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Alpha blocker and 5-alpha reductase versus alpha blocker alone in treatment of Lower Urinary Tract symptoms due to Benign Prostatic Hyperplasia

Research submitted to the department of surgery / college of medicine / AL-Nahrain University as part of M.B.Ch.B graduation requirements

Done by: Zina Amer Salman

Supervised by: Dr. Firas Salman

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بِسْمِ اللهِ الرَّحمنِ الرَحّيم

{...وَمَا أُوتِيتُم مِّنَ الْعِلْمِ إِلَّا قَلِيلا}

(صَدَق اللهُ العليُّ العَظيمْ)

سورة الإسراء (آية85)

Dedication

Every challenging work needs self-efforts as well as guidance of orders especially those who were very close to our heart.

Father and Mother,

Whose affection, love, encouragement and prays of day and night make me able to get such success and honor.

Acknowledgements

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List of Contents

Abstract: ……5

Introduction: ……7

Aim of Study: ……25

Patient and method: ……26

Results: ……28

Discussions: ……40

Conclusion: ……42

Conflict of study: ……42

Recommendation: ……42

References:……43

Abstract

Background

Benign prostatic hyperplasia is very common condition in males. It is defined as a deterioration of clinical variables such as lower urinary tract symptoms (LUTS), health-related quality of life and peak flow rate, increased prostate size, or unfavorable outcomes such as acute urinary retention (AUR) and benign prostatic hyperplasia-related surgery. The natural history is best analyzed from longitudinal studies of community-dwelling men.

Aim of Study

To compare between the effect of 5alpha reductase and alpha blocker as combination therapy versus alpha blocker alone on the lower urinary tract symptoms in benign prostatic hyperplasia.

Patient and method

This study is a prospective study conducted on male patients with history of lower urinary tract symptoms, performed during 10th of October 2018 to 1st March 2019. Twenty five patients enrolled in this study whom collected from AL-Emmamain AL-Kadhumain medical city (from outpatient urology clinic). Any patient labeled as having lower urinary tract symptoms sent for general urine examination and ultrasound and prostate specific antigen in order to be included in this study.

Results

Twenty five (25) patients were involved in this study, who had history of lower urinary tract symptoms who diagnosed as having benign prostatic hyperplasia. Randomly 12 patients (48%) of these 25 were given alpha blocker as only treatment . 13 patients(52%) of these 25 were given combination therapy of alpha blocker and 5- alpha reductase inhibitor as treatment. Patients with age below 50 years were 3 patients(12%) of 25, 2 of them (66.66%) treated with alpha blocker alone and 1 patient (33.33%) was treated with combination therapy, while patients above 50years were 22 patients(88%) of 25, 10 patients (45.45%) of 22 patients treated with alpha blocker, 12 patients (54.54%) of 22 treated with combination therapy. patients present with prostate size below 50cc were 14 patients (56%), 7 patients (50%) treated with alpha blocker, and 7 patients (50%) treated with combination therapy, while patients present with prostate size above 50cc were 11 patients (44%), 5 patients (45.45%) from 11 patients treated with alpha blocker alone, while 6 patients (54.54%) were treated with combination therapy.

Conclusion

The combination therapy of alpha blocker and 5-alpha reductase inhibitor is more effective than alpha blocker alone as monotherapy.

Key Words:

Benign Prostatic Hyperplasia, α-blocker, 5α-reductase inhibitor, lower urinary tract symptoms, prostate specific antigen, Acute urinary retention.

Introduction:

Benign Prostatic Hyperplasia is the most common benign tumor in men. It is progressive disease in many men. The term benign prostatic hyperplasia refers to histological presence of stromal glandular hyperplasia within the prostate [1].The condition that occurs when the prostate gland is increasing in size without there being any malignant cause. As the prostate enlarges it leads to compression and then obstruction of the urethra, which in turn affects urinary flow. The symptoms include urinary frequency, urinary urgency, and hesitancy in urination, poor stream and incomplete bladder emptying. Partial obstruction can ultimately become complete causing acute urinary retention and the urgent requirement for a bladder catheter. Benign prostatic hyperplasia is not however a pre-malignant condition [2].The process by which the prostate begins enlarging starts around the age of 30 and up to 50% of men will show histological signs (changes within the tissues) of benign prostatic hyperplasia by 50 years of age. Symptomatic benign prostatic hyperplasia occurs in up to 50% of men of middle age or older. it is necessary to define Benign Prostatic hyperplasia as microscopic Benign prostatic hyperplasia , macroscopic Benign prostatic hyperplasia , or clinical Benign prostatic hyperplasia. Microscopic Benign prostatic hyperplasia represents histologic evidence of cellular proliferation of the prostate. Macroscopic Benign prostatic hyperplasia refers to enlargement of the prostate resulting from microscopic one. Clinical Benign prostatic hyperplasia represents the lower urinary tract symptoms, bladder dysfunction, hematuria, and urinary tract infection (UTI) resulting from macroscopic Benign prostatic hyperplasia. Microscopic Benign Prostatic hyperplasia describes a proliferative process of the stromal and epithelial elements of the prostate[3].Risk factors for the development of benign prostatic hyperplasia are poorly understood It is rarely identified in men younger than 40 years [4]. Some studies have suggested a genetic predisposition and some have noted racial differences. Approximately 50% of men under the age of 60 who undergo surgery for benign prostatic hyperplasia may have a heritable form of the disease. This form is most likely an autosomal dominant trait, and first degree male relatives of such patients carry an increased relative risk of approximately fourfold [5].

Incidence and Prevalence:

The prevalence of histologic benign prostatic hyperplasia can be determined only from autopsy studies. In 1984, Berry and colleagues [6] summarized 5 autopsy studies addressing the prevalence of histologic benign prostatic hyperplasia according to age. Histologic benign prostatic hyperplasia was never observed in men under the age of 30 years. Approximately half of men in the sixth decade of life exhibited histologic evidence of benign prostatic hyperplasia. Almost 90% of men developed histologic benign prostatic hyperplasia by the ninth decade of life. A review of the literature provides compelling evidence that the prevalence of histologic benign prostatic hyperplasia is similar throughout the world [7].

Surgical Anatomy of Prostate:

The prostate is described as expressing zonal anatomy (McNeal zones), which differ based on their predominant cell type and anatomy. Benign prostatic hyperplasia mainly arises in the transition zone, and cancer mainly in the peripheral zone. The ejaculatory ducts run through the central zone and empty into the urethra at the verumontanum. The peripheral zone is wrapped around the central and transitional zones and is deficient anteriorly where the anterior fibromuscular stroma lies. Structurally, the prostate is composed of fibromuscular stroma and glandular epithelial cells. In childhood there are very few epithelial glands, they appear and develop in puberty. In old age hypertrophy of one or all three elements in the transition zone around the periurethral area gives rise to the nodules of benign prostatic hyperplasia. The prostate is closely related to the three elements of the urethral sphincter in the male [8]; these are as follow:

1. The bladder neck (internal sphincteric mechanism)
   is a collection of alpha-adrenergic smooth muscle and supplied by sympathetic nerve fibres.

2. The supramembranous external sphincter, partly smooth muscle, partly striated, is just distal to the verumontanum and is also supplied by sympathetic nerve fibres.

3. The levatorani, voluntary striated muscle that forms the pelvic floor looping around the urethra and supplied by the pudendal nerve.

