GERONTOLOGIA POLSKA 2026; 34; 3-11 ARTYKUŁ ORYGINALNY / ORIGINAL PAPER
zgłoszono 17.02.2026 – zaakceptowano 03.03.2026

Alpha-adrenergic blockers in the management of Benign Prostatic Hyperplasia: a review of contemporary treatment approaches

Artur Spyrka, Jakub Nocoń, Szymon Domagała, Kamil Kania, Michał Tkocz, Kamil Marczewski, Mateusz Marcinek

Department of Urology, Medical University of Silesia, Katowice

Abstract

Background. *Benign Prostatic Hyperplasia (BPH) is the primary cause of urinary symptoms in men over 50. Alpha-blockers provide rapid symptomatic relief but have a limited impact on prostate volume and disease progression.* **Aim.** *To evaluate the efficacy and safety of alpha-blockers and combination therapy in light of the most recent clinical studies.* **Materials and Methods.** *A review of the PubMed database (2020–2025) was conducted using the keywords "alpha blockers benign prostatic hyperplasia." Ten selected clinical trials were analyzed.* **Results.** *Alpha-blockers improve the peak urinary flow rate (Qmax) and reduce post-void residual volume. Combination therapy (with 5ARIs, anticholinergics, or PDE5is) offers complementary benefits. Tamsulosin has a favorable cardiovascular profile, though long-term use may be associated with neurodegenerative risk.* **Conclusions.** *BPH treatment requires individualization based on patient characteristics. Combination therapy effectively improves patients' quality of life, although further clinical trials are necessary to establish optimal treatment regimens. (Gerontol Pol 2026; 34; 3-11) doi: 10.53139/GP.20263407*

Keywords: *benign prostatic hyperplasia (BPH), lower urinary tract symptoms (LUTS), alpha-adrenergic antagonists, combination therapy, natural treatment*

Introduction

Benign prostatic hyperplasia (BPH) is one of the most prevalent urological conditions in older men. Worldwide prevalence of BPH is approximately 26% in males, 50-75% in men over 50 years of age, and up to 80% in patients over 70 years of age [1]. BPH is characterized by stromal and epithelial cell proliferation within the prostate's transitional zone encompassing the periurethral region. BPH development is testosterone- and derivative-stimulated and is accompanied by prostate enlargement with secondary bladder outlet narrowing [2]. Lower urinary tract symptoms (LUTS) are the most frequent clinical manifestation of BPH. Bladder outlet obstruction is the underlying fact of all these symptoms. Common BPH symptoms are: poor urine stream, prolonging of voiding time, sense of incomplete emptying of the bladder, urge to start urinating, urgency, and stop-and-start stream. If left untreated, BPH may advance to chronic retention of urine and infections of the urinary tract [3]. Optimal remedy for BPH is individualized and is depending upon the examination of LUTS and prostate volume. IPSS is typically utilized to quantify symptom severity, and IPSS stratifies patients into mild, moderate, and severe symptomatic groups. Prostate volume is best assessed by transrectal ultrasound (TRUS), by use of PSA levels, or by imaging procedures to delineate patients with large prostate glands (≥30 g). The combination of these two parameters-symptom strength and prostate volume-is significant during the selection of the appropriate treatment strategy, ranging from medical therapy and monotherapy to combination of therapies or surgery [4].

Various pharmacologic classes are utilized for the management of BPH based upon symptom strength, prostate size, and comorbidities. Alpha-adrenergic blockers are the most commonly utilized medications that inhibit alpha1-adrenergic receptors of prostate and bladder neck smooth muscle, resulting in muscle relaxation and improvement of urine outflow [5]. In those individuals with large prostate volumes, 5-alpha-reductase inhibitors may decrease prostate volume and prevent disease progression by blocking testosterone conversion to dihydrotestosterone [6]. Individuals with concomitant erectile dysfunction are recommended to take phosphodiesterase type 5 (PDE-5) drugs [7]. Anticholinergic drugs may be

