Al-Nahrain University / College of Medicine

Department of Surgery

Plastic surgery

The efficacy of Silver Sulfadiazine Versus Acetic Acid On Pseudomonas Wound Infection

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Dedication

To all whom had been there

for their love and support

To my family .

بسم الله الرحمن الرحيم

"وَقُل رَّبِّ زِدْنِي عِلما "

سورة طه/آية 114

صدق الله العظيم

Abstract

Background:

Pseudomonas aeruginosa is a significant cause of pressure sores ulcers, skin and soft tissue infections.

With current emerging of multidrug resistance strains of pseudomonas bacteria , the light should be directed toward using topical agents such as acetic acid which provides simple , cheap , and safe method to eradicate pseudomonas from pressure sores ulcers , and others.

Aim:

To verify the effectiveness of the diluted acetic acid in the treatment of the pseudomonas pressure sores infections in comparison to the silver sulfadiazine effects.

Patients and method:

A prospective study that was done randomly on 8 infected pressure sores ulcers in 5 Iraqi patients (consist of 3 men and 2 women) in the medical ward at Al-Imamain Al-khadimain medical city , from the 4th of November \ 2018 to the 19th of march \ 2019.

All patients were diagnosed as cases of pseudomonas pressure sores infection , depending on culture swab of the wounds.

Silver sulfadiazine was applied to the ulcers for 1-2 weeks, till culture swab confirmed the resistance of the bacteria to silver sulfadiazine, then diluted acetic acid applied and continued to the same period of silver sulfadiazine application.

The clinical improvement and culture swab results were compared between the effects of the two agents.

Results:

Conclusion:

Acetic acid is to be kept in mind as one of the alternatives when infection is caused by multiple antibiotic resistant strains of P. aeruginosa, which has the advantage of being cheap, safe, and available.

At a time when bacterial resistance to antibiotics is a matter of increasing concern , the value of topical agents such as acetic acid should not be forgotten.

Introduction

- The skin is the largest organ in the body.
- The skin is composed of three major tissue layers, the epidermis, dermis and hypodermis, and also of various structures known as appendages.

- The epidermis is the outermost, protective layer of the skin. The thick dermis lies beneath this layer and contains most of the skin appendages. The hypodermis lies beneath the dermis and is predominantly composed of adipose tissue (as shown in figure 1).

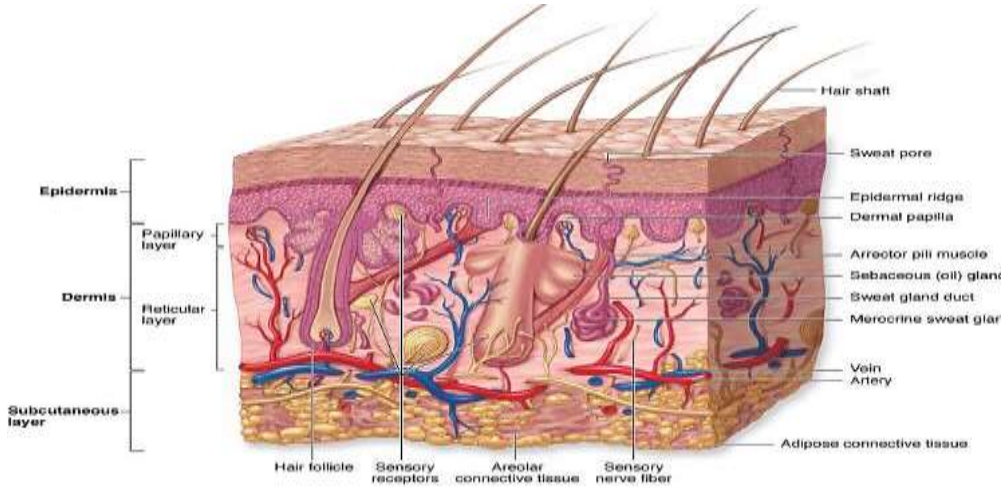

Figure (1): showing skin anatomy and histology.

- - Some of the functions carried out by this organ include physical protection, protection against ultraviolet light, protection against microbial invasion, prevention of fluid loss, regulation of body temperature, sensation , immunological surveillance, aesthetics and communication ,though one of the functions of the skin is physical protection, it is liable for breakdown and this is called wounding, wounding is the loss of continuity of epithelium, with or without loss of underlying connective tissue (i.e. muscle, bone, nerves)[1]

- Pressure ulcer is one of the forms of wounding.
- pressure sore is localized soft-tissue injury resulting from prolonged unrelieved pressure, usually over a bony prominence.

