needle aspiration cytology (FNAC) is a safe, simple and efficacious procedure for obtaining material for cytological diagnosis in space occupying superficial or deep-seated lesions[1,2], particularly when other routine non-invasive procedures have provided little diagnostic information.

Inadequate or inappropriate sampling can be minimized by precise localization of the lesion under ultrasound guidance, by experienced operator and by employing a rapid staining technique to assess the adequacy of the sample before releasing the patient out of the procedure room.

Objectives: The aim of the study to assess the value of using rapid staining technique in the assessment of cytological specimens obtained by ultrasonic guided FNAC and compares the success rate for securing an accurate diagnosis with that of the standard single sample method.

Methods: Over a 12 months period, 54 patients with different superficial and deep-seated lesions underwent ultrasonic guided FNAC by teamwork. After each sampling pass, the cytological specimen was stained by a rapid modified Leishman's staining method, and the smears were evaluated for adequacy. Subsequent passes were performed if the first pass was inadequate.

Results: The rapid staining technique gives a remarkably higher sensitivity than the standard technique (93.75%), vs. 75.5%), a higher specificity (100%, vs. 97.6%) and a remarkably higher diagnostic overall accuracy (96.15) compared with (78%) for the standard method. The overall complication rate with the rapid staining technique is 3.7%.

Conclusion: The use of rapid staining technique should be encouraged for its potential benefits, for the patients (less discomfort, less complication rate, and quicker diagnosis about the nature of the lesion).

Key words: Fine needle aspiration cytology, Leishman's stain, Rapid staining technique

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Introduction

Fine needle aspiration cytology (FNAC) is a safe, simple and efficacious procedure for obtaining material for cytological diagnosis in space-occupying superficial or deep seated lesions[1,2]; particularly when other routine non-invasive procedures have provided little diagnostic information.

Inadequate or inappropriate sampling can be minimized by precise localization of the lesion under ultrasonic guidance; by experienced operator and by employing a rapid staining technique to assess the adequacy of the sample before releasing the patient from the procedure room.

This paper describes the usefulness of employing rapid staining technique in the assessment of cytological specimens obtained by ultrasonic-guided FNAC and compares the success rate for securing an accurate diagnosis with that of the standard single sample method.

Materials and Methods

During the period from July 1999 to July 2001, a total of 54 patients underwent ultrasonic-guided FNAC from different superficial and deep-seated lesions including (thyroid, breast, liver, lung, retroperitoneal, pancreas and kidney) at the Radiology Department/Al-Kadhimiya Teaching Hospital. The procedure was done by a team work including radiologist and cytopathologist fellow, assisted by experienced staff of Radiology and Cytopathology Department.

The technique has been described elsewhere[3,4]. After each sampling pass, the cytologic specimen was stained using a rapid modified Leishman's staining method which takes five minutes[5], the smears were then evaluated for their adequacy by the same person who performed the FNAC at the Radiology Department procedure room. This rapid staining method did not attempt to make a diagnosis but just to assess the adequacy of the sample.

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Subsequent passes were performed only when this first specimen was inadequate.

A maximum of three adequate passes were done where the ultrasound clearly shown that the needle tip to be in the target lesion. Provided this is done properly, negative cytology indicates beginning of the lesion (whether neoplastic or non-neoplastic processes). Haematoxylin and Eosin staining method was routinely applied to the cytologic smears after de-staining. The diagnostic evaluation of the specimen was made by an experienced cytopathologist, and the confirmation of the diagnosis was based on subsequent histologic sampling, surgery or clinical and/or radiological follow up for more than six months.

The cytologic diagnoses were categorized as true positive (TPs); true negatives (TNs); false positives (FPs); false negatives (FNs) and non diagnostic (ND) = inadequate specimen; insufficient material. The sensitivity, the specificity and overall accuracy values of the overall results were calculated.

100 cases of FNAC done by the standard single sample method from sites comparable to those of the rapid staining technique (as control).

Results

There were 29 males (53.7%) with age range from 17 to 62 years and 25 females (46.3%) ranging in age from 22 to 51 years. The mean age for all patients was 43 years. Table 1 shows the results of cytologic diagnosis in 54 patients with ultrasonic guided-FNAC when compared with the biopsy. The overall results of the procedure from different sites gave a sensitivity of 93.75%, a specificity of 100% and an overall accuracy of 96.15%. The overall complication rate when using the rapid staining technique was 3.7% (two out of 54 patients had got non-specific general vasovagal attacks).

Table 1: Overall results of cytologic diagnosis in 54 patients with ultrasonic-guided FNAC

Target organ	TP	TN	FN	FP	ND
Thyroid	0	14	0	0	0
Breast	10	3	0	0	0
Liver	8	1	1	0	0
Kidney	3	1	0	0	1
Pancreas	3	0	0	0	0
Retroperitoneal	2	0	0	0	0
Lung	4	1	1	0	1
Total	30	20	2	0	2

Comparing between the results in Table 1 and Table 2, we can notice that the rapid staining technique gives remarkably higher sensitivity than the standard technique (93.75% versus 75.5%), a higher specificity (100% versus 97.6%) and remarkably higher diagnostic overall accuracy (96.15%) compared with (78%) for the standard technique.

Table 2: Shows the overall cytological results compared with biopsy in 100 patients with ultrasonic-guided FNAC done by the standard single sample method

Target organ	No. of cases	TP	TN	FN	FP	ND
Thyroid	30	2	25	3	0	0
Breast	25	11	12	1	0	1
Liver	16	10	2	4	0	0
Kidney	10	5	1	1	1	2
Pancreas	4	2	0	1	0	1
Retroperitoneal	5	3	0	1	0	1
Lung	10	4	1	1	0	4
Total	100	37	41	12	1	9

The overall complication rate when applying the rapid staining technique was 3.7% (two out of 54 patients had got non-specific general vasovagal attacks). The complication rate using the standard method was 4% (2 cases of spontaneous pneumothorax in FNAC of the lung which resolved spontaneously and 2 cases of fainting attack in FNAC from thyroid).

Table 3: shows a comparison between the rapid staining method and the standard method regarding accuracy and adequacy of aspirates

Technique	No.	Unsatisfactory aspirate	Accuracy
Standard	100	9	78%
Rapid staining	54	2	96.3%

Discussion

Despite the simplicity, rapidity and low cost, rapid staining techniques have rarely been used for the evaluation of FNAC specimens obtained under the guidance of expensive, time-consuming and/or potentially dangerous guidance technologies including C.T scan, MRI, Fluoroscopy, etc…

Most groups perform from two to five (or more) passes into target lesions to obviate the possibility of inadequate / insufficient

specimens[3,6-12]. Although there is a relationship between the number of complications and the number of passes for guided FNAC has been demonstrated, it seems reasonable to limit the number of passes to what are strictly necessary[9]. Moreover, there appear to have been no data published on the optimal number of passes to be performed in each lesion when rapid cytologic assessment was not employed. In addition, improved patient's care due to more specific and immediate selection of additional diagnostic tests and evaluated benefits for the staff were seen as a result of rapid cytologic assessment.

In our series, a careful evaluation of the diagnostic accuracy after each pass was made and from the analysis of our data, the following conclusions can be drawn:

1. The immediate rapid staining cytological assessment of the specimens obtained by ultrasonic-guided FNAC significantly reduced the number of puncture performed in each patient, thus reducing complication rate.
2. In most cases, it is possible to make a preliminary cytological assessment (whether benign versus malignant lesions) before the final cytological results. This is beneficial in giving at least some idea about the nature of lesion for both the patient and treating physician and to relive patient's anxiety.
3. In some cases, when a second pass into the lesions was needed, no significant improvement in diagnostic accuracy can be obtained provided the needle tip was in the target lesion.

The use of immediate rapid staining cytologic assessment should be encouraged for its potential benefits for both patients (less discomfort, less complication rate, quick orientative preliminary diagnostic idea about the nature of the lesion for future subsequent diagnostic assessment of the patients). When facilities for rapid staining cytological assessment are not available, we recommend performing a maximum of two passes from different sites for each lesion since the diagnostic yield did not improve with more passes.

Further large studies should be performed in order to elucidate the relationship between the number of passes, the rate of complication and the diagnostic yield.

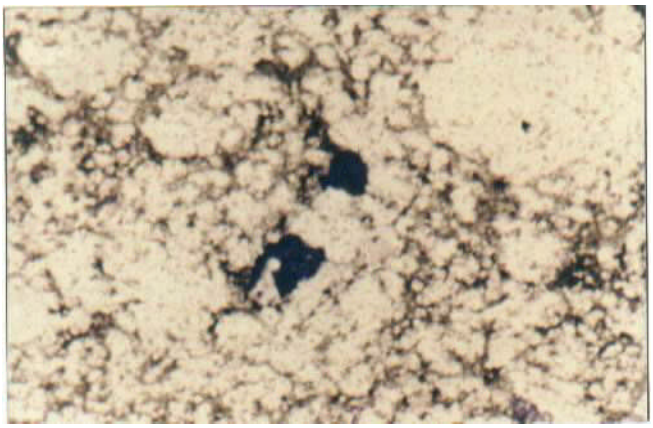

Figure 1: FNAC liver mass, modified leishman stain X 100; notice adequacy of the sample

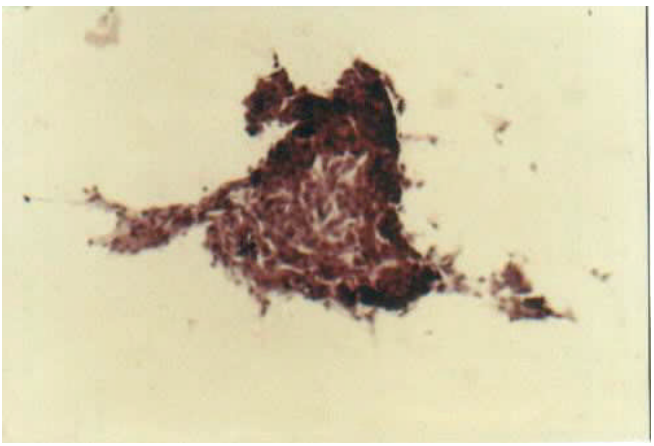

Figure 2: FNAC pancreatic carcinoma, H & E stain X 200

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PERIPHERAL BLOOD LYMPHOCYTES PROLIFERATION ASSAYS IN PATIENTS WITH HYDATID DISEASE (*ECHINOCOCCUS GRANULOSUS*)

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Abstract

Background: Hydatid disease represents a major public health problem. Little is still yet known about the establishment of the disease in humans and the role of the immune response in this process.

Objectives: To measure the mitotic and replicative indices (MI and RI) and cell cycle progression (CCP) in the peripheral blood lymphocytes (PBLs) of patients with hydatid disease.

Materials & Method: Ninety-six individuals were included in the study; fifty-eight with surgically confirmed hydatid disease and thirty-eight healthy controls. Blood was collected from each individual. The proliferation indices were measured in the PBLs according to Lamberti *et al.*, (1983).

Results: The proliferation indices were significantly lower in the patients when compared to the healthy controls.

Conclusion: MI, CCP and RI have relatively decreased values during hydatid disease infection. The decrease in proliferation measurements correlated with the immune unresponsiveness state associated with the disease.

Key words: Mitotic index, Replicative index, Hydatid disease, Peripheral blood lymphocytes, *Echinococcus granulosus*

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Introduction

The Mitotic Index (MI), Cell Cycle Progression (CCP), Replicative Index (RI) are of the most important parameters used in detecting agents which are mutagenic and/or carcinogenic in higher organisms including mammalian cells or human cells, in particular[1,2]. Several reports showed that parasitic infections such as schistosomiasis[3-5], visceral leishmaniasis[6] and trichomoniasis[7] in man, fascioliasis in sheep[8] and hydatid disease in mice[9] cause a significant reduction in MI, CCP and RI in host lymphocytes and bone marrow cells.

Hydatid disease still represents a major public health problem in Iraq. As a matter of fact, the number of cases recorded is indeed higher than the ones reported in many countries[10,11]. Yet still little is known about the establishment of this disease in the intermediate host and the immune status during the course of infection. Several mechanisms have been proposed for how the larval stages of *Echinococcus granulosus* manage to elude the immune response, and more recently, several studies suggest that the parasite exploits the immune response to its own benefit[12].

Because of the above, this study was conducted to record the proleifrative assays of PBLs during hydatid disease in humans.

Materials & Methods

Subject selection

Any individual who is smoker, alcohol consumer, has any disease other than hydatid disease or under any kind of therapy was excluded from the study. The individuals studied were divided into two groups as follows:

1. Hydatid cyst patients:

Blood samples of fifty-eight (58) surgically confirmed cases of hydatid patients of different organs involvement (single or multiple) were collected from three teaching hospitals in Baghdad; University Hospital of Saddam College of Medicine, Al-Shaheed Adnan Teaching Hospital, and Baghdad Teaching Hospital.

2. Healthy controls:

Thirty-eight control subjects were chosen on the bases that they were age and sex matched to the hydatid patients. The sera of this group were tested for hydatid disease (Echinococcosis) by the method of indirect hemagglutination (IHA) (bioMérieux, France). The positive samples were excluded from the study.

Blood samples collection

Two ml of venous blood was collected from the individuals after disinfecting the anti-cubital

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fossa with povidine-iodine (Povicenter, U.S.P, Jordan) and then with 70% ethyl alcohol (Riedel-de Häen, Germany). Veinpuncture was carried out with a 5-ml disposable syringe with a 22-gauge needle, after applying a tourniquet. The blood was placed aseptically in a sterile heparinized tube (B-D vacutainer brand) and mixed well to avoid clotting.

Mitotic index (MI) analysis

The MI was determined as a percent of the mitotic cells to interphase nuclei in 1000 cells, as shown in figure (1).

Cell cycle progression (CCP) analysis

The CCP was analyzed in 100 consecutive metaphase cells presented as percent of M_1 (figure 2), M_2 (figure 3), and M_3 (figure 4) cells. The replicative index (RI) was calculated using the following equation:

$$RI = \frac{(1\times\%M_1) + (2\times\%M_2) + (3\times\%M_3)}{100}$$ (Lamberti *et al.*, 1983)[13]

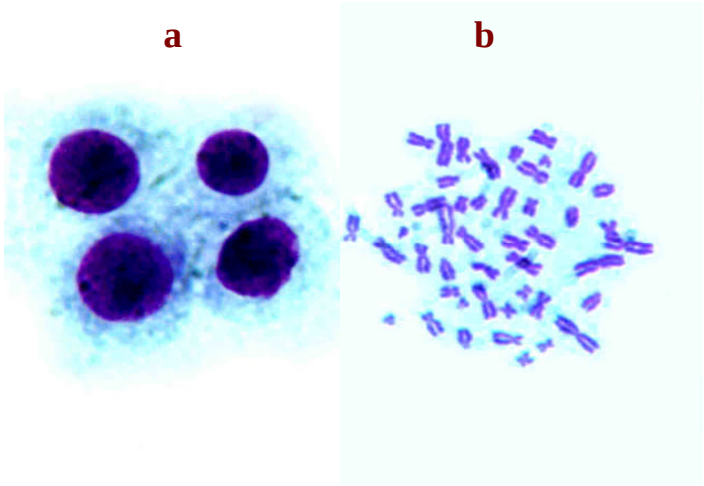


Figure 1: (a) human lymphoblasts (b) human lymphocytic metaphase (1000X, Giemsa stain)

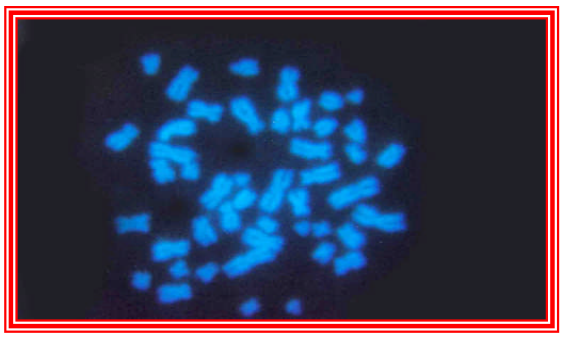


Figure 2: Human lymphocyte chromosomes at the first metaphase M_1 (1000X, DAPI-stain).

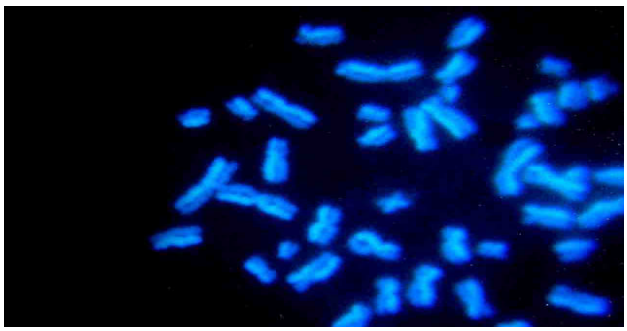


Figure 3: Human lymphocyte chromosomes at the second metaphase M_2 (1000X, DAPI-stain)

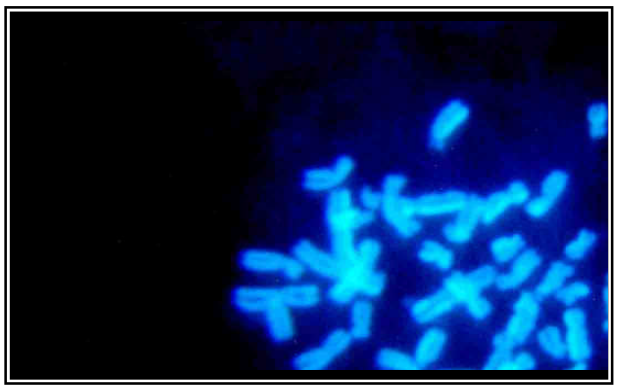


Figure 4: Human lymphocyte chromosome at the third metaphase M_3 (1000X, DAPI-stain).

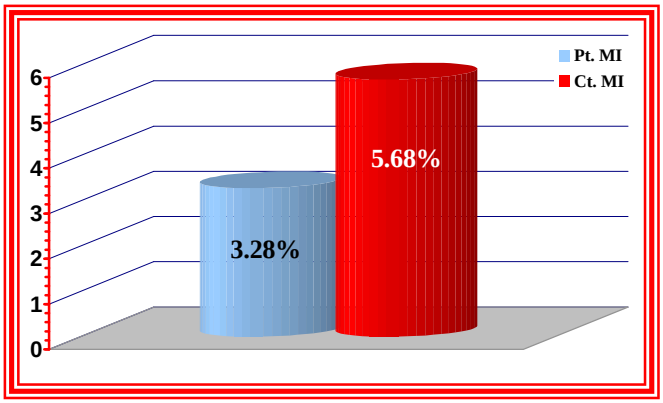
Results

1. The mitotic index (MI):

The mean MI of patients with hydatid disease (3.28% ± 0.19) was significantly lower ($P\leq 0.0001$) than that of the healthy controls (5.78% ± 0.21). No significant difference ($P\geq 0.05$) was found between the mean MI of the patients according to sex and the location of the cyst (figure 5, table 1).

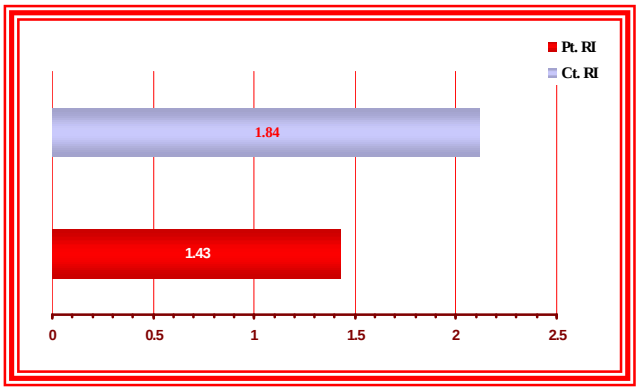
2. The cell cycle progression (CCP):

The mean replicative index (RI) of patients with hydatid disease (1.43 ± 0.02) was significantly lower ($P\leq 0.0001$) than that of the healthy controls (1.84 ± 0.02). No significant difference ($P> 0.05$) was found between the mean RI of the patients according to the sex and the cyst location (figure 6, table 1).



Pt. = Patients, **Ct.** = Controls, **MI** = Mitotic index

Figure 5: The mean mitotic index (MI) of the patients with hydatid disease and healthy controls.



Pt. = Patients, **Ct.** = Controls, **RI** = Replicative index

Figure 6: The mean replicative index (RI) of the patients with hydatid disease and healthy controls.

Table 1: The mean proliferative, cytogenetic parameters of patients with hydatid disease and healthy controls

	Hydatid disease patients					Healthy controls				
Sex	MI (%) ± SE	M_1 (%) ± SE	M_2 (%) ± SE	M_3 (%) ± SE	RI ± SE	MI (%) ± SE	M_1 (%) ± SE	M_2 (%) ± SE	M_3 (%) ± SE	RI ± SE
♂	3.09 ± 0.27	63.5 ± 2.18	29.7 ± 1.9	6.8 ± 0.94	1.43 ± 0.03	5.46 ± 0.32	37.7 ± 1.74	39.7 ± 2.13	22.6 ± 2.03	1.86 ± 0.03
♀	3.37 ± 0.25	65.1 ± 1.55	27.4 ± 1.38	7.5 ± 0.85	1.42 ± 0.02	5.79 ± 0.27	38.3 ± 1.47	42.3 ± 1.55	19.4 ± 1.55	1.82 ± 0.02
♂ + ♀	3.28 ± 0.19	64.4 ± 1.31	28.3 ± 1.17	7.3 ± 0.67	1.43 ± 0.2	5.78 ± 0.21	37.4 ± 1.09	41.2 ± 1.36	21.4 ± 1.3	1.84 ± 0.2

MI = Mitotic index (%), M_1 = First metaphase (%), M_2 = Second metaphase (%), M_3 = Third metaphase (%), RI = Replicative index, SE = Standard error

Discussion

One of the most sensitive tests for the effect of potentially mutagenic, carcinogenic and toxic agents is the quantifying of cytogenetic parameters including MI, RI and CCP[14]. The mean MI, RI of patients with hydatid disease in response to the nonspecific T-cells mitogen, the PHA, was significantly lower than those of healthy controls. This may indicate an immune unresponsiveness state against the parasite. The observed state of immune unresponsiveness against the parasite might be due to the release of immunoregulatory substances from the parasite. The above results are also supported by the results of previous workers in other parasitic infections like *Schistosoma haematobium*[3,5], *Schistosoma mansoni*[4], *Echinococcus granulosus* experimental infection in mice[9], visceral leishmaniasis in children[6], and *Fasciola gigantica* infection in sheep[8]. It is reported that chronic helminthic infections cause chronic immune activation and strong Th-2 type cytokine profile[15]. This polarization towards the Th-2 subtype and its cytokine profile that include the IL-4, IL-5, IL-6, IL-10 and IL-13 was reported in cases of hydatid disease[12,16,17]. This will cause inhibition of type-1 T-cells especially by the IL-10, and that is supported by the low concentration of IL-12 due to the toxic effect of hydatid antigens on macrophages[12,18]. This might be a good support and explanation of our result suggesting that the significantly low MI and RI in response to the stimulation by the mitogen in patients cells is due to this shifting in the T-cell subset leading to predominant Th-2. On the other hand, the controls group cells responded normally.

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SPECIFIC IGG AVIDITY TESTING IN DIAGNOSIS OF ACUTE TOXOPLASMOSIS AMONG WOMEN WITH HISTORY OF ABORTION

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Abstract

Background: Toxoplasmosis is a disease of importance because of it's effect on public health, especially that on fetus and pregnant women. Serological tests are most frequently used for diagnosing acute infection.

Objective: To detect recently acquired toxoplasmosis among women with first abortion.

Subjects & Methods: A cross-sectional study was conducted on 330 women with a history of abortions (first abortion and repeated abortion), and 40 women with no abortion. Their age ranged between 16-50 years. Using ELISA technique, women with history of first abortion and those with no abortion were screened for toxoplasmosis by specific IgM and IgG detection in their sera. Women with repeated abortion were screened for specific IgG in their sera. Specific IgG avidity index was evaluated, to confirm diagnosis of acute toxoplasmosis.