Correspondence address: ✉ Kamil Kania, Department of Urology, Faculty of Medical Sciences in Katowice, Medical University of Silesia, Pl. Medyków 1, 41–200 Sosnowiec ☎ (+48 32) 368 25 11 🖳 kania.kamil.lek@gmail.com
ORCID: Artur Spyrka 0009-0008-9772-0923, Jakub Nocoń 0009-0002-5253-121X, Szymon Domagała 0009-0000-7989-2942, Kamil Kania 0000-0002-7660-2505, Mateusz Marcinek 0000-0002-5784-5245 Kamil Marczewski 0000-0003-4250-8235, Michał Tkocz 0000-0001-5382-6787

utilized in patients with symptoms of overactive bladder [8]. Beta-3 adrenergic agonists relax the detrusor muscle and diminish symptoms of urination frequency, urgency, and nocturia through novel mechanisms [9]. Increasing interest is also being shown towards phytherapeutic medication such as pumpkin seed oil, saw palmetto, and pomegranate extract, which exert anti-inflammatory, anti-androgenic, and antioxidant activities, along with favorable safety profiles [10].

Alpha-adrenoreceptor blockers (alpha-blockers) constitute first-line medication to correct LUTS secondary to BPH. Their pharmacological mode of action consists of blocking α_1-adrenoreceptors in the smooth muscle of the prostate, bladder neck, and the urethra. Stimulation of these receptors by norepinephrine results in muscle contraction and higher resistance to urine flow. Alpha-blockers prevent it by inducing muscle relaxation and enhanced urine flow [11].

Alpha1 receptors can be distinguished into three principal subtypes:
- Alpha1A - most common in prostate and bladder neck.
- Alpha1B - receptors are mostly expressed in vascular tissues.
- Alpha1D - of bladder innervation and the spinal cord [12].

Tamsulosin and silodosin are significantly selective for the alpha1A receptor, therefore relieving voiding symptoms effectively with minimal effects on blood pressure. However, terazosin and doxazosin also involve alpha1B receptors of vessels, therefore posing higher risk for hypotensive side effects [13]. Alpha-adrenergic antagonists demonstrate a rapid onset of action, with clinically meaningful symptom relief typically observed within the initial days of therapy. Nevertheless, owing to their ineffectiveness for prostate volume and natural disease progression, patients with large prostate glands are advised to use these medications concomitantly with 5-alpha-reductase inhibitors to attain durable clinical improvements [14].

Aim

The primary objective of this study is to evaluate the clinical efficacy and safety of alpha-blockers and combination therapies in the management of Benign Prostatic Hyperplasia (BPH).

Based on a review of clinical trials from 2020-2025, the study specifically aims to:
- Assess improvements in Qmax and PVR.
- Compare the benefits of combination therapy (with 5ARIs, anticholinergics, or PDE5is) against monotherapy.
- Analyze the safety profiles of these treatments, focusing on cardiovascular effects and potential long-term neurodegenerative risks.
- Identify strategies for personalizing BPH treatment based on patient-specific clinical characteristics.

Materials and Methods

This review seeks not merely to summarize contemporary evidence regarding the efficacy and safety of alpha-adrenergic antagonists, but to offer a critical synthesis of the current literature, delineate unresolved clinical challenges, and outline prospective research directions aimed at advancing therapeutic understanding beyond the scope of existing guidelines.

The structured search was done on July 19, 2025, in PubMed.

Search Strategy:
- Search term: “alpha blockers benign prostatic hyperplasia”
- Filters used: Publication type - Clinical Study
- Time Limitation: From January 2020 to July 2025
- Database: PubMed only

This search yielded 49 records. Titles and abstracts were screened for relevance to the research question. Full-text articles were then assessed based on predefined eligibility criteria.

Inclusion Criteria:
- Studies published between 2020 and 2025
- Research studies on alpha-adrenergic antagonists in the treatment of BPH
- Outcome reporting, quantitative (e.g. IPSS, Qmax, PVR)
- Randomized controlled trials or prospective clinical studies

Exclusion Criteria
- Articles, reviews, editorials, or case reports, which aren’t
- Studies without outcome data or with unclear methods
- Duplicated publications
- Those involving only surgical or phytotherapeutic treatments

Although this review did not strictly follow the PRISMA checklist, its methodology was inspired by PRISMA principles, including structured search, transparent selection, and predefined eligibility criteria. While the core analysis was based exclusively on clinical studies published between 2020 and 2025, selected references outside this range were included to provide pharmaco-

logical background, mechanistic insights, or historical context essential for interpreting current evidence.

