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Options of Medical Management for Benign Prostatic Hyperplasia: Review Article

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ABSTRACT

Background: Ablative surgery has been the go-to method for treating benign prostatic hyperplasia (BPH), for the better part of the past 60 years. Recent discoveries in incidence and pathogenesis as well as physiology of prostatic hyperplasia, while conventional management guidelines are put to reconsider by urologists due to recent endocrine and urology studies, which have served as the foundation for diagnosis and therapy in the past.

Objective: Review literature about management options of benign prostatic hyperplasia.

Methods: We scoured scholarly papers and databases including PubMed, Google Scholar, and Science Direct for information on benign prostatic hyperplasia and management between December 1999 and July 2022. However, only the latest or most comprehensive study was considered. The authors also assessed the usefulness of references taken from similar books. Documents written in languages other than English have been overlooked because of lack of funding to translate them. Unpublished articles, oral talks, conference abstracts, and dissertations were all generally agreed upon to not constitute valid scientific investigation.

Conclusion: Over the course of the past ten years, a number of innovative approaches to the treatment of symptomatic BPH have come into existence. The number of possible treatments has increased, the spectrum of therapeutic choices, from careful waiting to open surgery, has broadened thanks to minimally invasive surgical techniques (MIST), novel drugs, and novel combinations of medical treatments. The range of possible symptoms is matched by the breadth of available therapies. Since deaths from BPH are uncommon, treatment typically centres on maintaining or enhancing quality of life.

Keywords: Management, Benign prostatic hyperplasia, Prostate.

INTRODUCTION

The prostate gland is a component of the male reproductive system and may be found in the true pelvis. Its function is to provide support. Its primary function is to release an alkaline fluid that acts as a barrier between the acidic vaginal environment and the sperm that live there. The fluid has the effect of bringing the acidity of the vagina back into balance, which in turn lengthens the total lifespan of the sperm and provides a greater window of opportunity for successfully fertilizing an ovum. The proteins and enzymes in the fluid are there to keep the sperm alive and healthy. When combined with the seminal fluid and sperm, the increased volume of the prostatic fluid makes it possible for easier mechanical propulsion through the urethra **(1).**

Benign prostatic hyperplasia is an expansion of the prostate that does not indicate the presence of malignancy. It's a common urological condition in middle-aged and elderly men, and it manifests with lower urinary tract symptoms. While, both the stromal and epithelial components of the prostate grow larger in men with BPH, it is the proliferation of stromal smooth muscle cells that is the primary factor in prostatic enlargement **(2).**

Both static and dynamic variables may play a role in the pathophysiology of urinary symptoms that are associated with BPH. The static part is a result of the expansion of the prostate impinging onto the prostatic urethra and bladder outflow, whereas the dynamic component is connected to the tension of prostatic smooth muscle. Because of an abnormally high rate of glandular tissue growth in the periurethral zone or stromal tissue growth in the transition zone, the static component may be responsible for urinary symptoms. The direction in which glandular tissue grows can have an effect on the flow of urine. A direct restriction of urine flow is likely to result from growth that is directed toward the interior. The early stage of an outward development of glandular tissue is less likely to induce an obstruction in the flow of urine in the urinary tract. It's possible that the prostatic capsule can stop the prostate from growing progressively more outward. As a consequence, continued outward development may eventually lead to compressive stresses being exerted on the prostatic urethra (Figure 1) **(3).**