- Factors contributing to the development of pressure sores include: decreased mobility, decreased sensation, spasticity, shearing forces, friction, and moisture. Compression of soft tissue impairs lymphatic drainage, leading to edema, ischemia, and other conditions favorable to colonization and infection by microorganisms.

- Both pulmonary and urinary sources cause seeding and subsequent infection of pressure sores.

- Indwelling bladder catheters or self-catheterization programs can result in urinary sepsis in one-third of paraplegic patients. If left untreated, urinary infections can be a constant source of bacteremia.

- The most widely accepted pressure sore staging system was revised by the National Pressure Ulcer Advisory Panel in 2007 to include the original four stages and an additional two stages regarding deep tissue injury and unstageable pressure sores.

1. **Stage I: includes intact skin with non-blanching erythema.**
2. **Stage II: includes partial-thickness loss of dermis.**
3. **Stage III: includes full-thickness tissue loss.**
4. **Stage IV: includes exposed bone, tendon, or muscle.**

- Additional classification includes suspected deep tissue injury, usually characterized by maroon localized intact skin or blood-filled blister, and unstageable, which is a full-thickness ulcer with eschar at the base.
- Limitations exist in this system include; signs like skin erythema can be present in more than one stage and dark skin pigmentation can actually obscure the presence of erythema, necessitating other diagnostic signs like increased skin temperature, edema, and induration, to accurately stage the wound.

- Pressure sores may or may not present with local infection (deep or superficial), the removal of all nonviable tissue is the essential first step, after a soft-tissue debridement, a specimen should be sent to the microbiology laboratory to assess not only the bacterial types and sensitivities but also for quantitative culture.

- A result of more than 100,000 organisms per gram of tissue is diagnostic for invasive infection and is predictive of failure of surgical closure.

- Swab cultures are generally discouraged because they often represent only surface contaminants.

- Indicators of infection include ‘serous exudate with erythema’, ‘swelling with increase in exudate volume’, ‘oedema’, ‘increase in local skin temperature’ and ‘unexpected pain/tenderness [2].

- Pseudomonas aeruginosa is a classic opportunistic pathogen with innate resistance to many antibiotics and disinfectants. It is resistant to some common antiseptics and disinfectants such as quaternary ammonium compounds (e.g., cetrimide and benzalkonium chloride), chloroxylenol and hexachlorophane. Its isolation has been reported from povidone-iodine, chlorhexidine, dettol and savlon solutions used in hospitals [3].

- In recent years, P. aeruginosa has acquired significance as an important cause of nosocomial infections because of its ability to survive in the hospital environment and because of its ability to develop resistance to antimicrobial agents. It is ubiquitous in the hospital environment and is the most frequently isolated non fermentative bacillus from various clinical specimens. It can infect almost any external site or organ in the body. It is a significant cause of burn wound infections, and skin and soft tissue infections and is associated with high morbidity, increased stay in the hospital and increase the cost of treatment because of its resistance to a variety of antipseudomonal agents commonly available.

- What has increased the mud wetness is that the increase in the frequency of strains resistant to several antimicrobial agents have been reported [4]. In spite of continuing introduction of potent antipseudomonal agents, it is the most difficult nosocomial pathogen to be eliminated from infection site. Growing resistance to antimicrobial agents seriously hampers the therapy of pseudomonas infections. The incidence of such multiple drug resistant isolates remains very high in burn units. P. aeruginosa is the most

commonly encountered and most difficult to eradicate, needs special attention, if uncontrolled, becomes life threatening. There is a substantial evidence that excessive use of antibiotics promotes the selection, propagation and maintenance of antibiotic resistant microbes, especially in the hospital environment. In the recent times, the advent of new antimicrobial agents has helped to decrease the seriousness of many types of infections but in case of nosocomial infections caused by P. aeruginosa, the results have been less satisfactory and still the nosocomial infections caused by P. aeruginosa present a serious problem. The burn wound infections and, skin and soft infections caused by P. aeruginosa are very difficult to treat, in spite of availability of newer antibiotics with broad spectrum of activity. Thus, P. aeruginosa continues to create a threat to patient care [5].

The optimal topical treatment is a balance between microbicidal activity and tolerability. Generally, highly reactive antiseptics are estimated as too toxic (though there are reports on the usability of agents like hypochlorous acid). Modern antiseptics are less reactive and need a little longer killing times against pathogens but are still efficient.