Results

To improve clarity and facilitate structured comparison, a summary table was constructed to present the key characteristics of the ten clinical studies included in this review. The table outlines study design, interventions, and main therapeutic outcomes related to the use of alpha-adrenergic antagonists in the treatment of benign prostatic hyperplasia

Clinical Efficacy

Alpha-adrenergic blocking agents are of paramount importance in the management of symptoms of the lower urinary tract that are related to benign prostatic hyperplasia. Their clinical effectiveness is because they possess the activity of relaxing the contractile tone of prostate smooth musculature, the musculature of the urethra, and the bladder neck. Several clinical studies have justified the clinical effectiveness of alpha-blockers.

Comparing the efficacy and adverse events of two doses of tamsulosin (0.4 mg/day and 0.8 mg/day) in 93 patients with BPH, two groups demonstrated substantial symptomatic improvement from LUTS. Group B (0.8 mg/day) yielded superior clinical outcomes to Group A (0.4 mg/day) for IPSS score, maximum flow rate of urine (Qmax), and post-void residual volume (PVR). It can be inferred from these findings that higher doses of tamsulosin may offer incremental therapeutic benefit for patients with severe LUTS [15].

In 222 men enrolled in a prospective, randomized trial, alpha-blocker discontinuation or discontinuation of 5α-reductase inhibitors (5-ARIs) was analyzed to find whether therapeutic benefits can be sustained in BPH patients formerly responsive to combination treatment, by at least seven-point IPSS-T improvement and ≥20% prostate volume reduction (PV). It was seen that alpha-blocker discontinuation didn't significantly deteriorate parameters after 6–24 months. IPSS, Qmax, and PVR didn't change. Also, only 5.6% of patients needed to be readmitted to alpha-blockers. These findings suggest that discontinuation of alpha-blockers is safely possible in men formerly responsive to combination treatment, with minimal risk of symptom return [16].

Combination Therapy

While treating benign prostatic hyperplasia (BPH), combination therapy is becoming increasingly prominent to increase the efficacy of treatment and improve the quality of patients' lives. It involves treating with alpha-adrenergic antagonists plus various other pharmacological classes. An example of such is a three-faceted therapeutic regimen of tamsulosin (alpha-blocker) plus dutasteride (5-alpha-reductase inhibitor) plus imidafenacin (anticholinergic medication).

The DIrecT trial examined the effectiveness of this combination in patients with BPH and accompanying overactive bladder (OAB) symptoms that were refractory to monotherapy with tamsulosin. The trial demonstrated that triple therapy (TDI) was significantly better at reducing symptoms of overactive bladder by Overactive Bladder Symptom Score (OABSS) assessment and by overall IPSS, IPSS-QOL, quality of life index, and post-void residual volume (PVR) improvement. These findings suggest that combination with an anticholinergic agent of standard alpha-blocker and 5-alpha-reductase inhibitor therapy could potentially significantly improve LUTS and symptoms of OAB, particularly in non-responders to monotherapy. TDI combination treatment may therefore be regarded as a potential alternative to individualized BPH management [17].

Alpha-blockers exert a marked relaxing capability upon the smooth muscle of the prostate and bladder neck, resulting in rapid improvement of urine outflow and relief of symptoms. However, their impact upon the natural course of the disease is limited. One randomized trial analyzed the efficacy of combining the use of a selective alpha-blocker (silodosin) with the botanical extract Garcinia cambogia in men diagnosed with BPH and LUTS. Study subjects were randomly assigned to either of three groups: silodosin given as monotherapy (8 mg/day), Garcinia cambogia given as monotherapy (500 mg/day), or combination therapy of the two substances. After 12 weeks of treatment, all groups showed significantly improved progress in Qmax, total IPSS score, and PVR. The greatest improvement was noted in the combination group, in whom Qmax showed 50% increment and IPSS showed 72% reduction, statistically significantly higher in comparison to monotherapy. Additionally, prostate volume and PSA levels showed reduction. Interestingly, no clinically relevant adverse events were reported nor drug interactions were noted. These findings suggest that combining silodosin with Garcinia cambogia may be an effective and tolerable therapeutic approach, especially for patients showing severe LUTS and contraindications to use of 5-alpha-reductase inhibitors [18].

A randomised trial compared combination treatments of tamsulosin/finasteride and tadalafil/finasteride in patients with prostate volume >40 ml and IPSS >7, for 4 and 12 weeks. Both combinations produced significant improvements in voiding parameters and quality of life.