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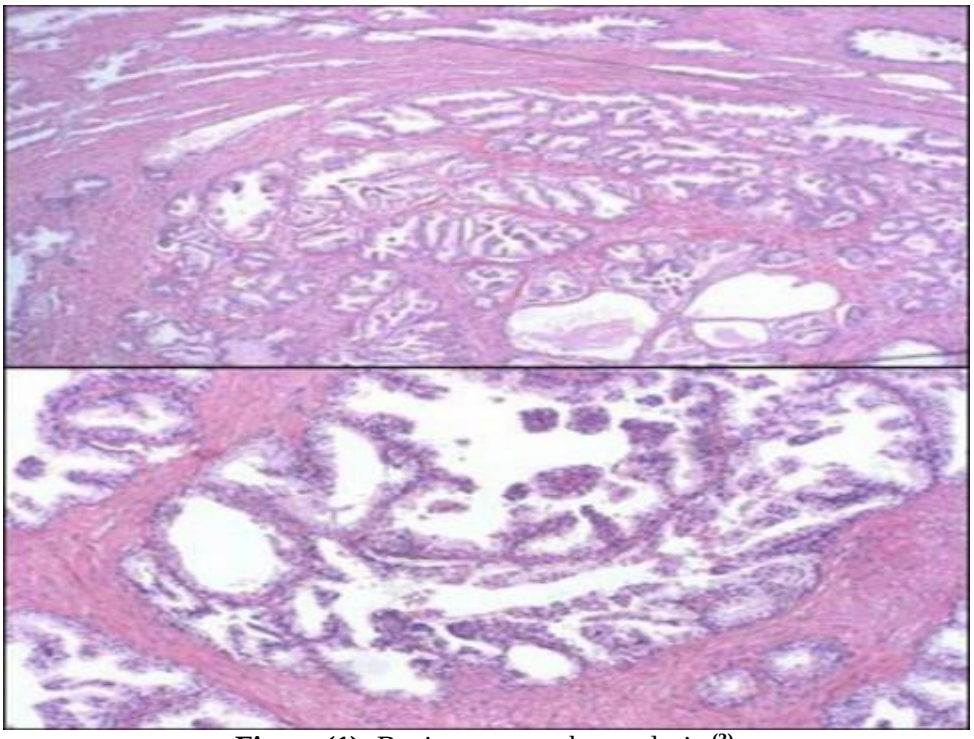

Figure (1): Benign prostate hyperplasia [3].

Therefore, the size of the prostate as determined by digital rectal examination (DRE), which correlates with outward growth, may not correlate with urine flow complaints. This is because outward growth correlates with prostate size. In addition, obstruction of the urinary tract can occur even in the absence of prostate growth if there is an increase in the tone of the prostatic smooth muscle. There is a correlation between being older and having higher levels of the enzymes involving aromatase as well as 5-alpha reductase. Androgen hormones are converted into oestrogen and dihydrotestosterone by the enzymes aromatase and 5-alpha reductase, respectively. Testosterone levels fall while dihydrotestosterone (DHT) and oestrogen levels rise as a result of androgen hormone metabolism. When oestrogen and DHT, an anabolic hormone that is several times stronger than testosterone and plays a vital role in the growth of cells in the prostate, are present together, they generate a synergy that leads to the development of BPH [3].

Excessive growth of the prostate as a natural consequence of ageing will lead to benign prostatic hyperplasia (BPH), which will eventually lead to lower urinary tract symptoms (LUTS). Many men suffer from LUTS and BPH, two disorders that worsen with time. Acute urine retention (AUR) and surgical procedures are two outcomes that can occur as a result of this progression, along with an increase in prostate size, increasing symptoms, discomfort, and a decline in flow rate and urodynamics. Over the course of the past ten years, a number of innovative approaches to the treatment of symptomatic BPH have come into existence. The number of possible treatments has increased, range from watchful waiting to full-blown surgery as a result of advances in MIST, novel pharmaceuticals, and novel combinations of medical therapy. The variety of possible treatments is just as wide-ranging as the symptoms that can be experienced. BPH is rarely fatal, hence care should most likely focus on safely improving quality of life. The goal of treatment for BPH is to improve quality of life by alleviating symptoms, boosting maximum flow rate, slowing disease progression, and lowering the risk of developing new morbidities [4].

Watchful waiting:

Watchful waiting, often known as active surveillance, is the treatment approach of choice for patients whose symptoms are quite modest. It's also a viable option for men with moderate-to-severe symptoms but no LUTS or BOO-related complications (such as renal insufficiency and urinary retention, or recurrent infection) yet. BPH can be managed with a strategy known as "watchful waiting," in which the patient is monitored by his doctor but is not given any treatment at this time. Even with a high AUA-SI score, patient may choose watchful waiting as his therapy of choice because the level of symptom unpleasantness that various patients are able to tolerate on a daily basis is quite variable [5].

The practise of watchful waiting relies on Alterations to one's lifestyle, such as reducing the amount of fluids consumed before going to bed and cutting back on alcohol and items containing caffeine, can help alleviate the symptoms of BPH. Patients may also be given opiates, antihistamines, decongestants, diuretics, and antidepressants that are of the tricyclic variety. Alpha blockers are by far the most often used option for the initial treatment [4].