To the clinician it is obvious that reducing the number of bacteria in wounds is ultimately aimed at accelerating wound healing. The antiseptic management has a dichotomous history anchored in tradition and science. It is an integral part of the management of acute as well as chronic wounds [6]. The ideal topical therapy is aimed at reduction of bacterial contamination

and removal of soluble debris without adversely affecting cellular activities vital to wound healing process. Although several studies support the value of topical antimicrobial agents, many commonly used antiseptic agents are not approved for use in wound infections. The safety and efficacy of many antiseptics as topical agents for local wound care is a questionable issue. A number of experimental studies both in vitro and in animal wounds suggest that many antiseptic agents including iodine, chlorhexidine, hydrogen peroxide, alcohol, silver sulfadiazine, mefenide acetate, sodium nitrate, sodium hypochlorite, etc. may be toxic to the cells involved in wound healing process. Available experimental data suggest that the antiseptics such as hydrogen peroxide and iodine are not only toxic to fibroblasts but also potentially retard the contribution of fibroblasts in healing process. Repeated and excessive treatment of wounds with antiseptic agents, except for short-time application to attack the causative pathogens and to control the infection, may have negative outcomes or promote a microenvironment similar to those found in chronic wounds [7].

Silver sulfadiazine has a broad spectrum of antibacterial, antifungal and antiviral activity. It is the most commonly used antiseptic agent in burn wound management but it is toxic to fibroblasts in culture. Also, it requires frequent dressing changes, delays re-epithelization and stains tissue. It may also cause allergic reaction and transient leucopenia [8].

As reported by various workers, these agents are cytotoxic, retard healing and can do more harm than good when they are not used in a proper concentration. They can interfere with the normal healing process, are toxic to fibroblasts and may permit more virulent microbes to dominate [9]

A variety of chemical agents are available, which are nontoxic, inexpensive and highly effective against nosocomial strains of P. aeruginosa .

The topical use of various organic acids such as boric acid, ascorbic acid, citric acid, salicyclic acid and acetic acid for elimination of P. aeruginosa from skin and soft tissue infections and from burn infections has been reported by various workers.

The use of acetic acid has been reported as potent topical agent for the treatment of pseudomonas infections of burns and, skin and soft tissue infections. Dilute acetic acid is used for the treatment of chronic wounds. It is effective against Gram-negative bacteria, especially against P. aeruginosa. Clinical antibacterial efficacy requires a concentration of a 0.5% at least. Though, the results of in vitro studies indicate that acetic acid is toxic to fibroblasts, these results are not considered as decisive. As acetic acid is well tolerated in vivo and gives better results in the treatment of wound infections caused by P. aeruginosa, its use has been reported from time to time as an effective topical agent [10]

Aim of the study:

To verify the effectiveness of the diluted acetic acid in the treatment of the pseudomonal pressure sores infections in comparison to the silver sulfadiazine effects.

Patient and methods

Study design: this is a prospective study that was done randomly on 8 infected pressure sores ulcers in 5 Iraqi patients (consist of 3 men and 2 women) in the medical ward at Al-Imamain Al-khadimain medical city , from the 4th of November \ 2018 to the 19th of march \ 2019.

For each patient, the form shown in table (1) was filled, wound swabs were taken prior to ulcer dressings, photographs were taken also.

Table (1): The patient document.

Name	
Age	
Gender	
Date of admission	
Date of taking history	
Cause of the ulcer	
Site of the ulcer	
Duration of the ulcer	

Grade and degree	
Co morbidities	
Clinical Signs of infection	Redness Hotness Tenderness Indurated edges discharge
Duration of infection	
Previous drugs	
Associated illnesses	
Culture and sensitivity	
Treatment	
Side effects of the local treatment	
Duration until micro-oraganism was cleared	
Duration until healthy granulation tissue formed	

The study was designed to take a wound swab from pressure sores before washing the ulcer sites with normal saline.

The wound swab was sent for culture and sensitivity to prove that there is pseudomonas resistance to silver sulfadiazine as proved by a previous trials period of frequent silver sulfadiazine wound dressings.

The ulcer sites were washed with normal saline, adding a sterile gauze containing silver sulfadiazine cream each 6 hours, last for 1 week duration, taking culture swab till having a proved silver sulfadiazine resistant pseudomonas infection, discontinued silver sulfadiazine then wound swabs were taken before and after application of acetic acid.

In these patients, ulcer sites also washed first with normal saline then a sterile gauze soaked in 1% diluted (1:3 natural acetic acid to distilled water) natural acetic acid (as shown in figure 2), replaced each 6 hours, the wound dressing and culture swab were continued till the improvement showed in form of absence purulent and foul smelling discharge, regression of inflammatory features (as shown in figure 3) and swabs yielded no growth of bacteria .

