

Review Article

Medical Management for BPH-Present Concept

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ABSTRACT

Purpose of review: Benign prostatic hyperplasia (BPH) is one of the most common disease to affect men beyond middle age to cause lower urinary tract symptoms (LUTS).

Medical therapy is now well established as the first option in the management of symptomatic BPH.

Selective α_1 blockers which relaxes the smooth muscle component of prostatic urethra and bladder neck and the 5 α reductase enzyme inhibitors (5ARI) which inhibit or regresses the growth of adenomatous component of prostatic gland have proved quite efficacious when given as a monotherapy or in combination.

Lately anticholinergic drugs like tolterodine or solifenacetin are given in combination with α blockers where irritative bladder symptoms like- urgency, frequency or urge incontinence predominates. Though these two drugs are physiologically antagonistic, each exerts its beneficial effect acting at different target sites eg., - overactive detrusor muscle and spasmodic bladder neck sphincter area.

More recently 5 phosphodiesterase inhibitors like Sildenafil citrate (Viagra) or the long acting variant Tadalafil citrate (Tazzele) are prescribed in combination with α blockers to enhance the effect of smooth muscle relaxation at the bladder neck and also to take care of the erectile dysfunction (frequently experienced by many ageing men with BPH)

Various phytotherapeutic products and food supplements used by traditional medical therapists failed to give a consistent favourable result.

The present review gives a bird's eye view on recent advances in the medical management of BPH.

Key Words: Benign prostatic hyperplasia, Medical therapy, 5 α reductase inhibitors, Selective α blockers, Phosphodiesterase inhibitors.

INTRODUCTION

BPH is characterised by the enlargement of the prostate gland resulting from benign proliferation of glandular component and the

stromal elements consisting of fibroblasts and smooth muscles. The enlarged gland leads to disease manifestation via two means-Static and Dynamic components

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STATIC COMPONENT

Enlarging adenomatous mass produces compression at the bladder neck and prostatic urethra causing bladder outlet obstruction (B.O.O).

DYNAMIC COMPONENT

Increased smooth muscle tone of the enlarged prostate gland leads to sphincter spasm enhancing further the symptom of B.O.O.

DISCUSSION

CLINICAL MANIFESTATIONS

The common manifestation of BPH is a constellation of symptoms described presently as lower urinary tract symptoms (LUTS).

LUTS are any combination of voiding symptoms (hesitancy, intermittency, weak stream and terminal dribbling) and storage symptoms of bladder (manifesting as frequency, urgency, urge incontinence and nocturia). Storage symptoms are caused by long standing bladder outlet obstruction (BOO) leading to over distension of bladder, fibrosis and detrusor denervation.

In terminal stages if untreated, one may develop retention of urine and/ or retention with overflow incontinence (false incontinence).

The size of the prostate is not directly related to

patient's symptoms. Not all men with BPH have LUTS and all men with LUTS have BPH.

To assess the severity of symptoms objectively and to decide whether one needs only observation (expectant management), medical treatment or surgical intervention, a scoring system called International Prostatic Scoring System (IPSS) is devised. The IPSS questionnaire is given to the patient to answer in the language he best understands (see Table 1).

An elderly man with BPH may also suffer from various co morbid conditions like Diabetes Mellitus, COPD, IHD, CNS disorders, UTI or erectile dysfunction. On such a situation additional treatment modifications may need to be made as per the need.

For decades, the primary treatment option for BPH remained surgical intervention. Medical treatment is now well established to manage BPH with mild to moderate symptoms or to treat the cases where the patient is not fit for surgery due to various cardiovascular co-morbidities. In fact medical treatment has

