Tamsulosin-Dutasteride Combination Therapy in Benign Prostatic Hyperplasia

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Introduction

Benign prostatic hyperplasia (BPH), a frequent cause of lower urinary tract symptoms (LUTS) in aging men, is characterized by non-malignant enlargement of the prostate gland. This is attributed to uncontrolled hyperplastic growth of fibromuscular and epithelial tissues in the transition zone and periurethral region.[1,2] Around 50% of men by the age of 60 years have BPH in India.[3]

Symptoms of BPH

Patients with BPH can present with symptoms like poor flow, hesitancy, nocturia, etc.[1] LUTS can be storage or voiding:[1,2]

Storage LUTS

Frequency, urgency, nocturia, incontinence (usually as a result of bladder overactivity)

Voiding LUTS

Weak or intermittent urine flow, hesitancy in starting to void, straining to urinate, extended duration of urination, incomplete bladder emptying, post-void dribbling of urine.

Risk Factors and Pathophysiology

Several risk factors have been linked to the development of BPH (Figure 1). These can be modifiable and non-modifiable.[1]

Figure 1. Risk factors for BPH development

- Diet
  Excess alcohol intake, caffeine, and high-dose vitamin C supplement can heighten the risk of BPH and symptoms
- Diabetes and insulin
- Genetic predisposition
- Obesity
- Localized inflammation

Both static and dynamic factors are implicated in the development of LUTS and bladder outlet obstruction in BPH. Prostatic enlargement leads to static obstruction. This leads to compression of the periurethral region and obstruction of the bladder outlet.[1]

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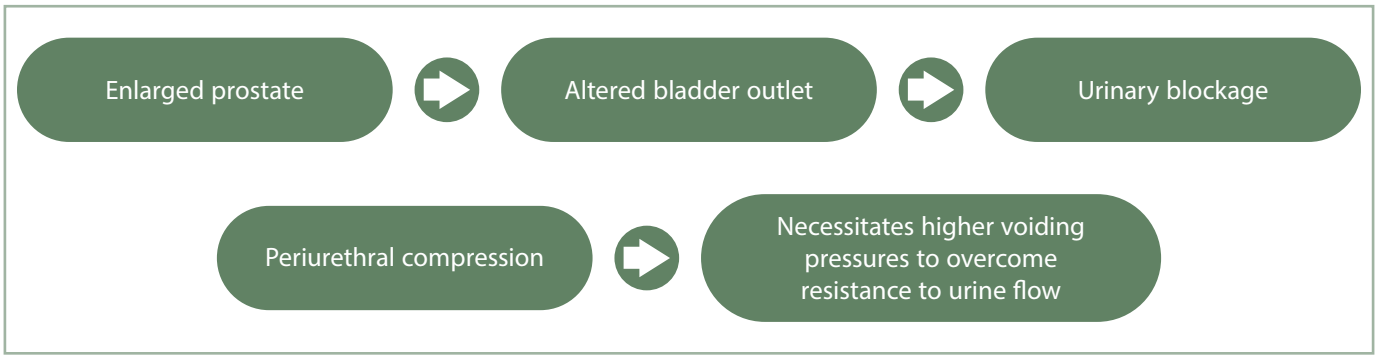


Tension in the prostatic smooth muscle constitutes the dynamic component.[1]