Results: Specific IgM antibodies were significantly observed in 40.3% of women with first abortion and 10% among women with no abortion. The positivity rate, as indicated by specific IgG, was 60.2% in women with repeated abortion. Specific IgG avidity index was evaluated in 20 sera positive for specific IgM and 12 sera negative for specific IgM. The avidity indices ranged from 2.4%-52.6% in the former group and 35.7%-96.6% in the later group. The sensitivity of this new technique was 100%, while its' specificity was 83.3%.

Conclusion: Determination of the avidity of *T. gondii* specific IgG is an efficient technique for defining recent infection with *T. gondii* among women with abortion.

Key words: Toxoplasmosis, IgG avidity, abortion

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Introduction

Toxoplasmosis, is a worldwide infection caused by the obligatory intracellular coccidian *Toxoplasma gondii*. It is estimated that up to 5×10^8 people worldwide are infected with *T. gondii*. Between 15% and 85% of the world adult human population is chronically infected with T. gondii. It is a disease of importance in community medicine because of it's ill effect on public health, especially that of the fetus and pregnant woman[1].

As seroconversion and a rise in IgG titers are seldom demonstrable, the detection of *T. gondii* specific IgM antibodies has been the most frequently used serological marker for diagnosing acute infection[2]. However, the persistence of specific IgM antibodies in some patients and the use of tests with a low specificity have complicated the interpretation of serological results when toxoplasmosis is suspected. Various confirmatory tests have been proposed to distinguish recent from past toxoplasmosis, including IgG avidity tests[3]. Avidity analysis is an important part of the diagnostic procedure in toxoplasmosis and other infections which carry a risk of congenital transmission[4]. Avidity analysis provides a useful tool in staging these infections and in predicting potential fetal loss[5].

Therefore, the aim of this study is to detect recently acquired toxoplasmosis among women with history of first abortion by surveying specific IgM antibody and by testing for low avidity of specific IgG antibody.

Materials & Methods

A cross sectional study was conducted on three hundred and thirty women with a history of abortion (women with first and repeated abortion), and forty women with no history of abortion, their ages range between 16-50 years, cases that had obstetric histories of D.M., H.T., uterin abnormality, hormonal insufficiency, smoking, cervical incompetence, emotional causes and trauma were excluded.

These samples were collected from women attending Al-Noor General Hospital and Al-Adel Primary Health Care Center from 21th of July 2001 to 14th of January 2002 the samples were classified into three main groups.

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Group I: One hundred and forty four women with history of first abortion were screened for toxoplasma infection based on detection of specific IgM and IgG antibodies by using ELISA test (Bio elisa toxo IgM kit (biokit, Spain) &Bio elisa toxo IgG kit (biokit, Spain)).

Group II: One hundred eighty six women with history of repeated abortion were screened for specific IgG antibody by using ELISA Test.

Group III: Forty women with no history of abortion (non pregnant) and had history of labors screened for specific IgM and specific IgG antibodies by using ELISA test.

Blood was collected from each subject enrolled in this study. Sera were separated and then stored at -20^{o}C until time of processing. An indirect enzyme immunoassay for the qualitative determination of IgM and IgG antibodies directed against *T.gondii* in human serum was carried out. Positivity and negativity of each sample for specific IgM and IgG antibodies were determined from the cut-off values that were calculated according to the manufacturers instructions.

The avidity of T. gondii IgG antibodies was measured with a commercial ELISA IgG kit, for detecting specific IgG antibodies to *T.gondii*. Each serum sample was analyzed in two rows (row A and row B) of the ELISA plate then incubated for 1 hour at 37^{o}C. Row (A) was washed three times with PBS-Tween 20 containing 6M. urea, whereas row (B) (control row) was washed three times with the washing solution (no urea) that accompanied the kit. The subsequent steps of the reaction, including incubation with conjugate (goat antihuman IgG labelled with peroxidase), washing, incubation with Substrate (3,3',5,5'-tetramethylbenzidine/H_2O_2) and the addition of stopping solution were performed as recommended by the manufacturer. The optical density of each well was read at 450 nm.

The avidity index was calculated as the mean absorbance of reactions when exposed to urea divided by the mean absorbance of reactions not exposed to urea, expressed as a percentage. Avidity indices $\leq$ 58 and > 58 were considered as indicative of recent and long-term infection respectively [2,6].

Analysis of data: The collected information was appropriately coded and fed into the computer files for storage and analysis through use of EPI 6 programs. Chi-square was used for analysis of the data. Results were considered significant at P<0.05.

Results

As shown in table 1, the percentages of positivity rate for specific IgM among women with history of first abortion (40.3%) was significantly higher than that in women with no history of abortion (10%), p = 0.00068. The frequency distribution of specific IgG among women with history of repeated abortion compared to those with history of first abortion, was demonstrated in table 2, where the positivity rate for specific IgG among the former group (60.2%) was significantly higher than that in the later group (33.6%), P = 0.00002.

Table 1: Frequency distribution of toxoplasma specific IgM by ELISA among women with history of first abortion compared to women with no history of abortion

Type of cases	IgM positive	IgM negative	Total	Yates corrected X^2 P value Odds ratio
First abortion group	58 (40.3%)	86 (59.7%)	144(100%)	Yates corrected X^2 = 11.53 P = 0.00068 Odds ratio = 6.07 2.00<OR<24.54
No abortion group	4 (10%)	36 (90%)	40 (100%)	
Total	62 (33.7%)	122 (66.3%)	184 (100%)	

Table 2: Frequency distribution of toxoplasma specific IgG by ELISA among women with repeated abortion compared to women with first abortion

Type of cases	IgG positive	IgG negative	Total	Yates corrected X^2 P value Odds ratio
Repeated abortion group	112 (60.2%)	74 (39.8%)	186 (100%)	Yates corrected X^2 = 18.14 P = 0.0000206 Odds ratio = 2.98 1.77<OR<5.07
First abortion group	36 (33.6%)	71 (66.35%)	107 (100%)	
Total	148 (50.5%)	145 (49.5%)	293 (100%)	

Twenty sera positively reactive to toxoplasma specific IgM and IgG and 12 sera negatively reactive to specific IgM but positively reactive to specific IgG were subjected for IgG avidity testing. In our analysis we considered sera with indices < 58 as having low avidity which reflects

recent infection with toxoplasmosis, while those > 58 as having high avidity (chronic infection)[2,6]. As shown in table 3A and 3B, the avidity indices for positively reactive sera to specific IgM ranged between 2.4% - 52.6% while the 12 sera that were negative for specific IgM ranged between 35.7% - 96.6%.

Table 3A: Avidity indices for 20 cases with acute toxoplasmosis

Duration since last abortion for 20 cases	Number of cases	Ranged of avidity
1-10 days	13 cases	2.4% - 40.5%
>10 days-2 months	4 cases	40.2% -52.6%
≥ 3 months	3 cases	40% -43.4%

Table 3B: Avidity indices for 12 cases with chronic toxoplasmosis

Duration since last abortion for 12 cases	Number of cases	Ranged of avidity
2 weeks – 2 months	8 cases	35.7% - 96.6%
>2 months – 4 months	1 case	68.9%
>4 months – 6 months	3 cases	37.5% -93.3 %

As shown in table 4 the sensitivity, specificity, positive and negative predictive values of the IgG avidity testing was 100%, 83.3%, 87.5% and 100% respectively.

Table 4: The sensitivity and specificity of the avidity index
ELISA IgM

Avidity Index	IgM +ve	IgM -ve	Total
≤ 58	12	2	14
> 58	0	10	10
Total	12	12	24

$$\text{Sensitivity} = \frac{12}{12} \times 100 = 100\%$$

$$\text{Specificty} = \frac{10}{12} \times 100 = 83.3\%$$

$$PV^{+} = \frac{12}{14} \times 100 = 87.5\%$$

$$PV^{-} = \frac{10}{10} \times 100 = 100\%$$

Discussion

Acute toxoplasmosis was detected in this study by measurement of specific IgM, in 58 (40.27%) women with history of first abortion, the results were significant statistically as compared to women with no abortion (P=0.0006).

Using the same technique (ELISA Technique), many researchers in the world have reported specific IgM antibodies that ranged from (4.2%-43.8%) of women[7,8]. In Iraq, previous studies have reported Toxoplasma specific IgM using ELISA Technique in (28.7%) of women[9]. However, the studied group was complicated pregnancy. While using other techniques the seropositivity rate was found to be 23-24% using IFAT[10], 7.3% and 27.6% by IHAT[11,12].

This study has demonstrated Toxoplasma specific IgG in 112 (60.21%) of women with history of repeated abortion, and that women with repeated abortion was statistically significant as compared to first abortion group p=0.00002. Niazi and coworkers (1992)[10] have reported a slightly lower results (39%). This is possibly due to the use of different serological test (IFAT) and their study was done on general population from the rural and urban areas. In other countries, many investigators have reported various results as 34% in United Arab Emirates[13] and 81.4% in Egypt[14]. In non Arabic countries Toxoplasma specific IgG, using different Techniques, was recorded in 39.14% in West China[7], 57% in France, 75% in El-Salvador and 60.4% in United States[15].

This discrepancy in the results in comparisons to this study is rather due to the number of cases included in the study, the variability of the techniques used for measurement of specific IgM or IgG antibodies as well as the socioeconomic status of the population chosen, as reflected by the custom in preparing meat and under cooked meat consumption in addition to animal contact. So these findings may have relations to the different environmental, cultural and hygienic factors prevalent in their place of origin[13]. The epidemology of toxoplasmosis in different population groups is affected partially by eating habits. Ingestion of inadequately cooked meat or food or water contaminated with cat feces is responsible for spread of the infection[16].

In recent years, several Immuno-enzymic assays for specific IgG have been adapted to estimate antibody avidity in certain infections, including toxoplasmosis[17,18]. In the solid-phase ELISA system, a hydrogen bond-disrupting agent is commonly used to elute low-avidity antibodies from Immobilized antigen[5]. In this study, the 20 cases that were reactive to specific IgM by ELISA gave a low range of avidity index (2.4%-52.6%) confirming the acute stage of toxoplasmosis. All the above cases gave history of their first abortion ranged from one day to 4

months. Moreover, out of 12 cases, that were negative for specific IgM, 10 women showed a high range of avidity index (more than 58%) and they gave history of their first abortion 7 or more months ago. This supports, that those women have chronic toxoplasmosis. The remaining 2 cases had low avidity indices (37.7% and 37.5%). The duration since their first abortions were one month and 5 months respectively. The possible explanation here is that IgM antibody level became low by that time and can not be detected by ELISA[19].

Variation in the ranges for low-and high -avidity antibodies varies due to several factors, including patient heterogeneity, immune status at time of blood collection , time of blood collection in relation to infection onset, assay technique, antigen preparation, type and concentration of hydrogen bond-disrupting agent and method of calculating antibody avidity[5,20]. From the analysis, the sensitivity of this new technique was [100%], and the specificity was [83.3%] which agreed with the results of others[21].The data suggest that determination of the avidity of *T. gondii* specific IgG is an efficient technique for defining recent infection with *T. gondii*[18].

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SERUM ADENOSINE DEAMINASE LEVELS IN INFANTS WITH CYTOMEGALOVIRUS INFECTION

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Abstract

Background: Human cytomegalovirus (HCMV) is the most common cause of congenital and perinatal infections. Adenosine deaminase (ADA) deficiency leads to B and T cell dysfunction resulting in immunosuppression thereby enhancing susceptibility to infections.

Objective: To investigate serum levels of ADA among infants infected with HCMV.

Patients & Methods: HCMV infection was diagnosed based on the detection of HCMV-specific IgM using ELISA among 62 symptomatic and 50 healthy looking infants. Then HCMV specific IgM positive sera and negative sera were subjected to measurement of ADA level.

Results: The mean serum ADA level of symptomatic infants infected with HCMV (3.16 ± 3.34 U/L) was found to be of significant difference when compared with that of both symptomatic and asymptomatic infants who were sero-negative for HCMV specific IgM (7.78 ± 4.71 U/L, P < 0.05) and (10.38 ± 5.54 U/L, P < 0.05) respectively.

Conclusion: Infants with serum ADA deficiency are susceptible to HCMV infection.

Key words: Human cytomegalovirus, adenosine deaminase, infants.

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Introduction

HCMV is the most common cause of congenital and perinatal infections throughout the world[1]. The most severe forms of this viral disease develop in 5-10% of infants infected *in utero* and these infants have signs of severe generalized infections involving the liver and CNS. Both humoral and cellular immune responses are important in protective immunity against HCMV infection[2].

Deficiency of ADA is severe combined immunodeficiency (SCID) that is inherited as an autosomal trait. The patient is presented in infancy with recurrent infections[3]. This deficiency is also responsible for enhancing susceptibility to congenital infections[4]. Immune deficiency is thought to occur by lymphoid cells that are particularly sensitive to the toxic effects of adenosine and 2-deoxyadenosine that accumulate due to ADA deficiency[5]. Hence, the aim of this study was to investigate the deficiency of ADA among HCMV infected infants.

Patients & Methods

A total of 112 cases (from Al-Kadymia teaching hospital) were included in this study. They were divided into two groups; group A included 62 symptomatic babies clinically suspected to be infected with HCMV, those include babies born with various manifestations like jaundice, rash, hepatomegaly, neurological manifestations (like microcephaly, hydrocephaly, intracerebral calcification, meningocele), intrauterine growth retardation and eye abnormalities (like chorioretinitis, cataract, absence of eye). However, all the cases were presented with various combinations of symptoms. Their ages ranged between one and sixty days. Group B included 50 healthy looking newborns as indicated by general clinical examination in the labor room from which cord blood was collected.

Blood samples were collected from each individual included in this study. Serum was then separated and dispensed into tightly closed capped tubes in 0.2ml aliquots and stored at -20^{o}C until use. All sera were screened for HCMV specific IgM using ELISA (Biokit-Spain). Procedures and interpretation of the results were followed as written in the instructions supplied with the kit.

Total ADA levels were measured [(6)] in the sera of each individual which were grouped as

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follows according to the HCMV specific IgM results: Group 1 (G1): includes all sera found to be positive for HCMV specific IgM using the ELISA technique (N=9). Group 2 (G2): includes randomly chosen sera from symptomatic infants found to be negative for HCMV specific IgM using ELISA technique (N=8). Group3 (G3): includes randomly chosen sera from healthy looking newborns (group B) and all were negative for HCMV specific IgM using ELISA technique (N=22).

Results

HCMV infection, as indicated by specific IgM measured by ELISA was detected in 9 out of 62 (14.52%) symptomatic infants. None of the cord sera obtained from healthy looking newborns was infected with HCMV as evidenced by the negative result by ELISA for specific IgM.

The mean value of serum ADA of symptomatic HCMV infected infants (G1) was found to be of statistically significant difference ($P < 0.05$) when compared with that of both symptomatic non HCMV infected ones (G2) (Tables 1, 2) and asymptomatic non HCMV infected infants (G3). However, no significant difference ($P > 0.05$) was found regarding the mean value of serum ADA of symptomatic and asymptomatic non HCMV infected infants (Table 3).

Table 1: Mean ± SD of serum adenosine deaminase (ADA) level in U/L among symptomatic infants with or without human cytomegalovirus (HCMV)

Symptomatic infants	Number of cases No. (%)	Mean ADA ± SD
HCMV infected	9 (52.94%)	3.16±3.34
non HCMV infected	8 (47.06%)	7.78±4.71
Total	17	

t = -2.31, P< 0.05, SD= standard deviation

Table 2: Mean ± SD of serum adenosine deaminase (ADA) level in U/L among symptomatic human cytomegalovirus (HCMV) infected and asymptomatic non HCMV infected infants

Group of infants	Number of cases No. (%)	Mean ADA ± SD
Symptomatic, HCMV infected	9 (29.03%)	3.16 ± 3.34
Asymptomatic, Non HCMV infected	22 (70.96%)	10.38 ± 5.54
Total	31	

t= 4.46, P< 0.05, SD= standard deviation

Table 3: Mean ± SD of serum adenosine deaminase (ADA) level in U/L among symptomatic non human cytomegalovirus (HCMV) infected and asymptomatic non HCMV infected infants

Group of infants	Number of cases No. (%)	Mean ADA ± SD
Symptomatic, Non HCMV infected	8(26.66%)	7.78 ± 4.71
Asymptomatic non HCMV infected	22(73.33%)	10.38 ± 5.54
Total	30	

t= 1.27, P > 0.05, SD= standard deviation

Discussion

HCMV is the most common cause of congenital infections, affecting 0.2% of all live births in industrialized countries and up to 3% in developed countries[7]. Specific as well as non specific immune surveillance mechanisms play a role in controlling HCMV infection[8]. Cell mediated immunity is important for the recovery from HCMV infection[9]. Although HCMV infection causes few symptoms in immunocompromized adults, about 10% of newborns with congenital infections develop symptoms[7]. It is generally accepted that the fetus and infants have a high susceptibility to viral infections related to the immaturity of the immune system. However, the mechanisms involved remain poorly understood[10].

ADA deficiency is an autosomal recessive character that leads to SCID. The pathophysiology and molecular biology vary, however, the lack of T and B cell function is the common end point in all forms of SCID. In this study, a significant difference was found regarding the mean value of serum ADA among HCMV infected infants when compared with the control groups. It seems likely that such findings agree with others who documented that patients with ADA deficiency are susceptible to TORCH, as the enzyme deficiency results in B and T cell dysfunction resulting in a state of immunosuppression[4]. In addition, such children usually succumb to infection early in life[11, 12].

It will be of both interest and importance to screen cord sera for the prevalence of this type of SCID, for these children should not receive live vaccines especially OPV and BCG. It is also of interest to perform molecular studies to identify any specific genetic defects regarding this type of immune deficiency.

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PRIMARY GASTRIC LYMPHOMA IN CLINICAL PRACTICE 1994-2002

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Abstract

Objectives: Is to identify the clinicopathological characteristics, the investigations to reach the diagnosis, and the therapeutic way of management of gastric lymphoma.

Subjects & Methods: A retrospective analysis of 17 patients admitted to Al-Kadhimiya Teaching Hospital from March 1994 to February 2002. The data were collected from three sources: registration department, oncology and histopathology departments. The data include full history and clinical examination of the patients, investigations done, histopathological result and the line of management.

Results: The study shows, male more than female (1.4:1 ratio), the age range 61-65 years, main symptoms and signs, are weight loss epigastric pain and pallor, the most common site is in the pyloric area. Histopathological result in most cases is of low grade lymphoma. 10 cases treated surgically but the remaining 7 cases were inoperable.

Conclusion: Gastric lymphoma is uncommon tumor of the stomach but its incidence was increased in the recent years. Surgery has the main role in the treatment especially in the early stage, chemotherapy used in all patients.

Keywords: Primary Gastric Lymphoma, Chemotherapy

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Introduction

Primary gastric lymphoma accounts for between 1-5% of all gastric malignancies[1]. Even when confounding factors such as the decreased incidence of gastric carcinoma are taken into account the incidence of primary gastric lymphoma seems to be increasing[2]. Survival has been shown to depend on the histological grade at presentation[3]. Patients with low-grade disease with low depth of infiltration and radical resection of the gastric lymphoma have been shown to have the best prognosis[4]. In a prospective study Ruskone-Foumestraux et al[4] showed that the combination of surgery and chemotherapy in patients with high grade disease was associated with an improved survival compared with patients treated with chemotherapy alone.

Recent interest in the relation between Helicobacter (H) pylori and gastric carcinoma[4] has prompted an analysis of the presence of this organism in patients with gastric lymphoma. Wotherspoon et al[4] found a 92% incidence of H pylori in 110 patients with gastric lymphoma, an order similar to that found in patients with gastric carcinoma but much higher than in the general population. Many primary gastric lymphomas are now recognized to be B cell lymphomas of mucosa associated lymphoid tissue (MALT). While MALT is not normally found in the gastric mucosa, it may develop after chronic inflammation such as is seen with H pylori infection. It has been proposed that MALT, acquired in response to infection provides a background for the development of both gastric carcinoma and lymphoma[5]. In five of six patients with low-grade primary gastric lymphoma, H pylori eradication therapy has been shown to lead to a regression of the lymphoma[6].

Clinical experience in routine general hospital practice suggests that very few cases of primary gastric lymphoma, even in patients with low-grade disease, present at such an early stage as those seen in a tertiary referral center[9].

This study aimed to identify the clinicopathological characteristics, the investigations and the therapeutic way of management. We also assessed the presentation and importance of the stage and grade of these tumors at diagnosis, the prognosis, how the patients were treated (by radiotherapy or chemotherapy with or without surgery).

Subjects & Methods

For the period 1994-2002 a retrospective analysis of 132 patients attended to Al-Kadhimiya Teaching Hospital were identified from Registration Department and Oncology Department as gastric malignancy, 17 cases were

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included as primary gastric lymphoma proved by histopathological examination.

All cases notes were retrieved and details recorded of patient age, sex, presenting symptoms, clinical features, investigations done including the result of histopathological examination. The diagnosis of primary gastric lymphoma was based on the criteria described by Isaacscon et al[7].

The sites of the tumors were localized and they were staged according to the Ann Arbor classification (stage IE, confined to the stomach; stage IIE, with local lymph node spread). The presence or absence of 'B' symptoms (which includes weight loss), was also recorded. Patients with secondary involvement of the stomach by either Hodgkin's disease or non-Hodgkin's lymphoma were excluded.

The method of treatment of the patients were recorded, (whether the tumors are operable or not), by surgery, chemotherapy alone or after surgery. All the above findings are compared with the results of studies done on primary gastric lymphoma in other parts of the world.

Results

In this retrospective study the total cases of primary gastric lymphoma is 17 cases, 10 males and seven females, sex ratio of 1.4:1. (Table-1) Their ages ranged from 25 to 75 years, but the highest percentage in the age group ranging from 61-65 years, 3 patients were under 40 years. No distinctive racial or geographical pattern in Iraq was noticed.

Table 1: Sex and gastric lymphoma

Sex	Number	%
Male	10	58.8
Female	7	41.1
Total	17	100

The duration of symptoms ranged from 1 to 9 months with a mean of 6.2 months. The clinical presentation was non specific, weight loss 82.3%, and abdominal pain 70.5%, vomiting 52.9%, loss of appetite 35.2%, bleeding in form of melaena 23.5%, and heamatemesis 5.8% (Table-2). On examination of those patients 47.1% have pallor, epigastric mass in 41.1%, and upper abdominal tenderness in 29.4% and hepatomegaly in 11.7% (Table-3).

Table 2: Symptoms in gastric lymphoma

Symptom	No.	% from total
Abdominal pain	12	70.5
Vomiting	9	52.9
Weight loss	14	82.3
Loss of appetite	6	35.2
Malena	4	23.5
Hematamesis	1	5.8

Table 3: Signs in gastric lymphoma

Sign	No.	% from total
Pallor	8	47.1
Epigastric mass	7	41.1
Upper abdominal tenderness	5	29.4
Hepatomegally	2	11.7

All patients were investigated for their illnesses; ultrasound was done to see the thickness of the wall of stomach and any metastasis to the adjacent structure or to the liver. While OGD was done in 88.2% (15 patients) and in 11.7% (2 patients), OGD showed the site of the tumor and taking biopsy for histopathological examination, Ba-meal was done 47.1% (8 patients) which show filling defect (fingerprint-like appearance), dilated stomach due to obstruction in the pylorus. C.T scan was perform in 17.6% (3 patients), and not available in the rest patients.

Eleven patients were treated surgically 64.7%, while the remaining were treated by chemotherapy with or without surgery 29.4% (5 patients), or palliative 23.9 % (4 patients) because they are inoperable (Tables 5 & 6). The tumor was localized in 15 cases (8 in pylorus, 3 in the fundus, 2 in prepyloric area, 2 in the lesser curvature) and diffuse type involving the entire stomach in 2 (Table-4). As far as histopathological characters, the low grade types of lymphomas have the highest percentage 53%, while the high grade types of lymphoma account for 35%.

Table 4: Site of the tumor

Site of tumor	No.	%
Pylorus	8	47.1
Fundus	3	17.6
Prepyloric	2	11.7
Lesser curvature	2	11.7
Diffuse	2	11.7
Total	17	100

Table 5: Mode of treatment in gastric lymphoma

Mode of treatment	No.	% of total
Surgery	11	64.7
Chemotherapy after surgery or alone	5	29.4
palliative	4	23.5

Table 6: Role of surgery in the removal of the tumor

Surgical operation & removal of the tumor	No	% of total
Operable	8	72.7
Inoperable	3	27.2
Total	11	100

The regional lymph nodes were hugely enlarged, oedematous, but discrete in all patients. The liver and spleen were free of tumor in all cases. Grossly the localized tumors were indistinguishable from carcinoma, but usually there is no sharp demarcation between the tumor and the surrounding gastric mucosa in primary lymphoma. The diffuse tumors were seen in a bulky stomach with extensive oedema and increased vascularlity of the gastric wall. The cut section was typically of fish-flesh appearance. The regional lymph nodes were grossly enlarged, congested, oedematous, and fleshy in consistency and not matted together.