PROSTATE PROBLEMS

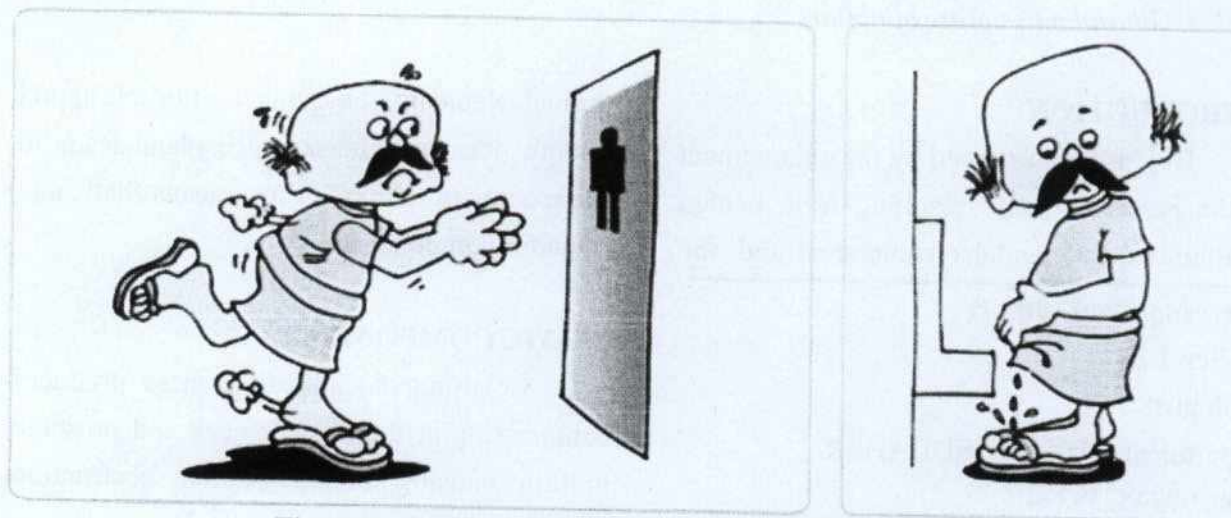


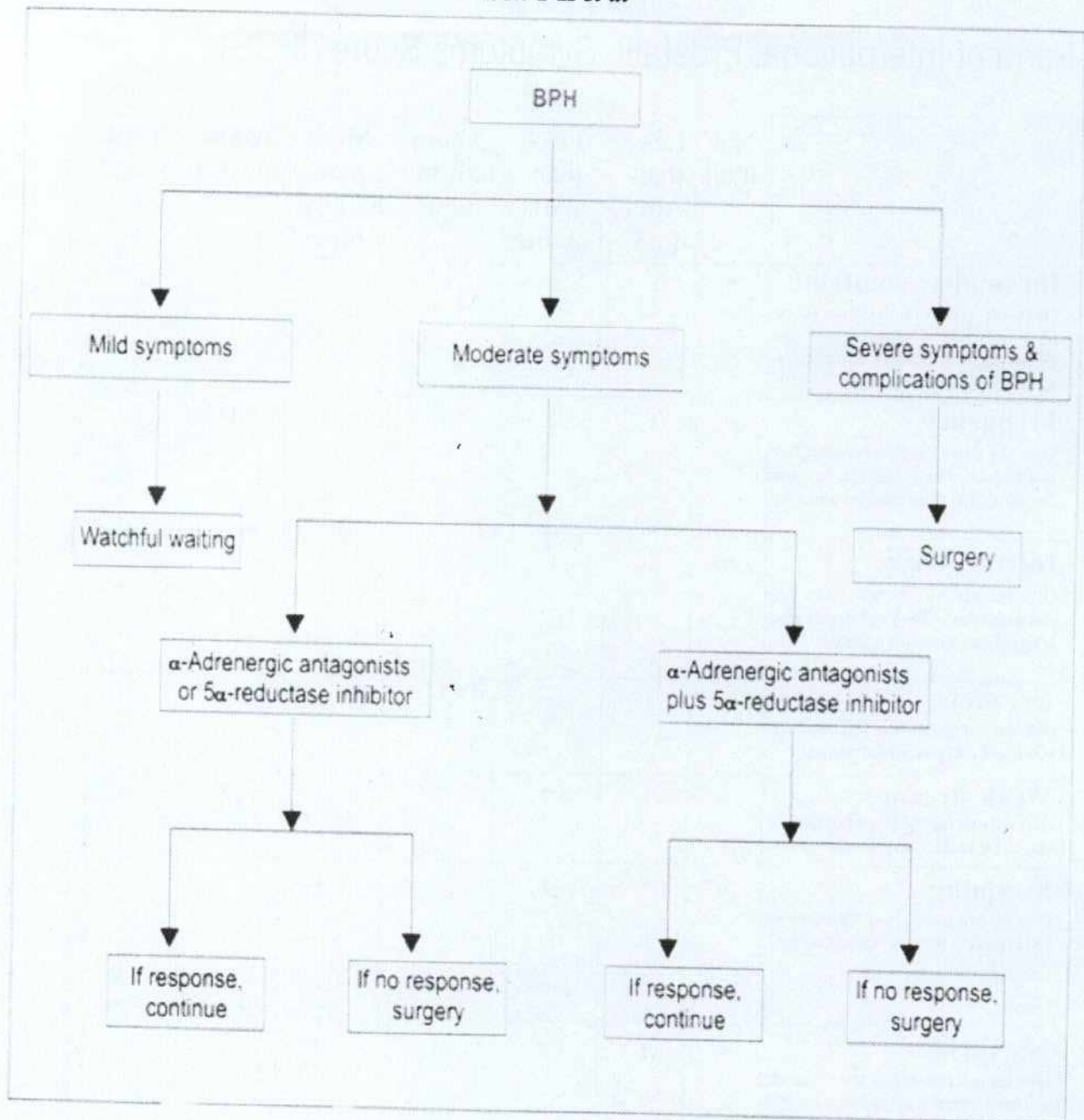
Figure 1: Frequency, Urgency and urge incontinence