Alpha one adrenoreceptor blockers:

Alpha one adrenergic receptors (AR), are responsible for mediating a large number of the physiological processes that are caused by the endogenous catecholamines noradrenaline and adrenaline. These functions include the contraction of smooth muscle and the hypertrophy of cells. In addition, drugs now used in clinical practice target them at the molecular level to treat disorders including arterial hypertension and benign prostatic hyperplasia. Due to the frequency of 1-AR in the bladder neck or prostate, studies on alpha 1-adrenergic blocking drugs have concentrated on the treatment of symptomatic benign prostatic hyperplasia (BPH) (40 times the concentration in the bladder). Alpha 1-blockers including doxazosin, terazosin, tamsulosin, and alfuzosin are commonly prescribed by doctors to treat LUTS caused by BPH. By inhibiting stimulation of sympathetic alpha 1-receptors, they alleviate tension in the prostate and treat the dynamic aspect of benign prostatic hyperplasia (BPH). Regardless of blood prostate specific antigen levels or prostate volume, each of these medications can cause the desired effects on urination **(6).**

Alpha 1-blockers have the ability to quickly alleviate urinary symptoms and increase urine flow by decreasing smooth muscle tone in the prostate. Drugs like tamsulosin, a highly selective 1A-blocker, and the nonselective 1 blockers terazosin, doxazosin, and alfuzosin are currently on the market **(7).**

Because 1A-receptors are more common in the male bladder outflow tract than 1B-receptors, silodosin is a highly selective medication for these receptors. According to in vitro studies, silodosin has an extremely high ratio of 1A to 1B binding affinity (162 to 1), this may have a significant beneficial effect on blood pressure regulation by decreasing the amount of dynamic neutrally generated smooth muscle relaxation in the lower urinary tract. High uroselectivity and a favourable cardiovascular safety profile have been reported for silodosin, and these claims have been supported by both preclinical and clinical research. Silodosin is selective for the 1A-AR subtype, which may be due to the drug's favourable safety profile. When it comes to treating LUTS caused by BPH, silodosin is both fast-acting and long-lasting **(8)**.

On the other hand, silodosin is associated with a significantly greater risk of ejaculatory dysfunction. In reality, the latter is an ejaculation, despite the fact that it is commonly referred to as a retrograde ejaculation. Then, especially those who are younger or sexually active, need to be advised that this side effect will go away after they stop taking the medicine, which something needs to be thoroughly discussed with patients **(9).**

Naftopidil, an alpha D-selective blocker, was discovered in a recent study to lower the likelihood of generating ejaculatory irregularities. The effects of the alpha-1a blockers silodosin and naftopidil on LUTS are very similar, with silodosin having a minor advantage in voiding symptoms. The most serious risk associated with these medications is the development of vasodilatory symptoms. Naftopidil, an alpha 1A selective blocker, may have a better track record of preserving sexual function (especially ejaculation) than silodosin, a 1-selective blocker **(7).**

Although alpha 1-adrenergic receptor (AR) antagonists are generally well tolerated, they can cause serious adverse events such cardiovascular problems and even death in some patients. Tamsulosin's safety in high-risk populations is better documented than that of other -AR antagonists, although the available data are inconclusive. Patients with LUTS/BPH who fall into one of these risk categories should utilise this knowledge to guide their treatment selection **(4).**

5-alpha reductase inhibitors:

Although alpha 1-adrenergic receptor (AR) antagonists are generally well tolerated, they do carry the risk of cardiovascular adverse effects, which in turn increase the risk of serious adverse events such falls and fractures. Although current results are inconclusive, tamsulosin's safety in such high-risk populations is more documented than that of other -AR antagonists. These data should influence the treatment options considered by patients with LUTS/BPH who fall into one of the aforementioned risk categories **(4)**.

Inhibiting type 2 5-alpha-reductase reduces DHT production in the prostate by blocking the initial step in the conversion of testosterone to DHT. This results in a reduction in the size of the prostate, as well as apoptosis and involution. There is a lack of consensus on the precise function of 5-alpha-reductase type 1 in both normal and pathological prostatic development. 5-alpha-reductase inhibitors treat LUTS by reducing the volume of the prostate. As a result, people whose prostates are larger may have a higher improvement. In addition, the optimal reduction in prostate volume requires treatment for a period of six months **(10)**.

