

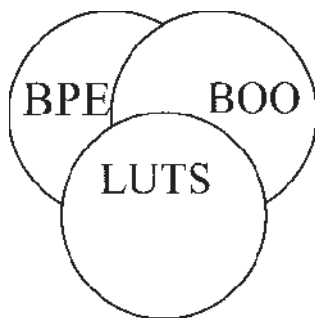
CAN BENIGN PROSTATIC HYPERPLASIA BE MANAGED BY PILLS? - OUR EXPERIENCE

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Abstract : This communication is to provide a critical overview of the currently available guidelines in management of benign prostatic hyperplasia & also to give the revolution of changes that has taken place in its management paradigm in the last four decades. Open prostatectomy was the only treatment modality available till 1970. Development of transurethral procedure by Nesbit in 1943 brought a total revolution in its management in 1970 till dates. Many other minimally invasive procedure have developed in the recent past using different source of energy like laser, heat, radio frequency and ultrasound. Medical management for BPH using pills was dream till 1910 when α -adrenergic receptors were identified by Shapirio in 1967 with these recent developments, now a days, management of BPH has not only become very safe with low morbidity, no morbidity but also cost effective giving better quality of life to the patient.

INTRODUCTION

Until recently benign prostatic hyperplasia (BPH) was thought of as a relatively uncomplicated disease process, resulting from age related enlargement of the prostate gland. Current thought leaders view BPH as a syndrome in which BPE (Benign Prostate Enlargement), BOO (Bladder Outlet Obstruction) and LUTS (Lower Urinary Tract Symptoms) are inter related but distinct entities with possibly different etiologies and divergent natural histories. (Figure below)



Benign hyperplasia of the prostate (BPH) usually affects men after 40 years of age. It is the commonest disorder of ageing males worldwide, affecting one out of four men over 50 years of age. The prevalence is expected to increase as the mean age of the male population is increasing in our society and in years to come this malady will be a great health problem in ageing males of our society. Although 70% of men over 60 years of age will develop BPH, but only 35% of them may require surgical intervention for relief of their symptomatology. Therefore, there is a need for medical management of rest of BPH patients who are symptomatic. Again various co-morbid factors in the geriatric age group may be a contraindication for undergoing surgical treatment. This group would greatly benefit from medical management.

The *weight of the prostate* at birth is 1gm in weight. This gland undergoes first involution at the age of 14 years when man enters adulthood. From 14 years to 40 years of age the prostate growth is

slow as its main function remains as an accessory gland for sexual activity of the man. After 40 years of age when the peak sexual activity of man starts declining, serum testosterone level also falls, an imbalance occurs between serum testosterone and oestrogen resulting in uncontrolled enlargement of prostate gland. The size and the degree of growth vary from individual to individual depending on the stimulation of various growth factors like EGF (epidermal growth factor), FGF (fibroblast growth factor) and TGF (transition growth factor). The *prevalence of BPH* is 8% at the 4th decade of life, rises to 50% by 6th decade of life and 80% by 8th decade of life.

The concept of *medical management* of BPH came into focus after the identification of effect of α -adrenergic receptors at the bladder neck, prostate capsule, smooth muscle of prostate and prostatic urethra in 1970-75 when it was proved that stimulation of these receptors control the tonicity at the bladder neck & prostate resulting in obstruction to urinary flow i.e. the dynamic factor. Hence relaxation of these receptors by giving α -adrenergic antagonist will relax the tonicity at the bladder neck thereby releasing obstruction. Simultaneously it was proved that the increased volume of the prostate gland also results in obstruction at the bladder neck i.e. the static factor. Therefore, shrinkage of the prostate gland can be achieved by giving 5 α reductase inhibitors so that DHT (di-hydro testosterone) production from serum testosterone and androgens can be reduced thereby causing reduction in volume of prostate adenoma.

Age is the greatest prognostic factor for BPH. BPH decreases quality of life. Raised serum insulin, waist to hip ratio and coffee drinking increase incidence of BPH. Incidence of BPH is declining in developed countries but mortality is on rise in underdeveloped countries.

AUTHOR'S EXPERIENCE

The author in the last ten years has tried to establish the importance of medical management in BPH and herewith present his experience & research work with result chronologically.

The first α -selective α -adrenergic blocker available in Indian market was *Terazocin* in 1990. We conducted a trial using Terazocin 5mg once a day (in divided dose) for three months on BPH patients not having absolute indication for surgery but symptomatic of

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prostatism. These patients showed 50-55% improvement in their subjective and 40-45% improvement in their objective symptoms at the end of therapy but showed adverse side effects in the form of postural hypotension, dizziness, headache in 20% of patients and had symptoms returned once drug was stopped. (Paper published – Indian Journal of Urology, March 1998)

With the introduction of *Doxazocin* later in 1998 as a highly selective α -adrenergic blocker with a longer half life (22 hours) and gradual onset of action 2-6 hours we conducted a trial in 1999 using 4mg of *Doxazocin* once a day at night for three months. At the end of the therapy we recorded 50-55% subjective improvement and 60% in objective improvement with a decrease in the post residual urine volume by 21%. Though there was no significant improvement in symptoms score and flow rate as compared to *Terazocin* but the incidence of adverse side effect was comparatively much lower than *Terazocin*. In *Doxazocin* group, headache, dizziness and hypotension was seen in 10% only. (Paper published – Indian Journal of Urology, Sept. 2000).