Form of International Prostatic Symptoms Score (IPSS)

	Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almst always	Your score
Incomplete emptying Over the past month, how often have you had a sensation of not emptying your bladder completely after you finish urinating?	0	1	2	3	4	5	
Frequency Over the past month, how often have you had to urinate again in less than two hours after you finished urinating?	0	1	2	3	4	5	
Intermittency Over the past month, how often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5	
Urgency Over the last month, how difficult have you found it to postpone urination?	0	1	2	3	4	5	
Weak stream Over the past month, how often have you had a weak urinary stream?	0	1	2	3	4	5	
Straining Over the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5	
	None	1 time	2 times	3 times	4 times	5 times or more	Your score
Nocturia Over the past month, how many times did you most typically get up to urinate from the time you went to bed until the time you got up in the morning?	0	1	2	3	4	5	
TOTAL IPSS SCORE							
Quality of life due to urinary symptoms	Delighted	Pleased	Mostly satisfied	Mixed about equally satisfied and dissatisfied	Mostly dis satisfied	Unhappy	Terrible
If you were to spend the rest of your life with your urinary condition the way it is now, how would you feel about that?	0	1	2	3	4	5	6

From the American Urology Association(AUA) Symptom Index for BPH

Total score: 0-7 Mildly symptomatic; 8-19 moderately symptomatic; 20-25 severely symptomatic.



Various treatment options for BPH

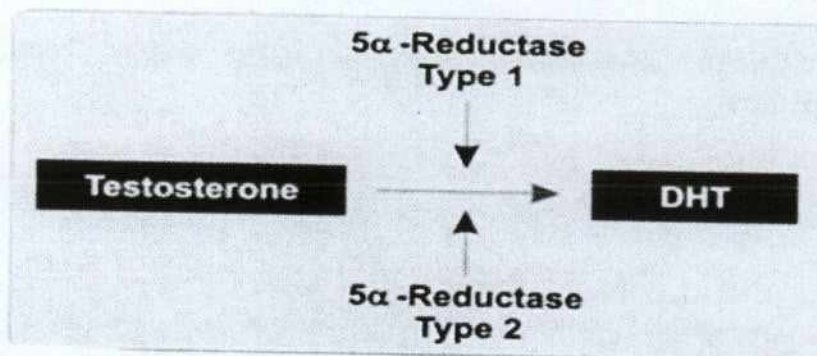


Figure 2 : Mechanism of 5αRI

become the first option in the line of management of symptomatic BPH.

MEDICAL MANAGEMENT

Medical treatment of symptomatic BPH is aimed at improvement of symptomatic score, lowering the risk of disease progression, improving the patient reported quality of life (QOL) and patient satisfaction.^[1] It typically targets one or both main disease components eg: static and dynamic component by 5 α reductase inhibitors or selective α 1 blockers.

Lately the medical therapy has been further modified and tailored to include anticholinergic drugs to look into the aspects of overactive bladder (BOO) and phosphodiesterase inhibitors to overcome the problem of erectile dysfunctions.

ALPHA ADRENERGIC BLOCKERS

Alpha adrenergic receptors are located in abundance in prostate stromal smooth muscles and in the smooth muscles of arteries and veins. Activation of these receptors enhances the prostatic smooth muscle tone resulting in impaired urine flow.

Blockage of these receptors by alpha blockers results in relaxation of the spincteric and easy passage of urine. However the similar effect of the drug at the arteriolar level lead to the fall of BP and postural hypotension and syncopal attacks. Earlier generation of non selective α blockers like prazosin, terrazosin and dazosocin fell into disrepute due to this major side effect.