Following 12 weeks of treatment, patients in the tamsulosin/finasteride combination showed significantly marked improvements in Qmax, reduction in PVR, and total IPSS score reduction. Interestingly, relief of symptoms was demonstrated by week 4 and continued for all the duration of treatment. Tamsulosin has proven to be of high efficacy in decreasing LUTS, whether as monotherapy and combined with additional agents [19].

A multicenter, prospective, randomized clinical trial, published in the World Journal of Urology (2022) studied the efficacy of three therapeutic regimens for LUTS due to BPH: monotherapy with tadalafil (5 mg) alone, monotherapy with silodosin (8 mg) alone, and combination of both drugs. The trial enrolled 308 patients. The patients were followed up for changes in Qmax, IPSS, International Index of Erectile Function (IIEF), and PVR. It was demonstrated that combination therapy was significantly superior to either monotherapy.

At 12 weeks of treatment:

– Qmax rose to mean 15.8 ml/sec in combination therapy in comparison to 14.4 ml/sec (tadalafil) and 15.2 ml/sec (silodosin).
– IPSS was lowered to 15.6 points in the combination group, from 17.6 and 16.7 points in the two monotherapy groups.
– The IIEF was significantly better in the combination group (21.9), verifying additional efficacy in sexual function.

These outcomes suggest that silodosin-tadalafil combination may be particularly effective in patients with LUTS and ED, with simultaneous relief of urinary symptoms and sexual quality of life [20].

Safety and Adverse Effects

Alpha-adrenergic antagonists usually are tolerated quite well and exhibit favorable safety profiles. Alpha-blockers, although having good safety, do not come without side effects.

As part of research to evaluate the efficacy and safety of two doses of tamsulosin (0.4 mg vs. 0.8 mg) in patients with LUTS due to BPH, utilization of the higher dose was significantly related to higher occurrence of dizziness ($p < 0.001$). Other side effects including retrograde ejaculation, orthostatic hypotension, and headache were noticed, but occurrence difference between the two groups didn't meet the criteria of statistical significance [15].

One cohort of more than 1.1 million Medicare beneficiaries aged over 65 investigated the influence of many medications for BPH that are chiefly alpha-blockers on risk of developing Parkinson's disease (PD) and Alzheimer's disease (AD) and rates of all-cause mortality. Tamsulosin was selected as the comparator medication for alpha-blocker comparison by virtue of it being the alpha-blocker that is most commonly used. The findings indicated that use of tamsulosin was significantly correlated with risk of developing neurodegenerative diseases when matched against various alpha-blockers. For instance, terazosin demonstrated 26% risk reduction of developing Parkinson's disease (HR 0.74) and doxazosin demonstrated 21% reduced risk (HR 0.79) to make tamsulosin the comparator with significantly higher risk. Similar patterns were unearthed for Alzheimer's disease, where terazosin demonstrated risk reduction of 27% and doxazosin of 16%. Secondly, analysis demonstrated use of tamsulosin to be correlated with higher rates of all-cause mortality when matched against alfuzosin (HR 0.73) and against doxazosin (HR 0.94). These results indicate that while use of tamsulosin is convenient and tolerable in the short term, repeated use throughout the lifecycle in older adults may bear many severe health risks [21].

The profile of adverse effects associated with alpha-blockers is affected by their selectivity towards particular receptor subtypes as well as their influence on the cardiovascular system. A clinical investigation conducted in Kolkata assessed the effects of tamsulosin and prazosin on blood pressure response during the isometric handgrip (IHG) test, a method for evaluating autonomic nervous system function. The study comprised 97 hypertensive men with BPH, allocated into two distinct groups: one administered tamsulosin and the other prazosin. Post-IHG test results indicated a significantly greater increase in diastolic blood pressure (DBP) within the tamsulosin group in comparison to the prazosin group. This outcome is ascribed to the high selectivity of tamsulosin for alpha1A receptors, which are primarily situated in prostatic tissue, along with its low affinity for vascular receptors, leading to minimal impact on blood pressure levels. Conversely, prazosin demonstrates lesser selectivity and induces hypotensive effects through its action on vascular smooth muscle. These results imply that tamsulosin could represent a more advantageous choice for hypertensive patients [22].