Pathology

Benign prostatic hyperplasia is nodular hyperplasia and not diffuse hyperplasia, affecting the transitional and periurethral zones of the prostate [9]. Often the hyperplasia is multinodular, coalescing to form adenomata. Adenomata from the transitional zone form the lateral lobes while adenomata from the periurethral zone form the middle lobe in clinical disease [10]. Benign prostatic hyperplasia gives rise to obstruction by compression as well as by distortion of the bladder outlet. In flow dynamics, distortion causes more obstruction than compression. Using the analogy of a garden hose, it is easier to stop the water flow by distorting (bending) rather than compressing the hose. At the prostate, the lateral lobes tend to compress the bladder outlet while the middle lobe tends to distort it. A third factor which may play a part in bladder outlet obstruction (BOO) is the decrease in elastic system fibers and collagen in the prostatic urethra [11]. There may also be an increase in chondroitin sulphate proteoglycans in BPH [12]. These may affect the plasticity of the prostatic urethra, influencing the distortion and compression. This may explain why in some older patients, the prostate can grow to a large size with minimal obstruction, possibly because the prostatic urethra becomes more rigid or less elastic and therefore more difficult to bend or compress.

Pathophysiogy

The prostate is an accessory sex gland whose primary function is the support and promotion of male sperm function and fertility [13]. During ejaculation it is thought that the prostate secretes about 0.5–1.0 mL of fluid, which is added to the ejaculate. The acini of these ducts are composed of secretory cells, basal cells and neuroendocrine cells. It is the epithelial secretory cells that produce both prostate-specific antigen (PSA) and prostatic acid phosphatase [14].One can relate the symptoms of benign prostatic hyperplasia to either the obstructive component of the prostate or the secondary response of the bladder to the outlet resistance. The obstructive component can be subdivided into the mechanical and the dynamic obstruction .The ability to ultimately prove or disprove the causal relationship between benign prostate enlargement, bladder outlet obstruction, and lower urinary tract symptoms required the availability of noninvasive and reliable methods for assessing prostate volume, bladder outlet obstruction, and lower urinary tract symptoms [15]. It is well recognized that a digital rectal examination is an unreliable method for measuring prostate volume. As prostatic enlargement occurs, mechanical obstruction may result from intrusion into the urethral lumen or bladder neck, leading to a higher bladder outlet resistance. Prostatic size on digital rectal examination (DRE) correlates poorly with symptoms, in part, because the median lobe is not readily palpable [16].The dynamic component of prostatic obstruction explains the variable nature of the symptoms experienced by patients. The prostatic stroma, composed of smooth muscle and collagen, is rich in adrenergic nerve supply. The level of autonomic stimulation thus sets a tone to the prostatic urethra. Use of alpha-blocker therapy decreases this tone, resulting in a decrease in outlet resistance. The irritative voiding complaints of benign prostatic hyperplasia result from the secondary response of the bladder to the increased outlet resistance. Bladder outlet obstruction leads to detrusor muscle hypertrophy and hyperplasia as well as collagen deposition. Although the latter is most likely responsible for a decrease in bladder compliance, detrusor instability is also a factor. On gross inspection, thickened detrusor muscle bundles are seen astrabeculation on cystoscopic examination. If left unchecked, mucosal herniation between detrusor muscle bundles ensues, causing diverticular formation (so-called false diverticula composed of only mucosa and serosa)[17].

Etiology

The etiology of benign prostatic hyperplasia is not completely understood, but it seems to be multifactorial and endocrine controlled [18]. The prostate is composed of both stromal and epithelial elements, and each either alone or in combination, can give rise to hyperplastic nodules and the symptoms associated with benign prostatic hyperplasia [19]. Each element may be targeted in medical management schemes .Observations and clinical studies in men have clearly demonstrated that benign prostatic hyperplasia is under endocrine control.Castration results in the regression of established benign prostatic hyperplasia and improvement in urinary symptoms. Additional investigations have demonstrated a positive correlation between levels of free testosterone and estrogen and the volume of benign prostatic hypertrophy. The latter may suggest that the association between aging and benign prostatic hyperplasia might result from the increased estrogen levels of aging causing induction of the androgen receptor, which thereby sensitizes the prostate to free testosterone. However, no studies to date have been able to demonstrate elevated estrogen receptor levels in human benign prostatic hyperplasia.

Symptoms:

- Irritative symptoms (voiding): frequency, urgency, nocturia.
- Obstructive symptoms (storage): hesitancy, sensation of incomplete emptying, weak stream, poor straining, post void dribbling, intermittency[20].

The self-administered questionnaire developed by the American Urological Association (AUA) is both valid and reliable in identifying the need to treat patients and in monitoring their response to therapy. The American Urological Association Symptom Score questionnaire is perhaps the single most important tool used in the evaluation of patients with benign prostatic hyperplasia and is recommended for all patients before the initiation of therapy [21]. This assessment focuses on 7 items that ask patients to quantify the severity of their obstructive or irritative complaints on a scale of 0–5. Thus, the score can range from 0 to 35. A symptom score of 0–7 is considered mild, 8–19 is considered moderate, and 20–35

is considered severe. The relative distribution of scores for benign prostatic hyperplasia patients and control subjects is, respectively, 20% and 83% in those with mild scores, 57% and 15% in those with moderate scores, and 23% and 2% in those with severe scores[22].A detailed history focusing on the urinary tract excludes other possible causes of symptoms that may not result from the prostate, such as urinary tract infection, neurogenic bladder, urethral stricture, or prostate cancer.

Signs:

A physical examination, Digital Rectal Exam, and focused neurologic examination are performed on all patients. The size and consistency of the prostate is noted, even though prostate size, as determined by DRE, does not correlate with severity of symptoms or degree of obstruction. benign prostatic hyperplasia usually results in a smooth, firm, elastic enlargement of the prostate. Induration, if detected, must alert the physician to the possibility of cancer and the need for further evaluation (prostate-specific antigen [PSA], trans-rectal ultrasound and biopsy)[23].

Investigations:

-Urinalysis

To exclude infection or hematuria, the presence of urinary tract infection or hematuria requires additional testing to exclude genitourinary malignancies and other conditions unrelated to benign prostatic hyperplasia. Urine cytology should be considered in men with severe irritable symptoms, especially if they have a history of smoking. If a dipstick approach is used, the test should include leukocyte esterase and nitrite tests for the detection of pyuria and bacteriuria .There is insufficient evidence to support urinalysis as an effective screening procedure in asymptomatic men [24].

-serum creatinine measurement

The measurement of serum creatinine has been recommended in the initial evaluation of all patients with lower urinary tract symptoms to exclude renal insufficiency caused by the presence of obstructive uropathy. However, in men with an elevated serum creatinine level, the etiology is rarely associated with acute or chronic urinary retention secondary to benign prostatic hyperplasia. Obtaining a serum creatinine measurement may be an appropriate screen for renal disease unrelated to benign prostatic hyperplasia.

-Prostate specific antigen measurement

Normal values for age:

40 to 49 is 0 to 2.0ng/ml

50 to 59 is 0 to 3.0ng/ml

60 to 69 is 0 to 4.0ng/ml

70 to 79 is 0 to 5.0ng/ml

Advanced prostate cancer can lead to lower urinary tract symptoms by producing urethral obstruction similar to that in men with benign prostatic hyperplasia. In men with clinically localized cancer, the distribution of American Urological Association symptom scores is similar to that in age-matched men in the general population, suggesting that it is the benign prostatic hyperplasia that causes the symptoms [25]. Prostate cancer commonly coexists with benign prostatic hyperplasia and in most men with a 10-year or longer life expectancy, a finding of concomitant prostate cancer may well alter management of the benign prostatic hyperplasia component. The detection of a large nodular prostate cancer on digital rectal examination would no doubt alter therapy; however, the “early detection” of small-volume prostate cancer in an 80-year-old man is unlikely to be beneficial. A prostate specific antigen test and digital rectal examination increase the detection rate of prostate cancer over digital rectal examination alone. Therefore, measurement of the serum Prostate specific antigen value should be performed in patients for whom the identification of cancer would clearly alter Benign prostate

hyperplasia management. There is significant overlap between the serum prostate specific antigen values of men with benign prostate hyperplasia and those of men with clinically localized prostate cancer. Twenty-eight percent of men with histologically proven benign prostatic hyperplasia have a serum prostate specific antigen level greater than 4.0 ng/mL [26]. Serum prostate specific antigen trends over time (PSA velocity), measurement of free versus complex prostate specific antigen, and prostate specific antigen density may help to improve the specificity of Prostate specific antigen testing in men with Benign prostatic hyperplasia. McConnell and colleagues have demonstrated a strong correlation between prostate volume and serum prostate specific antigen levels [27].