According to Ann Arbor system[8] all our patients were in stage IE or IIE as in no case was there any evidence of extra- abdominal spread. All of the 6 patients in stage IE (tumor localized to the stomach and regional lymph nodes free) underwent radical subtotal gastrectomy. The 2 patients in stage IIE (tumor in the stomach with involvement of regional lymph nodes) were treated by total gastrectomy (Table-7).

Table 7: Type of surgical operation in treatment of gastric lymphoma

Type of surgery	No.	% of total
Total gastrectomy	2	25
Subtotal gastrectomy	6	75
Total	8	100

The remaining patients in our study was inoperable at time of presentation diagnosed by OGD and biopsy and they were treated by chemotherapy alone or palliative by correction the anemia and nutritional supports.

Discussion

Although this series of patients with primary gastric lymphoma is small, certain features of the disease as seen in Iraq are noteworthy and may be compared with those reported from other parts of the world.

Most published reports put the occurrence of primary gastric lymphoma at about 1-5% of total gastric malignant tumors[1,2], the 17 patients with primary gastric lymphoma who are the subject of this study were encountered among 132 patients with malignancy of the stomach, an incidence of 12.3% which is more than double the highest reported figure in the other series .This increased prevalence of primary gastric lymphoma relative to carcinoma of the stomach in Iraq probably reflects the increased incidence of gastrointestinal lymphomas in general in this part of the world .

The average age at diagnosis of primary gastric lymphoma was 62.5 years, considerably higher than that reported in other studies[9]. As reviewed by Hertzer and Hoerr[10], the average age of the patients at the time of diagnosis in four series reported from North America was between 55-60 years. The male predominance and the other features of the disease in our cases are similar to those reported by other workers[1,9].

The common site of the tumors were in the pylorus followed by the lower third of the body of the stomach which is approximately like what in far east and Japan[11], this may be due to similar nutritional habits.

As far as histopathological characters, the low grade types of lymphomas have the highest percentage 53%, while the high grade types of lymphoma account for 35%, this is opposite to what is mention by other reports[11,12], which could be due to the small population have been calculated. Early MALT tumors are being missed because of their non-specific symptoms and their "gastritis" type of appearance at endoscopies. Testes for H pylori are not available during our study and H pylori eradication therapy was used in last years of the study.

Over the past few years, flexible endoscopic ultrasonography provides the more sensitive modality for diagnosis and staging of primary gastric lymphoma, it is also reliable in assessing the depth of the invasion and to lesser extent in detecting metastatic spread to the regional lymph

nods[13] while C.T. scan with contrast can detect lymph nods enlargement especially in the celiac and para-aortic lymph nods but unreliable in assessing the extent of mural invasion[14].

In agreement with other authors[15], we found the stage of the disease, the grade of the tumor and the resection of the tumor to be the most important prognostic indicators in primary gastric lymphoma. Patients whose tumor was resected at the time of diagnosis had the most favorable prognosis and the longest symptoms free survival.

In this series as well as those of others[15] surgical resection of the tumor, with or without chemotherapy seems to offer the best chance of long survival.

Early diagnosis must be attempted in any case of upper abdominal pain and weight lost in elderly patients. Wider use of endoscopy with biopsy may increase the number of accurate diagnosis at an early and respectable stage.

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BRACHIAL PLEXUS PALSY IN THE NEWBORN

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Abstract

Background: Brachial plexus palsy is still a potential complication of difficult childbirth. Many affected infants recover with little or no residual deficits; however, others never regain sufficient extremity and go on to have functional limitations, bony deformities, and joint contractures.

Material & Method: The study included all children with weakness in the upper limbs who were admitted to the orthopedic clinic between January, 2000 and December 2001. This study was designed to determine the incidence of brachial plexus injuries in newborns at Al-Kadhimiya Teaching hospital and tried to follow the natural history of this problem.

Results: Of the 6221 live births at our hospital during the period of the study, 35 infants were diagnosed to have brachial plexus palsy, giving an incidence of 5.6 per 1000 live births. The affected infants were followed for at least one year. Thirty one (88.5 %) of these patients had full recovery by one year. Four patients (11.5 %) who were followed for at least two years had residual weakness

Conclusion: The over-all recovery from the injury was excellent in this study. The results justify the use of conventional non-operative management. Also identification of the maternal, fetal and delivery risk factors should alert physicians and led to appropriate corrective measures, when indicated to help prevent these neonatal complications.

Keywords: Brachial plexus, Newborn

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Introduction

Brachial plexus palsy in the newborn was first described in 1764[1], and its natural history has been discussed by many authors over the past century. The reported incidences have been ranged from 0.4 to 4.17 per 1000 live births, and these rates have not declined in the last few decades. The prognosis for full recovery, however, may have improved. Earlier studies reported complete recovery in only 13 to 18 percent of these patients[2,3], but more recent studies have claimed full recovery in 70 to 95 percent[4,5].

This study was designed to determine the incidence of brachial plexus injuries in newborns at Al-Kadhimiya Teaching hospital and tried to follow the natural history of this problem.

Materials & Methods

This is a prospective study conducted at Al-Kadhimiya Teaching Hospital. The study included all children with weakness in the upper limbs who were admitted to the orthopedic clinic between January, 2000 and December 2001.

A full detailed history from the parents of the child and from the medical records including age, sex, type of delivery, involved side, any associated fractures. All these children were examined by pediatrician, neurologist, and orthopedician for muscle tone, reflexes, passive and active range of motion to determine the type pf palsy (whether upper or lower brachial plexus involvement); loss of continuity or tender swelling over clavicle, presence or absence of Horner's syndrome or phrenic nerve palsy were sought. X-ray was carried out to rule out a fracture of clavicle or humerus in all affected infants.

The patients were followed up on an outpatient basis, the visits being scheduled once a week for one month, once a month for six months, and once every two or three months thereafter. At each examination, motion, motor strength, and function were documented.

The parents were taught how to put all of the joints of an involved upper extremity through a full range of movement several times a day. No orthosis were used.

Results

Of the 6221 live births at our hospital during the period of the study, 35 infants were diagnosed to have brachial plexus palsy, giving an incidence of 5.6 per 1000 live births. Of these, there were 20 (57 %) left side, 15 (43%) right side and no

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bilateral palsies. Thirty-two (91.5 %) were upper brachial plexus palsies, three (8.5 %) were lower brachial plexus palsies, four had associated homolateral fractured clavicle and humerus, and none had Horner syndrome or phrenic nerve palsy.

There were 21 affected males (60 %) and 14 females (40%). All but one infant were delivered vaginally (97%) (32 infants with vertex presentation, while two with breech presentation). One singleton (3 %) was delivered by cesarean section for fetal distress.

The affected infants were followed for at least one year. Thirty one (88.5 %) of these patients had full recovery by one year (Table 1). The average time to full recovery was three months, and the range was two weeks to twelve months. Four patients (11.5 %) who were followed for at least two years had residual weakness (Table 1).

Table 1: Birth and Recovery Factors in Brachial Plexus Palsy

Factor	Number (%)
GENDER	
Female	14 (40%)
Male	21 (60%)
DELIVERY	
Vertex	32 (91.5%) (18 forceps delivery)
Breech	2 (5.5 %)
Cesarean section	1 (3 %)
INVOLVED SIDE	
Left	20 (57%)
Right	15 (47%)
FRACTURES	
Clavicle	2
Humerus	2
Total	4 (11.5%)
DISTRIBUTION	
Upper plexus palsy	32 (91.5%)
Lower plexus palsy	3 (8.5%)
Total plexus palsy	none
RECOVERY	
Spontaneous	31 (88.5%)
Residual paralysis	4 (11.5%)

The patients who had residual weakness of an upper extremity all had a palsy of the fifth, sixth, and seventh cervical nerves. One of them had fracture of the clavicle, while the other patient had fracture of the humerus (Table 2).

Table 2: Patients with Incomplete Return of Neurological Function

Sex	Side	Palsy	Associated fracture	Residual paralysis
Male	Right	$C_5C_6C_7$	-	Shoulder & elbow
Female	Right	$C_5C_6C_7$	Clavicle	Shoulder & elbow
Male	Left	$C_5C_6C_7$	-	Shoulder & elbow
Female	Right	$C_5C_6C_7$	Humerus	Shoulder & elbow

Discussion

The incidence of brachial plexus palsy in our study was 5.6 per 1000 live births, compared with 0.4 to 4.17/1000 in other reports[6-8]. This high incidence could be attributed to many factors including: high incidence of maternal diabetes in our population, high parity, fetal distress, vaginal delivery, dystocia, perineal laceration, high birth weight, instrumental delivery, and bad obstetrical management.

The great majority of infants (88.5%) recovered normal brachial plexus function except four infants (11.5%) who had persistent weakness, after two years. None required surgery at the time being and all are develop mentally normal. The immediate and long term prognosis for this complication is therefore excellent in the great majority, as found in other studies[6-8].

Two patients had humeral and clavicular fractures that were due to birth trauma. Both had residual paralysis at the time of follow up. This could be due to the forced delivery that causes both the fracture and the brachial plexus palsy. However, the cases of so few patients do not yield sufficient data for us to conclude that a patient who had birth palsy and associated fractures due to birth trauma will have a poor prognosis than one who does not have these findings.

The patients who recovered fully all did so within one year. Several authors have concluded that major recovery may continue for as long as twelve months and that minor improvements may be seen in the span of an additional twelve months, but we know of no reports of improvements after two years.

The author does not believe in the use of abduction splintage, and recommends that the parents be carefully instructed how to put all upper limb joints of the affected limb through a full range of movement, each time the child is fed after the first week of life. A physician should check that this technique is being properly practiced at regular intervals.

Thus, the over-all recovery from the injury was excellent in this study. The results justify the use of conventional non-operative management. Also identification of the maternal, fetal and delivery risk factors should alert physicians and led to appropriate corrective measures, when indicated to help prevent these neonatal complications.

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GALLBLADDER DISEASES IN CHILDREN

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Abstract

Background: Cholecystectomy is a relatively uncommon operation in children, and diseases of the gallbladder have been considered uncommon; where a review of the recent literature reveals that this entity is not rare, and our experience indicates that it is common enough to be considered in any patient with abdominal pain or jaundice.

Objective: The aim of this article is to review all cases of pediatric cholecystectomy at two institutions to determine indications for gallbladder surgery.

Subjects & Methods: The medical records of all children 16 years old and younger, who underwent surgery for cholelithiasis and/or cholecystitis at Al-Kademyia Teaching Hospital and Al-Eskan Central Teaching Hospital for Children between 1998 and 2003, were reviewed.

Results: Cholecystectomy was performed in 15 patients. The mean age was 5 years old (range: 1 to 12 years old). There were 9 boys (60%) and 6 girls (40%). The cause for gallbladder disease was identified as hemolytic disorder in 8 patients (53%). Family history of gallbladder disease was observed in 9 patients (60%). Splenectomy was performed in combination with cholecystectomy in 5 patients (33%). Postoperative complications were developed in 2 patients (13%).

Conclusion: Gallbladder diseases are being diagnosed with increasing frequency in the pediatric population. The single most important factor leading to the diagnosis is awareness that cholelithiasis and cholecystitis can occur in children.

Keywords: cholecystectomy, gallbladder disease, children

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Introduction

Cholecystitis in childhood was first reported in 1722 by Gibson. Little was subsequently written on this disease until Potter[1] reviewed the subject in 1938. Ulin, Nosal, and Martin[2] in 1952 reviewed cases in the literature up to 1948. After further review of the literature it can be concluded that cholelithiasis has been increasingly diagnosed in childhood during the past two decades. Whether the incidence is actually escalating or the diagnostic accuracy is improving because of the readily available use of ultrasonography is unclear[3].

The gallbladder functions as a reservoir for bile storage and concentration. With meals, the gall bladder contracts as the sphincter of Oddi relaxes in response to the hormone cholecystokinin and related peptides. Following cholecystectomy, the flow of bile depends on the sphincter of Oddi[4]. Absence of gallbladder is rarely of physiologic significance in the child or adult. Although congenital anomalies of the gallbladder are rare, acquired conditions of the gallbladder are of clinical importance in a significant number of infants and children. These conditions are usually related to (1) gallstones and their complications, (2) inflammation of the gallbladder with or without stones, and (3) dilatation (hydrops) of the gallbladder in response to a systemic ailment.

The most common cause of gallstones, at urban academic medical centers is hemolytic diseases where there is a large population of children with sickle cell disease[4]. More than 50% of children with sickle cell disease have evidence of cholelithiasis by the age of 18 years[5]. Thalassemia & spherocytosis are also associated with an increased incidence of gallstones. Other causes that are nonhemolytic include long term use of total parenteral nutrition, obesity, history of ileal resection, cystic fibrosis, oral contraceptive use, and pregnancy[7].

Subjects & Methods

This is a retrospective study, including all children 16 years old and younger, who underwent surgery

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for cholecystitis or cholelithiasis; at Al-Kademyia Teaching Hospital and Al-Eskan Central Teaching Hospital for Children between 1998 and 2003.

The medical records of 15 patients were reviewed and the results were analyzed, regarding the age, sex, clinical presentation, duration of symptoms, etiology, family history, type of operation and the complications. Infants with biliary atresia or choledocal cyst were not included in this series.

Results

Cholecystectomy was performed in 15 patients. The mean age was 5 years old (range: 1 to 12 years), there were 9 boys (60%) and 6 girls (40 %) as shown in Table 1. The cause for gallbladder disease was identified as hemolytic disease in 8 patients (53 %), other medical diseases or risk factors for gallstone disease were identified in 2 patients and included congenital heart disease (1 patient) and obesity (1 patient). In addition one patient had a history of abdominal trauma (Table 2). The family history of gallbladder disease was observed in 9 patients (60 %) and family history of hematological disease was positive in 5 patients (33 %).

Duration of symptoms varied from few days to 4 years with an average of 1year. Abdominal pain, the most common presenting symptom, was noted in 10 patients (66%). Jaundice or a history of jaundice was present in 9 patients (60%). One patient (6.6%) was asymptomatic & diagnosed incidentally.

The diagnosis depends on ultrasonography in 15 patients (100 %), while plain films of the abdomen demonstrated right upper quadrant opacifications in 2 of 10 patients (20 %) who had a radiographic examination performed.

In all the 15 patients cholecystectomy was performed & in 5 of them (33%) splenectomy was also performed at the same time (Table 3). There were 2 complication in the 15 patients (13%); wound infection and intraabdominal abscess, both of which occurred in the combined splenectomy & cholecystectomy.

Table 1: Age and sex in 15 patients with gallbladder disease

AGE	BOYS	GIRLS
1 year through 3 years	2	2
4 years through 6 years	3	2
7 years through 9 years	2	1
10 years through 12 years	2	1
Total	9	6

Table 2: Etiology factors in 15 patients with gallbladder disease

etiology	No.
Hematological disorders	8
Sickle cell disease	3
Spherocytosis	3
Thalassemia	2
Obesity	1
Congenital heart diseases	1
Trauma	1
No etiology discernible	4
Total	15

Table 3: Modalities of operative treatment

Operation	No.
Cholecystectomy	10
Cholecystectomy + splenectomy	5
Total	15

Discussion

In adults, gallbladder disease is more common in the female than in the male. However among children the rate is equal, or with male predominance. In our series of 15 patients; all of them under 12 years of age, there were 9 boys (60%) with a male to female ratio of 1.5:1. Nilsson[8] concluded that until puberty the incidence is equal for boys and girls, and that after puberty there is a sharp increase in the incidence for girls. The incidence of gallbladder disease in boys in other studies varied from 41% to 57%[9,10].

A considerable amount has been written concerning the etiology of gallbladder disease. Unlike adults who usually undergo cholecystectomy for cholesterol cholelithiasis and have no other medical conditions, pediatric cholecystectomies were historically performed in patients with an underlying medical illness. The commonest cause of cholelithiasis in our series is hemolytic disease. It was found in 8 patients (53%). The same was noticed by Bruce[9] and Seiler[10]. While others like Darlene[11] and McEvay[12] suggested a higher incidence of nonhemolytic cholelithiasis in recent years. We found 4 patients (26%) with no etiology for their gallbladder disease, while 1 patient was obese, one with congenital heart disease and another with abdominal trauma 6 weeks before the development of cholecystitis. Other causes of gallbladder disease were noticed by others[4,9-11] like total

parenteral nutrition, ileal resection, cystic fibrosis, use of contraceptives and pregnancy.

The family history of gallbladder disease was positive in 9 patients (60%), and 5 of them (33%) had a family history of hematological disease. Seiler [10] reported in his series that 40% of patients had family history of gallbladder disease and another 40% had family history of hematological diseases. While Bruce[9] reported that 30% of his patients had family history of hematological diseases, but stated that family history was usually not helpful.

Duration of symptoms varied from few days to 4 years with an average of 1 year. Abdominal pain, the most common presenting symptom was noted in 10 patients (66%), while jaundice or a history of jaundice was present in 9 patients (60%). These results are similar to those by Bruce[9] and Potter[1], although Ulin[2] reported an incidence of jaundice of 92%. This incidence of jaundice is far greater than that reported in similar adult series.

The diagnosis of cholelithiasis and/or cholecystitis; in our series depended mostly on ultrasonography (100%), although plain films of the abdomen demonstrated right upper quadrant opacification in 2 of 10 patients (20%) who had a radiographic examination performed. The high rate accuracy of ultrasonography and awareness of gallbladder diseases were responsible on the recent rise in gallbladder surgery in children and this was noticed by others[3,11,12]. This awareness may be attributed to the routine use of ultrasound in the evaluation of abdominal pain. While the high rate accuracy make ultrasound replaces oral and intravenous cholecystography, which were not used in our patients.

Cholecystectomy was performed in 15 patients. Only in 5 patients (33%) it was combined with splenectomy for hematological indications. Choledocotomy was not needed in our patients. The indications for choledocotomy include; small gallstones, dilatation of the common bile duct, and common duct stones. In order to avoid operative complications to the small common bile duct in this age group, one should have a clear indication for exploration of this duct in children. Operative cholangiography is of great value and should be done, if there is indication to explore the common duct[9].

There were 2 complications (13%) in the 15 patients, both of which occurred in those who had a combined splenectomy and cholecystectomy. Probably because this group of patients had a longer operative time, had to wait an extra day before starting to eat, and stayed in the hospital longer[11].

Although we do not have experience with pediatric laparoscopic cholecystectomy, but it seems that children enjoy the same benefits of laparoscopic cholecystectomy as adults. In a recent review Miltenburg et al[13] showed that although pediatric laparoscopic cholecystectomy took longer time than open cholecystectomy, it resulted in less post operative narcotic use and a shorter post operative stay.

Conclusion

Gallbladder diseases are being diagnosed with increasing frequency in the pediatric population. The single most important factor leading to the diagnosis is awareness that cholelithiasis and cholecystitis can occur in children.

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TREATMENT OF RECTAL PROLEPSES IN INFANTS AND CHILDREN WITH INJECTION OF HYPERTONIC SALINE

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Abstract

Objectives: The aim of this study is to determine the efficacy of submucosal injection of 30% hypertonic saline solution in treatment of partial rectal prolapse in infants and children.

Subjects & Methods: One hundred patients of partial rectal prolapse in infants and children were treated with 30% hypertonic saline injection into the submucosal layer at the Department of General Surgery in the University Hospital of Iraqi College of Medicine during the period from October 1998 to October 2002. Ninety two patients were treated in the outpatient while the other 8 patients were treated as day cases under general anesthesia.

Results: Seventy-three patients were males and 27 were females with a male-to-female ratio of 2.7:1. The age ranged from 6 months to 13 years, with the most common age of 1-3 years (74%). The duration of symptoms varied from 2 months to 2 years with 47% of patients presented within 2-3 months of initial compliant. Chronic diarrhea was the main precipitating factor (55%).

Ninety-four patients (94%) were cured by a single injection, 6 patients (6%) needed a second injection, while no patients needed a third injection. The overall success rate was 100%. There were no significant complications.

Conclusion: Injection treatment of partial rectal prolapse in infants and children using 30% hypertonic saline in submucosal layers is less invasive than operation, safe, easy, very effective and without any significant complications.

The simplicity of the injection treatment, availability of the sclerozing agent and the possibility of the treatment at the outpatient level are the main advantages of this treatment.

Key words: Rectal prolapse, Injection, Hypertonic saline

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Introduction

Rectal prolapse is known since 1500 B.C[1].It is defined as a circumferential descent or protrusion through the anus of one or more coats of the rectum. It is classified into two types, INCOMPLETE rectal prolapse (partial) where mucous membrane alone descends, and COMPLETE (full thickness) in which all coats of the rectum are involved, which rarely occurs in infants and children[2,3].

The partial prolapse is distinguished from complete prolapse (procidentia) by prolapsing of the rectal mucous membrane for a half inch to one inch from the anal verge with characteristic radiating folds while in the complete prolapse all coats of rectum protrude for two inches or more with characteristic circular folds[4].

The rectal prolapse can be managed conservatively, by injection or by operation[5-8]. The steps of management can be conveniently remembered as a memonic SEVEN's, the 1st 4S are conservative include stool, seat, sedation and strapping, and the last3S' are surgical include sclerosing agents injection, suturing and surgical operations.

The condition is regarded as being minor by surgeon but not by parents. Conservative measures have frequently failed and there are troublesome cases with frequent prolapse managed by manual reduction, thus an injection of a sclerosing solution into the rectal submucosa proved longstanding results and success in many centers[7,8].

Solutions can be used include 70% ethylalcohol, 5% phenol in almond oil[8,9] or hypertonic glucose[2,3,10,11] and in this study, hypertonic saline (30%) has been used[9,12-17]. Injection of hypertonic saline solution into the submucosal layer promotes a vigorous inflammatory reaction. In the immediate post-injection period, edema resulting from the injection provides mechanical support for the rectum to prevent prolapse. The edema disappears in 2-3 days and the resulting fibrosis of the perirectal tissue should prove adequate to prevent recurrence of the prolapse[15,18]. In spite of the proven efficacy of this simple treatment, elaborate operations base largely on adult experience continue to be advocated. These operations include subcutaneous perianal suture[18,19], linear

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cauterization of the mucosa[8,20], the Lockhart-Mummery operation and even pelvic floor repair[2,3,11,21-25].

Subjects & Methods

This is a prospective study of 100 patients with partial rectal prolapse who were treated at the Department of General Surgery in Al-Kadhimiya Teaching Hospital during the period from October 1998 to October 2002 with submucosal injection of hypertonic (30%) saline solution.

Ninety-two patients were treated in the outpatient while the other 8 patients were treated as day cases under general anesthesia. The six cases, who received second injection, were treated in outpatient .The requirements are 10ml. syringe, surgical gloves, 10 ml. of solution and an anal speculum. The rectum is emptied, short-term general anesthesia is required in eight patients and lithotomy position is preferable. About 7-8 cm. above the anal verge 2 ml. of 30% saline solution is injected into the submucosa at three sites around the circumference, one in the posterior midline and other two on each side. The injection can be performed under vision as in Figure 1 or by using a guiding finger in the rectum for a needle passed through the perianal skin as in Figure 2.

Post-injection, the patient is kept for observation for 1-2 hours and then allowed to go home with analgesics. Follow up examinations were made weekly for 4 weeks and afterward at longer intervals. If further injections are needed, they are usually given at the end of the third week. A maximum of 3 sessions can be given if necessary. The longest period of follow up was 4 years.

The following factors regarding rectal prolapse itself has been studied as well: the duration of the prolapse, the frequency of attacks, reducibility (spontaneous, manual or obstructed) and the type of prolapse.

Results

This study included a total of 100 patients with rectal prolapse, 73 patients were males (73%) and 27 were females (27%) with sex ratio 2.7: 1 (Table 1).

Sixteen patients were 6-12 moths of age, 74 patients were within the age of 1-3 years, 6 patients were 3-5 years and only 4 patients were more than 5 years old. The most common age of presentation was 1-3 years and the mean age was 2.2 years (Table 2).