TURP vs. Alpha-Blockers

Transurethral resection of the prostate (TURP) is still considered the standard for surgical intervention in BPH for those patients not achieving satisfactory relief from medical therapy. In a prospective cohort study of TURP outcomes for 87 patients with BPH, the patients were stratified by duration of preceding medical therapy: less

than 3 months, 3 to 12 months, and more than 12 months. Although no significant difference was identified in baseline characteristics (age, prostate size, operative time, complications) between the groups, patients treated pharmacologically for over one year showed significantly less benefit after TURP for:

– Percentage reduction in IPSS
– PVR
– Rise in storage and voiding pressures as observed during urodynamic investigation

Research findings reveal that although alpha-blockers are effective in the short-term treatment of LUTS, ongoing use can defer intervention to surgically correct procedures that might otherwise compromise TURP outcomes. Therefore, consideration of surgical management by referral should be considered at an earlier date for patients experiencing recurrent symptoms despite medical management [23].

Pumpkin Seed Oil in Alleviating Symptoms of Benign Prostatic Hyperplasia-An Alternative to Tamsulosin

In recent years, there has been growing interest in natural alternatives to standard medications used in the treatment of BPH. Among the most frequently studied are pumpkin seed oil, saw palmetto, and pomegranate juice, which exhibit anti-inflammatory, anti-androgenic, and antioxidant properties. Their favorable safety profiles make them potential therapeutic options for patients who prefer plant-based treatments or experience adverse effects associated with alpha-blockers.

While seeking natural alternatives to standard medications for treating BPH, pumpkin seed oil has become of growing interest. The efficacy of pumpkin seed oil was tested in a randomized clinical trial comparing it to that of tamsulosin in 73 BPH patients followed up for 3 months. Participants were randomized to take either 0.4 mg of tamsulosin once daily at bedtime or capsules of 360 mg pumpkin seed oil twice daily.

Both groups significantly improved symptoms by IPSS and QoL parameters. While tamsulosin demonstrated significantly greater efficacy to diminish IPSS scores at the first and third month of treatment ($p = 0.048$ and $p = 0.020$, respectively), the level of improvement from month 1 through month 3 was statistically comparable ($p = 0.728$). Interestingly, no side effects were observed for the pumpkin seed oil group, in contrast to the cases of occurrence of dizziness (5.9%), headache (2.9%), retrograde ejaculation (2.9%), and erythema with itching (2.9%) that occurred for the tamsulosin group.

Its mode of activity of pumpkin seed oil may encompass 5-alpha-reductase inhibition and reduced synthesis of dihydrotestosterone. It is also anti-inflammatory and diuretic in character.

Seed of pumpkin may serve as a viable adjunctive or alternative therapeutic option that can be utilized for individuals who tend to use natural cures or individuals that are suffering from unwanted side effects of alpha--blockers. But additional studies should prove these outcomes [24].

To support interpretation of the results, a summary of alpha-blocker characteristics is included (table I) prior to the discussion section.

Table I. Pharmacological comparison of alpha-adrenergic blockers used in BPH treatment

Drug	Receptor selectivity	Key clinical benefits	Most common adverse effects reported in the study
Tamsulosin [13,15-17,21]	High α1A selectivity	Rapid LUTS improvement, increased Qmax, reduced PVR; favorable cardiovascular profile; highly effective in monotherapy and combination therapy (e.g., with dutasteride, tadalafil)	Dizziness (more common at 0.8 mg), retrograde ejaculation, orthostatic hypotension; potential increased risk of neurodegenerative diseases with long-term use in older patients
Silodosin [13,18,20]	Very high α1A selectivity	Significant LUTS improvement; best outcomes when combined with tadalafil in patients with concomitant ED; beneficial when combined with Garcinia cambogia	No significant adverse effects reported in included studies
Doxazosin [13,21]	α1A + α1B	Clinical efficacy in LUTS; potentially neuroprotective compared to tamsulosin in epidemiological analysis	Hypotension
Terazosin [13,21]	α1A + α1B	Effective in LUTS treatment,potentially more favorable neurological profile (lower PD/AD risk vs tamsulosin)	Hypotension
Prazosin [22]	Non-selective α1	Option in patients with hypertension; in the study caused a greater blood pressure decrease during the isometric handgrip test compared to tamsulosin	Hypotension; greater impact on blood pressure than tamsulosin

Discussion

The cumulative evidence verifies that alpha-adrenergic antagonists constitute the foundation of pharmacotherapy of BPH and specifically of the pharmacotherapy of LUTS. Their quick pharmacodynamic activity, that is obtained through the relaxation of prostate and bladder neck smooth muscle, is translated into the improvement in urinary flow and the relief of symptoms during the first few days of treatment [15]. Nevertheless, as has been shown by several studies, their influence on prostate volume as well as the natural course of has no impact on disease progression, therefore supporting the widespread use of combination treatment with 5-alpha-reductase inhibitors [4,14]. This therapeutic rationale is further supported by clinical evidence showing that alpha-blockers, while effective in relaxing smooth muscle and improving urinary flow, do not reduce prostate volume or prevent disease progression. Their role remains primarily symptomatic, which underscores the need for adjunctive agents that target hormonal mechanisms of prostate enlargement [25].