-Abdominal ultrasound

The volume of urine remaining in the bladder can be measured by abdominal ultrasound. This may vary from day to day and may be caused by bladder outflow obstruction, detrusor failure or both [28].The abdominal ultrasound may also detect dilatation of the ureters and renal pelvis in chronic high-pressure urinary retention and gross bladder trabeculation and diverticula [29].

-Trans-rectal ultrasound

The volume of the prostate can be measured from the ultrasound image (width, height and length) and may help in planning treatment [30].

-Urodynamic studies

The only way of making certain that lower urinary tract symptoms are due to bladder outflow obstruction is by means of a cystometrogram. Flow rates vary from day to day, and a poor flow may not necessarily mean obstruction: it may result from a weak detrusor, while on the other hand if the detrusor has undergone considerable hypertrophy, it can compensate for obstruction and produce a good flow rate. Nevertheless an impaired flow rate of <10 mL/s is a significant part of the clinical pattern [31].

Treatment of Benign Prostatic Hyperplasia

A wide variety of treatments are available for enlarged prostate, including medication, minimally invasive therapies and surgery. The best treatment choice depends on several factors[32,33] including:

- The size of prostate
- Age
- Overall health
- The amount of discomfort

Watchful waiting and active surveillance—

For patients with IPSS of 0-7 and include[34,35]:

1- Decrease liquid intake at special time to reduce frequency.
2- Use of relaxed and double voiding techniques.
3- Avoidance or moderation of alcohol, tea and coffee.
4- Urethral stripping to prevent post micturation dribbling.
5- Distraction technique such as breathing exercise.
6- Bladder retraining where the patient is encouraged to hold his urine to increase bladder capacity.
7- Treatment of constipation.

Medical Therapy

5alpha-reductase

Androgens play an essential role in prostatic development and function, but are also involved in prostate disease pathogenesis. The primary prostatic androgen, dihydrotestosterone (DHT), is synthesized from testosterone by 5alpha-reductase types 1 and 2. Inhibition of the 5alpha-reductase isoenzymes therefore has potential therapeutic benefit in prostate disease by reduction in the size of the gland and improvement in symptoms. The two currently approved 5alpha-reductase inhibitors (5ARIs), finasteride and dutasteride, have demonstrated long-term efficacy and safety in the treatment of benign prostatic hyperplasia[36,37].

Alpha-blockers

Also known as α-blockers or α-adrenoreceptor antagonists ,are a class of pharmacological agents that act as antagonists on α -adrenergic receptors (α-adrenoceptors)[38].The evolution of alpha blocker therapy for benign prostatic hyperplasia (BPH) has focused on improving convenience and tolerability. Indications for treating benign prostatic hyperplasia include reversing signs and symptoms or preventing progression of the disease[39]. The indication that most commonly drives the need for intervention is relief of lower urinary tract symptoms (LUTS) with the intent of improving quality of life. Alpha blockers are the most effective, least costly, and best tolerated of the drugs for relieving lower urinary tract symptoms. The non- selective alpha blocker is phenoxybenzamine effective drug but high side effect profile. No more used in treatment of benign prostatic hyperplasia. Alpha-1blocker are prazosin, Terazosin, Doxazosin effective drugs, with typical side effects :orthostatic hypotension , dizziness, retrograde ejaculation, rhinitis, and headache. Alpha-1a blocker are tamsulosin , silodosine.

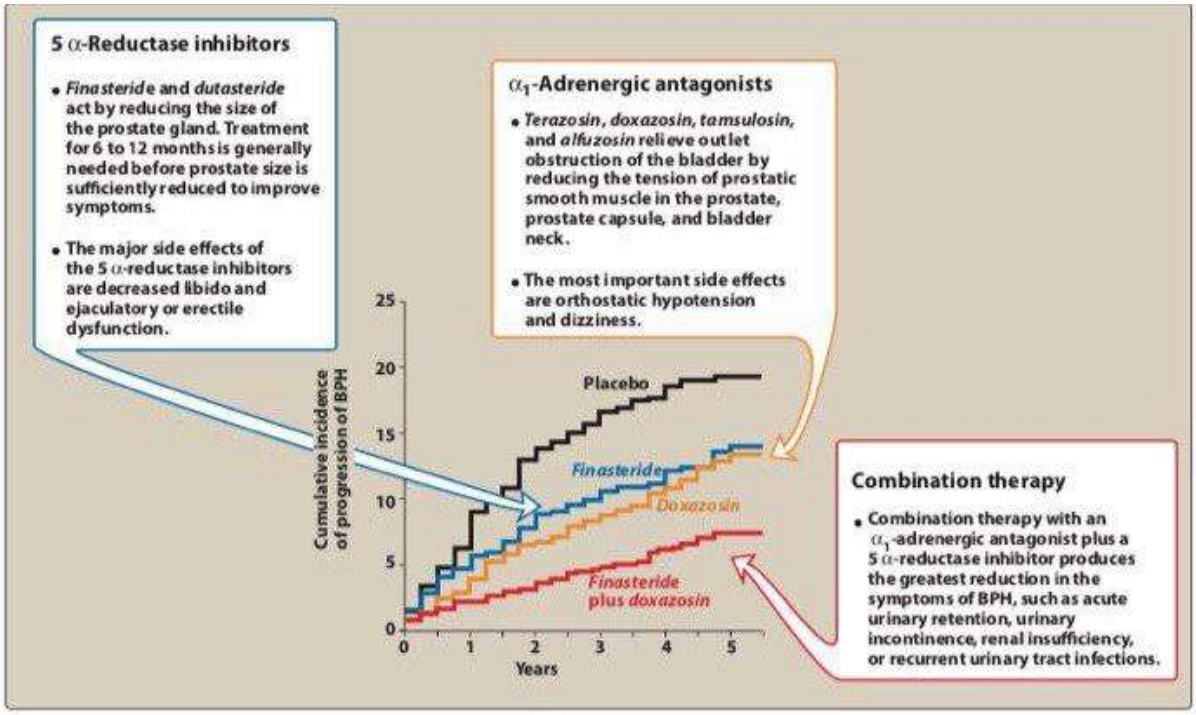


Figure 25.13
Therapy for benign prostatic hyperplasia (BPH).

Combination Therapy

An underlying scientific rationale exists for combining α-adrenergic blockade and 5α-reductase inhibition for the treatment of lower urinary tract symptoms (LUTS) in men with benign prostatic hyperplasia (BPH), given that their modes of action in managing lower urinary tract symptoms secondary to BPH are different and complementary. Both α-blockers and 5α-reductase inhibitors (5-ARIs) provide sustainable reductions in symptom scores. Although both classes of agents have data to support delays in acute urinary retention (AUR) and the need for invasive BPH therapy, only the 5-ARIs reduce the long-term risks of both events. Current evidence suggests that initiation of combination therapy should be considered in men with prostatic enlargement, elevated prostate-specific antigen (PSA) level, lower urinary tract symptoms, and moderate or severe bother. The Medical Therapy of Prostate Symptoms (MTOPS) study provided evidence that the prostate volume threshold for benefit of a 5-ARI, and therefore of combination therapy, is lower than previously thought (>25 cc)[40]. Cost effectiveness in this population has been demonstrated to increase in men with severe symptoms, although transurethral resection of the prostate (TURP) is probably more favorable in the long-term from a cost perspective. However, many men wish to avoid surgery, and for them, combination therapy offers significant benefits over monotherapy, especially over α-blocker therapy where no long-term reductions in the risk of acute urinary retention or surgery have been demonstrated[41].