Table 1: Sex distribution of patients with rectal prolapse

Sex	Male	Female
No. of patients	73	27
Percentage	73%	27%

*Sex ratio 2.7:1

Table 2: Age distribution of patients with rectal prolapse

Age	6-12 months	1-3 years	3-5 years	>5 years
No. of patients	16	74	6	4
Percentage	16%	74%	6%	4%

* The oldest patient was 13 years old.
* Mean age was 2.2 years.

Forty-seven patients presented to us within 2-3 months of initial complaint, (Table 3). Regarding the frequency of prolapse attacks, 48 patients had the prolapse every bowel motion (Table 4). Rectal prolapse was spontaneously reducible in 43 patients while manuale reduction was needed in 57 patients. No patient presented with irreducible prolapsed rectum (Table 5).

Table 3: Duration of rectal prolapse

Duration of prolapse	2-3 months	4-6 months	7-12 months	1-2 years
No. of patients	47	26	18	9
Percentage	47%	26%	18%	9%

Table 4: Frequency of attacks of rectal prolapse

Frequency of attacks	Occasional	Every 2-3 months	Every bowel motion
No. of patients	18	34	48
Percentage	18%	34%	48%

Table 5: Type of reduction of rectal prolapse

Type of reduction	Spontaneous	Manual	Irreducible (obstructed)
No. of patients	57	43	0
Percentage	57%	43%	0%

The tone state of the anal sphincter was assessed clinically by per rectum examination, 42 patients had normal sphincter tone while 58 patients had relaxed sphincter (Table 6).

Table 6: State of anal sphincter in patients with rectal prolapse

State of anal sphincter	Relax	Normal
No. of patients	58	42
Percentage	58%	42%

Precipitating factors for the attacks of rectal prolapse were diarrhea mainly chronic type in 55 patients, constipation in 34 patients and chronic respiratory tract infection in11 patients. Thus diarrhea was the major precipitating factor (Table 7).

Table 7: Factors precipitated the attacks of rectal prolapse

Factors precipitated the attacks	Diarrhea	Constipation	CRTI*
No. of patients	55	34	11
Percentage	55%	34%	11%

*CRTI = Chronic respiratory tract infection

All patients included in this study had partial prolapse. Of the 100 patients of prolapsed rectum who received injection treatment, 85 patients had no further prolapse after first injection, while 9 patients had transient attacks of prolapse that stopped soon after without more injections; making 94 of 100 patients required no further treatment. Prolapse recurred in 6 patients, surprisingly long after treatment (Figure 3), suggesting that faulty technique was not responsible. Those 6 patients were cured by a second injection in outpatient No child needed a third injection.

Complications, including rectal stenosis, perirectal abscesses, urine retention and bleeding were not recorded in this series. One of patients had recurrence after Thiersch's operation also received injection treatment successfully. Nine patients were missed after the first injection, thus were not included in this study.

Discussion

Rectal prolapse is found to affect mostly children of 6-36 months of age; the majority of them are males[3]. This age is the time for toilet training, and because the child in this age is hyperkinetic, he (or she) spends little time during the act of defecation. Therefore; a little time is permitted for molding of stool by pelvic floor muscles[10].

The most common age group in our study was 1-3 years (73%) which is comparable to many other studies[2,3,11-16,21], on the other hand, Groff et al (1990)[18] showed that the most common age group is more than 2 years.

In our study males were affected more than females (2.7:1), like other studies[9,12-16,18]. This may be due to the fact that males are more hyperkinetic in this age than females. In some studies the incidence of occurrence in females is more than in males[5,25] while Marvin (1985)[21] showed an equal incidence .

Diarrhea is the main precipitating factor of rectal prolapse in our study (55%) as in other studies[2,5,12-14,25], this can be explained by the fact that diarrhea leads to loss of weight and consequent diminution of fat in the ischio-rectal fossa[2] and lack of rectal support[3,5,11,26]. On the other hand, constipation is the main cause of rectal prolapse in other studies[11,25], this can be due to an increase in the intra-abdominal pressure and straining effort during defecation which may lead to prolapse of rectum. Like other studies, 47% of the patients in our study presented within 2-3 months of initial complaint[14,25].

Norman (1995)[2] and Scott (1979)[3] showed that the majority of the prolapse was reduced spontaneously, while our study showed that manual reduction of prolapse was used in 57% of our patients and spontaneous reduction occurred in 43%, this may be attributed to that parents consider spontaneous reduction of rectal prolapse is a self-limiting problem and they do not need to seek a medical advise till the prolapse becomes manually reducible. Furthermore, most of mothers are afraid of manual reduction since the prolapsed rectum bleeds when it touches the underwear. This makes the parents seek a medical advice rapidly.

In our study, treatment of rectal prolapse by submucosal injection of (30%) hypertonic saline has a successful result in 94% of the patients after the first injection and 100% after the second

injection. The overall success rate in our study was 100%. A third injection was not needed in any patient.

Kayan Zachary[15] reported 51 patients of rectal prolapse treated by the injection of 30% saline, of whom 11 patients (21.56%) required a second injection, 3 patients (5.88%) of them required a third injection.

Dutta[16] reported 30 patients of rectal prolapse that received 30% saline injection treatment, 25 patients (83.4%) were cured by the first injection, 4 patients (13.3%) needed a second injection, while only one patient (3.3%) needed a third injection.

The reported complications after injection therapy are[9,14-16]:

1. Rectal stricture.
2. Perirectal abscess.
3. Urine retention.
4. Damage to the nerve supply of the bladder, if injection was done too far in front of the rectum.

These complications were not encountered in our patients.

Comparison of success rate of injection in our study with that in other studies using the same agent or other is shown in Table 8. The difference in success rate in various studies may be due to the type of sclerosing agents and its effects on pararectal tissues in producing inflammatory reaction.

Table 8: Comparison of success rate after injection treatment in different studies

The study	Type of sclerosing agent	Success rate
Kayon Zachary (1970) [15]	30% saline	100%
Dutta (1977) [16]	30% saline	100%
Wrman (1985) [21]	30% saline	100%
Wyllie (1979) [9]	5% phenol in almond oil	100%
Malyshev (1973) [14]	70% alcohol	96%
Fehri (1988) [5]		98%
Our study	30% saline	100%

Conclusions

Injection treatment of partial rectal prolapse in infants and children using 30% hypertonic saline in submucosal layers is less invasive than operation, safe, easy, very effective, and without any significant complications.

Recommendations

1. The major cause of rectal prolapse in Iraqi children is diarrhea associated with weight loss, so the prevention and treatment of diarrhea and the improvement of nutrition can decrease the Incidence of rectal prolapse.
2. Children with rectal prolapse should be treated at an early stage by means of an injection, in order to reduce the discomfort of recurrent manipulative reductions of the prolapse in the child and alleviate the anxiety of the parents.
3. The use of submucosal injection of hypertonic saline (30%) gives excellent success rate in the treatment of rectal prolapse in infants and children and can be used as an alternative to the 5% phenol in almond oil or other sclerosants because it is available, cheaper, easily prepare and does not need special syringe for injection.

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THE SEASONAL VARIATION OF GUILLIAN-BARRE SYNDROME IN IRAQ

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Abstract

Background: Guillain-Barre syndrome is viewed as reactive, autoimmune disease triggered by a preceding bacterial or viral infection. The variety of antecedent infections may contribute to the clinical and immunologic heterogeneity of the syndrome. No seasonal variation in the incidence of Guillain-Barre syndrome was found in many surveys in the most of western countries. But there was seasonal preponderance found in Taiwan, Sweden and Saudi Arabia.

Objective: To evaluate the distribution of the numbers of cases admitted to the hospital over different months of the year for significant seasonal variation in the incidence of Guillain-Barre syndrome.

Patient & Methods: The monthly rate of admission of patients with Guillain-Barre syndrome was obtained as recorded in hospital discharges data during the years 1993-1995 and 1999-2001 from the university Hospital of Iraqi Medical College. Patients were examined and diagnosed according to Asbury criteria. . A total of 98 patients were studied for age, sex and distribution over different months of the year.

Result: Statistical analysis of the number of the cases admitted to the hospital each month by rejection null hypothesis of no difference in frequency of admission from an average eight cases per months by P (χ^2)=0.007. There was a significant seasonality of Guillain-Barre syndrome with a peak incidence in May and June. The higher incidence of Guillain-Barre syndrome in the study was below the age of twenty years with male: female ratio of 3:2.

Conclusion: There was a significant seasonality of Guillain-Barre syndrome with a peak incidence in May and June.

Keywords: Guillain-Barre syndrome

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Introduction

Guillian-Barre syndrome (GBS) also known as acute inflammatory demyelinating polyradiculo-neuropathy is a common cause of acute generalized paralysis, with an estimated incidence of 1.5 to 2 cases per 100,000 population[1]. It affects both genders, involves people of all ages, is reported worldwide, and in the post-polio era, it is the most common cause of an acute generalized paralysis[2].

The diagnosis of GBS requires the presence of relatively symmetric progressive muscle weakness and areflexia. Cerebrospinal fluid findings that support the diagnosis are an elevated protein content with a normal cell count. Electrophysiological studies provide confirmation of the diagnosis with evidence of a demyelinating polyneuropathy[1].

In the early phases, laboratory tests are helpful only to exclude other disorders that can resemble GBS. Electrodiagnostic features may be minimal and the cerebrospinal fluid protein level may not rise until in the end of the first weak. If the diagnosis is strongly suspected treatment should be initiated without waiting for evolution of characteristic electrodiagnostic and CSF finding to occur[3].

The variety of antecedent infections may contribute to the clinical and immunologic heterogeneity of GBS. Multivariate analysis showed that in GBS patients, infections with campylobacter Jejuni, cytomegalovirus, and Epstein-Barr virus were significantly more frequent than in controls[4]. Mycoplasma pneumonia infections occurred more often in GBS patients than in controls in univariate analysis. Infections with Haemophilus influenzae, Para influenza I virus, influenza A virus, influenza B virus, adenovirus, herpes simplex virus, and varicella zoster virus were also demonstrated in GBS patients, but not more frequently than in control[4].

No seasonal variation in the incidence of GBS was found in many surveys in the most of western countries[5,6]. But there is seasonal preponderance in spring was found in Taiwan[7]. There was a moderate but significant seasonality with a peak in August[7], particularly among the

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young age groups observed in Sweden[8]. A seasonal peak was found in winter in Saudi Arabia[9].

Patients & Methods

A hospital based retrospective study. We obtained the monthly rate of admission of patient with GBS as recorded in hospital discharges data during 1993-1995 and 1999-2001 from the university Hospital of Iraqi Medical College and they were collected and studied. These years were chosen according to the availability of the data in the hospital records. Patients were examined and diagnosed as GBS according to Asbury and Cornblath criteria[10]. A total of 98 patients were studied for age, sex and distribution over different months of the year.

The total of patients were recorded, they were referred from different hospitals and private clinics from different parts of Iraq for evaluation and management. GBS cases referred to the teaching hospitals due to accessibility of the respiratory Care Units in these hospitals. Many patients referred to the Respiratory Care Unit directly.

Statistical analysis of the age, sex and number of the cases admitted to the hospital each month. The results were recorded and analyzed and organized into tables and graphs to show sex and ages as well as distribution of the number of the cases admitted to the hospital each month.

Results

The study included 98 cases of Guillain-Barre syndrome 59 males (60.2%) and 39 females (39.8%) admitted within the six years of study. The number of patients who were involved in the study in each calendar month is shown in (table 1).

Table 1: Frequency distribution of GB cases by year and month of admission

	1994	1995	1996	1999	2000	2001	Total
January	2	3	0	2	0	2	9
February	1	5	0	3	0	1	10
March	0	5	1	2	1	1	10
April	0	0	2	0	1	1	4
May	0	2	1	7	2	5	14
June	2	1	2	3	2	6	17
July	3	0	0	1	2	1	7
August	1	0	2	1	1	1	6
September	0	0	1	0	1	1	3
October	1	1	1	1	1	0	5
November	1	1	0	0	2	0	4
December	3	0	2	1	1	1	8
Total	14	18	12	20	14	20	98

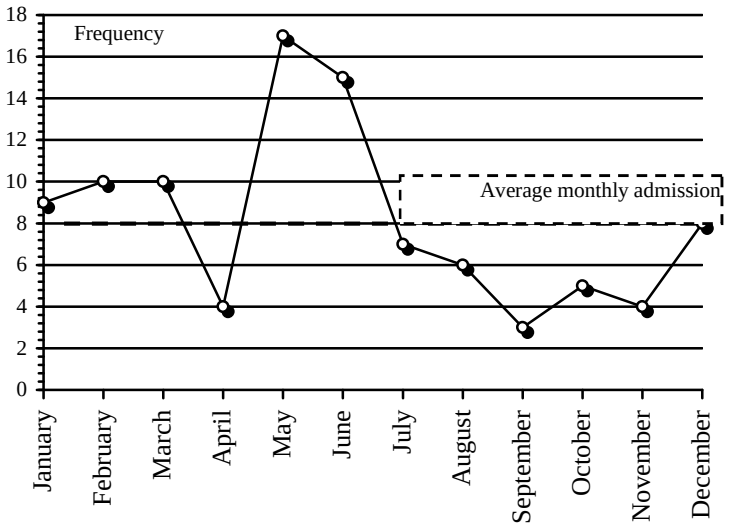

Figure 1: Bar chart showing the time trend of 6 years total monthly admission of GB cases

Statistical analysis of the number of the cases admitted to the hospital each month by rejection null hypothesis of no difference in frequency of admission form an average eight cases per months. P (χ^2)=0.007 for the null hypothesis that the observed monthly frequencies do not significantly differ from an average of eight cases/month.

There was a significant seasonality of Guillain-Barre syndrome found with a peak incidence in May and June (Figure 1).

In (table 2) gender distribution in the study show Male: Female ratio of 3:2. The higher incidence of Guillain-Barre syndrome in the study was below the age of twenty years (Table 2 and Figure 2).

Table 2: showing the distribution of the study sample by age and gender

	Number	%
Age (years)		
<10	27	27.5
11-20	38	38.8
21-30	9	9.2
31-40	5	5.1
41-50	5	5.1
>51	14	14.3
Gender		
Female	39	39.8
Male	59	60.2
Total	**98**	**100**

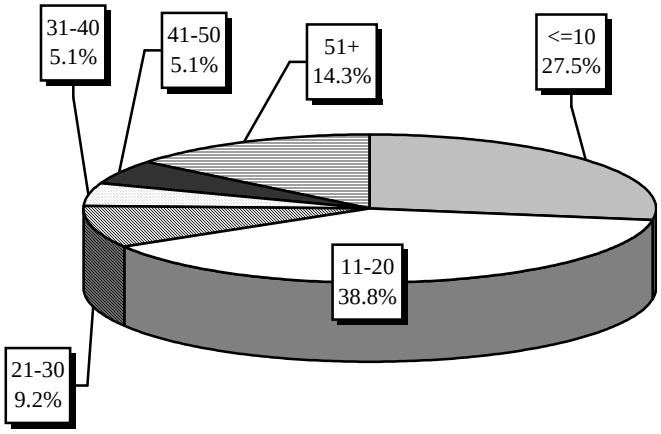

Figure 2: Pie chart showing the distribution of the study sample by age

Discussion

Guillain-Barre syndrome is viewed as reactive, autoimmune disease triggered by a preceding bacterial or viral infection[11]. More recently a distinction has been made between pure motor forms, severe sensory form, and primary axonal and primary demyelinating varieties[12].

There was a significant seasonality of GBS with a peak in May and June and another peak in February and March. There is seasonal variation in the same geographical distribution and there is variable distribution and seasonal difference in the antecedent infection in the different parts of the world.

Various diseases are described as antecedents of the syndrome particularly gastroenteritis and respiratory infectious diseases, but epidemiological survey is rare[13].

Hughes-Ra and Ree-JH claimed that there is no seasonal variation in the western countries because the most frequent antecedent events, respiratory and enteric infections have opposite seasonality[6].

C Jejuni a major cause of bacterial gastroenteritis worldwide has become recognized as the most frequent antecedent pathogen for GBS. Serological or culture evidence of a recent C. Jejuni infection ranged from 26 to 41% in series of sporadic GBS cases from the UK, the Netherlands, the USA and Japan[11]. Cytomegalovirus antecedent infection, account for 13% in Guillain Barre syndrome[4]. A seasonal DNAemia variation in cytomegalovirus seropositive subject was found by Dumon et al. in 2001[14].

In china in 1995, forty cases of GBS were reported, in that the clinical electrophysiological and pathological features of GBS in north China were similar to those of atypical GBS cases in western countries, though there seemed to be some special epidemiological features in age, seasonal and regional distribution[15].In northern China, serological evidence of recent C. Jejuni infection was found in 66% of GBS patients in rural area, as opposed to only 16% of village controls[11]. This may explain the yearly epidemics among rural children in north China.

In Japan, Hao Q et al suggest that Campylobacter Jejuni- associated GBS was more frequent in early spring than in other season [16].And van-der-Meche-FG et al found that Campylobacter Jejuni infection are the most frequent trigger of the Miller Fisher syndrome[17].Seasonal preponderance in spring was found in GBS patients in Taiwan and high frequency of fissure syndrome not seen in other series[7]. This observation strongly suggests the association between the peculiar type of GBS and Campylobacter Jejuni infection.

In a study done in our country cytomegalovirus infection was found in 14.3% of the patients which is comparable to the findings in other series, but Epstein-Barr virus was found to be less frequent and herpes simplex virus (HSV-1) acute infection was found in 28.6% of the patients, which is significantly high[18].

So the seasonal variation in the same geographical distribution may be related to the variable distribution and seasonal difference in the antecedent infection in the different parts of the world. And seasonal difference in Iraq may be related to the high incidence of HSV-1 antecedent infection incomparable to the western countries.

The higher incidence of Guillain-Barre syndrome in the study was between the ages of 11-20 years. Most surveys show a slight peak in late adolescence and young adulthood[11]. In our study there is a small peak at age above 50 year, which is compatible to the series of Hughes and Rees[19], and high incidence in age group less than 10 years similar to what is found in Taiwan[7]. The variation in age distribution may also be related to the incidence of the antecedent infections among the age groups.

Male predominance in this series is compatible to the series of Al-Araji[17]and Bahou YG in Saudi Arabia[9] with no definite explanation.

Conclusion: There was a significant seasonality of Guillain-Barre syndrome.

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A REVIEW OF 210 DIABETIC CHILDREN ATTENDING PRDIATRIC DIABETIC CLINIC IN AL-KADHIMIYA TEACHING HOSPITAL FROM 1990-1999

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Abstract

Background: Insulin dependant diabetes mellitus (IDDM) is one of the chronic irreversible diseases that lead to major complications for children.

Aims: To study some of the factors associated with IDDM.

Subjects & Methods: A review was carried out on 210 newly diagnosed children with IDDM attending the pediatric diabetic clinic in Al-Kadhimiya teaching hospital over 10 years period (January 1990-December 1999).

Results: The majority (82.8%) of our patients aged 6-14 years while the minority (1.4%) was less than two years of age. Male: female ratio was 1.3:1. Family history of IDDM was present in 5.7% of cases. More than half (59%) of cases of our patients live in urban areas, while the rest reside in rural areas. The majority (73.8%) presented with classical symptoms of IDDM, while the rest presented with diabetic ketoacidosis. Around one third of patients presented in winter months. Sixteen patients had preceding history of viral illness or emotional stress.

Conclusion: Factors found to be associated with IDDM were increasing age, male sex, family history, and winter season.

Key words: Diabetes mellitus, Pediatrics, review

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Introduction

Insulin dependant diabetes mellitus (IDDM) is a chronic irreversible disease of any age characterized by insulinopenia and dependence on injected insulin to sustain life. This clinical entity may be an outcome of different pathological processes; however the exact etiologic mechanism remains unknown. About 25-50% of patients are diagnosed by the age of 15 years[1,2]. In northern Europe and North America, IDDM is the third most frequent severe chronic disease of childhood, second only to asthma and cerebral palsy[3]. In a population that is at modest risk, 3 out of 1000 children develop IDDM. Inter and intra country variation exists in the incidence and prevalence of IDDM[3]. The collection of sound epidemiological data from different geographical parts of the world is vital if the puzzle of pathogenesis of this disease is to be solved, much information on the epidemiology of IDDM from northern hemisphere, but there are only sparse data from Asia. Comparisons of international IDDM registries have shown that a child in Finland is over 60 times more likely than a child in Korea to develop IDDM[3,4]. The first finding reported the seasonal pattern of IDDM incidence roughly correlating with occurrence of infectious diseases. The second finding was the isolation of Coxsackie's virus from a child with diabetic ketoacidosis[5].

Aims of the study:

To study some of the factors that may be associated with IDDM such as age, sex, residency, and seasonality.

Subjects & Methods

A review was done for 210 medical records for children newly diagnosed as cases of IDDM. Those children were attendees of the diabetic clinic for children in Al-Kadhimiya teaching hospital from the period Jan.1990-Dec.1999 (inclusive). The variables studied were age, season of diagnosis, duration of symptoms between onset and diagnosis, residency whether urban or rural, family history of IDDM and non-IDDM (NIDDM). Parental consanguinity, mode of clinical presentations, and the presence of any possible precipitating factors as viral illness or psychological stress. Regarding statistical analysis, X2 test of association was used whenever applicable.

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Results

Table 1 showed that in around one third (30.5%) of patients the age of onset of IDDM was 12-14 years old. It is evident from the same table that 27.6% of patients presents at the age of 6-8 years, whereas few patients presents at the age of two years or less. The trend of patients' attendance to the center was increasing throughout the period of the study.

Table 1: Distribution of patients by age of onset of IDDM and year of attendance

Age years	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	Total No.	%
≤ 2	0	0	0	1	1	0	0	1	0	0	3	1.4
3-5	1	2	1	1	3	4	5	5	6	5	33	15.7
6-8	3	4	5	5	6	5	7	7	8	8	58	27.6
9-11	3	4	5	4	4	6	5	6	7	8	52	24.8
12-14	3	4	6	4	7	6	7	9	9	9	210	30.5
Total	10	14	17	15	21	21	24	28	30	30	210	100

In table 2, it is evident that the number of male patients overweighed the number of female patients in all age groups. The male to female ratio was 1.36:1.

Table 2: Distribution of patients by age of onset and gender

Age (years)	Male		Female		Total	
	No.	%	No.	%	No.	%
≤ 2	2	66.6	1	33.4	3	100
3-5	20	60.6	13	39.4	33	100
6-8	34	58.6	24	41.4	58	100
9-11	31	59.6	21	40.4	52	100
12-14	34	53.1	30	46.9	64	100
Total	121	57.6	89	42.4	210	100

Table 3 and figure 1 showed that greater proportions of patients were diagnosed in winter months, and the least number of patients were diagnosed in summer months, and this is applied to all age groups except the age of two years or less. It is evident in figure 2 that more patients (59%) live in urban areas, and the rest live in rural areas.

Ninety six patients (45.7%) had positive family history of diabetes; out of those patients 12 (12.5%) had family history of IDDM, and the rest (87.5%) had family history of NIDDM. Results showed that 12 out of the 96 patients were first degree relatives. The parental consanguinity was found in 21% of patients.

Table 3: Distribution of patients by age and seasonality

Age years	Winter No.	%	Spring No.	%	Autumn No.	%	Summer No.	%	Total No.	%
≤ 2	1	33.3	1	33.33	1	33.30	0	0.00	3	100
3-5	12	36.36	8	24.24	7	21.21	6	18.18	33	100
6-8	20	34.48	17	29.3	12	20.68	9	15.52	58	100
9-11	15	28.85	13	25	13	25	11	21.15	52	100
12-14	20	31.25	16	25	14	21.87	14	21.87	64	100
Total	68	32.40	55	26.20	47	22.40	40	19.00	210	100

Regarding signs and symptoms, 155 patients (73.8%) presented with polyurea and polydipsia, and 138 patients presented with weight loss in addition to the symptoms mentioned.

Forty three patients (20.5%) presented with frank clinical picture of DKA (dehydration, kussmaul respiration, and cerebral obtundation). Eighty three (39.5%) presented with urinary tract infections one presented with failure to thrive and gastroenteritis, and one presented with pneumonia.