Clinically, combination of alpha-blockers with other classes of medications, including dutasteride, tadalafil, or imidafenacin, may elicit notable improvements for both parameters of voiding and sexual quality of life, and for OAB symptoms control. Systematic review by Kim et al. supported combination treatment with anticholinergic medications to significantly enhance the control of symptoms of the LUTS with only negligible increment of risk of side effects [26]. Notable are the results pertaining to TDI that revealed enhanced efficacy over dual treatment for relief of symptoms of OAB and IPSS parameters [18]. Consistent herewith was another systematic overview that came up with similar results, revealing that combination of alpha-blocker medications with anticholinergic medications improves LUTS control without appreciable increments of risks of side effects [26]. However, certain trials have stressed the fact that supplementation with anticholinergic medications can elevate the risk of side effects such as dry mouth and constipation, especially in geriatric patients. Thus, the need to weigh the benefits against side effects in treatment approaches cannot be understated [27].

On the other hand, more prominence is being assigned to the long-term safety of alpha-blocker use. Though agents like tamsulosin are typically well tolerated short term,cohort studies point to the possibility of increased risk of neurodegenerative diseases and increased rates of fatality among aged patients [21]. Also in question is the influence of pharmacotherapy length on TURP efficacy. As shown, medically treated patients for more than one year prior to surgery showed less improvement after TURP, possibly as a consequence of secondary deterioration of detrusor muscle function. These findings signify that determination of continuation of pharmacotherapy must be established individually, taking into consideration risks of postponed surgical intervention [23]. Adding evidence to support this is the fact that Zhu et al. found patients with more than one year of alpha-blocker usage before TURP had significantly lower detrusor contractility following the procedure, which indicated irreversible changes due to prolonged medications [28].

Other therapeutic agents, for example, Garcinia cambogia extract or pumpkin seed oil, revealed potential efficacy for augmentation of voiding parameters and quality of life through the minimization of side effects [24]. Their actions involve anti-inflammatory, antiandrogen activity and dihydrotestosterone metabolism modulation. Review of literature concludes that herbs like Serenoa repens, Pygeum africanum, and nettle can complement BPH therapy, particularly in patients with preference for natural drugs [10]. However, a 2024 Cochrane-based systematic review by Franco et al. concluded that Serenoa repens provides little to no benefit in relieving LUTS associated with BPH, with outcomes comparable to placebo. These findings challenge its role as a standalone treatment and support its use, if at all, only as an adjunct to conventional pharmacotherapy [29].

Where combination treatment is concerned, it is of interest that the combination of alpha-blockers with PDE5 inhibitors shows synergistic effects for the relief of both urinary symptoms and of erectile function. Evaluation of clinical trials has shown that combination of tadalafil with tamsulosin or silodosin is of special value for patients with LUTS with concomitant erectile dysfunction [20,30].

Treatment of BPH as a whole must be personalized to consider not only the severity of symptoms and prostate volume but also safety profiles, patients' expectations, and the value of combination treatment. Future research must focus on identification of target therapies, strategy by biomarkers, and combined use of traditional and evidence-based natural therapies. Furthermore, the integration of biomarkers such as urinary nerve growth factor (NGF) and inflammatory cytokines may help identify patients most likely to benefit from specific therapies. Jiang et al. highlighted the potential of such markers in guiding personalized treatment strategies for BPH [31].

The synthesis of the presented clinical studies, in the context of the European Association of Urology (EAU) guidelines [4], enables the formulation of practical implications regarding the selection of specific alpha-adrenergic antagonists for defined patient subgroups. Accor-

ding to current recommendations, treatment choice should be individualized, taking into account the side effect profile and coexisting medical conditions.