Phytotherapy

Phytotherapy has become a more popular treatment option among American men with benign prostatic hyperplasia (BPH). The most popular herbal agent is saw palmetto (*Serenoarepens*), which is derived from the berry of the American dwarf palm tree. *Pygeumafricanum* and beta-sitosterol are also used by many patients with BPH, either alone or in combination with saw palmetto. A significant limiting factor to our understanding of the use and effectiveness of phytotherapy is the lack of standardization of these products. Despite this lack of standardization and the variation in results that may be seen with herbal products, there is growing evidence from well-conducted clinical trials that

phytotherapeutic agents may lead to subjective and objective symptom improvement beyond a placebo effect in men with BPH. In addition, histologic evidence has been presented demonstrating that saw palmetto causes atrophy and epithelial contraction within the prostate gland. Overall, it is likely that herbal therapy will continue to be used by a growing number of Americans to treat a variety of ailments. Physicians should attempt to remain open-minded regarding alternative approaches and educate themselves so that they may counsel patients in an informed and credible fashion[42].

Surgery

Transurethral resection of the prostate (TURP)

is a surgery used to treat urinary problems due to an enlarged prostate . A combined visual and surgical instrument (resectoscope) is inserted through the tip of penis and into the tube that carries urine from bladder (urethra). The prostate surrounds the urethra. Using the resectoscope, doctor trims away excess prostate tissue that is blocking urine flow. TURP is generally considered an option for men with moderate to severe urinary problems that haven't responded to medication. Traditionally, TURP has been considered the most effective treatment for an enlarged prostate [43]. However, a number of other, minimally invasive procedures are becoming more effective, due to improved techniques and surgical tools. These minimally invasive procedures generally cause fewer complications and have a quicker recovery period than TURP. The risk of bleeding is generally higher with TURP, so it might not be the best option for certain men who take blood-thinning medications. TURP helps reduce urinary symptoms caused by benign prostatic hyperplasia (BPH), including [44]:

- Frequent, urgent need to urinate
- Difficulty starting urination
- Slow (prolonged) urination
- Increased frequency of urination at night
- Stopping and starting again while urinating
- The feeling can't completely empty bladder
- Urinary tract infections

TURP might also be done to treat or prevent complications due to blocked urine flow, such as:

- Recurring urinary tract infections
- Kidney or bladder damage
- Inability to control urination or an inability to urinate at all
- Bladder stones
- Blood in urine

Transurethral Incision of The Prostate

A Transurethral Incision Of The Prostate (TUIP) is a prostate surgery that is performed to relieve the symptoms associated with an enlarged prostate gland, a condition known as benign prostatic hyperplasia (BPH). When the prostate becomes enlarged it can put pressure on the urethra and cause difficulty with urination. In the more severe cases of BPH the patient's ability to pass urine can become completely blocked. TUIP is a viable option for the treatment of an enlarged prostate depending on the severity of symptoms and only if the swollen gland is relatively small, generally no more than an ounce or 30 milliliters in size.

Simple (open) prostatectomy

This differs from radical prostatectomy in that the former consists of enucleation of a hyperplastic prostatic adenoma, and the latter involves removal of the entire prostate, the seminal vesicles, and the vas deferens. When medical and minimally invasive options for benign prostatic hyperplasia (BPH) have been unsuccessful, the more invasive treatment options for BPH should be considered, such as transurethral resection of the prostate (TURP) or open prostatectomy. Patients who present for open (simple) prostatectomy are typically age 60 years or older [45].The advantages of open (simple) prostatectomy over TURP include the complete removal of the prostatic adenoma under direct visualization in the suprapubic and retropubic approaches. However, these procedures do not obviate the need for further prostate cancer surveillance because the posterior zone of the prostate remains as a potential source of carcinoma formation. Open (simple) prostatectomy has 3 different approaches: retropubic, suprapubic, and perineal.

Simple retropubic prostatectomy is the enucleation of a hyperplastic prostatic adenoma through a direct incision of the anterior prostatic capsule. Simple suprapubic prostatectomy is the enucleation of the hyperplastic prostatic adenoma through an extraperitoneal incision of the lower anterior bladder wall[46].

Risk of surgery

Problems specific to prostate surgery can include:

- problems controlling the urge to urinate
- difficulty controlling bowel movements
- scar tissue that blocks part of the urethra
- infertility
- problems maintaining an erection
- injury to internal organs

Principles of Laser Therapy

There are 2 basic principles of laser therapy for Benign prostatic hyperplasia. These are determined by the final tissue effect (what the laser does to the tissue). The 2 principles are laser coagulation and laser vaporization.In laser coagulation, relatively low-density laser thermal energy is used to produce tissue coagulative necrosis, with a potential for delayed anatomical debulking. Clinically significant anatomical debulking occurs only if the tissue is allowed to slough, which takes place when the prostatic urothelium is involved in the process. Preservation and protection of the prostatic urothelium from laser thermal damage prevents tissue sloughing. For laser vaporization, higher-density laser thermal energy is used. This high energy raises the tissue temperature to several hundred degrees Celsius, causing its vaporization. Additionally, various degrees of coagulation necrosis take place in the adjacent residual tissue. This principle is used in different ways to achieve a variety of objectives, depending on the amount and site of tissue vaporization. These range from complete tissue vaporization to incision, resection, or enucleation of the obstructing prostatic tissue. Irrespective of the technique used, the final common result is “opening” (anatomical de-obstruction) of the prostatic urethra.

Advantages of Laser Therapy

Laser therapy has a number of potential advantages over other methods for treating Benign prostatic hyperplasia, such as transurethral resection of the prostate (TURP) and open prostatectomy. These advantages include [47]:

Lower risk of bleeding :Because there is a low risk of bleeding with laser surgery, it can be a good option for men who take medication to thin their blood or who have a bleeding disorder that doesn't allow their blood to clot normally.

Shorter or no hospital stay :Laser surgery can be done on an outpatient basis or with just an overnight hospital stay.

Quicker recovery time: Recovery from laser surgery generally takes less time than recovery from TURP or open surgery.

Quicker results: Improvements in urinary symptoms following laser therapy are noticeable right away, while it can take several weeks or even months to see any noticeable improvement with medications.

Transurethral electrovaporization of the prostate (TUVP)

It is one of the alternative, minimally invasive procedures to treat BPH with promising initial results. Data were analysed for improvement of IPSS and Q(max), operation time, hospital stay, perioperative bleeding, postoperative irritative symptoms, long-term side effects and reoperation rate. reviewed a total of 244 TUVP compared to 259 TURP patients in six prospective randomized studies that reached 1 y follow-up. Less perioperative bleeding, shorter catheterization time (mean of TUVP: 30 hour vs TURP: 61 hour) and shorter hospital stay (mean of 1.4 days vs TURP: 3.4 days) were reported in the TUVP patients. The improvement in IPSS (71%) and mean Q(max) (20 ml/s) was similar in both groups. The reoperation rate was 2% per year in both vaporization and resection patients. In conclusion, analysis of the prospective randomized trials that reached 1 year follow-up revealed that TUVP is as effective as standard TURP in the treatment of Benign prostatic hyperplasia. Long-term side effects and reoperation rates are comparable and the initial improvement was maintained over 1 year for the majority of patients [48].