Sixteen patients (7.6%) had preceding illness or stress: 7 had history of upper respiratory tract infections 2-3 weeks prior to the onset of symptoms, 5 had history of mumps 3-4 weeks prior to the onset of symptoms, and 4 had history

of psychological trauma with an average of 2 weeks before onset of symptoms.

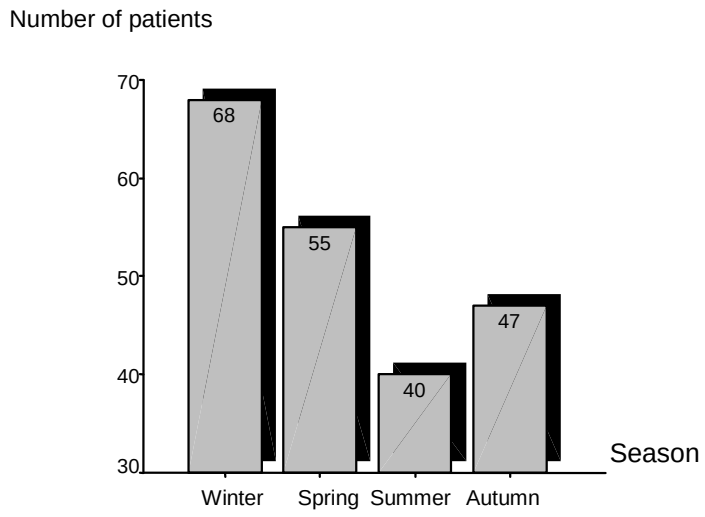

Figure 1: Distribution of patients according to season of diagnosis

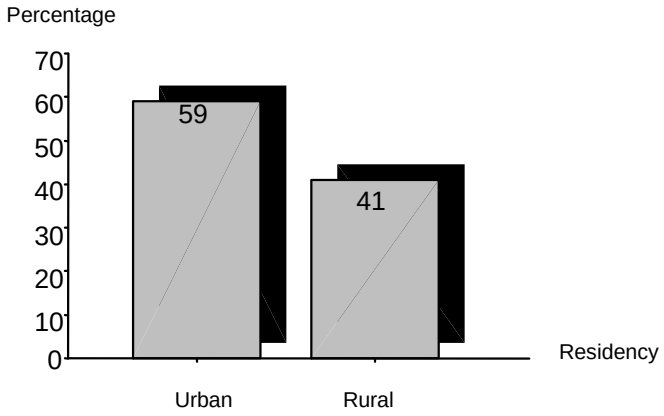

Figure 2: Distribution of patients according to residency

Discussion

In a study done by Ellient et al, the mean age of onset of IDDM was reported to be around 12 years with an increase incidence in the age group 4-6 years and 10-13 years[6]. Results of another study showed that the frequency is highly correlated with increasing age[1]. In our study the peak of presentation occur in two age groups: at 6-8 years of age and 12-14 years of age, comparable results were reported from Alabama[1], Oxford[7], and Sweden[8]. The lowest frequency of cases was found among patients aged 2 years or less, comparable results were observed in other studies[9,10].

The first peak corresponds to the time of increased exposure to infectious agents coincident with the beginning of school, the latter to the pubertal growth hormone secretion, which antagonizes insulin action and to the psychological stresses accompanying puberty[9,11].

Males were predominant in all age groups, similar results were reported from Oxford[7], Saudi Arabia[12], Denmark[13], and Norway[14], but were opposite to that experienced by Lynne from Alabama[1] who stated that males and females are equally affected.

The family history of DM was positive in (40% of cases) higher figures were reported from Saudi Arabia[15] (56.7%) and U.K[7]; in our study 12 (5.7%) had positive family history of NIDDM, this is less from that reported from Sweden[16] which stated that the family history of DM by Joner was Positive in 8.7% and 43% for IDDM and NIDDM, respectively.

The parental consanguinity rate (21%) was slightly higher from that reported in Saudi Arabia[12]. The frequency of cases in the first degree relatives was 5.7% which was similar to reported from U.K[7,13].

More cases resided in urban areas. This may be explained by the fact that the hospital is located in an urban area, and may be related to exposure to toxic substances or stressful life events in urban areas, or to differences in feeding habits in the two areas.

In our study frank clinical picture of DKA was found in 20.5% which is higher than that reported from USA (10%)[5,15,17], this may be due to difference in health care and educational level.

The predominance of viral infections in winter and autumn may give an explanation to our findings (more cases during these seasons).

Conclusion

In this ten years review the frequency of cases was increasing through out the years in all age groups except fewer than 2 years of age, with male predominance.

Recommendation

We need further and strenuous efforts to find out reliable data for incidence of IDDM in children less than 18 years of age in Iraqi population and then to use this data base to study the impact of environmental factors with special emphasis on changes in living conditions, panorama of viral

infection, immunization practice, breast feeding habits and socioeconomic status through the establishments of an Iraqi diabetic association registry.

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CHILDHOOD ASTHMA AND GROWTH

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Abstract

Background: Asthma is an Umbrella term, which involves reversible airway obstruction caused by different mechanisms. It's the most common chronic disease of childhood. The prevalence, morbidity and mortality of asthma have increased during last two decades without obvious specific causes. The hyper responsiveness manifest itself as bronchoconstriction following URTI, exercise, strong odor or irritant fumes, tobacco smoke, cold air, drugs…etc.
Does asthma affect growth of the patient? If it is any relation of that to severity of asthma?

Aim: To study growth parameters of asthmatics i.e weight, height and head circumference and to show any effect of asthma on growth and relation of that to severity of asthma.

Subjects & Methods: A total number of 110 asthmatic patients subjected to study of growth parameters (weight, height and head circumference) and put these measurements on centile chart with assessment of severity of asthma according to specific clinical criteria and study of growth failure in relation to severity of asthma had been done.

Results: The results show that 16.28% of mild asthmatic patients have weight on him 10th centile while 44.18% on 50th centile and 39.5% on 90th centile. In moderate asthma 12.24% of patients on 10th centile for weight, 67.34% of patients on the 50th centile and 20.4% about 90th centile.
In sever asthmatics 50% were on 10th centile and 38.8% on 50th centile and 11.11% about 90th centile. By statistical analysis by qui square there is decrease of weight of asthmatics with increase severity of asthma ($P< 0.05$) i.e there is a growth failure in asthma (mainly the weight) but no significant decrease in height and head circumference). The more severe the asthma the more negative correlation to growth.

Conclusion: Chronic asthma affects the growth of asthmatic patients especially in moderate to ever asthma.

Key words: asthma, growth, severity

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Introduction

Asthma defined as reversible airway obstruction due to hyper- reactivity of the airway[1]. It's the most common chronic disease in childhood. Both small (<2mm) and large (>2mm) airways involved to varying degree in this hyper reactivity[2].
Asthma in fact an umbrella term which may brought about by different mechanisms, bronchoconstriction, mucosal edema and thick viscid secretion are three main pathological factors share together in narrowing of the airways[3].
The hyper responsiveness manifest itself as airway obstruction following triggering factors which are URTI, exercise, strong odors or irritant fumes, tobacco smoke, cold air, drugs (e.g. NSAID) and other predisposing factors which differ from patient to another[4].
The prevalence, morbidity and mortality of asthma have increased during the last two decades, without specific causes, its responsible for significant proportion of school days lost because of chronic illness[4].
Asthma is a complex disorder involving autonomic, immunologic, infectious, endocrine and psychological factors.
Does asthma affect growth of the patient? And if it's is there any relation to severity. This question to be discussed by this study.

Subjects & Methods

A cross sectional study done from August 2001 to August 2002 which a total number of 110 asthmatic patients subjected to study regarding growth parameters i.e weight, height and head circumference for each patient and put those on centile chart and compared them with 10th , 50th and 90th centiles.
Also these patients assessed clinically for severity of asthma according to following criteria:
Mild Asthma: patients with mild asthma have less frequency of attacks, good exercise tolerance, good school attendance, little or no interruption of sheep and good response to

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treatment. They have normal chest- X ray and no hyper inflation of the chest and patient is symptoms free between the attacks.

Moderate asthma: Children of moderate asthma have more frequent attacks than the mild disease and often have cough and mild wheezing between more sever exacerbations, school attendance may be impaired, exercise tolerance is diminished and child may lose sleep at night during attack, such children will generally require continuous rather than intermittent bronchodilator therapy and sometimes steroid to control the symptoms. Hyperinflation may be evident clinically and roentgenographically.

Sever asthma: Children with sever asthma have daily wheezing and more frequent and more sever exacerbations and require recurrent hospitalization which is rarely required for mild or moderate asthma. They miss significant days of school, have their sleep interrupted by asthma and have poor exercise tolerance.

They have chest deformity as a result of chronic hyperinflation. Bronchodilator required continuously and steroid regularly. The correlation of the growth parameters with the severity of asthma analyzed by Chi square. For each asthmatic patient we compare the severity of asthma with the centile for weight, height and head circumference.

Results

The results showed that the weight of the patients (16.28%) which are labeled as mild asthma is about 10th centile and 19 patients (44.18%) are about 50th centile and 17 patients (39.5%) are about 90 centile (Table 1, Figure 1).

While the patient's moderate asthma, 6 patients (12.24%) with weight about 10th centile and 33 patients (67.34%) their weight on 50th centile and 10 patients (20.4%), their weight on 90 centile (Table 1, Figure 1).

Table 1: Correlation of severity of asthma with weight centile

Percentile	Mild	Moderate	Severe
10th **50th** **90th**	7 (16.28%) 19 (44.18%) 17 (39.5%)	6 (12.24%) 33 (67.34%) 10 (20.4%)	9 (50%) 7 (38.88%) 2 (11.11%)
Total	43	49	18

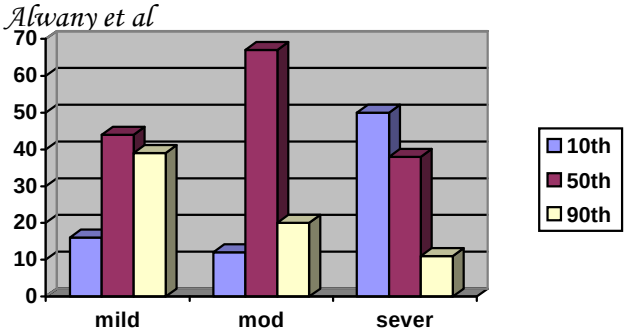

Figure 1: Weight centile in relation to severity of asthma

Regarding the patients with severe asthma, 9 patients (50%) were on the 10th centile for weight and 7 patients (38.88%) were on the 50th percentile and 2 patients (11.11%) about the 90th centile (Table 1, Figure 1).

The statistical analysis of these data by qui square showed that there is decrease of weight of the patient with the increase of severity of asthma ($P < 0.05$).

The results of the height of the mild asthmatic patients showed that 12 patients (29.9%) were about 10th centile, 18 patients (41.86%) were on the 50th centile and 13 patients (30.23%) on the 90th centile table 2 figure 2 while patients with moderate asthma, 8 of those (16.32%) were about 10th centile and 20 (40.8%) patients were on 50th and 21 (42.86%) were on 90th centile (Table 2, Figure 2).

Table 2: correlation of severity of asthma with height centile

Percentile	Mild	Moderate	Severe
10th **50th** **90th**	12 (29.9%) 18 (41.86%) 13 (30.23%)	8 (16.32%) 20 (40.8%) 21 (42.86%)	5 (27.7%) 7 (38.88%) 6 (33.3%)
Total	43	49	18

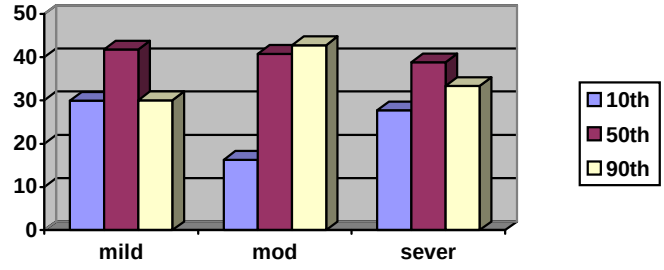

Figure 2: Height centile in relation to severity of asthma

The results of head circumference showed that 5 patients of mild asthma (11.6%) were on 10th and 22 (51.16%) patients were on 50th and 16 (37.2%) patients were on 90th centile (Table 3, Figure 3) while 5 patients of moderate asthma (10.2%) were about 10th and 22 (44.89%) patients were on 59th centile and 22 (44.89%) were on 90th centile (Table 3, Figure 3).
While 5 patients of sever asthma (27.7%) were on 10th centile and 6 patients (33.3%) were on 50th and 7 patients (38.8%) were on 90th centile (Table 3, Figure 3).

Table 3: Correlation of severity of asthma with head circumference centile

Percentile	Mild	Moderate	Severe
10th **50th** **90th**	5 (11.6%) 22 (51.16%) 16 (37.2%	5 (10.2%) 22 (44.89%) 22 (44.89%)	5 (27.7%) 6 (33.3%) 6 (38.8%)
Total	43	49	18

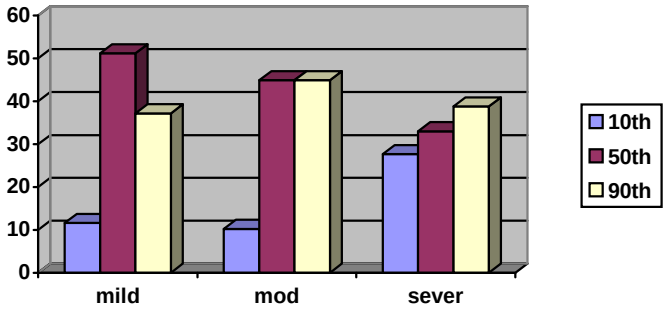

Figure3: Head circumference centile in relation to severity of asthma

By analysis of those data of height and head circumference by qui square, we found no significant decrease of height and head circumference with increase of severity of asthma in this sample of patients (P > 0.05).

Discussion

1. The results of the study showed growth failure (mainly weight) of the patient correlate with the severity of asthma, the more severe the asthma (i.e moderate to sever) the more failure to thrive.
2. The failure to gain weight in severe asthmatic goes with the fact that the weight is first to be affected in any chronic disease, followed by height then the head circumference.
3. The non-significant correlation of height and head circumference with the severity of asthma in this study may be due to short duration for the study and may need more longer follow up to manifest.
4. The growth failure in asthmatics has many causes, It may be due to disease itself or may be due to treatment (mainly steroid) and this is so difficult to estimate because usually those patients received steroid frequently.

Many studies worldwide discussed this issue:
Abrom[5] estimated that any chronic lung disease leads to growth failure and delayed development. Baum et al[6] showed that asthma affect growth and the more sever the asthma the more negative growth. Kloditz[7] showed that asthmatics have tendency to retard growth and hyposomia in childhood and also estimated that B2 agonist decrease growth hormone (GH) secretion. Sharek and Bergman[8], Fernando et al. showed that inhaled steroid leads to decrease growth.
Kisson et al. showed that steroid affect growth of the asthmatic patients. Silver-stain et al.[10] showed that adult height of asthmatics is not significantly different from peers. Patel et al. showed that growth impairment is temporary and reversible.

Conclusions

* Chronic asthma affects growth of the patient mainly the moderate to sever type.
* Mild asthmatic has the chance to grow as peers.
* Height and head circumference is not significantly affected by asthma.

Causes of growth failure of asthma are difficult to be estimated because the variety of causes that affect growth of asthmatics which needs more specific sophisticated studies.

Recommendations

1. Measurements of growth parameters are important in asthmatic patients because it correlate with severity of asthma, so there measurements should be included in the follow up of asthmatics.
2. Good control of asthma in children may give good chance for better growth.
3. The steroids is still highly recommended in moderate to severe asthma regardless of possibility of growth suppression that is because of risk-benefit ratio of sever asthma which may danger the life of the asthmatics and a lot of studies showed that the growth failure is

reversible in asthma i.e normal adult growth may be catch up as his normal peers.

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PICA IN CHILDREN

Faris B. Al-Sawaf *MRCP*

Abstract

Objectives: To see how frequent pica among children; to look at other signs and symptoms of malnutrition as anemia and rickets that are associated with pica; and to see how frequent worm infestations among those children with pica.

Participants and Setting: Children visiting a private clinic during 3 years.

Main outcome measures: Full information was taken from their mothers and thorough examination was done, full blood count was done to 160 patients and stool examination was done to 42 patients.

Results: Pica was found in 11.56% of them whom their age was between 10 and 36 months. Sixty seven percent of them came from presumably poor families. Sixty two percent of them showed signs of rickets. All the infants were pale, and the RBCs were hypochromic microcytic in 91.25% of them. Worm infestation was found in 14.36 %. Six percent of them had splenomegaly.

Conclusion: Pica is not uncommon problem among children and it is frequently associated with iron deficiency anemia, rickets, and worm infestation.

Key words: Pica. Iron deficiency, rickets, pinworm.

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[1]Introduction

Pica is defined as persistent eating of non-nutritive substances for a period of at least one month without an association with an aversion to food[1], but it is a normal transitory phenomenon during the toddler period[2,3], it is frequently associated with mental retardation, but it has been seen in all ages and both sexes[4] and in patients of lower socioeconomic status[5] and under developed areas[5-8].

It is also found in some cases of iron-deficiency anemia as well as in deficiencies of other nutrients such as zinc[6]. In some cultures pica is considered normal and even therapeutic[9].

The etiology can be explained from nutritional (iron and zinc deficiencies), sensory, physiologic (enjoy the taste, texture, or smell of the item), neuropsychiatric (association with certain patterns of brain disorder), cultural or psychosocial (family stress)[5,7], sometimes it is regarded as addictive behavior or part of the obsessive-compulsive disorder[6,10]. The effects of pica have been classified into five groups[1,6]:

1. Inherent toxicity (direct toxic effects of the substance).
2. Obstruction {trichophagia (eating hair)}.
3. Excessive calorie intake related to amylophagia (starch eating).
4. Nutritional deprivation
5. Parasitic infections and dental injury[7]

The diagnosis can be difficult and could be missed easily without a high degree of suspicion. Treatment includes education about nutrition along with iron therapy or transfusion, psychological counseling or behavior therapy can also be useful adjuncts[1]. Not all forms of pica are dangerous and some might not require intervention. Severe or recalcitrant cases could require referral to a mental health specialist.

The Aim of the study is to look at:-

1. The frequency of pica among children.
2. The associated deficiencies.
3. The frequency of worm infestation.

Patients & Methods

Three thousand two hundred and fifty infants' between 10 and 36 months of age were reviewed in the private clinic during 3 years.

There were 1805 boys and 1445 girls, their mothers were asked about pica and other symptoms as anorexia, fretfulness, pruritus ani (irritable sleep), excessive sweating, family history of worm infestation. Examination was done to them looking for nutritional status, pallor, organomegaly, signs of rickets (cranio tabes, wide wrist, rickety rosary, bow legs …etc). Full blood count was done to 160 patients who had history of pica and stool examination for worm was done to 42 patients who had history of pruritus ani. Other investigations as serum ferritin, serum iron and total iron binding

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capacity were not done because of difficulties (not available and costy).
Those with pica were given oral or parenteral iron for an adequate time together with vitamin D supplementation if needed; Albendazole was also given in 2 doses for those with worm infestation.

Results

Three hundred seventy six patients (11.56%) had pica. Two hundred and two (53.7%) were boys and 174 (46.3%) were girls as shown in table (1).

Table 1: Shows the sex distribution

Sex	Number	%
Male	202	53.7
Female	174	46.3
Total	376	100

Two hundred fifty two of them (67%) came from presumably poor families who don't eat meat and eggs. The non food materials ingested were sandstones, soil, papers, paint, dirt, and soap. Two hundred thirty three patients of those 376 (61.98%) had signs of rickets. The mothers of seventy one patients (18.88%) were doubtful about their children whether they were harboring worms or not and 59 of them (83%) had positive family history of worm.
Fifty four children (14.36%) had definitely worm infestation from their complaint (pruritus ani) and all had positive family history of worm infestation as shown in table 2.

Table 2: History of worm infestation

History of worm infestation	Number	%	Positive family history of worm infestation	
			Number	%
Doubtful	71	18.88	59	83
Definite	54	14.36	54	100

All the 376 children were pale. Twenty three patients (6.12%) had a palpable spleen.
The haemoglobin level was between 9.5-11.5gm/dl in 55 of those who had their blood tested (160) (34.38%) and it was 6.5-9gm/dl in 105 patients (65.62%) as shown in table 3.

Table 3: The level of haemoglobin

Hb (gm/dl)	Number	%
9.5-11	55	34.38
6.5-9	105	65.62
Total	160	100

Table 4: The shape of RBCs

Shape	Number	%
Hypochromic microcytic	146	91.25
Normochromic normocytic	14	8.75
Total	160	100

The RBCs were hypochormic microcytic in 146 patients (91.25%) and normochromic normocytic in 14 patients (8.75%) as shown in table (4).
Eosinophilia was found in 95 patients (59.37%).
Stool examination showed the eggs of pinworms in 35 samples (83.33%).
Iron therapy with vitamin D supplementation and antihelminthic drug when needed were marvellous in curing these patients and no one came back with the same problem.

Discussion

Pica was more commonly found in those children with the age range 10-36 months and this is in agreement with that reported by Scott and Dalton[3]. Sixty seven percent of patients came presumably from low socioeconomic families and this is consistent with Edwards[5] and others[6-9].
Nearly 62% of the children with pica had signs of rickets which was mainly nutritional due to vitamin D deficiency and it is part of the nutritional deprivation imposed on the child by pica by eating substances instead of nutritive foods, similar findings were found by Weaver[2].
Worm infestation was found in (14.36%) of the patients and was doubtful in 18.88% of the patients with high index of suspicion because of the high positive family history of worm infestation, in a study of Jamaican children with pica, worm infestation was found in more than 70%[(11)].
The haemoglobin level was 9.5-11.5gm/dl in (34.38%) of those who had their blood tested and it was 6.5- 9 gm/dl in the remaining 65.62% and the majority of them 91.25% had hypochromic microcytic anaemia so pica has frequently been described as a symptom of iron deficiency although it occurs often in those who have normal haemoglobin levels[4,6-8]. Eosinophilia was found in (59.37%) of the patients and eosinophilia should be looked for in patients with pica as claimed by Waller[12]. Helminthic infection causing eosinophilia and gastrointestinal symptoms has been described

and the stool was positive for eggs of pinworms in (83.33%) of those who had their stool tested.

The response to iron therapy was dramatic in all the patients but Mitchell[10] claimed that cessation of pica behavior with iron replacement does not happen often, however, whether continued pica behavior constitutes an addiction or simply a learned pattern of behavior is unclear[10]. Also still it is unclear whether pica causes the anemia or the anemia causes pica[9].

So in conclusion pica is a frequent problem in children and it is frequently associated with iron deficiency anemia and rickets together with worm infestation and it can be cured with iron therapy in addition to other necessary drugs.

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EXPERIENCE IN LAPAROSCPIC TREATMENT OF ECTOPIC GESTATION

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Abstract

Objectives: to assess the value of operative laparoscopy in the management of ectopic gestation in term of diagnosis, treatment, post-operative complication and post-ectopic pregnancy.

Materials & Methods: 12 cases of ectopic gestation treated by operative laparoscopic surgery. 4 cases presented as acute abdomen. Average age 25 years. History of infertility found in 5 cases (41.6%), three primary and two secondary infertility.

Results: 12 ectopic gestation were treated laparoscopically; 7 ruptured, 4 unruptured and one tubal abortion. Eight in the right tube and four in the left tube. Salpingostomy was the treatment in 7 cases and partial salpingectomy was the treatment in 5 cases. All cases discharged home with in 24 hours without complication and none required another laparoscopy or laparotomy. Four patients conceived within 10 months.

Conclusion: 12 ectopic gestations treated successfully by the laparoscope with no operative or post- operative complication. Operation time ranged between 45 minutes-1 ½ hour. These results are very encourging in comparism with conventional surgery. Keeping in mind the short hospital stay & better cosmotic results to the patients. Ectopic gestation can be treated successfully by the laparoscope even if the patient in acute abdomen, but the procedure has to be conducted by an experienced laparoscopic surgeon.