In our study, there were no surgical debridement, and the patients were under systemic antibiotic cover.

Figure (2): shows the natural acetic acid used in the treatment.

A B

Figure (3): shows chronic infected pressure sore ulcer in an 54- years old male

(A): ulcer site after application silver sulfadiazine and before acetic acid applying.

(B): ulcer site after 1 week of acetic acid application.

Results:

The study showed that pressure sores were more common in males (as shown in figure 4):

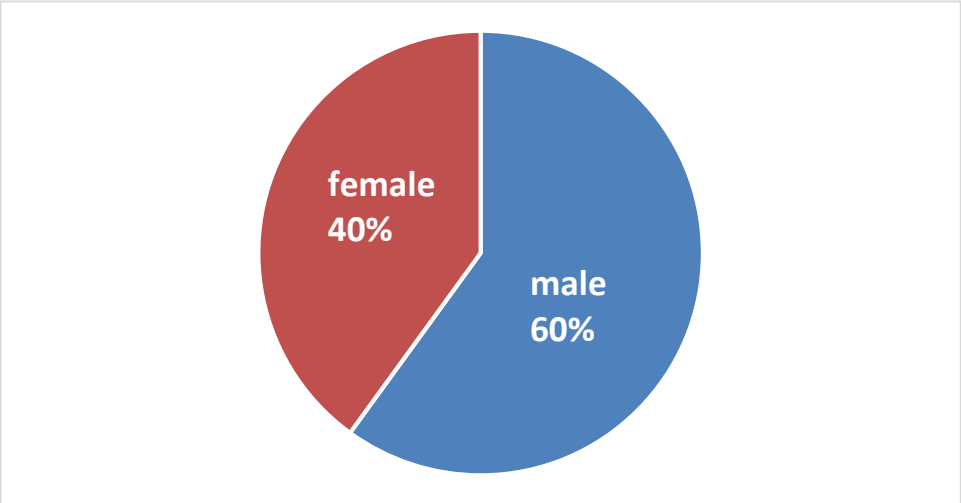

Figure (4): show the distribution of patients according to gender

It also showed that pressure sores were less common among patients who are less than 60 years old (as shown in figure 5):

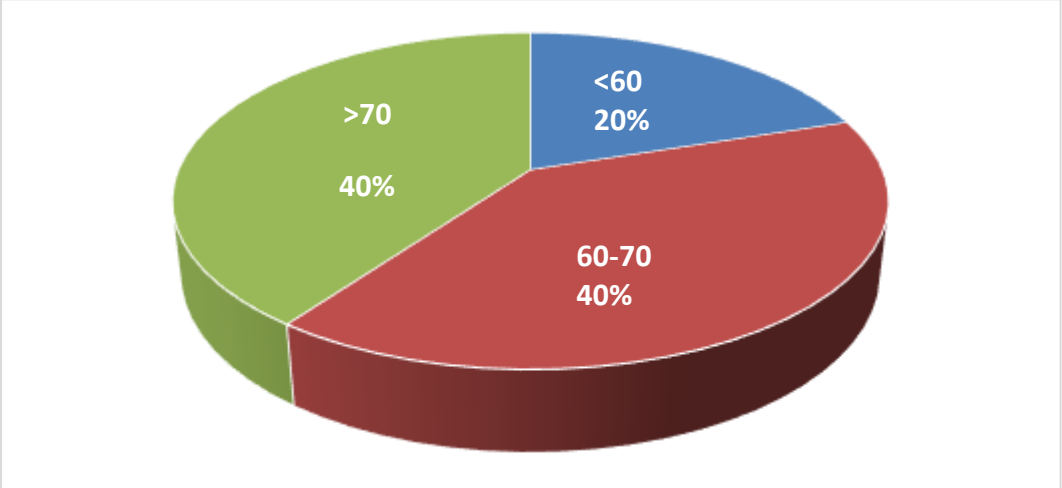

Figure (5): show the distribution of patients according to age.