Hyperthermia and thermotherapy of benign prostatic hyperplasia

The indications, risks and benefits of surgical treatment of benign prostatic hyperplasia (BPH) have recently been scrutinized, and interest in the development of less invasive alternative nonsurgical approaches has emerged. Among the nonsurgical alternatives, thermal treatments have been clinically introduced for a few years but are still under evaluation. Microwaves and radiofrequency waves are generated by various devices applied by the trans-rectal or transurethral approach, with different treatment and temperature schedules. Results achieved with the various devices did not show large significant differences. Improvement is mainly observed by a decrease in irritative symptoms rather than by modifications of obstructive parameters. The placebo effect must not be underestimated in all these new alternative methods [49]. Fifty percent of patients in retention and unfit for anesthesia voided satisfactorily after thermal treatment. Pathological studies of operative specimens after transurethral thermotherapy showed coagulative necrosis with destruction of smooth muscle and glandular components. The destruction of alpha-receptors or sensory nerves in the prostate stroma is a possible explanation for the reduction of irritative symptoms. No significant histological lesions were found however after trans-rectal hyperthermia. Various factors such as differences in tissue thermo sensitivity, tissular architecture and thermoregulation related to variation in the prostate blood supply may all play a part in the final heating effect and determine the clinical response for a given patient. Better understanding of these various factors may improve patient selection. Although thermal treatment of Benign prostatic hyperplasia cannot be seen as a substitution for surgery, it may represent an alternative option in selected patients essentially to alleviate irritative symptoms[50].

Transurethral needle ablation (TUNA)

It is an outpatient procedure to treat urinary symptoms caused by an enlarged prostate, a condition known as benign prostatic hyperplasia (BPH). This procedure is also called radiofrequency ablation or RF therapy. A specially adapted visual instrument (cystoscope) is inserted through the tip of your penis into the tube that carries urine from bladder (urethra). Using the cystoscope, doctor guides a pair of tiny needles into the prostate tissue that is pressing on the urethra. Then radio waves are passed through the needles to create scar tissue. This scarring shrinks prostate tissue, opening up the urinary channel so that urine can flow more easily[51].

Balloon dilatation of the prostate

Transurethral balloon dilatation of the prostate is a safe method of treating benign prostatic hyperplasia; it has been largely free of complications, and does not produce retrograde ejaculation. However doubts remain over its efficacy.

Aim of study:

To compare between the effect of 5alpha-reductase inhibitor and alpha blocker as combination therapy versus alpha blocker alone on the lower urinary tract symptoms in Benign Prostatic Hyperplasia.

Patient and method

This study was done in AL-Emmamain AL-Kadhumain medical city from (outpatient Urology clinic) in the period between **October**2018-**March** 2019.

Twenty five patients enrolled in this study. Any patient labeled as having lower urinary tract symptoms did for him clinical examination, then sent him for general urine examination , ultrasound and prostate specific antigen in order to ensure the diagnosis of benign prostatic hyperplasia .

For each patient taken, we took history from patient and do clinical examination and sent for general urine examination, ultrasound and prostate specific antigen in order to ensure the diagnosis of benign prostatic hyperplasia .

All patients were diagnosed by Urologist surgeon in hospital. Information collected from records of **25** patients randomly depend on data according to following questionnaire.

From questunnaire:

International Prostate Symptom Score (I-PSS)

Patient Name: _____ **Date of birth:** _____ **Date completed** _____

In the past month:	Not at All	Less than 1 in 5 Times	Less than Half the Time	About Half the Time	More than Half the Time	Almost Always	Your score
1. Incomplete Emptying How often have you had the sensation of not emptying your bladder?	0	1	2	3	4	5	
2. Frequency How often have you had to urinate less than every two hours?	0	1	2	3	4	5	
3. Intermittency How often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5	
4. Urgency How often have you found it difficult to postpone urination?	0	1	2	3	4	5	
5. Weak Stream How often have you had a weak urinary stream?	0	1	2	3	4	5	
6. Straining How often have you had to strain to start urination?	0	1	2	3	4	5	
	None	1 Time	2 Times	3 Times	4 Times	5 Times	
7. Nocturia How many times did you typically get up at night to urinate?	0	1	2	3	4	5	
Total I-PSS Score							

Score: 1-7: *Mild* 8-19: *Moderate* 20-35: *Severe*

Quality of Life Due to Urinary Symptoms	Delighted	Pleased	Mostly Satisfied	Mixed	Mostly Dissatisfied	Unhappy	Terrible
If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?	**0**	**1**	**2**	**3**	**4**	**5**	**6**

Statistical Analysis:

The analysis of data was carried out using Microsoft excel 2010 program and tables was made by Microsoft word 2010 program.

Ethical issues:

Prior to data collection, verbal consent of each participant was obtained after explaining the purpose of study and ensuring the privacy of data.

Results:

25patients were involved in this study, The exclusive critia:

1 - Huge prostate>80cc

2- patients with high prostate specific antigen >20

3- patients with compromised renal function (elevate blood urea, elevate serum urea).

classify them according to:

1- patients treated with alpha blocker alone were 12 patients (48%) from total 25 patients , and patients treated with combination therapy were 13 patients (52%) from total 25 patients.

2- The age whether below or above 50 years old, patients presented with age below 50 years were 3only(12%) and patients with age more than 50 years were 22 patients (88%).

3- The prostate size whether below or above 50cc, patients presented with prostate size below 50cc were 14 patients(56%) and patients presented with prostate size more than 50cc were 11 patients (44%).

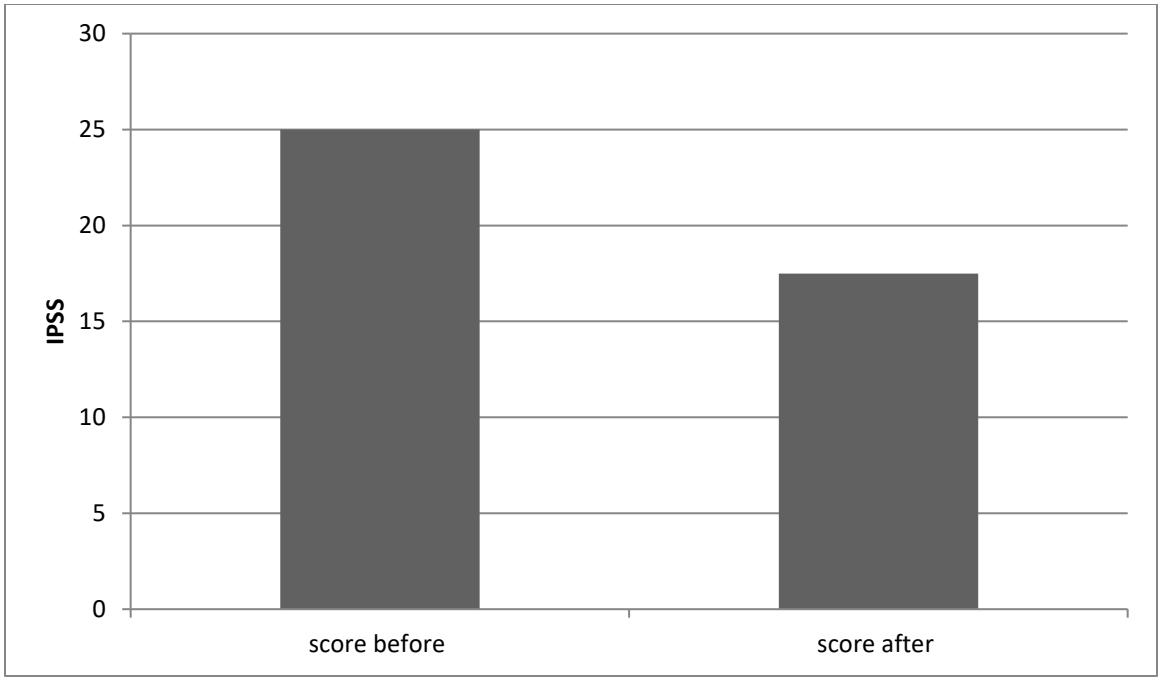
See table 1.