Key words: Operative laparoscopy, Tubal ectopic gestation, Salpingostomy, Salpingectoimy

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Introduction

Ectopic pregnancy is implantation occurring elsewhere than the cavity of the uterus, 99% of extra-uterine pregnancies occur in the fallopian tube. Incidence of extra-uterine pregnancy has increased from0.5% thirty years ago, to a present day 1-2%[1]. Incidence in the UK is 1 per 150 mature births, but much higher in other countries as France 20.2/1000 live -births, Finland 28/1000 births, USA 22/1000 live births, etc. The overall incidence is increasing, but the case fatality rate has decreased[2]. Mortality rates dropped, from 1.7% in the 1970s to 0.3% in the 1980s.

Presentation of ectopic pregnancy could be acute abdomen that required immediate interference when rupture occurred, but in the majority it is the subacute or asymptomatic form & in the last form especially unruptured small ectopic a non-surgical treatment could be feasible with systemic methotrexate or by local injection of drugs into the gestational sac, either laparoscopically, trans-vaginally, or by transcervical tubal cannullation. Fertility rates after salpingotomy via laparoscopy or Lparotomy are similar.

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Long term follow up shows similar tubal patency rates, whereas the no. of repeat ectopic pregnancies lowers, although these differences are not statistically significant. The laparoscopic approach is less costly as a result of significantly less blood loss and analgesia requirement, and a shorter duration of operation time, hospital stay, and convalescence time. Systemic methotrexate in a single dose intramuscular regimen is not effective enough in eliminating tubal pregnancy compared to laparoscopic salpingostomy. Only in patients with low initial serum hCG level systemic methotrexate leads to cost saving compared to laparoscopic salpingostomy[3].

Laparoscopy can be used for diagnosis & treatment of ruptured and unruptured ectopic pregnancy. Laparoscopic surgical treatment of ectopic gestation offers numerous advantages: reduced operating time, hospital stay and cost, earlier return to activity & improved cosmetic results[4].

Ectopic pregnancy is one of the life threatening disease in which prevalence has increased as mortality has declined. The life threatening ectopic pregnancy is now evolving into a medical disease, with the possibility of lower-cost treatment, faster recovery, & higher subsequent fertility.

The above has been achieved by: increased sensitivity of serum beta human gonadotrophin (B-hCG) immunoassay & improved quality

transvaginal sonography, combined with a heightened awareness and increased suspicion of the condition among clinicians which has allowed early detection of ectopic pregnancy. Laparotomy once the standard treatment of ectopic pregnancy has been replaced mostly by operative laparoscopy. Laparotomy however remains necessary in cases with haemodynamic instability & with exceptional locations, e.g. cervical, abdominal, and interstitial implantation. Methotrexate or other treatment therapies can be employed with some success and lastly expectant management involving follow up using serial hCG measurements & ultra-sound scans[1,2,4].

The standard surgical treatment for ectopic tubal gestation is either salpingostomy especially with unruptured tubes or partial salpingectomy especially with ruptured and damaged tubes and when bleeding control is inadequate[5].

Fimbrial evacuation or squeezing is better avoided and should be abondaned if anything more then very minor tubal pressure does not affect evacuation of the distal pregnancy[6]. It should be noted that there is a 5-10 % risk of persistent trophoblast remaining after conservative treatment, i.e both medical and surgical that might require a further treatment[7]. After conservative surgery approximately 50% of patients will have a subsequent intra-uterine pregnancy; 40% a live birth and 12% a repeat ectopic pregnancy

Fertility rate after laparoscopic salpingostomy is similar to that after Iaparotomy. The rate of intra-uterine pregnancy after radical procedures 45% is not significantly different to that after conservative surgery, but the repeat ectopic pregnancy rate is lower 9%.

Women with only one fallopian tube undergone salpingostomy or salpingotomy for ectopic gestation have a live birth rate of approximately 40% and a repeat ectopic pregnancy rate of 20%. The presence of risk factors increases the chances of recurrent ectopic and reduces the likelihood of intra-uterine pregnancy[2].

Fertility prospects after ectopic pregnancy treatment is not correlated to the features, but depends mainly on patients' age and past history[8]. In comparing Laparoscopic surgery with Iaparotomy to treat ectopic pregnancy after exclusion of patients with shock, laparoscopic surgery offered a significant shorter post-operative hospital stay (mean 2.7 days versus 5.5 days), a slightly lower peri-operative complication rate (8.1% versus 13.9%) and more conservative surgery (90.1% of all salpingotomies) than Laparotomy. A longer operating time was needed for Laparoscopic surgery (1.2 hours versus 1.01 hours)[9].

Operative laparoscopy is currently the best treatment for ectopic pregnancy and it can be conservative (salpingostomy), or radical (salpingectomy).

Materials & Methods

From January 2000 till January 2001, 12 cases of ectopic pregnancy were treated by laparoscopy at Elwiya maternity teaching hospital and Kamal Al -Sammariae fertility and IVF center.

Average age 27 years (youngest 22 and oldest 34). 5 patients were nullipara, while the rest have one or more children.

Infertility of more than one year encountered in 6 cases 50% (two primary and 4 secondary infertility). Three cases gave history of IUCD of more than 3 years duration and one was on oral combined contraceptive, but irregular use.

Table 1: Signs and symptoms of ectopic pregnancy

Sign and symptom	Number	%
Amenorrheoa	8	66.6
Abdominal pain	9	75
Irregular vaginal bleeding	10	83.3
Acute abdomen	4	33.3
Incomplete abortion evacuated 1 month before	1	8.3

Table 1 showed the frequency of signs and symptoms: the commonest presenting symptom was irregular vaginal bleeding which was encountered in 83.3% of cases. HB %, blood grouping and Rh were performed in all cases prior to surgery with preparation of 2 units of blood. Sonography performed in 8 cases because in the rest the cases were in acute state.

Operating Technique:

Laparoscopy confirmed the diagnosis and permitted assessment and surgery. Blood transfusion was given before surgery to the acute abdomen cases (4 cases), while the other ruptured ectopic pregnancies required blood transfusion during operation or in the post-operative period. None of the unruptured ectopic required blood transfusion.

Laparoscopy was performed under general anesthesia with endotracheal intubation, CO_2 used for insufflation, 10 mm laparoscope was introduced subumbilically and another two

portae for the introduction of two 5mm trocar and cannulae were introduced into the iliac fossae, one for the atraumatic forceps and the other for introduction of 5mm scissor that attached to a unipolar diathermy probe (Karl-Storz autocon 200 unipolar) high frequency elector-surgical and thermo-coagulation generator. A bipolar probe also available and used sometimes to control bleeding. Suction and irrigation is essential to wash the peritoneal cavity with normal saline before embarking on surgery.

In few cases we might require a fourth porta for fixation of the tissues and was usually introduced in the suprapubic region (2 Cases). The standard procedure is salpingostomy; trying to conserve the tubal function by making incision along the ante-mesenteric border over the ectopic 1-2 cm length, then the product of gestation are flushed with the suction irrigation system. Bleeding points controlled by cauterization with unipolar or bipolar diathermy, then operation area are flushed again to ascertain haemostasis, and then peritoneal cavity was washed with normal saline to ascertain no bleeding or left trophoblasts

If we could not control bleeding or the tube is damaged and conservative surgery is not feasible, partial salingectomy was performed with the use of scissor attached to unipolar diathermy to control bleeding and the same steps taken to control bleeding as before.

All patients were given antibiotic cover started before surgery & continued for 5 days (ampicillin 500mg QDS + metronidazol 500mg TDS), to guard against infection especially conserving future fertility.

Results

All 12 cases of ectopic pregnancy treated by laparoscope, no one required laparotomy i.e. no failure. Cases treated, laparoscopic finding and method of treatment employed are presented in tables 2, 3 and 4. Table 2 showed the treatment employed to treat the 12 cases.

Table 2: Results of treatment

Technique	Number of cases	%	Failure
Salpigostomy	7	58	nil
Salpingectomy	5	42	nil

There were 7 cases (58.3%) ruptured ectopic pregnancies; 4 out of them are in acute abdomen state that required resuscitation and blood transfusion before Laparoscopy; 6 on the right tube and one on the left tube (3 at the ampulla and 4 at the fimbria). 4 unruptured ectopic (33.3%); 2 on the right side and 2 on the left side, (one ampullary and 3 fimbrial) and one tubal abortion (8.3%) on the left side.

So the right side affected 66.6% while the left side affected in 33.4 %. Salpingostomy was the treatment in all unruptured ectopic and tubal abortion & was successfully performed in another 2 cases of ruptured ectopic pregnancies; (table 3 cases no. 7, 8). Average operation time 1 hour 10 minutes.

Blood transfusion was not required in all unruptured ectopic and tubal abortion, but was required (1-3 units) in all ruptured ectopic. All patients discharged home within 24 hours. No case required another laparoscopy or laparotomy. No post operative complications encountered. 4 cases conceived (cases 3, 5, 7, and 12) Table 2; 2 pregnancies occurred in the unruptured ectopic (5 and 12), one in the tubal abortion (case 3) and the 4th pregnancy in a ruptured ectopic (cases 7) that was treated by salpingostomy.

Table 3: Cases, presentation, laparoscopic findings and treatment

No	Age	Presentation	Laparoscopic findings	Treatment	Blood given
1	22	1ry infertility 3years	Rt. unruptured fimbrial ectopic ==	Salpingostomy	No
2	24	Para 1+2	Lt. fimbrial tubal abortion	Partial Salpingectomy	2 unit
3	21	Married 9 months	Rt. Ruptured ampullary	Partial	no
4	32	Para 5+1 2ndary infertility 2 years	ectopic (acute abdomen)	salpingectomy	2 unit
5	31	Para 2 2ndary infertility 2 years	Lt. unruptured ampullary ectopic	Salpingostomy	no
6	34	Para 6+3	Rt. unruptured ampullary ectopic (acute abdomen)	Salpingostomy	2 unit
7	26	1ry infertility 2 years	Rt. Ruptured fimbrial ectopic	Salpingostomy	2 unit
8	29	para 2+1	Lt. Ruptured fimbrial ectopic	Salpingostomy	2 unit
9	25	para 1+5	Lt. unruptured fimbrial ectopic	Salpingostomy	no
10	27	para 3+4	Rt. Ruptured ampullary ectopic (acute abdomen)	Partial salpingectome	2 unit
11	25	1ry infertility 2 years	Rt. Ruptured fimbrial ectopic (acute abdomen)	Partial salpingectomy	3 unit
12	28	para 2+1	Rt. Unruptured fimbrial ectopic	Partial salpingectome	no

Table 4: Side and site of ectopic pregnancies

Rt. Tube	Lt. tube
8 (66.6%)	4 (33.3%)
6 ruptured	1 ruptured
2 unruptured	2 unruptured
	1 tubal abortion
3 ampullary	1 ampullary
5 fimbrial	3 fimbrial

Discussion

Laparoscopy has evolved the management of ectopic pregnancy dramatically. Nowadays there is no way to keep patients in hospital as had practiced before with a diagnosis of suspected ectopic pregnancy because these patients has to be scoped to ascertain the diagnosis and treat accordingly .

Laparoscopic treatment of ectopic pregnancies started by Bruhat and Manhes in France and Decherney and Diamond in USA in the late 1970s and early1980s. Many authors reported a better results of Laparoscopic treatment of ectopic pregnancies to laparotomy[4,9,15].

The study covered 12 cases of ectopic pregnancies treated successfully by the laparoscope and included 4 cases acute abdomen which were managed after resuscitation by the laparoscope. Sultana et al[15] reported that significant haemoperitoneum was the indication of Laparotomy in cases of ectopic pregnancy & reported 25% of attempted Laparoscopy for ectopic cases were eventually converted to Laparotomies. Laparoscopy was significantly less expensive, with shorter hospital stay. Lowe et al[6] mentioned that the major contraindication to Laparoscopy are massive intra-abdominal bleeding and extensive intra-abdominal adhesions.

Tubal evacuation or aspiration was not attempted because of the fear of persistent trophoblast and recurrence[4]; Timonen et al[11] reported a recurrence in 2 out of 14 cases. Bruhat et al[12] quoted that precautions has to be taken to reduce the risk of leaving pregnancy in place:

1. To examine the aspirated fluid for the presence of product of gestation.
2. Intense and close post-operative follow-up to detect any failure and its consequences.

The study showed, that no case required Laparotomy and no post-operative complications, recurrence or persistance of trophoblast, but the number of cases treated was small (12 cases) and the sites were ampullary and fimbrial regions which are the easiest sites for laparoscopic treatment.

Tubal patency after laparoscopic treatment of ectopic pregnancy was not checked by the usual methods of tubal patency i.e. laparoscopy or HSG, but was proved by the occurrence of 4 pregnancies (33.3%). This figure is comparable to the average figure quoted by Henri-Suhet et al[16], but lower than the figure quoted by Bruhat et al[12].

All pregnancies occurred in the cases treated by salpingostomy, table 3 cases 3, 5, 7, and 12, but because number of cases is too small for these results to be statistically significant. Salpingostomy should be the standard treatment of unruptured ectopic and should be tried in ruptured ectopic if the rupture is small and bleeding is minimal. In this series, we managed to treat one of the ruptured ectopic (case no. 7) with salpingostomy.

Reproductive outcome laparoscopy or laparotomy performed for the treatment of ectopic is more or less the same and the crucial factor for future reproductive outcome after surgical treatment of ectopic gestation is the status of contralateral tube[10].

The risk of subsequent recurrence of ectopic pregnancy is 15-30 %, being more after conservative than after radical surgery and subsequent intra-uterine pregnancy rate is 30-50%[2].

Laparoscopic treatment of ruptured ectopic with acute abdomen was successful in 4 cases, while acute abdomen was a contra-indication to laproscopy in many other studies[6,15].

The present study showed that laparoscopic treatment of ectopic pregnancy is possible in almost all cases even the acute abdomen, but we should follow the laparoscopic golden rule that we have to revert to laparotomy when it is needed sooner and not later. Tubal aspiration was not attempted as mentioned before for the fear of leaving trophoblast leading to recurrence[6,11,12].

Conclusion:

Laparoscopy gives a better panoramic view of the peritoneal cavity than laparoscopy. If we standardize Laparoscopic treatment of ectopic pregnancy, it can be used for early diagnosis and treatment. Although the number of cases is small, the study showed that Laparoscopic

treatment of ectopic pregnancy is quick, safe, with short hospital stay even in acute cases, and better cosmetic results and very good fertility prospects. A multi-center study is required to ascertain these findings.

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Case Report

DOUBLE APPENDIX: CASE REPORT

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Abstract
A 31 year old male patient presented with signs and symptoms of acute appendicitis, operated on. Per-operatively revealing 2 perforated appendices one was in retrocecal area and the other was voluntary appeared subcecaly.

Appendectomy was done for 2 appendices with more than one drain. The patient passes in smooth postoperative course.

Keywords: Double Appendix, Appendicitis

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Case Report

A 31 year old male patient working as a butcher and living in Al-Aadhamiya presented to Al-Kadhimiya Teaching Hospital with abdominal pain of 48 hours duration.

The condition started gradually as a dull central abdominal pain shifted to right lower abdomen after few hours. The pain was squeezing in nature, increasing by movement, relieving by lying still. The condition associated with nausea and vomiting (3 times), the vomits was yellow in color, little amount, contain no blood and not projectile. The patient presented with loss of appetite with no alteration of bowel habit. Also the condition associated with fever which was associated with sweating and was relieved only by medication.

The patient went to other hospital before he was admitted to our center and treated as a case of abdominal colic with no benefit.

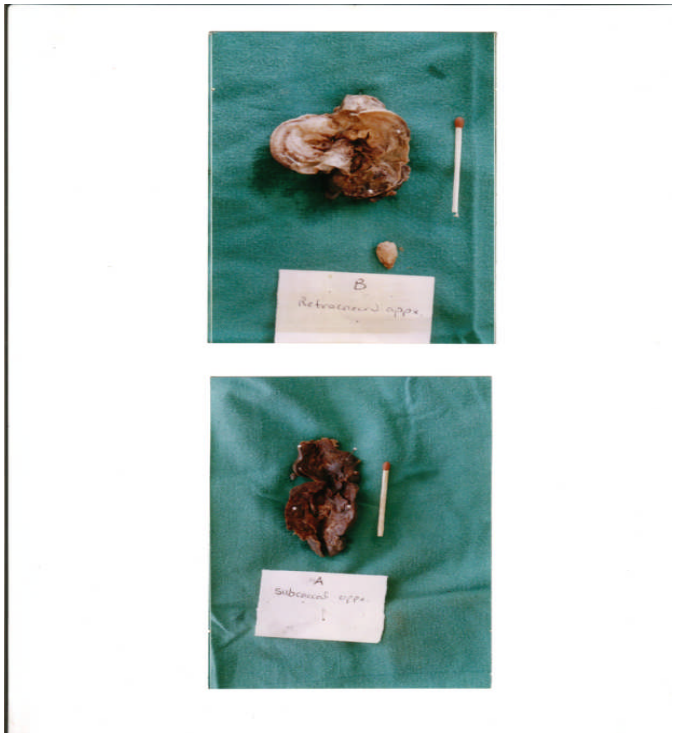
On examination the patient was conscious, oriented, of a body temperature 38.1 C, pulse rate 120 / min and blood pressure 120/90 mmHg. The abdomen was flat did not move with respiration, by palpation there was rigidity and tenderness particularly in right iliac fossa and umbilical region. Cough sign, rebound tenderness and Rovsing's sign were positive. No organomegally, no palpable mass. The percussion revealed tympanic abdomen and the auscultation showed, negative bowel sound.

Emergency laboratory investigations were done, including PCV which was normal, WBC count was slightly elevated, urinalysis was normal.

Decision was made to be operated on as a case of acute appendicitis.

The operation: After the Grid-Iron incision that was made, two perforated appendices were revealed. One was retrocecal, obstructed contain feacolith (Picture No.1B) and the other was subcecal (Picture No.1A), they had 2 separated bases 1.5cm apart. Appendectomy was done for both of them, washing the peritoneal cavity with normal saline was done. Tow tube drains were put, in the pelvis and the other retrocecally, other corrugated drain was put near the area of muscle cutting then the wound was closed in layers.

First postoperative day the patient passed flatus and started oral fluid, in second postoperative day the patient pass motion and pelvic tube drain and the corrugated drain were removed, while the retrocecal tube drain was removed on third postoperative day then the patient discharged in good general condition.



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Discussion

The common congenital abnormalities of the appendix are: agenesis of appendix, left sided appendix, double appendix[1,2]. Duplication of the appendix is a rare congenital abnormality and less than 100 cases were reported since the first description in 1892[5]. Embryological origin is controversial, but duplications would occur in the absence of the involution of the appendicular process after eightieth week gestation. According to the definition of Ladd and Gross, they explained that the duplication of appendix just like any other of digestive system[3]. One of explanation of the origin is offered by Kelly and Herdon (1905) who described a second transient appendix appearing in 10mm embryos. Mitchell (1905) who postulated the occurrence of a double appendix as a phylogenetic reversion to the paired caecal arrangement found in birds. This theory is not acceptable on the grounds that birds are not direct ancestors of man in evolutionary development[4].

Cases of double appendix may be classified as the following:

Type A: Which is called double-barreled appendix[5]. A single caecum and one appendix exhibiting various degrees of partial duplications[4].

Usually two separate tubes, each is lined by mucosa and is separated by submucosa, and is enclosed in a single common muscle coat[5].

Type B: A single caecum with two completely separate appendices. This group can further be subdivided into:

Type B (I): It is called the bird-like type due to the resemblance to the normal arrangements in birds, here there are two appendices symmetrically placed on either side of the ileocaecal valve[4]. It described only in infants with multiple abnormalities[5].

Type B (II): It is called the taenia-colic where one appendix comes of the caecum at the usual site, the other usually rudimentary, and arising from the caecum almost always along the lines of the taenia at the varying distance from the first. In our case one was retrocaecal which was in normal position (Picture No.1B), the other was subcaecal which was voluntary (Picture No.1A).

TYPE C: It is a double caecum, each with an appendix[4].

In some instances one of the twin appendices has been found acutely inflamed and the other uninvolved[1].

The condition must be distinguished from a solitary diverticulum of the caecum which is found on the inner side of the ileocaecal angle; and histologically the wall of the diverticulum does not contain lymphoid tissue[4].

Duplication of the appendix is usually an operative diagnosis and when it found treatment will follow the same rules of acute appendicitis in which appendicactomy should done for both appendices with or without drainage of the operative area.

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تمايز الخلايا الجذعية الجنينية الى خلايا شبيهة بالخلايا العصبية في الوسط الزرعي و في داخل الجسم بعد زرعها في المخلص

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الخلاصة:
خلفية الدراسة: توفر الخلايا الجذعية الجنينية متعددة الأمكانيات مصدرا غير محدود لزراعة الخلايا، في ضوء تطور طرق توليد خلايا عصبية في الوسط الزرعي.
هدف الدراسة: وصف الشرزط التي تؤدي الى حث تمايز الخلايا الجذعية الجنينية للتطور باتجاه الخلايا العصبية.
طريقة العمل: تم الحصول على خلايا جذعية جنينية للفار من استزراع الأريمة و اعيد زرع هذه الخلايا بعد اضافة خلاصة دماغ جنين الفار. زرقت هذه الخلايا، و كذلك خلايا جذعية لم تعامل بخلاصة دماغ الفار الى دماغ فئران بالغة باستخدام جهاز التوجيه المحوري المجسم (sterotaxic). اضيفت مادة (Horse Raddish Peroxidase) الى وسط الزرع بهدف وسم الخلايا الجذعية المستزرعة للتمكن من ملاحظة الخلايا التي تم حقنها الى دماغ الفار البالغ.
النتائج: اظهرت النتائج ان مقدمات الخلايا العصبية الناشئة من الخلايا الجذعية الجنينية و التي تم زرقها في دماغ الفار البالغ موقع الزرق ربما لتحل محل الخلايا التي تعرضت للتلف في الموقع او في مسافات ابعد.
الأستنتاج: ان خلاصة الدماغ تعمل كمصدر للعوامل المغذية و عوامل النمو التي تؤدي الى الخلايا الجذعية الجنينية لتمايز نحو خلايا عصبية (او شبه عصبية) . و بهذا للخلايا الجذعية ان تكون مصدرا مهما لزرع الخلايا العصبية التعويضية. كما اظهرت النتائج ان الوسم بواسطة (Horse Raddish Peroxidase) و الذي استعمل لأول مرة في هذا المجال باضافته الى الوسط الزرعي قد ادى الى تعليم هذه الخلايا في الوسط الزرعي او في داخل الجسم مما يمكن من تتبع مصير الخلايا التي تم حقنها.

مفتاح الكلمات: الخلايا الجذعية الجنينية، التشكل العصبي، عوامل النمو العصبي، زرع الخلايا الجذعية الجنينية

المجلة العراقية للعلوم الطبية ٢٠٠٤ م، المجلد ٤ ، العدد ٢ ، ص ١٠٠ ـ ١٠٧

دراسة كيمانسجية لخلايا شوان في الارنب

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الخلاصـــة:
خلفية الدراسة: تمت دراسة العمليات الايضية في أغشية الاعصاب المحيطية للارنب بأستخدام فعالية أنظيمات هايدرولازات استرات الكاربوكسيل غير المحددة بمستوى المجهر الالكتروني .
طريقة العمل: استعملت عينات بمقدار (١ سم) من العصب النسوي للارنب بعد تثبيتها وصباغتها لكل من أسترات اليورانيل وأسترات الرصاص .
النتائج: لوحظ أن فعالية الانظيمات تتركز في غلاف خلية شوان وحول فجوات الغلاف وعدم وجود فعالية في متن السايتوبلازم الموجود في محاور الخلايا العصبية او في الانابيب الدقيقة والخيوط الدقيقة داخل هذا السايتوبلازم.
الأستنتاج: من خلال هذه الدراسة يمكن أستنباط النتائج ان لهذا الانظيمات دورا" مهم في عملية البناء والهدم التي تتضمن خلايا شوان ومكوناتها او أفرازاتها.