In this study the ulcers were mostly between (2-3) weeks duration (as shown in figure 6):

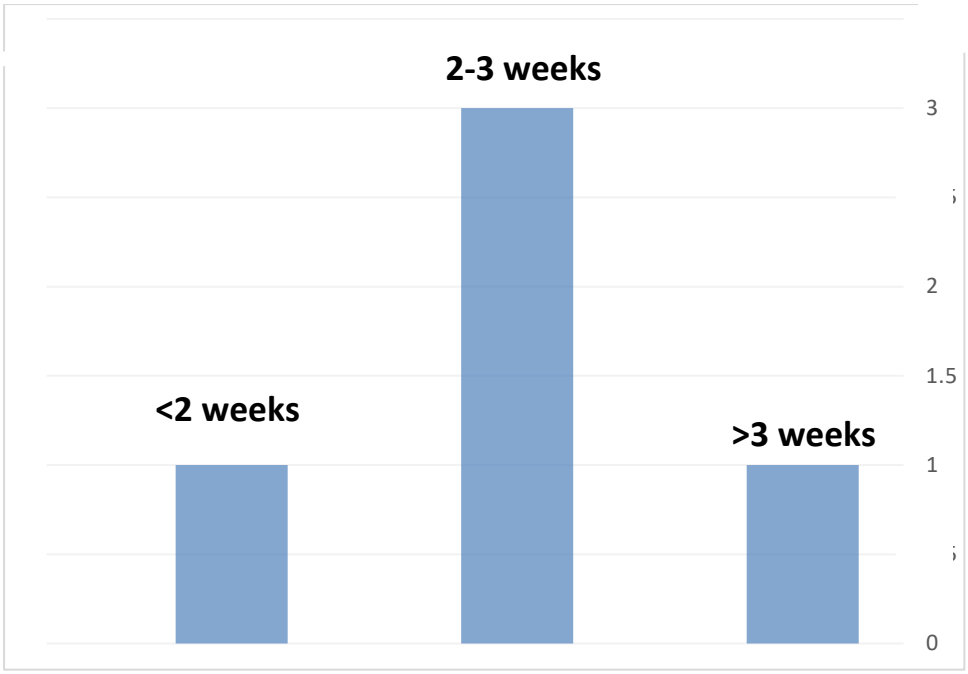

Figure (6): show the distribution of ulcers according to the duration.

Most of ulcers in were of stage II (as shown in figure 7):

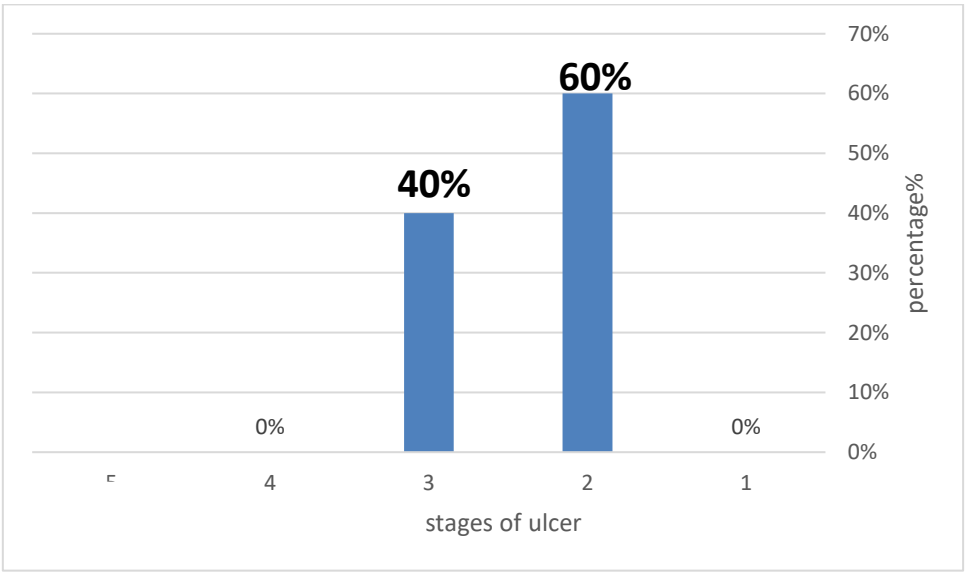

Figure (7): show the distribution of ulcers according to stage

Also this study showed that most of ulcers were on the sacrum and the greater trochanter (as shown in figure 8):