Table(1): Base line characteristic

Criteria	Group	Number of cases	Percentage %
Type of medical treatment	Patients treated with Alpha blocker alone	12	48%
	Patients treated with combination therapy	13	52%
Patients age	Below 50 years	3	12%
	Above 50years	22	88%
Prostate size	Below 50cc	14	56%
	Above 50cc	11	44%

Table (2): patients treated with alpha blocker alone

No.	Cases	Score before	Score after	P-value
1	Case 1	30	17	*0.04*
2	Case2	27	16	
3	Case3	17	13	
4	Case4	25	21	
5	Case5	19	13	
6	Case6	26	13	
7	Case7	21	13	
8	Case8	27	16	
9	Case9	23	18	
10	Case10	26	21	
11	Case11	32	27	
12	Case12	27	22	



Figure(1): show change in IPSS before and after treatment with alpha blocker alone.

Table (3): patients treated with combination therapy(5-alpha reductase inhibitor and alpha blocker)

No.	Cases	Score before	Score after	p-value
1	Case1	29	15	
2	Case2	13	8	
3	Case3	24	11	
4	Case4	29	15	
5	Case5	12	3	
6	Case6	24	12	
7	Case7	24	12	
8	Case8	27	19	0.001
9	Case9	25	14	
10	Case10	24	13	
11	Case11	26	13	
12	Case12	19	8	
13	Case 13	17	11	

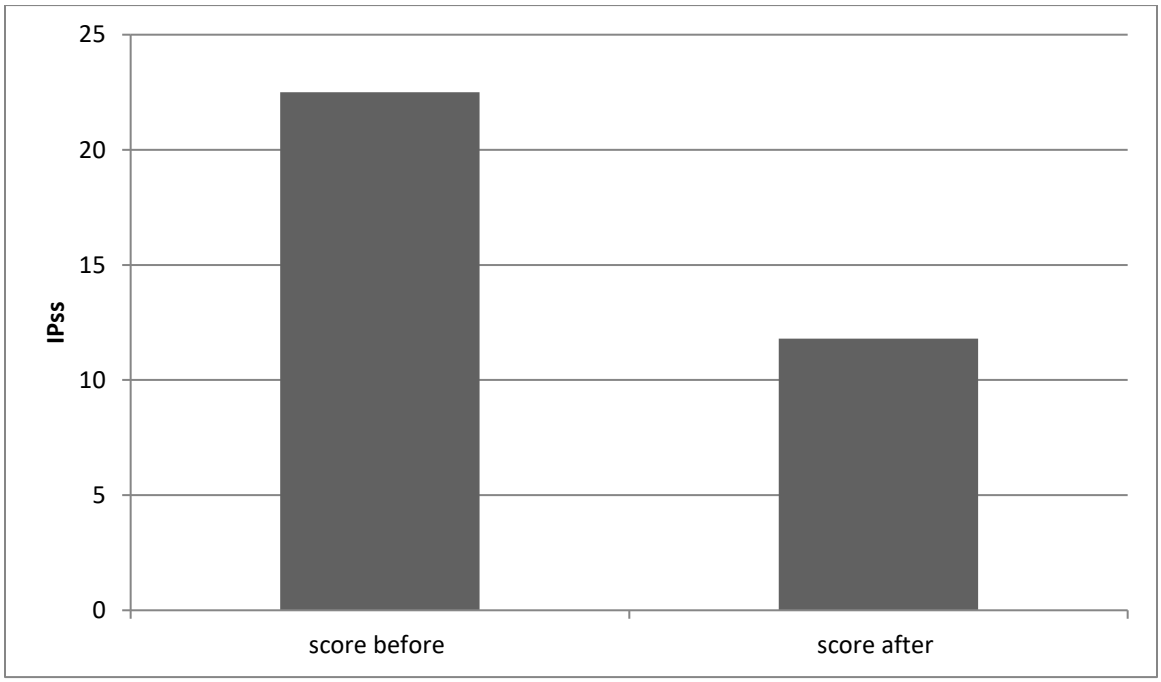
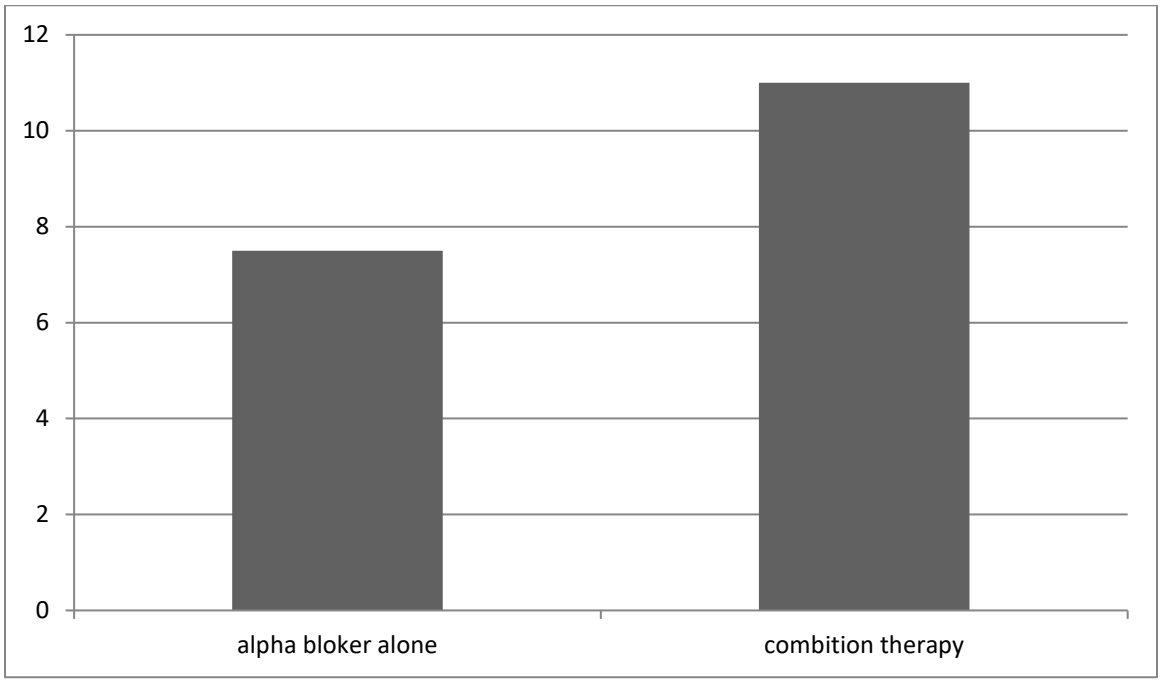


Figure (2): show changes in IPSS before and after combination therapy.



Figure(3): show changes in IPSS between patients treated with alpha blocker alone and patients treated with combination therapy.

Table (4): patients below age of 50years and their response to treatment

No.	Patient case	Treated with Alpha-blocker		p-value	Treated with Combination therapy		p-Value
		Before	After		Before	After	
1	Case1	----------		0.19	25	14	0.22
2	Case2	27	16		----------		
3	Case3	30	17		----------		