مفتاح الكلمات: الميالين، استيريز غير خاصة، الفا نفثيل اسيتيت

المجلة العراقية للعلوم الطبية ٢٠٠٤ م، المجلد ٤ ، العدد ٢ ، ص ١٠٨ ـــ ١١١

فعّالية أنزيم صوديوم بوتاسيوم أي تي باز في متلازمة تناذر الكليتين التجريبي

ابتسام العبوسي (قسم الكيمياء)، إسراء فائق السامرائي (قسم وظائف الأعضاء)،
فائزة الراوي (قسم الأمراض) كلية الطب /جامعة النهرين

الخلاصة:
خلفية الدراسة: متلازمة تناذر الكليتين بالادريامايسين هي نموذج للبروتين في الإدرار المزمن الغير ناتج عن تحفيز الجهاز المناعي والذي يسبب بحقن الجرذ في الوريد الذيلي بهيدروكلوريد الدوكسوروبسين. إنّ تكوّن الورم وانتفاخ البطن المائي في هذا النموذج هو ناتج عن سحب الصوديوم.
هدف الدراسة: لتقييم ما إذا كانت زيادة فعالية إنزيم صوديوم بوتاسيوم أي تي باز في الكليتين هي صفة عامة لتناذر الكليتين التجريبي وهل زيادة هذه الفعالية مسؤولة عن قلة إفراز الصوديوم في الإدرار.
طريقة البحث: تضمن العمل ١٢ جرذ: مجموعة المقارنة (حقنت ب ١٥ ملغم لكل ١٠٠ غم من وزن جسم بالادريامايسين) أعطيت في وريد ذيل الجرذ. المجموعة الأخرى أخذت كلوريد الزنك ٠,٢ ملغم /كغم وزن جسم بالإضافة إلى نفس جرعة الأدريامايسين. بعد أسبوعين تم قتل الحيوانات. تحليل الإدرار تم بواسطة أشرطة لقياس نسبة البروتين في الإدرار. أخذت عينات الدم قبل وبعد إعطاء الأدريامايسين وفي كلتا العينات تم قياس فعالية إنزيم صوديوم بوتاسيوم أي تي باز. تمت عملية مجانسة الكلى لقياس فعالية الصوديوم بوتاسيوم أي تي باز في الأنسجة في المجموعتين. وأخيراً تم تشريح الكلى وفحصت بواسطة المجهر الضوئي والمجهر الالكتروني.
النتائج: العينات النسيجية لكلى الجرذ المعالجة بالادريامايسين بيّنت تغيرات لمتلازمة تناذر الكليتين. فعالية إنزيم صوديوم بوتاسيوم أي تي باز ازدادت زيادة معنوية في الجرذان المصابة بتناذر الكليتين ($P<0,05$) وكانت هناك زيادة أكثر في الجرذان التي أخذت زنك ($P<0,01$). المقاطع التي فحصت بالمجهر الالكتروني أكدت تشخيص التناذر وأظهرت ذوّي في الخلايا القنوية في الجرذان المصابة بالتنا ذر.
الاستنتاج: كان هناك زيادة واضحة في فعالية إنزيم صوديوم بوتاسيوم أي تي باز (مرتين) في مجموعة التناذر وزيادة أكثر في مجموعة إضافة الزنك.

مفتاح الكلمات: صوديوم بوتاسيوم أي تي باز، أدريامايسين، متلازمة تناذر الكليتين.

المجلة العراقية للعلوم الطبية ٢٠٠٤ م، المجلد ٤ ، العدد ٢ ، ص ١١٢ ــ ١١٦

الملخصات العربية
مقالات مبتكرة

دراسة سريرية مقارنة لعقار فينيستراید المستخدم موضعيا كعلاج جديد لمرض حب الشباب

اديب الزبيدي، فاروق الجواد (قسم العقاقير و التداوي)، نضير مطلوب (قسم الطب-الجلدية)
كلية الطب-جامعة النهرين

الخلاصة:

خلفية الدراسة: إن تنظيم إفراز المادة الدهنية في الجلد يتطلّب تحوّل موضعي للهرمون الذكري (تيستوستيرون) إلى ما هو أكثر فعّاليّة (دايهايدروتيستوستيرون) بمساعدة الأنزيم ٥-ألفا- ريدكتيس. لذا فأنّ عقار فينستيراید (المثبّط للأنزيم آنف الذكر) يمكن أن يكون ذا فعّاليّة في علاج مرض حب الشباب وأمراض جلديّة أخرى متسبّبة من زيادة فعّاليّة الهرمون الذكري.

هدف الدراسة: لتقييم كلاً من الفعّاليّة والسلامة السريرية لعقار فينستيراید ذي التركيز(٠,٠١٪) المستخدم موضعياً كعلاج جديد لمرض حب الشباب.

طريقة العمل: تمّ تقسيم المشمولين بهذه الدراسة (٦٠ مصاباً بمرض حب الشباب) بشكل عشوائي إلى مجموعتين متساويتين(٣٠ مريض لكل منهما) يعالجون بمسح المنطقة المصابة موضعيّا مرّتين يوميّاً لمدة ثلاثة أشهر إما بسائل فينستيراید(٠,٠١٪) أو بسائل كلندامايسين(١٪). لقد تمّ تقييم فعّاليّة العقارين ومقارنتهما ببعض اعتماداً على تحديد عدد المرضى المستجيبين للعلاج وفقاً لكلّ فترة من فترات النسبة المئوية للشفاء.

النتائج: لقد تم تشخيص الاستجابة الأولية بعد مرور ما معدّله(± الانحراف المعياري للمعدّل)٤,١٥ (± ٠,١٥) أسابيع من بدء العلاج بعقار فينستيراید في مقابل ٣,٥٦ (± ٠,١٣) أسابيع من بدء العلاج بعقار كلندامايسين على أنّ هذا الفرق ممّا لا يعتدّ به إحصائيا. أمّا تشخيص الاستجابة القصوى فقد احتاج إلى فترة إضافية لتصل إلى ما معدّله(± الانحراف المعياري للمعدّل)٨,٢ (± ٠,٢٣) أسابيع من بدء العلاج بعقار فينستيراید في مقابل ٨ (± ٠,١٤) أسابيع من بدء العلاج بعقار كلندامايسين على أنّ هذا الفرق ممّا لا يعتدّ به إحصائيا كذلك. إن نسبة المرضى المستجيبين بشكل جلّي بعد ١٢ اسبوعاً من العلاج بعقار فينستيراید كانت ٦٦,٦٧٪ وهي نسبة مقارنة لنسبةاولئك المماثلين لهم في مجموعة الكلندامايسين حيث كانت ٨٠٪ وبعبارة أخرى فانّ الفرق بين النسبتين ممّا لا يعتدّ به إحصائيا.

أضف الى ما تقدّم فانّ كلا العلاجين في هذه الدراسة كانا أمينين سريريا ولم يحدثا أعراضاً جانبية تذكر.

الاستنتاج: أنّ سائل عقار فينستيراید ذي التركيز(٠,٠١٪) المستخدم موضعياً مرتين يومياً لمدة ١٢ أسبوعاً يمثّل علاجاً فعّالاً و أميناً و جديداً لمرض حب الشباب الملتهب ذي الشدة البسيطة أو المتوسطة.

مفتاح الكلمات: فينيستيراید، كلندامايسين، حب الشباب

المجلة العراقية للعلوم الطبية ٢٠٠٤ م، المجلد ٤ ، العدد ٢ ، ص ١١٧ ـــ ١٢٤

الملخصات العربية
مقالات مبتكرة

الفحص الخلوي لنماذج غسل القصبات في تشخيص أمراض الرئة

فائزة عفتان زغير الراوي (قسم علم الأمراض-كلية الطب-جامعة النهرين)

الخلاصة

هدف الدراسة: إجراء الفحص الخلوي لغسل القصبات ومقارنة النتائج مع الفحص النسيجي وفحص الناظور.

طريقة العمل: أجري الفحص الخلوي ل ٤٩٥ نموذج غسل قصبات، وقورنت النتائج مع فحص الناظور و الفحص النسيجي.

النتائج: أظهرت الدراسة ان التوقع الصحيح لتشخيص الورم (حساسية الفحص الخلوي) تم الحصول عليه في ٨٢٪ من نماذج غسل القصبات و ارتفعت إلى ٩٥٪ عندما اقترن غسل القصبات مع تخدش القصبات بالفرشاة.

الأستنتاج: أظهرت الدراسة أن الفحص الخلوي لغسل القصبات أعطت قيم نتائج تشخصيه عاليه وحساسية جيده في تشخيص أمراض الرئة.

مفتاح الكلمات: ناظور القصبات، غسل وتخدش القصبات.

المجلة العراقية للعلوم الطبية ٢٠٠٤ م، المجلد ٤ ، العدد ٢ ، ص ١٢٥ ــ ١٢٧

طريقة الفحص بالإبرة الدقيقة باعتماد الخاصية الشعرية. هل الرشف مع المص ضروري ؟ دراسة ثلاثون حالة لمختلف الآفات المرضية

يعرب إدريس خطاب، علاء غني حسين (قسم الأمراض-كلية الطب-جامعة النهرين)

الخلاصة:

خلفية الدراسة : إن طريقة الفحص الخلوي بالإبرة الدقيقة باعتماد الخاصية الشعرية قد اكتسبت حاليا كطريقة تشخيصية. وقد نشر القليل حول كفاءة هذه الطريقة والتي يتم الحصول على مادة الفحص الخلوي فيها باستخدام خاصية الأنبوب الشعري بدلا عن الرشف.

هدف الدراسة: تقييم أهمية وموضعية طريقة الفحص الخلوي بالإبرة الدقيقة باعتماد الخاصية الشعرية في آفات مرضية متعددة.

طريقة العمل: خلال فترة ١٩ شهر، تم إجراء طريقة الفحص الخلوي بالإبرة الدقيقة باعتماد الخاصية الشعرية لثلاثين مريضا يعانون من آفات مرضية مختلفة وتم إجراء بعضها تحت توجيه السونار تم تثبيت المسحات الخلوية بالكحول الاثيلي بتركيز ٩٥٪ ومن ثم صبغها بصبغة الهيماتوكسلين والايوسين وفحصها من قبل نفس الاختصاصي بالفحص الخلوي. تم تقييم الطريقة باعتماد نظام نقطي ذو خواص خمسة وتم التأكد من نتائج التشخيص الخلوي بإجراء الفحص النسيجي.

النتائج: تم احتساب معدل النقاط المسجلة للحالات الثلاثين من الإناث المرضية في المواقع المختلفة باستخدام نظام الخواص الخلوية الخمسة المذكورة آنفا. وتم التأكد من نتائج الفحص الخلوي جميعا بإجراء الفحص النسيجي (الخزع النسيجية).

الاستنتاج: بتطبيق نظام نقطي موضوعي، فان طريقة الفحص الخلوي بالإبرة الدقيقة باعتماد الخاصية الشعرية قد أنتجت نتائج مقاربة في ما يخص النتائج الخلوية، والدقة التشخيصية لفحص الرشف بالإبرة الدقيقة. ومن جهة أخرى فقد كانت الطريقة المستخدمة في هذه الدراسة اقل أذى وصاحبها عدد اقل من النتاجات الخلوية الملوثة بالدم، وسمحت بإحساس finger tip للآفة المرضية .

مفتاح الكلمات: الرشف الخلوي، الفحص الخلوي بالإبرة الدقيقة، الفحص الخلوي بالإبرة الدقيقة باعتماد الأنبوب الشعري، الفحص الخلوي من دون الرشف.

المجلة العراقية للعلوم الطبية ٢٠٠٤ م، المجلد ٤ ، العدد ٢ ، ص ١٢٨ ــ ١٣١

الملخصات العربية
مقالات مبتكرة

قياس معدل ترسب الكريات الحمراء باستخدام K_3EDTA

رعد جابر موسى، سعد شوقي منصور، حسام حسون علي
(قسم الأمراض-كلية الطب-جامعة النهرين)

الخلاصة :

خلفية الدراسة: ان الطريقة الروتينية لقياس معدل ترسب الكريات الحمراء هي باستخدام طريقة الوستركرين. في هذه الدراسة استخدمت الطريقة الجديدة وذلك باستخدام مادة بديلة مضادة للتخثر وهي (K_3EDTA) لقياس معدل ترسب الكريات الحمراء.

هدف الدراسة: اهداف هذه الدراسة هي لمقارنة النتائج بالطريقتين وكذلك لتحديد المعدل الطبيعي لترسب الكريات الحمراء بالطريقة الجديدة.

النتائج: في هذه الدراسة تم تسجيل معدل ترسيب الكريات الدموية الحمراء باستخدام طريقة ويستركرن المعدلة عند ١٠٠ شخص.وتبين وجود توافق ممتاز بين الطريقتين وكان متوسط معدل ترسيب الكريات الدموية الحمراء في الطريقة القياسية ٢٥,٠١ملم/ ساعة وفي الطريقة المعدلة ٢٤,٦٩ ملم/ ساعة حيث لا يوجد فرق احصائي بين الطريقتين. وكذلك تم تثبيت القيم الاعتيادية لمعدل ترسيب الكريات الدموية الحمراء باستخدام الطريقة المعدلة عند (٦١) من الأشخاص الأصحاء ظاهريا تبين إن معدل ترسيب الكريات الدموية الحمراء عند النساء هو أعلى من الموجود عند الرجال ذوي الأعمار المتقاربة.

الاستنتاج: هي طريقة جيدة وممكن استخدامها في العمل الروتيني بدل الطريقة القديمة.

مفتاح الكلمات: وستر غرين، مادة بديلة مضادة للتخثر

المجلة العراقية للعلوم الطبية ٢٠٠٤ م، المجلد ٤ ، العدد ٢ ، ص ١٣٢ ـــ ١٣٥

تقييم أهمية طريقة الاصطباغ السريعة المستخدمة في الفحص الخلوي باعتماد الرشف بالإبرة الدقيقة

يعرب إدريس خطاب، علاء غني حسين (قسم الأمراض-كلية الطب-جامعة النهرين)

الخلاصة:

خلفية الدراسة: تعد طريقة الفحص الخلوي باعتماد الرشف بالابرة الدقيقة طريقة امينة، بسيطة وفعالة لاستحصال التشخيص الخلوي في حالات الافات المرضية السطحية والعميقة. وخصوصا حين تكون الفحوص الروتينية الاختراقيةالاخرى ذات اهمية تشخيصية محدودة. ويمكن التقليل من امكانية الحصول على نماذج غير مناسبة وغير كافية للتشخيص بالتحديد الدقيق للافة المرضية باستخدام توجيه جهاز الفحص بالموجات فوق الصوتية يجريه كادر متمرس وباستخدام طريق الصبغة السريعة لتقييم مدى كفاية النموذج الخلوي للتشخيص قبل السماح للمريض بمغادرة غرفة السحب.

هدف الدراسة: هدفت الدراسة الى تقييم اهمية طريقة الاصطباغ السريعة لنماذج الفحوص الخلوية المستحصل عليها باستخدام طريقة الفحص الخلوي باعتماد الرشف بالابرة الدقيقة الموجهة بالسونار ومقارنة معدل النجاح في الوصول الى تشخيص دقيق مع الطريقة القياسية المعتادة.

طرائق العمل: اجراء الفحص الخلوي باعتماد الرشف بالابرة الدقيقة على ٥٤ مريض لديهم افات مرضية سطحية وعميقة وبتوجيه من جهاز الفحص بالامواج فوق الصوتية. تم اجراء الفحص من قبل فريق عمل. وبعد كل فحص بهذه الطريقة تم صباغة الانموذج لصبغة اللشمان المحورة السريعة ومن ثم تم تقييم المسحات الخلوية حول مدى كفايتها للتشخيص الخلوي. تم اعادة الفحص مرة او مرات اخرى اذ اظهر الفحص الاولي عدم كفاءة التشخيص.

النتائج: اظهرت طريقة الاصطباغ السريعة حساسية عالية مقارنة بالطريقة القياسية المعتادة (٩٣,٧٥ ٪ مقابل ٧٥,٧ ٪) ونوعية عالية (١٠٠٪ مقابل ٩٧,٦٪) وكانت ذات دقة تشخيصية عالية (٩٦,١٥٪ مقابل ٧٨٪) للطريقة القياسية. بلغ معدل المضاعفات باستخدام طريقة الصبغ السريعة ٣,٧ ٪.

الاستنتاج: يجب تشجيع استخدام طريقة الاصطباغ السريعة لفوائدها الملحوظة للمريض (شعور اقل بعدم الارتياح، معدل اقل للمضاعفات، تشخيص اسرع لطبيعة الافة المرضية).

مفتاح الكلمات: الفحص الخلوي باعتماد الرشف بالابرة الدقيقة، صبغة اللشمان، طريقة الصبغ السريعة.

المجلة العراقية للعلوم الطبية ٢٠٠٤ م، المجلد ٤ ، العدد ٢ ، ص ١٣٦ ـــ ١٣٩

قياسات إنتاجية الخلايا الليمفاوية المحيطية في المرضى المصابين بمرض الأكياس العدرية (المشوكات الحبيبية)

علي حسين العبيدي، طارق إبراهيم الجبوري، أمينة صباح محمود جمعة
(قسم الأحياء المجهرية، جامعة النهرين، كلية الطب)

الخلاصة

خلفية الدراسة: يمثل مرض الأكياس العدرية مشكلة صحة عامة رئيسية. القليل يعرف عن كيفية تطور المرض في الإنسان لحد ألان، و دور الاستجابة المناعية في هذه العملية.

هدف الدراسة: قياس معاملي الانقسام و التضاعف و تطور دورة انقسام الخلايا في الخلايا الليمفاوية المحيطية للمصابين بمرض الأكياس العدرية.

طريقة العمل: تضمنت الدراسة ستة و تسعون شخصا، ثمانية و خمسون من هؤلاء ثبتت إصابتهم جراحيا بمرض الأكياس العدرية و ثمانية و ثلاثون شخص صحي كسيطرة. تم جمع الدم من كل شخص. تم قياس معاملات الإنتاجية للخلايا الليمفاوية المحيطية باستخدام طريقة Lamberti *et al* لعام ١٩٨٣ .

النتائج: كانت معاملات الإنتاجية اقل معنويا في المرضى مقارنة بالأشخاص الأصحاء.

الاستنتاج: انخفاض نسبي في قيم معاملي الانقسام و التضاعف و تطور دورة انقسام الخلايا خلال الإصابة بمرض الأكياس العدرية. الانخفاض في قياسات الإنتاجية له علاقة بحالة عدم الاستجابة المناعية المتعلقة بهذا المرض.

مفتاح الكلمات: معامل الانقسام، معامل التضاعف، مرض الأكياس العدرية، الخلايا الليمفاوية المحيطة، طفيلي الأكياس العدرية

المجلة العراقية للعلوم الطبية ٢٠٠٤ م، المجلد ٤ ، العدد ٢ ، ص ١٤٠ ــ ١٤٣

استعمال قوة الاجتذاب للمضاد المناعي ج في تشخيص داء المقوسات الحاد عند النساء اللواتي يشكين من الاجهاض

مي محي الدين عباس، امجد نيازي (قسم طب المجتمع)، منال عدنان حبيب (قسم الاحياء المجهرية الطبية) كلية الطب- جامعة النهرين

الخلاصة:

خلفية الدراسة: داء المقوسات الحاد يعتبر احد الامراض المهمة لكونه ذا تاثير على الصحة العامة و خاصة على المراة الحامل و الجنين و ان استخدام الاختبارات المصلية هو الاكثر شيوعا في تشخيص الاصابة بهذا المرض.

هدف الدراسة: تشخيص الاصابة بداء المقوسات الحاد عند النساء اللواتي يعانين من الاجهاض الاولي.

طريقة العمل: اجريت دراسة مقطعية على (٣٣٠) امرأة تعاني من الاجهاض (اولي ومتكرر) و (٤٠) امرأة لا تعاني من الاجهاض تتراوح اعمارهم بين (١٦–٥٠) سنة. تم فحص جميع النساء بفحص الـ (ELISA) للمضاد المناعي نوع (م ، ج). تم فحص النساء اللواتي يعانين من الاجهاض الاولي والنساء اللواتي لا يعانين من الاجهاض لتشخيص داء المقوسات الحاد من خلال تواجد المضاد المناعي نوع م في حين فحصت النساء اللواتي يعانين من الاجهاض المتكرر بوساطة نسبة ظهور المضاد المناعي نوع ج في مصولهن. استعملت قوة الاجتذاب للمضاد المناعي ج في تشخيص داء المقوسات الحاد في مصول (٣٢) امرأة وهي طريقة حديثة للتشخيص.

النتائج: اظهرت النتائج ان نسبة تواجد الاجسام المضادة نوع م لطفيلي التوكسوبلازما بنسبة ٤٠,٣ ٪ عند النساء اللواتي يعانين من الاجهاض الاولي و ١٠٪ عند النساء اللواتي لا يعانين من الاجهاض بينما بلغت نسبة ايجابية الفحص عند النساء اللواتي يعانين من الاجهاض المتكرر ٦٠,٢٪ كان مؤشر قوة الاجتذاب قليل ويتراوح بين ٢,٤ – ٥٢,٦ ٪ بالنسبة الى ٢٠حالة تعاني من داء المقوسات الحاد، موجب IgM وسالب IgG. في ١٢ حالة كان IgM سالباً و IgG موجباً ، كان مؤشر قوة الاجتذاب عالياً ويتراوح بين ٣٥,٧– ٩٦,٦ ٪ . كانت حساسية هذه الطريقة ١٠٠٪ ودقتها ٨٣,٣ ٪.

الاستنتاج: ان اختبار قوة الاجتذاب للمضاد المناعي ج يعتبر ذو دقة و حساسية عاليتين لتشخيص الاصابة بداء المقوسات الحاد عند النساء اللواتي يعانين من الاجهاض الاولي.

مفتاح الكلمات: داء المقوسات، قوة الاجتذاب للمضاد المناعي ج، الاجهاض.

المجلة العراقية للعلوم الطبية ٢٠٠٤ م، المجلد ٤ ، العدد ٢ ، ص ١٤٤ ــ ١٤٧

قياس مستوى انزيم الادينوسين دي امينيز في مصل الدم عند الاطفال المصابين بالفايروس المضخم للخلية

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كلية الطب-جامعة النهرين

الخلاصة:
خلفية الدراسة: يعتبر الفايروس المضخم للخلية من الفايروسات أكثر شيوعا في تسببها للالتهابات في الاجنة و حديثي الولادة. النقصان في انزيم الادينوسين دي امينيز يؤدي الى عدم عمل الخلايا المناعية T و B مؤدية الى تثبيط المناعة و بذلك يزيد من احتمالية الالتهابات.

هدف الدراسة: هو قياس مستوى انزيم الادينوسين دي امينيز في مصل الدم عند الاطفال المصابين بالفايروس المضخم للخلية.

طريقة العمل: تم تشخيص الاصابة بالفيروس عن طريق التحري عن المضاد الخاص بالفايروس المضخم للخلية نوع IgMباستخدام الاليسا في٦٢ طفل يحملون الاعراض و ٥٠ طفل يبدون بصحة جيدة. تم قياس مستوى انزيم الادينوسين دي امينيز في مصل دم المصابين و غير المصابين.

الأستنتاج: كان معدل مستوى انزيم الادينوسين دي امينيز في الاطفال المصابين اقل معنويا (١٦و٣ ±٣٤و٣) عند المقارنة مع الاطفال الذين يحملون الاعراض أو لا يحملوها والذين اعطوا نتيجة سلبية لل IgM (٧٨و٧ ±٧١و٤) ($p<0.05$) و (٣٨و١٠ ±٥٤وه) ($p<0.05$) على التوالي.

الاستنتاج: يمكن الاستنتاج بان الاطفال المصابين بنقص في انزيم الادينوسين دي امينيز هم اكثر عرضة للاصابة بالفايروس المضخم للخلية.

مفتاح الكلمات: الفايروس المضخم للخلية، الادينوسين دي امينيز، الاطفال

الورم اللمفي الأولي للمعدة: ممارسة سريرية ١٩٩٤-٢٠٠٢

حكمت عبد الرسول حاتم، اكثم رشيد الصالحي، حامد هندي سرحان
(قسم الجراحة-كلية الطب-جامعة النهرين)

الخلاصة

هدف الدراسة: إن هدف البحث هو دراسة العلامات السريرية والمرضية والتحليلات النسيجية للوصول إلى تشخيص وعلاج أورام المعدة اللمفاوية.

طريقة العمل: تم دراسة حالة ١٧ مريض ادخل إلى مستشفى الكاظمية التعليمي في الفترة من آذار ١٩٩٤ وشباط ٢٠٠٢. البيانات التي تم جمعها كانت من أقسام الإحصاء والأورام والتحليلات النسيجية وكانت هذه البيانات تشمل التاريخ المرضى والعلامات السريرية والتحاليل المختبرية والنسيجية وطرق العلاج.