The Food and Drug Administration in the United States gave its approval to finasteride as the first steroidal 5'-reductase inhibitor (USFDA). In humans, it brings the level of prostatic DHT down by 70–90% and shrinks the size of the glands that produce it. In 2002, approval was given to yet another similar counterpart called dutasteride. After one year of oral medication, dutasteride reduces DHT levels by more than 90%, whereas finasteride only inhibits type I isozymes of the 5 alpha-reductase enzymes **(11).**

A new 5'-reductase inhibitor called epristeride has shown promise as a potential treatment for benign prostatic hyperplasia (BPH). Carboxy steroid describes this chemical. Due to its preferential attachment to an enzyme binary complex containing NADP, its inhibitory effect is not overcome by increases in testosterone concentration, despite being an uncompetitive inhibitor against both testosterone and NADPH. The type II 5'-reductase isoenzyme is the

target of this inhibitor. Androgen-sensitive prostate cancer development is also suppressed. Both finasteride and dutasteride have demonstrated therapeutic and preventative efficacy in men at high risk for developing prostate cancer [(12)].

Treatments with 5ARI have been shown to have a number of adverse effects, the most of which are related to sexual function. Reduced libido, erectile dysfunction, and ejaculatory frequency have all been reported by up to 8% of individuals on sildenafil (compared with 3 percent, 4 percent and 1 percent, respectively, for placebo) [(13)].

Combination therapies:

More beneficial than 5-ARI therapy and as safe as alpha blocker medication, combination therapy was proven to be useful in treating hypertension. Combination therapy, on the other hand, was found to be superior to alpha-blocker therapy or 5-ARI therapy in the Medical Therapy of Prostate Symptoms (MTOPS), study in terms of avoiding progression and relieving symptoms among men with bigger prostates [(14)].

It has been hypothesised that this could be an indication that the short-term benefits of 1-blockers, specifically the relaxing of the smooth muscle to ease urinary stress, are nullified by the ongoing growth of the prostate. This can be stopped and reversed by inhibiting the 5a-reductase enzyme in its own right. It has been demonstrated that the use of combination therapy with doxazosin and finasteride can provide rapid relief from symptoms, as well as a reduction in the growth of the prostate, a lower chance of developing AUR, and a decreased need for surgery associated to BPH [(15)].

Anticholinergic Agents:

Anticholinergic drugs are appropriate and effective therapy choices for the management of lower urinary tract symptoms (LUTS) that are caused by BPH in men who do not have an elevated post-void residual (PVR) and whose LUTS are mostly irritative [(15)].

The incidence of urinary retention was similar to that of placebo in two of the largest randomised controlled trials (RCTs). In addition, the incidence of side effects such constipation, diarrhoea, and sleepiness were similar to those seen in the placebo group. In the available randomised controlled trials (RCTs), the overall withdrawal rate from tolterodine therapy ranged from 11% to 12%. Adverse events caused between 0.02 and 0.33% of individuals to withdraw from the study [(16)].

Tolterodine use on its own or in combination with tamsulosin did not result in any cases of erectile dysfunction (ED) or ejaculatory problems being reported by patients. In none of these random controlled trials (RCTS), the use of tolterodine was associated with a significant increase in morbidity or mortality. Anticholinergic medicines, as antimuscarinic agents, inhibit the action of the neurotransmitter acetylcholine. Through a process known as competitive inhibition, the effects of acetylcholine on the receptors of neurons in the bladder can be mitigated by the use of this category of pharmaceuticals [(17)].

Phytotherapy:

Cernilton is just one of many phytotherapeutic drugs used to treat BPH nowadays. Secale cereal, which comes from rye grass, provides the pollen for this product. Millions of men throughout the world utilise this drug, which has been approved for sale in various nations. It is particularly popular in Western Europe, Japan, Korea, and Argentina [(18)].

The investigated cernilton trials were short in duration, had a small sample size, and failed to provide important results, and the uncertain quality of the preparations that were used were all limitations. In the comparison studies, there was no active control that could be verified. According to the evidence that is now available, cernilton is safe to use and shows only a moderate improvement in urological symptoms generally, including nocturia [(18)].

CONCLUSION

Over the course of the past ten years, a number of innovative approaches to the treatment of symptomatic BPH have come into existence. The number of possible treatments has increased, the spectrum of therapeutic choices, from careful waiting to open surgery, has broadened thanks to MIST, novel drugs, and novel combinations of medical treatments. The range of possible symptoms is matched by the breadth of available therapies. Since deaths from BPH are uncommon, treatment typically centres on maintaining or enhancing quality of life.

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