Though medical management with above α -adrenergic blocker showed 50-55% improvement in symptomatology and flow rate but it did not bring satisfaction to the patient as was expected as patients continued to have lower irritative symptoms like urgency, frequency & nocturia.

In 2001, *Tamsulosin* a new uroselective α -adrenergic receptor antagonist was introduced for medical management of BPH. This salt has the advantage of being uroselective as it takes care of both the bladder outlet obstruction symptoms hesitancy, intermittency, terminal dribbling & weak stream and bladder instability symptoms like nocturia, frequency and urgency. Since it has a dual mode of action blocking not only α_{1a} but also α_1 responsible for bladder irritative symptoms.

We undertook a trial to study the safety & efficacy of *Tamsulosin* in management of BPH using a dose of 0.4mg once a day at night for three months. At the end of therapy there was 70-75% improvement in subjective symptoms score and 75-80% improvement in objective symptoms. Post residual urine volume decreased by 39% from baseline.

The adverse effect in the form of dizziness & headache was found in 7% of patients and less than 4% of patients had postural hypotension as compared to *Terazocin* & *Doxazocin* because the ratio of binding affinity for α_{1a} receptor to α_{1b} receptors was 29 times for *Tamsulosin* as compared to 1-2 times for *Terazocin*, *Doxazocin* & *Prazocin*, thereby making *Tamsulosin* a much safer drug. (Paper published – Indian Journal of Urology, Sept. 2003 & Annals of the College of Surgeons, Aug. 2003)

Since at present medical management is a well established modality of management of BPH for patients not having absolute indication for surgery, more and more geriatric males and males not suitable for surgery due to associated co-morbid factors are willing for medical management as the first line of treatment for their prostatism symptoms.

The MTOPS (Medical Therapy of Prostatic Symptoms Trial) study have established the use of two drugs – a uroselective α -blocker in combination with 5 α -reductase inhibitor (type I & type II) is very effective in management of BPH.

To give more benefit to the patients the author undertook another trial in 2003-04 using a combination of α -adrenergic blocker (*Tamsulosin* 0.4mg OD) and 5 α -reductase inhibitor (*Finasteride* 5mg OD) for six months. The result of this combination has proved to be most beneficial in improving the symptoms score, urinary obstruction and greatly reducing irritative symptoms and post residual urine volume as compared to all other previous trial therapy. Before starting this combination a baseline PSA is mandatory and periodic PSA estimation during course of therapy is recommended as 5 α -reductase inhibitor cause reduction in PSA. (Accepted for publication in Indian Journal of Urology 2004-05). The result of this study is very encouraging with regard to reduction in prostate size, post residual urine volume, improve IPS score, uroflow rate & decrease hesitancy time with the minimum adverse effect.

The author invariably faces one query while treating such patients. *How long can I continue with medical management?* The author is of the opinion to continue medical management on BPH patients as long as the patients do not develop absolute indication for surgery. In authors opinion retention of urine and back pressure changes of kidneys are the two only indications for surgery for BPH. At present the author has patients who are satisfied with medical management for more than five years.

DISCUSSION

Medical management with α -adrenergic antagonist and 5 α -reductase inhibitor as monotherapy or in combination is a well established modality of management of BPH patients not having absolute indication for surgery but symptomatic or having associated risk co-morbid factors as contraindication for surgery.

Selection of patients with periodic follow up should be meticulously done so that patient gets maximum benefits.

By doing so the author in the last ten years have not only prevented unnecessary prostate surgery or over-doing of prostate surgery in many patients of BPH but also has reduced the surgical morbidity & mortality rates from prostate surgery in the department apart from establishing medical management of BPH as a reality and there by giving better quality of life in a sizeable geriatric male population of our society.

Currently the author is involved in management of BPH with newer drug combination and phytotherapies. *Alfuzosin* and *Dutasteride* are newer drug on study trial with the author. *Lycopene* an antioxidant derived from tomatoes and guava have shown to reduce serum testosterone in human beings and causes apoptosis in prostate of rats in experimental study.

CONCLUSION

Medical management is now the first line treatment option for patients with BPH not having indication for surgery. In the past five years medical management for BPH has greatly reduced the incidence of surgery for prostate worldwide simultaneously reducing the mortality & morbidity incidence resulting from the same.

The author is of the firm opinion that 65-70% of patients with BPH not requiring surgical intervention greatly benefit from medical management as first line of treatment option for their prostatism.