Subsequent discovery lead to the finding of various subtypes of alpha receptors eg: α 1a,

1b and 1d. Alpha 1a receptors are predominantly located at the prostatic smooth muscles and α 1b receptors are predominantly located in the smooth muscles of arteries and veins. α 1d receptors are mainly located in the bladder wall body and dome and also in the spinal cord. Alpha 1d receptors have been proposed to mediate the irritative components of LUTS due to BPH (see Figure 1).

Selective α 1a blockers like Tamsulosin Hydrochloride and Silodocin are now widely used as first line of drug treatment for BPH with no side effects of postural hypotension (as seen with drugs of earlier generation of non selective blockers).^[2]

Alfuzosin though not a pure alpha 1a blocker, is considered uroselective α blocker as it exerts least cardiovascular side effects.

Naftopidil is another new selective alpha blocker which also has blocking effect of both α 1a and α 1d receptors and is found to be useful when the bladder irritative symptoms predominate.

Retrograde ejaculation due to bladder neck relaxation with α blockers is a known side effect though not commonly seen when these drugs are given in the standard therapeutic dosages.

5 α REDUCTASE INHIBITORS

Testosterone, the primary circulatory androgen needs to be converted into dihydrotestosterone (DHT) to act on the target organs like prostate cells. 5 α reductase enzyme is responsible for conversion of testosterone to DHT(see Figure 2).

Finasteride and dutasteride are two drugs

which block the action of 5 alpha reductase enzyme and prevents formation of DHT. Finasteride (Proscar) was the first drug of this group but it inhibits only the type 1 of the isoenzyme.^[3]

Dutasteride on the other end inhibits both type 1 and type 2 of the isoenzyme of 5 α reductase and is found to be more effective than finasteride. However it takes 4-6 weeks for these drugs to show its beneficial effects of shrinkage of prostate size (unlike alpha blockers which are effective within 24-48 hours).

Both finasteride and dutasteride bring down the level of PSA by 50%, hence base line PSA study is desirable for future comparison and references if doubt of malignancy exists. Decrease in libido is a common side effect complained by few patients.

ANTIMUSCARINIC AGENTS

Cases where the bothersome bladder storage symptoms manifesting in the form of frequency, urgency or urge incontinence predominates, antimuscarinic agents like tolterodine, solifenacin or darifenacin may be added in small doses along with the α blocker. One such available drug combination is Rolliflow (Tolterodine 5mg with Tamsulosin 0.4 mg)

PDES INHIBITORS

Addition of Sildenafil or Tadalafil with α blockers may potentiate the effect of smooth muscle relaxation at bladder neck and prostatic urethra. Besides it takes care of erectile dysfunction commonly experienced by the men of advanced age group.^[4,5,6]

ALGORITHMIC APPROACH

Following initial analysis with symptom analysis, Digital rectal examination (DRE), ultrasound studies with postvoidal residual urine (PvRu), PSA estimation and uroflowmetry, patients are classified into classes of mild, moderate and severe symptoms with or without complications.

Patients with mild symptoms not bothersome enough to carry out day to day activities are managed with watchful waiting with modulation of fluid and alcohol intake and avoidance to cold and humid conditions. Patients with bothersome moderate to severe symptoms are subjected to single drug or combination of two or three drugs depending on the nature of the prevailing symptomatology.

Surgical management is indicated in patients with bothersome symptoms refractory to medical treatment or having developed complications like urinary retention, recurrent UTI, haematuria, renal insufficiency or bladder stones (please refer to flow chart-Table 2).

CONCLUSION

Medical treatment with single drug or combination of Dutasteride and Tamsulosin is well established in the management of moderate to severe LUTS due to BPH. The treatment is strongly supported world over and reduces the risk of clinical progression, acute urinary retention and BPH related surgical interventions. However once subjected to medical treatment, patient needs to be closely observed and followed up every 3-6 months to assess the progress and failure of medical treatment. Till date there is no unanimous

opinion regarding the duration of treatment. The treatment should continue till the beneficial effects are seen. However at the end of 6 months period, one of the components of combination drug treatment may be withdrawn and assess the beneficial effects continue or not.

Various phytotherapeutic agents like saw palmetto(*Serenoa repens*), soya(*Glycine soja*), gokshur(*Tribulus terrestris*) African ray grass etc, are popular with people practising traditional medicine.

Phytotherapy cannot be recommended due to heterogeneity of the products and no strong evidence supporting its effectiveness.

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