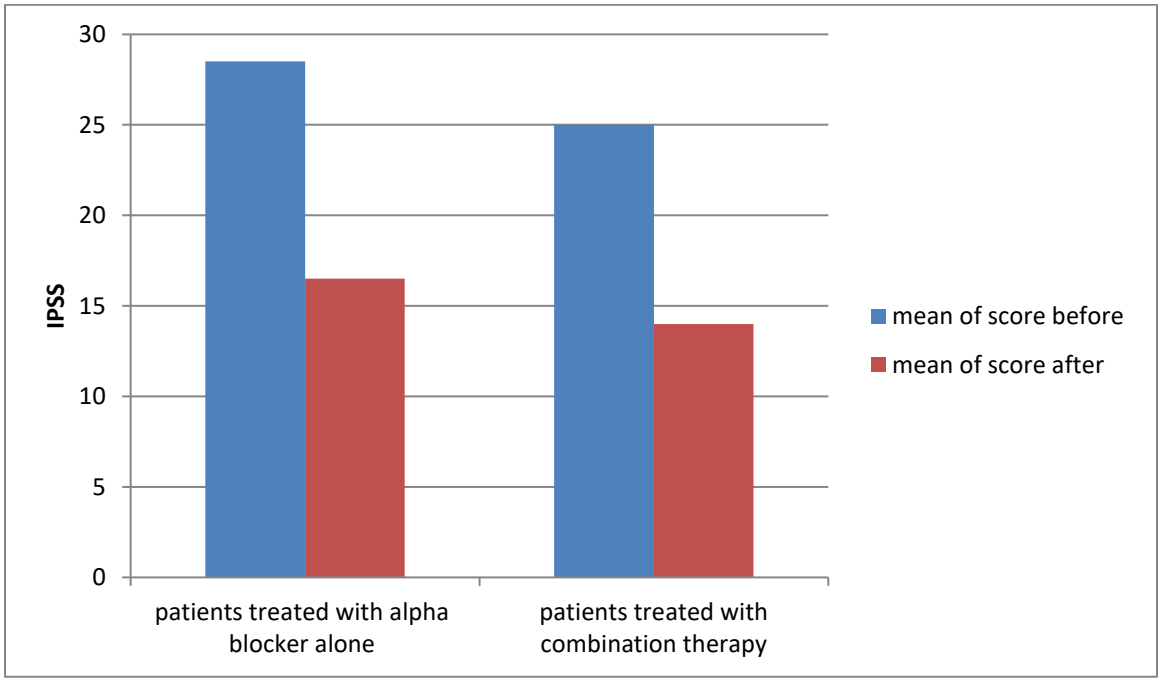


Figure (4): show changes in IPSS between patients treated with alpha blocker alone and those who treated with combination therapy in age below 50 years.

Table (5): Patients above age of 50 years and their response to treatment

No.	Patient case	Treated with Alpha-blocker		p-value	Treated with Combination therapy		p-value
		Before	After		Before	After	
1	Case1	23	18		----------		
2	Case2	26	13		----------		
3	Case3	26	21		----------		
4	Case4	27	16		----------		
5	Case5	17	13		----------		
6	Case6	21	13		----------		
7	Case7	25	21		----------		
8	Case8	32	27		----------		
9	Case9	21	13		----------		
10	Case10	27	22	0.14	----------		0.25
11	Case11	----------			24	13	
12	Case12	----------			29	15	
13	Case13	----------			24	12	
14	Case14	----------			27	19	
15	Case15	----------			13	8	
16	Case16	----------			26	13	
17	Case17	----------			19	8	
18	Case18	----------			29	15	
19	Case19	----------			12	3	
20	Case20	----------			24	11	
21	Case21	----------			25	14	
22	Case22	----------			24	12	

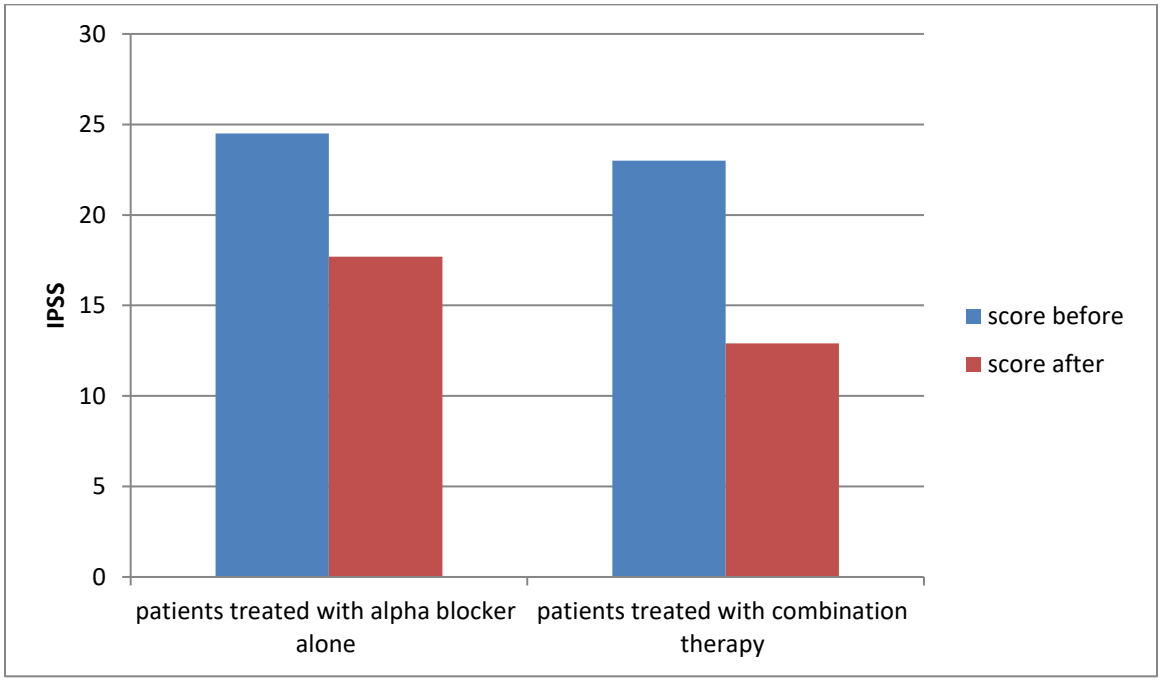


Figure (5): show changes in IPSS between patients treated with alpha blocker alone and those who treated with combination therapy in age above 50 years.

Table (6): Patients with prostate size below 50cc and their response to treatment

No.	Patient case	Treated with Alpha-blocker		p-value	Treated with Combination therapy		p-value
		Before	After		Before	After	
1	Case1	26	13	0.02	----------		0.04
2	Case2	23	18		----------		
3	Case3	27	22		----------		
4	Case4	26	21		----------		
5	Case5	27	16		----------		
6	Case6	17	13		----------		
7	Case7	21	13		----------		
8	Case8	----------			13	8	
9	Case9	----------			24	12	
10	Case10	----------			24	11	
11	Case11	----------			12	3	
12	Case12	----------			29	15	
13	Case13	----------			19	8	
14	Case14	----------			26	13	

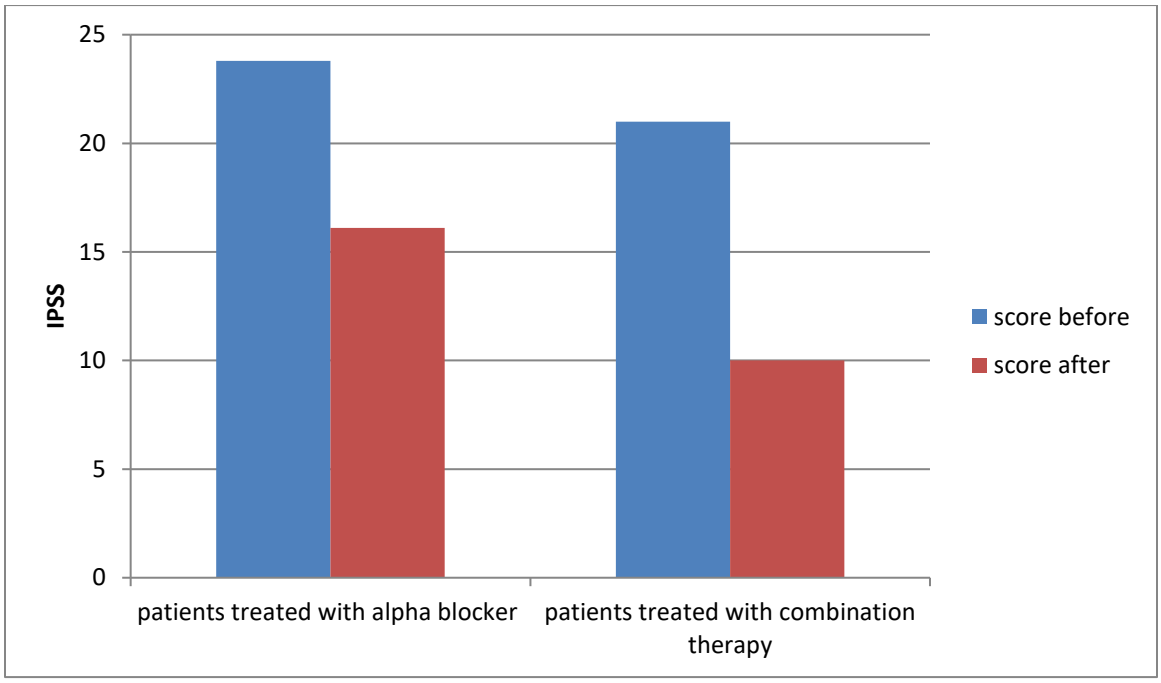


Figure (6): show changes in IPSS between patients treated with alpha blocker alone and those who treated with combination therapy with prostate size below 50cc.