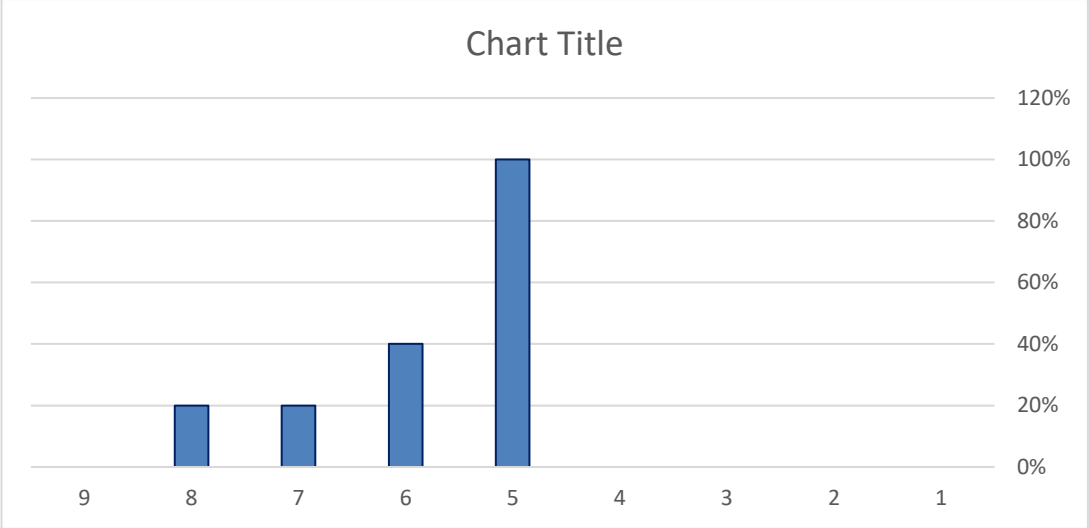

Figure (8): distribution of ulcers according to the site.

1. occiput
2. upper back and shoulder
3. lower back
4. malleoli
5. sacrum
6. greater trochanter
7. ischium
8. buttock

This study shoes a proven culture -ve for pseudomonas infected ulcer treated by silver sulfadiazine by 25% (as shown in figure 9):

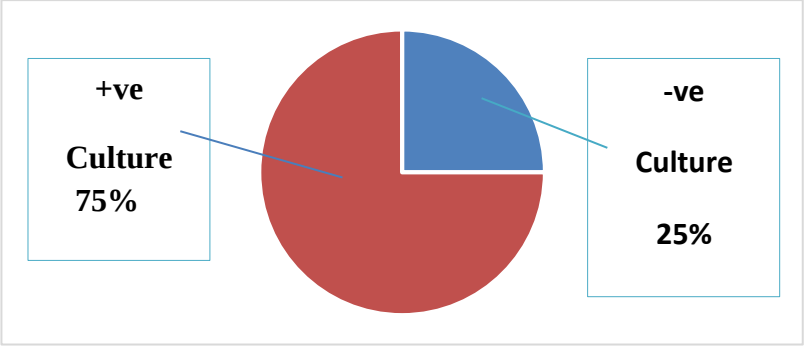

Figure (9): frequency of culture –ve for pseudomonas infected ulcer treated by silver sulfadiazine.

This study shows a proven culture –ve for pseudomonas infected ulcer treated by acetic acid by 60% (as shown in figure 10):

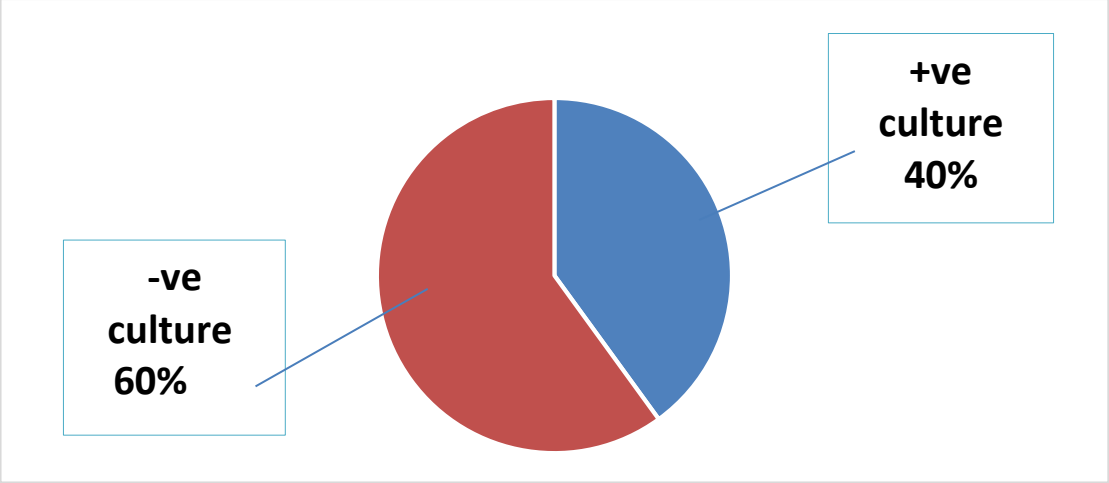

Figure (10): frequency of culture - ve for pseudomonas infected ulcer.