Treatment of BPH

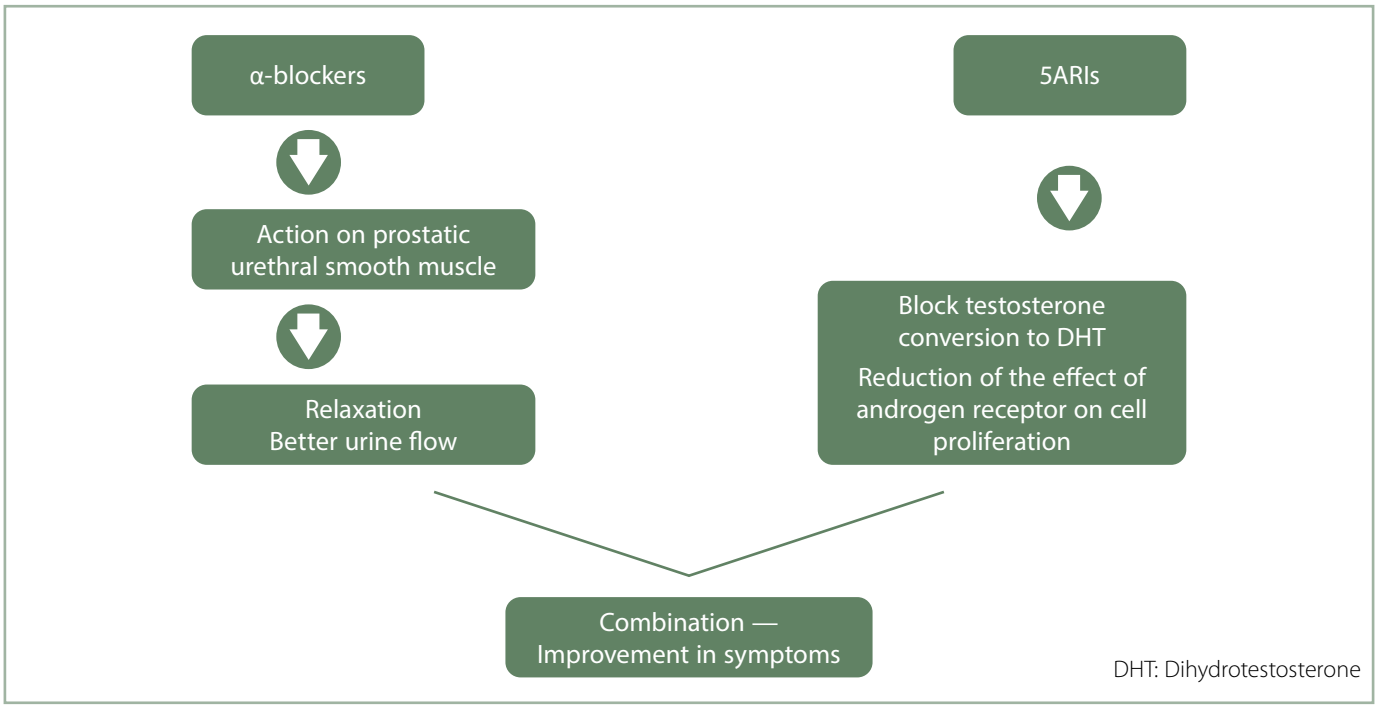
Watchful waiting

This involves lifestyle modification, such as decreased caffeine consumption, weight loss, decreased fluid intake in the evening, measures to avoid constipation, and pelvic floor muscle exercise.[1]

Medical treatment

Both static and dynamic factors, involved in the development of BPH, are targeted by medical treatments. It includes the use of α-blockers and 5 α-reductase inhibitors (5ARIs). Other agents include phosphodiesterase type 5 (PDE5) inhibitors and antimuscarinic agents.[1] A combination of α-blockers and 5ARIs is also used.[2] Figure 2 summarizes the action of these two groups of drugs.[2]

Figure 2. Action of α-blockers and 5ARIs



Surgical management

Surgical treatment can be considered for patients who do not respond to medical treatment or cannot tolerate medical therapy. Surgical intervention includes procedures like transurethral resection of the prostate (TURP), transurethral incision, holmium laser enucleation, vaporization, and minimally invasive techniques like aquablation, paclitaxel-coated prostatic balloon dilation, prostatic urethral lift, transurethral microwave thermotherapy, and selective prostatic artery embolization.[1]

Tamsulosin-Dutasteride Combination Therapy

Selective α1-adrenergic antagonists work by relaxing the prostate and bladder neck smooth muscles and do not impact the detrusor muscle of bladder wall. Resistance to urine flow is reduced while not impairing bladder contractility.[4] Tamsulosin is one of the only two α-blockers that has selectivity for α1a over α1b receptor.[5] Dutasteride is a 5ARI that can inhibit type 1 and 2 5α-reductase isoenzymes. Finasteride, on the other hand, inhibits type 2 only.[4] 5ARIs, either as monotherapy, or in combination with α-blockers have been recommended for the prevention of progression of LUTS/BPH or to diminish urinary retention risk and requirement for prostate-related surgical intervention.[5] The combined use of α-blockers and 5ARIs, owing to their distinct mechanisms of action, can provide more effective symptom control and improved quality of life.[6]

Several studies have evaluated the potential role of a combination of tamsulosin and dutasteride in LUTS/BPH management. Roehrborn and colleagues noted in a study that dutasteride and tamsulosin combination therapy at 4 years offered significantly greater benefit in terms of symptoms compared to either monotherapy. The findings thus supported long-term dutasteride and tamsulosin combination therapy for moderate-to-severe LUTS from BPH and prostate enlargement.[7]

Among males with moderate-to-severe BPH symptoms, the improvements in patient-reported quality of life and treatment satisfaction were significantly greater with combination treatment with dutasteride and tamsulosin compared to either monotherapy over a 4-year period.[8]

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Based on 4-year data from the Combination of Avodart and Tamsulosin (CombAT) study, Montorsi and colleagues evaluated the impact of dutasteride and tamsulosin combination therapy on symptoms of voiding and storage vs. those of either monotherapy. Among men with prostate volume of 30 mL or more, combination therapy demonstrated superior long-term management of both storage and voiding LUTS in comparison with tamsulosin alone. Additionally, among men with prostate volumes ranging from 30 to less than 58 mL, combination therapy was found to be better than dutasteride alone.[9]

A recent randomized trial compared the efficacy, side effects, and the time gap with combination treatment using different doses of dutasteride or finasteride combined with tamsulosin for treating BPH. Dutasteride proved to be superior to finasteride in improving maximum urinary flow rate (Qmax) at 6 months. It might offer somewhat greater advantages as part of combination therapy in BPH management.[10] In a real-world study on the experience of physicians using tamsulosin and dutasteride combination for BPH, around 88.86% of the physicians regarded tamsulosin and dutasteride combination as the gold standard for BPH treatment. Most common comorbidity considered by the physicians included cardiovascular (62.61%).[11]

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Conclusion

BPH, a non-malignant enlargement of the prostate, commonly leads to LUTS among aging men. Treatment of BPH includes observation, medical management, and surgery. Guidelines advocate the use of α-blockers and 5ARIs in the management of BPH, both alone and as combination therapy. Tamsulosin and dutasteride are potential agents in these classes that have shown benefits in the management of BPH as combination therapy. The combined use of α-blockers and 5ARIs, owing to their distinct mechanisms of action, can provide more effective symptom control and improved quality of life.

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