Table (7): Patients with prostate size above 50cc and their response to treatment

No.	Patient case	Treated with Alpha-blocker		p-value	Treated with Combination therapy		p-value
		Before	After		Before	After	
1	Case1	30	17		----------		
2	Case2	25	21		----------		
3	Case3	32	27		----------		
4	Case4	21	13		----------		
5	Case5	27	16		----------		
6	Case6	----------		0.03	24	13	0.001
7	Case7	----------			24	12	
8	Case8	----------			27	19	
9	Case9	----------			17	11	
10	Case10	----------			29	15	
11	Case11	----------			25	14	

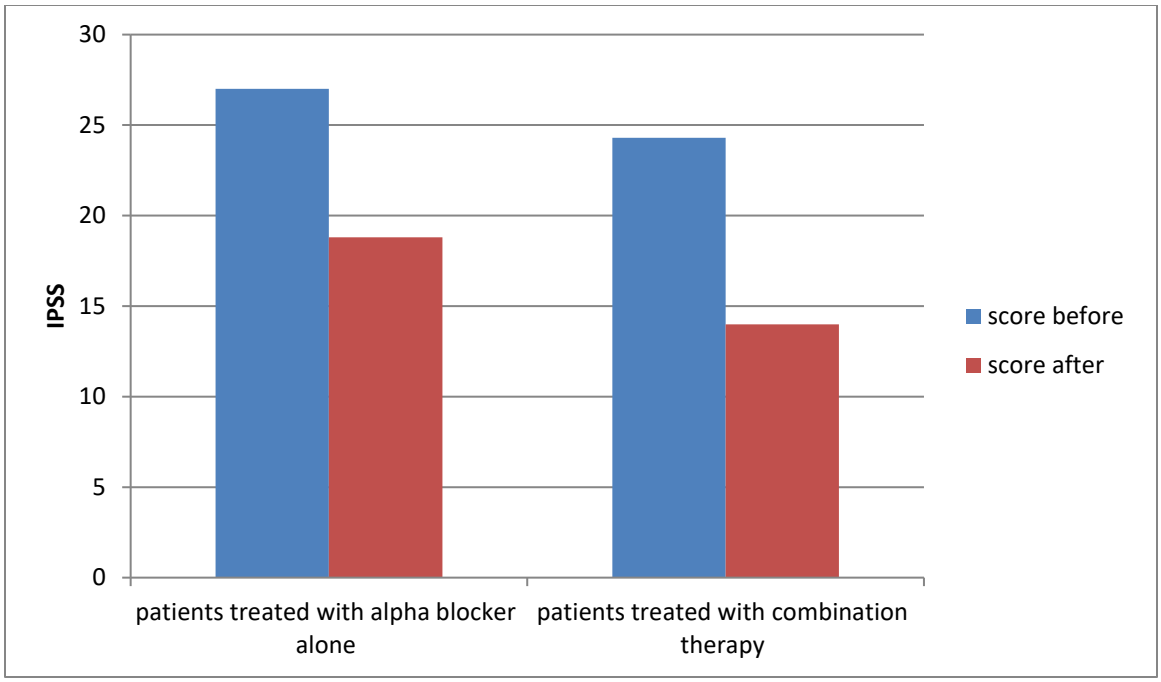


Figure (7): show changes in IPSS between patients treated with alpha blocker alone and those who treated with combination therapy with prostate size above 50cc.

Discussion:

Twenty five (25) patients were involved in this study, who had history of lower urinary tract symptoms. Randomly 12 patients(48%) were given alpha blocker alone and 13 patients(52%) were given 5-alpha reductase inhibitor and alpha blocker as combination therapy, as treatment for lower urinary tract symptoms in patients who first diagnosed for having benign prostatic hyperplasia .the mechanism of action of alpha blocker by relaxing smooth muscle tissue found in prostate and bladder neck, this allows urine to flow out of the bladder more easily ,while the most common side effect of alpha blocker is headache and orthostatic hypotension. The mechanism of action of 5 alpha reductase by suppressing serum dihydrotestosterone levels by inhibiting the conversion of testosterone to dihydrotestosterone , while most common side effect is erectile dysfunction and decrease libido. The p-value for patients treated with alpha blocker alone was 0.04 which means that the treatment was significant, while the p-value for patients treated with combination therapy was 0.001 which means it is significant and more effective than the monotherapy, also the changes in mean of IPSS in patients with combination treatment was more than the change in mean of IPSS in patients treated with alpha blocker alone. This study according to results, combination therapy is more effective than mono therapy and this study is supported by previous reported data , Using of a combination therapy of an alpha blocker and 5 alpha reductase inhibitor long term may help to reduce symptoms more than either medicine alone [52]. In the past, however, most studies were skeptical about the effects of combination therapy with alpha-blockers and 5-alpha reductase inhibitor . The Veterans Affairs Cooperative Study showed that alpha-blocker monotherapy and 5-alpha reductase inhibitor combination therapy for 12 months decreased the American Urological Association symptom score to 6.1 and 6.2, and increased Qmax to 2.7 and 3.2, with no significant differences between the two therapies [53]. When we classify patients according to age patients with age below and above 50 years . patients with age below 50 years were only 3patients (12%) from 25 patients 2of them(66.6%) were treated with alpha blocker alone as monotherapy, the p-value of them was 0.19 which not very significant, and 1 of them (33.3%) was treated with combination therapy with p-value of 0.22 which is also not signifcant. Patients with age more than 50 years were 22 patients (88%) from 25 patients 10 0f them (45.45%) were treated with alpha blocker alone, with

p-value 0.14 which is not very significant , and 12 of them (54.54%) from 22 patients were treated with combination therapy with p-value 0.25 also here is not very significant. That mean the response to treatment is effected by age, But according to patients symptoms We see that also the combination therapy had better effect on lower urinary tract symptoms regarding the age. Patients presented with prostate size below 50cc were 14 patients (56%) from 25 patients, 7 patients (50%) were treated with alpha blocker alone, with p-value 0.02 which means that the treatment is significant ,and 7 patients (50%) were treated with combination therapy, with p-value of 0.04 which means that its significant. Patients present with prostate size above 50cc were 11 patients (44%) , 5 of them (45.45%) were treated with alpha blocker alone, with p-value of 0.03 that means that the treatment was significant , and 6of them (54.54%) were treated with combination therapy with p-value of 0.001 which means that the treatment is very significant. we see that regarding prostate size the combination therapy was more effective on the lower urinary tract symptoms in patients with benign prostatic hyperplasia.

Limitations

Our study has limitations, including a small sample size, short time and filling the questionnaire is from old patients, some cases did not return back for flow up.

Conclusion

The combination therapy of alpha blocker and 5-alpha reductase inhibitor is more benefit and effective than alpha blocker alone as monotherapy.

Conflict of interest

The author has no conflict of interest.

Recommendations

Further studies with a larger sample size, multi centric approach, over longer time period are recommended to further confirm the result, with prospective design.

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