this study shows that most common side effect of silver sulfadiazine usage is the cost (as shown in figure 11) :

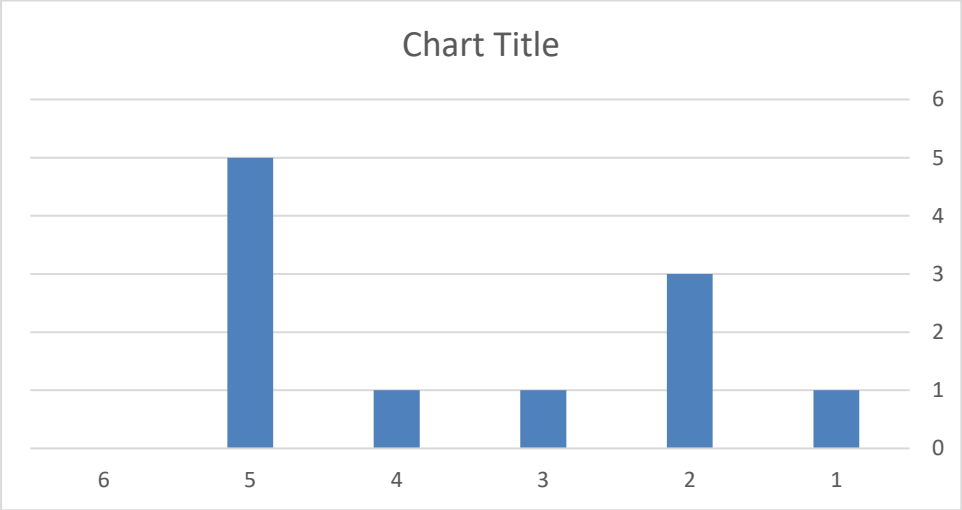

Figure (11): distribution of the side effects of silver sulfadiazine application

1. Bad odor
2. Cost

3. Pain
4. Burning
5. Delay time for healing

This study shows that bad odor was the most common side effect for using acetic acid in the process of treatment (as shown in figure 12):

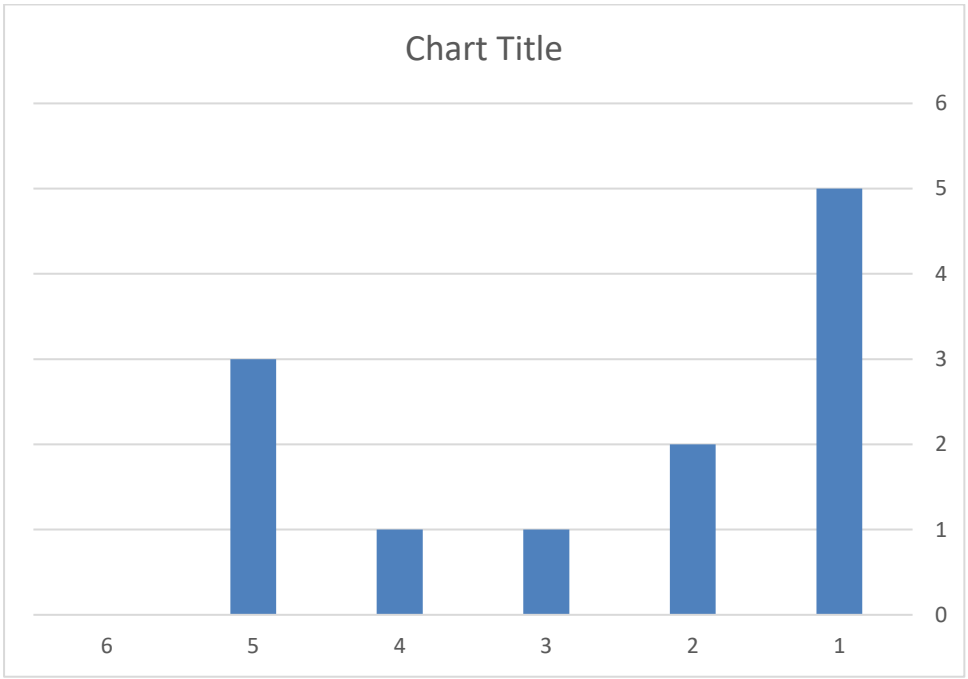

Figure (12): distribution of the side effects of acetic acid application.