النتائج: أظهرت الدراسة إن نسبة الرجال إلى النساء هي ١ : ١و٤ ومعدل العمر هو بين ٦١ – ٦٥ سنة وان العلامات السريرية السائدة هي فقدان الوزن وفقر الدم وألام في البطن وان معظم الأورام توجد في منطقة بواب المعدة. نتائج التحليل النسيجي بينت أن معظم الأورام هي من نوع الأورام اللمفاوية واطئة الشدة. عشرة حالات عولجت جراحيا أما بقية المرضى (سبعة) منها من غير الممكن علاجهم جراحيا لتقدم الحالة.

الاستنتاج: أورام المعدة اللمفاوية هي أورام غير منتشرة بكثرة في المعدة ونسبة حدوثها ازدادت في الأعوام الماضية ولا يزال التداخل الجراحي وخاصة في المراحل الأولية للمرض هي طريقة العلاج الأولي وان استعمال المواد الكيماوية يستعمل في كل المرضى.

مفتاح الكلمات: ورم المعدة اللمفاوى الأولي، العلاج الكيماوي.

المجلة العراقية للعلوم الطبية ٢٠٠٤ م، المجلد ٤ ، العدد ٢ ، ص ١٥١ ـــ ١٥٤

دراسة اصابات الضفيرة العصبية في الرقبة لدى الاطفال حديثي الولادة

محمد ياسين حاجم، سنان حسن مكي (قسم جراحة الكسور-كلية الطب-جامعة النهرين)

الخلاصة

خلفية الدراسة: تحدث اصابات الضفيرة العصبية لدى الاطفال حديثي الولادة اثناء الولادات المتعسرة. يحدث الشفاء في معظم الاطفال المصابين بدون مضاعفات مستقبلية، ومع ذلك فأن العديد منهم لا يتم شفائهم بشكل كامل مما يؤدي الى حدوث تشوهات عظمية وعضلية وضعف في وظيفة الطرف العلوي.

طريقة العمل: اجريت دراسة لـ ٣٥ مريضاً من الاطفال حديثي الولادة محالين الى قسم جراحة العظام والكسور من قسم الولادة للفترة من كانون الثاني ٢٠٠٠ الى كانون الاول ٢٠٠١، للاشتباه باصابتهم بشلل في الضفيرة العصبية في الرقبة. اخذت معلومات من ذوي الاطفال ومن ملفاتهم .

اجريت هذه الدراسة لبيان نسبة حدوث اصابات الضفيرة العصبية لدى الاطفال ومتابعتهم لبيان درجة شفائهم.

النتائج: وجد ان نسبة حدوث الاصابات هي ٥,١٧ لكل ١٠٠٠ ولادة حية. حيث تم اكتشاف ٣٥ حالة اصابة للضفيرة العصبية. تمت متابعة المرضى لفترة تراوحت بين سنة الى سنتين.

وجد ان واحد وثلاثين مريضا(٨٨,٥٪) قد اكتسبوا الشفاء الكامل في حين ان اربعة مرضى (١١,٥٪) لم يكتسبوا الشفاء التام.

الاستنتاج: ان نسبة حدوث اصابات الضفيرة العصبية لدى الاطفال في العراق هي من اعلى النسب في العالم.كما ان نسبة الشفاء عالية ايضاً وهذا يعني انه يمكن معالجة معظم الحالات تحفظياً.

مفتاح الكلمات: الضفيرة العصبية في الرقبة، الأطفال حديثي الولادة، اصابات

المجلة العراقية للعلوم الطبية ٢٠٠٤ م، المجلد ٤ ، العدد ٢ ، ص ١٥٥ ــ ١٥٧

امراض كيس الصفراء عند الاطفال

حكمت عبد الرسول حاتم، حسين تركي ناجي (قسم الجراحة-كلية الطب-جامعة النهرين)

الخلاصة:
خلفية الدراسة: تعتبر امراض كيس الصفراء غير شائعة عند الاطفال، غير ان الدراسات الحديثة تؤكد ان هذه الامراض شائعة بما يكفي للتفكير بها عند اي طفل يشكو من الام في البطن او اليرقان.
هدف الدراسة: هدف هذه الدراسة هو مراجعة كل حالات عملية رفع كيس الصفراء عند الاطفال لمعرفة سبب العملية.
طريقة العمل: تمت مراجعة كل السجلات الطبية للاطفال الذين كانت اعمارهم ١٦ سنة فما دون واجريت لهم عملية رفع كيس الصفراء في مستشفى الكاظمية التعليمي ومستشفى الاسكان المركزي للاطفال للفترة مابين ١٩٩٨–٢٠٠٣.
النتائج: اجريت عملية رفع كيس الصفراء على ١٥ مريض. كان معدل الاعمار ٥ سنوات(النطاق ١–١٢ سنة). كان بينهم ٩ اولاد(٦٠٪) و ٦ بنات(٤٠٪). كان السبب وراء مرض كيس الصفراء هو امراض الدم عند ٨ مرضى(٥٣٪). التاريخ العائلي لامراض كيس الصفراء كان موجودا عند ٩ مرضى(٦٠٪). اجريت عملية رفع الطحال مصاحبة لعملية رفع كيس الصفراء عند ٥ مرضى(٣٣٪). حصلت مضاعفات ما بعد العملية لمريضين فقط (١٣٪).
الاستنتاج: امراض كيس الصفراء اصبحت تشخص بصورة متزايدة عند الاطفال. العامل الوحيد المهم للتشخيص هو الانتباه الى ان حصاة كيس الصفراء والتهابها تحصل عند الاطفال.

مفتاح الكلمات: عملية رفع كيس الصفراء، امراض كيس الصفراء، الاطفال.

المجلة العراقية للعلوم الطبية ٢٠٠٤ م، المجلد ٤ ، العدد ٢ ، ص ١٥٨ ـــ ١٦١

علاج هطول المستقيم في الأطفال و الرضع بحقن محلول الطعام عالي التركيز

حكمت عبد الرسول حاتم، حامد هندي سرحان، اكثم رشيد الصالحي
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الخلاصة

هدف الدراسة: ان الهدف من هذه الدراسة هو تحديد مدى فعالية طريقة معالجة هطول المستقيم الجزئي عند الرضع و الاطفال بحقنهم بمادة محلول الطعام العالي التركيز في الطبقة تحت المخاطية للمستقيم .

طريقة العمل: دراسة مستقبلية تضمنت مائة مريض من الرضع والاطفال يعانون من هطول المستقيم، تم علاجهم بنجاح باستعمال محلول ملح الطعام عالي التركيز (٣٠٪)، حيث تم حقن هذه المادة تحت غشاء بطانة المستقيم. تمت هذه الدراسة في قسم الجراحة العامة في مستشفى الكاظمية التعليمي خلال الفترة الممتدة من شهر تشرين الاول ١٩٩٨ و حتى شهر تشرين الاول عام ٢٠٠٢. اربع و تسعون حالة تمت معالجتها في الاستشارية الجراحية، اما الثمان حالات المتبقية فقد عولجت كحالات يومية و تحت التخدير العام .

النتائج: ثلاث وسبعون مريضا كانوا ذكورا وسبع وعشرون مريضا منهم كانوا اناثا أي ان نسبة الذكور الى الاناث كانت ٧و٢ : ١ . أعمار المرضى تتراوح بين ستة اشهر الى ثلاثة عشر سنة .اكثر المرضى كانت أعمارهم تتراوح بين سنة الى ثلاث سنوات ويشكون نسبة (٧٤٪) ، فترة الاعراض تتراوح من شهر الى سنتين مع نسبة (٤٧٪) منهم نمت أعراضهم في غضون شهرين الى ثلاثة اشهر من بداية ظهور المرض. الاسهال المزمن كان العامل المسبب الرئيسي و شكل نسبة (٥٥٪) من الحالات. من مجموع مائة مريض مصابون بهطول المستقيم والذين عولجوا بالحقن الموضعي فأن اربع وتسعون مريضا (٩٤٪) اكتسبوا الشفاء من الجلسة الاولى بينما ستة مرضى (٦٪) احتاجوا الى جلسة ثانية. لم يحتاج أي مريض الى جلسة ثالثة. المعدل الكلي لنجاح هذا العلاج (١٠٠٪). لم تكن هناك اية مضاعفات ذات اهمية.

الاستنتاج: معالجة هطول المستقيم الجزئي عند الرضع و الاطفال بحقنهم بمادة محلول الطعام العالي التركيز في الطبقة تحت المخاطية للمستقيم هي طريقة فعالة و سهلة و أمينة و بدون مضاعفات. الفوائد الرئيسية من استعمال طريقة العلاج هذه هي توفر المادة وسهولة تحضيرها و رخص سعرها وسهولة حقنها كونها لا تحتاج الى حقنة خاصة، كذلك امكانية استعمال هذه الطريقة العلاجية في الاستشارية الجراحية .

مفتاح الكلمات: هطول المستقيم، الحقن، محلول الطعام عالي التركيز.

المجلة العراقية للعلوم الطبية ٢٠٠٤ م، المجلد ٤ ، العدد ٢ ، ص ١٦٢ ـــ ١٦٦

التغيير الموسمي لمتلازمة كيليان بارى في العراق

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الخلاصة
خَلفِيَّة الدراسة: تُعتبر متلازمة كيليان بارى من أمراض اضطراب المناعة المُثار بواسطة عدوى فايروسيّة أو بكتيريّة سابقة. ربّما قد يُسَاهِمُ تنوّع العدوى السابقة فى التباين السَرِيرِيّ و المناعى لهذه المتلازمة. لا تغيير موسميّ في حدوث أعراض متلازمة كيليان بارى وُجِدَ في العديد من الدراسات دَاخل أكثر البُلْدَان الغربيّة. لكن كَانَ هناك تفوق موسميّ مَوْجُود في تايوان، السويد و العربية السعودية.
هدف الدراسة: تُقَيِّمَ توزيع عدد الحالات الداخلة إلى المستشفى خلال أشهر السنة ولعدة سنوات كتغيير موسميّ هامّ في حدوث متلازمة كيليان بارى.
طريقة العمل: تسجيل مُعَدَّل الدخول الشهريّ لمُرَضى متلازمة كيليان بارى المُسَجَّل في ارشيف مستشفى الكاظمية التعليمى للفترة من ١٩٩٣–١٩٩٥ و ١٩٩٩–٢٠٠١. شَخَّص المُرَضى إستنادا إلى معاييرأزبرى. لما مجموعه ٩٨ مَريض دُرِسَ العمر، الجنس و التوزيع خلال أشهر السنة.
النتائج: التحليل الإحصائيّ لعدد الحالات الداخلة إلى المستشفى من مرضى حدوث متلازمة كيليان بارى فى كلّ أشهرالسنة بواسطة رفض فرضيّة لاتغييرفي ذبذبة أدخال المرضى بمعدل ثمانية كل شهر بواسطة(P =٠,٠٠٧) كَانَ هناك تغيير موسمىهامّ مع بالغ الذروة في مايو/أيار و يونيو/حزيران.
كَانَ العدد الأكبر لمرضى متلازمة كيليان بارى في الدراسة تحت عمر العشرون السنة مع نسبة الذكورللأناث ٢:٣.
الأستنتاج: كَانَ هناك تغيير موسميّ هامّ في حدوث متلازمة كيليان بارى هامّ مع حدوث بالغ الذروة في مايو/أيار و يونيو/حزيران.

مفتاح الكلمات: متلازمة كيليان بارى

المجلة العراقية للعلوم الطبية ٢٠٠٤ م، المجلد ٤ ، العدد ٢ ، ص ١٦٧ ــ ١٧٠

مراجعة ٢١٠ طفلا مصابا بداء السكرى يراجعون عيادة مرض السكري لدى الاطفال في مستشفى الكاظمية التعليمي للفترة ١٩٩٠-٩٩٩.

نشأت عزيز نشأت، شذى حسين علي (قسم طب الأطفال)، نمير غانم الطويل (قسم طب المجتمع) كلية الطب-جامعة النهرين

الخلاصة

خلفية الدراسة: مرض البول السكرى المنوط بالانسولين احد الامراض المزمنة والغير منعكسة والتى تؤدي الى مضاعفاات كبيرة لدى الاطفاال.

هدف الدراسة: لدراسة بعض العوامل المرتبطة بمرض البول السكري المنوط بالانسولين

طريقة العمل: تمت مراجعة ٢١٠ طفلا مريضا جديدا بمرض البول السكري المنوط بالانسولين واللذين راجعوا عيادة مرضى السكري لدى الاطفال في مستشفى الكاظمية التعليمي خلال الفترة(كانون الثاني ١٩٩٠– كانون الأول ١٩٩٩).

النتائج: كان معظم المرضى(٨٢,٨٪) اعمارهم (٦–١٤ سنه) بينما القله (١,٤٪) كانت اعمارهم اقل من سنتين و نسبة الذكور الى الاناث (١/١,٣). التاريخ الاسري لمرض البول السكري المنوط بالانسولين كان موجودا في العائلة بنسبه (٥,٧٪) من الحالات. كان اكثر من نصف الحالات(٥٩٪) يعيشون في المدن بينما الباقي في مناطق ريفيه، و معظم المرضى (٧٣,٨٪) كانوا يعانون من اعراض تقليديه لمرض البول السكري المنوط بالانسولين بينما الباقي يعانون من حموضه كيتونيه سكريه وحوالي ٣/١ المرضى اصيبوا بالمرض في فصل الشتاء و ١٦ مريضا كان لديهم امراض فايروسيه قيل بدايه المرض مع اضطرابات انفعاليه.

الاستنتاج: العوامل التي وجدت مرتبطه بمرض البول السكري المنوط بالانسولين لوحظت تزداد مع ازدياد العمر، الجنس الذكري، التاريخ العائلي، و فصل الشتاء.

مفتاح الكلمات: **داء البول السكري، الاطفال، مراجعه**.

المجلة العراقية للعلوم الطبية ٢٠٠٤ م، المجلد ٤ ، العدد ٢ ، ص ١٧١ ـــ ١٧٤

الربو القصبي لدى الاطفال وتأثيره على النمو

حسام محي العلواني، نشأت عزيز نشأت، نهلة الكبان
(قسم طب الأطفال-كلية الطب-جامعة النهرين)

الخلاصة:

خلفية الدراسة: الربو هو مصطلح طبي شامل والذي يتضمن انسداد المجاري الهوائية القابل للانبراء ويتسبب بوسائل مختلفة. الربو هو أكثر الامراض المزمنة شيوعاً لدى الاطفال، ولقد زادت نسبة الاصابة به والوفيات الناتجة عنه خلال العقدين الماضيين بدون سبب واضح. شدة تحسس القصبات والتي ينتج عنها تضيق القصبات بعد الاصابة بالبرد او التمرين او الغبار او الرائحة القوية او العطور او دخان السجائر او الهواء البارد او بعض الادوية ... الخ. هل يؤثر الربو على نمو الطفل، ولو كان هذا صحيحاً، هل له علاقة بشدة الربو؟

هدف الدراسة: دراسة نمو الطفل. أي قياس اوزانهم واطوالهم وقياس محيط الرأس، ودراسة تأثير مرض الربو على نمو الاطفال وهل هناك علاقة مع شدة المرض لديهم.

طريقة العمل: اخذت عينة من (١١٠) طفل مصاب بالربو القصبي واخضعوا لدراسة مؤشرات النمو لديهم (الطول، الوزن ومحيط الرأس) وقيمت هذه القراءات بجدول النمو العالمي (Centile Chart) وقيمت شدة الربو لديهم حسب مقاييس سريرية معينة ودرست حالة تأخر النمو مع شدة المرض.

النتائج: بينت الدراسة ان هناك (١٦,٢٨ ٪) من المرضى المصابين بربو خفيف تقع اوزانهم على (١٠٪) من سلم النمو (Centile) بينما (٤٤,١٨ ٪) على النمو المتوسط (٥٠٪) و (٣٩,٥ ٪) على الـ (٩٠٪) من السلم (Centile) . اما في حالة الربو المتوسط فـ (١٢,٢٤٪) يقع على الـ (١٠٪) من السلم و (٦٧,٣٤٪) على الـ (٥٠٪) من السلم و (٢٠,٤) على الـ (٩٠٪) من السلم. اما في حالة الربو الشديد يقع (٥٠٪) على الـ (١٠٪) من الجدول و (٣٨,٨٪) على الـ (٥٠٪) و (١١,١١٪) على الـ (٩٠٪) من سلم النمو. بالتحليل الاحصائي بمعامل (qui) هناك نقص بالوزن لدى المريض مع زيادة شدة الربو ($P<0.05$) أي هناك تأخر بالنمو بصورة اكبر (الوزن) لكن لم يتأثر الطول ومحيط الرأس كثيراً كما في الوزن. أي كلما زادت شدة الربو كلما كان التأثير سلبياً على النمو.

الاستنتاج: الربو القصبي المزمن يؤثر على نمو الاطفال خاصةً في الحالة المتوسطة والشديدة من حالات الربو.

مفتاح الكلمات: الربو القصبي، النمو، شدة الربو

المجلة العراقية للعلوم الطبية ٢٠٠٤ م، المجلد ٤ ، العدد ٢ ، ص ١٧٥ ــ ١٧٨

تناول المواد غير الغذائية عند الأطفال

فارس بكر الصواف (قسم طب الأطفال-كلية الطب-جامعة الموصل)

الخلاصة:

أهداف البحث: التعرف على مدى انتشار هذه الظاهرة عند الأطفال، التعرف على بقية أعراض سوء التغذية المصاحبة لهذه الظاهرة مثل فقر الدم والكساح، التعرف على مدى انتشار الديدان عند هؤلاء الأطفال.

التصميم: دراسة سريرية.

المشاركون والمكان: الأطفال الذين تتراوح أعمارهم بين ١٠-٣٦ شهر والذين زاروا العيادة الخاصة لمدة ثلاث سنوات. أخذت كافة المعلومات من الأمهات وتم الفحص الدقيق للأطفال، أخذت عينة من الدم من ١٦٠ طفلا وتم فحص البراز للديدان من ٤٢ طفلاً.

النتائج: وجدت ظاهرة تناول المواد غير الغذائية في ١١,٥٦٪ من هؤلاء الأطفال الذين تتراوح أعمارهم بين ١٠-٣٦ شهر، ٦٧٪ من الأطفال كانوا من عوائل تبدو وبأنها فقيرة. ٦٢٪ من هؤلاء الأطفال كانت لديهم علامات الكساح المتعددة، جميع هؤلاء الأطفال كان لونهم شاحباً وأوضحت نتائج فحص الدم بأن فقر الدم لديهم كان على الأغلب نتيجة نقص الحديد. ١٤,٣٦٪ من هؤلاء الأطفال كانوا يعانون أيضا من الديدان الدبوسية. وتضخم الطحال وجد في ٦,١٪ منهم.

الاستنتاج: ظاهرة تناول المواد غير الغذائية هي مشكلة منتشرة عند الأطفال ويصاحبها كثيرا فقر الدم والكساح والتعرض للإصابة بالديدان.

مفتاح الكلمات: تناول المواد غير الغذائية، فقر الدم، الكساح، الديدان الدبوسية.

المجلة العراقية للعلوم الطبية ٢٠٠٤ م، المجلد ٤ ، العدد ٢ ، ص ١٧٩ ــ ١٨١

خبرة علاج الحمل خارج الرحم بواسطة التنظير الجراحي

محمد غني جابك (مستشفى العلوية للولادة التعليمي)

الخلاصة

هدف الدراسة: الحمل خارج الرحم هو حصول الحمل في مكان خارج التجويف الرحمي و في ٩٩ ٪ من حالاته يحصل في قناة فالوب. و الإحصائيات تشير الى حصوله بنسبة واحد الى ١٥٠ حمل كامل في المملكة المتحدة ولكنها أعلى في بلدان أخرى مثل فرنسا والولايات المتحدة و النسبة في تزايد في العالم ولكن الوفاة بسبب هذه الحالة في تناقص.

علامات الحمل خارج الرحم متباينة، فقد تكون حالة طارئة جدا وتحتاج لعملية جراحية مستعجلة ولكن في اكثر الأحيان تكون علامات الحالة غير حادة و في بعض الأحيان خاصة" قبل انفجار القناة الحاوية للحمل قد تشخص بصورة عرضية مثلاً خلال الفحص السريري أو الفحص بواسطة الأمواج فوق الصوتية لحالات أخرى.

نتائج العلاج لحالات الحمل خارج الرحم بواسطة التنظير الجراحي متقاربة لتلك النتائج بواسطة الجراحة التقليدية من ناحية الخصوبة المستقبلية ولكن نسبة تكرار الحمل خارج الرحم اقل جزئيا.

يعتبر التنظير الجراحي في الوقت الحاضر الطريقة المثلى لعلاج الحمل خارج الرحم.

طريقة العمل: من شهر كانون الثاني ٢٠٠٠ لغاية كانون الثاني ٢٠٠١ تم علاج ١٢ حالة حمل خارج الرحم بواسطة التنظير الجراحي في مستشفى العلوية التعليمي للولادة و كان متوسط عمر المرضى هو ٢٧ سنة (٢٢ – ٣٤ سنة). تم أجراء التنظير للتشخيص اولا" و من ثم اجراء العملية بالتنظير الجراحي أما بالعلاج التحفظي او العلاج الجذري.

النتائج: تم علاج جميع الحالات المشمولة بالدراسة (١٢) حالة بواسطة التنظير الجراحي. منها ٧ حالات (٥٨,٣ ٪) انفجار الحمل في التجويف البطني و ٤ حالات (٣٣,٣ ٪) حمل خارج الرحم قبل انفجار القناة و قد شخصت بواسطة التنظير، و واحدة فقط هي حالة إجهاض للحمل من خلال بوابة قناة فالوب. كانت إصابة الأنبوب الايمن في ٦٦,٦ ٪ (٨) حالات و الجانب الأيسر في ٣٣,٤ ٪ (٤) حالات. نجح العلاج التحفظي في سبعة حالات ٥٨ ٪ واحتاجت خمسة حالات ٤٢٪ لاجراء أستئصال جزئي للانبوب (العلاج الجذري). تم أخراج جميع المرضى الى البيت في أقل من ٢٤ ساعة و لم تحصل أية مضاعفات أو أختلاطات. و قد حصل الحمل في أربع حالات من التي عولجت بواسطة التنظير الجراحي خلال ٦ أشهر من العملية.

الأستنتاج: التنظير الجراحي أحدث ثورة في الجراحة خاصة" في علاج الحمل خارج الرحم من حيث التشخيص والعلاج و قد بدأت عمليات علاج الحمل خارج الرحم بالتنظير الجراحي في أوائل السبعينات من القرن الماضي في فرنسا و الولايات المتحدة. و قد أثبتت البحوث المتعددة التي أجريت بأن التنظير الجراحي متفوق على الجراحة التقليدية من حيث الدقة في أجراء العملية، و السرعة في الخروج من المستشفى و الشفاء بالاضافة لنتائجه الممتازة من

الناحية الجمالية مع التذكير بإمكانية أجراء التنظير الجراحي في جميع الحالات ماعدا حالات أنخفاض ضغط الدم الشديد (الصدمة الجراحية).

مفتاح الكلمات: التنظير الجراحي، الحمل خارج الرحم، العلاج التحفظي للحمل خارج الرحم، العلاج الجذري للحمل خارج الرحم

زائدة دودية مضاعفة

اكثم رشيد الصالحي، اباء محمود صبري (قسم الجراحة-كلية الطب-جامعة النهرين)

الخلاصة

مريض ذكر عمره ٣١ سنة يشكو من أعراض التهاب الزائدة الدودية ، أجريت له عملية جراحية فتبين أثناء العملية وجود زائدتين دوديتين واحدة تقع خلف الأعور منفجرة في التجويف البريتونى والأخرى وجدت تحت الأعور. تم استئصال الزائدتين مع وضع أنبوب تصريف في البريتون. حالة المريض بعد العملية كانت مستقرة.

مفتاح الكلمات: التهاب الزائدة الدودية،زائدة دودية مضاعفة.

المجلة العراقية للعلوم الطبية ٢٠٠٤ م، المجلد ٤ ، العدد ٢ ، ص ١٨٧ ــ ١٨٨

المجلة العراقية للعلوم الطبية
قائمة المحتويات

مقالات مبتكرة