1. Bad odor
2. Cost
3. Pain
4. Burning
5. Delay Time for healing

Discussion:

It has been reported that in some cases of local applications, chemical agents have advantages over antibiotics, especially in controlling hospital strains of P. aeruginosa, which are resistant to multiple antipseudomonal agents commonly used in the treatment of pseudomonal wound infections. These agents can be used locally in the treatment of pseudomonal wound infections and the use of antibiotics can be avoided to some extent. Krasilnikov et al. studied susceptibility of P. aeruginosa against antibiotics and antiseptic preparations currently used in medical practice and found that in some cases of local application antiseptic preparations have advantages over antibiotics, especially in controlling hospital strains of microorganisms

Philips et al. was first to report use of acetic acid as a topical agent for the treatment of superficial wounds infected by P. aeruginosa [11] Sloss et al. reported topical use of acetic acid at concentrations between 0.5% and 5% to eliminate P. aeruginosa from the burn wounds and soft tissue wounds. They found that all strains of P. aeruginosa exhibited a minimum inhibitory concentration of 2% in vitro. They successfully eliminated P. aeruginosa from wounds of 14 of the 16 patients within two weeks of treatment. Acetic acid was shown to be an inexpensive and efficient agent for the elimination of P. aeruginosa from burn and soft tissue wounds

Mujumdar in 1993 reported use of ascorbic acid in 35 cases with second degree burn injury involving 20–40% of body surface area infected with P. aeruginosa. He used 2% ascorbic acid to wash wound thoroughly and to create acidic medium in tropical climate where warm weather and alkalinity of the medium renders 0.1% silver sulfadiazine less effective. This treatment modality showed a dramatic reduction (88%) in pseudomonas infection from 94% (pre-treatment) to 6% (post-treatment)[12]

The clinical research was conducted to compare the efficacy of the acetic acid versus silver sulfadiazine in treating pseudomonal infected pressure sore ulcers.

The clinical improvement was detected in 6 ulcers from whole 8 ulcers to be treated , in form of granulation tissue formation , decreased foul smell , decreased redness and the discharge , using the acetic acid and the culture swab was negative for pseudomonas bacteria also , after 1 week duration of starting treatment , this result was not obtained with as such during the same period using silver sulfadiazine , in addition to the low cost , absence of emerging bacterial resistant , a wide availability and less side effects on the ulcer sites encountered to the acetic acid in contrary to the silver sulfadiazine , makes the use of acetic acid and such topical agents in treating infected wounds and ulcers of a big clinical importance , and direct the light upon the use of such topical agents in our country , with the increasing in the emerging of multiple antibiotic resistant bacteria.

Pressure ulcers were more common in males 8(54%), in the pelvic region 12(60%), and the mean age was (67) years old, this is similar to another study that was done in NAGHAPOUR , INDIA in 2012 which revealed that (56.4%) of cases were males, (86%) of pressure ulcers were in the pelvic region, and the mean age was (68) years old[13]. male predominance may be explained by small sample size, the higher incidence of traumas and accidents in males, as well as social and cultural factors that are not allowing females to seek medical advice, while old age predominance explained by the presence of co morbidities.
ulcers were mostly stage II and were subacute (2-3 weeks) and this may be explained by small sample size and early recognition and management

The clinical improvement of the ulcers and culture swab negativity found in 60% of the patient encountered to acetic acid versus flamazine , in contrast to a study research done in India , which reveal that 100% of the ulcers were of clinical improvement and culture swab negativity , this may be explained by the short period of the research , the small sample size , the multidrug resistanat strains of pseudomonas bacteria in our country, and the poor compliance of the family and the medical staff with the research program .

Conclusion:

Acetic acid was found to have bacteriostatic activity against P. aeruginosa, including multiple antibiotic resistant strains of P. aeruginosa. Acetic acid in a concentration of 1%-5% was found efficient in elimination of P. aeruginosa from superficial infection site. Such local antiseptic preparations have advantages over antibiotics in that their use does not encourage evolution of multiple drug resistant .strains of microorganisms in hospital environment It is to be kept in mind as one of the alternatives when infection is caused by multiple antibiotic resistant strains of P. aeruginosa, in which there is shortage of therapeutic options. At a time when bacterial resistance to antibiotics is a matter of increasing concern, the value of topical agents such as acetic acid should not be forgotten.

Recommendations:

1. Future study with increase sample size.

2. Confirm the infection by ulcer biopsy rather than swab.

3. Wide coverage of using acetic acid and other topical agents rather than antibiotcs.

Limitations:

1. Biopsies could not be done due to uncooperative laboratory staff.

2. Poor compliance with the treatment and follow up by the patients families.

3. Cost of the research.

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