For younger, sexually active men in whom preservation of sexual function is a priority, alpha-blockers with high selectivity for the α1A receptor-such as silodosin or tamsulosin-represent a more favorable option than non-selective agents, despite their association with retrograde ejaculation. Notably, in this demographic, combination therapy with a phosphodiesterase type 5 inhibitor such as tadalafil [20], may be particularly beneficial, offering simultaneous improvement in both LUTS and erectile dysfunction.

In contrast, among elderly patients with concomitant hypertension or heart failure-where the risk of orthostatic hypotension and drug interactions is elevated-tamsulosin demonstrates a more favorable hemodynamic profile than non-selective agents (e.g., prazosin) or even doxazosin. This finding reflects the high α1A receptor selectivity of tamsulosin within prostatic tissue [22]. However, in light of emerging data suggesting a potential increase in neurodegenerative risk associated with long-term tamsulosin use [21], consideration of doxazosin as an alternative-despite its stronger impact on blood pressure requiring cautious monitoring-may be justified in the oldest patients with elevated dementia risk.

In summary, despite the well-established and indisputable role of alpha-adrenergic blockers in the management of BPH, this review highlights several unresolved challenges that continue to limit the optimization of patient care.

The most pressing need is the personalization of therapy. As demonstrated by Osman et al. [15], a higher dose of tamsulosin (0.8 mg), while more effective, is associated with a significantly increased risk of dizziness. This dose-response-tolerability relationship underscores a fundamental gap: the absence of predictive biomarkers that could guide individualized treatment selection. A promising direction is suggested by studies such as Jiang et al. [31], which propose the use of urinary inflammatory markers. Identifying such indicators could enable a shift away from the current trial-and-error approach toward a personalized medicine paradigm.

Another critical gap concerns the optimal timing of combination therapy initiation. While the study by Lee et al. [17] suggests that discontinuation of alpha-blockers is feasible following a period of combination treatment, it leaves unanswered a key strategic question: is upfront combination therapy superior to stepwise escalation following monotherapy failure? Current guidelines are based on efficacy data, yet direct, long-term comparisons of these treatment pathways are lacking. Randomized trials assessing disease progression and quality-of-life outcomes are urgently needed to resolve this uncertainty and inform more precise clinical algorithms.

Finally, growing concerns regarding long-term safety demand urgent clarification. The observational study by Fung et al. [21], which identified a potential association between tamsulosin and increased risk of neurodegenerative diseases, presents clinicians with a difficult dilemma: how to balance its well-documented efficacy against possible long-term risks [15]. Further analyses are needed to determine whether the benefits of treatment outweigh the risks in specific age groups, and whether alpha-blockers with alternative receptor profiles such as doxazosin [21], should be preferred in patients with elevated neurodegenerative risk.

Conclusions

Medical treatment of BPH, specifically alpha-adrenergic antagonist administration, is a prime and expedient approach to treat LUTS. These drugs exhibit swift pharmacologic activity, resulting in expedient relief of patient comfort and health-related quality of life. Nevertheless, limited efficacy for prostate volume reduction and disease progression necessitates frequent use of combination pharmacotherapy with 5-alpha-reductase inhibitors.

Clinical trial outcomes indicate that alpha-blocker in combination with other medications, including dutasteride, tadalafil, or imidafenacin, significantly enhances measures of urine flow and of sexual function, as well as regulation of the symptoms of OAB. It is notable that outcomes for TDI are especially encouraging, as they reflect favorable results over dual therapy for the regulation of symptoms of OAB.

Increasing emphasis is, however, being placed upon the question of the safety of prolonged use of alpha-blockers. An epidemiological survey has shown the possible risk of neurodegenerative diseases, particularly with reference to tamsulosin. Certain of the alternative therapies, for example, botanical drugs (e.g., Serenoa repens and pumpkin seed oil), could prove to be of interest for alternative therapies for selected patients.

Timing of pharmacotherapy preceding TURP may influence surgery results and therefore continuation of medical therapy should be considered with possible delay of operative intervention.

The findings of this analysis are that optimal BPH care is personally tailored to the requirements of the patient and account is taken not only of the presence of symptoms and prostate volume, but also of safety concerns, patient preference, and the presence of concomitant con-

ditions such as erectile dysfunction or overactive bladder symptoms.

Conflict of interest:
None

References

1. Wei H, Zhu C, Huang Q, Yang J, Li YT, Zhang YG, et al. Global, regional, and national burden of benign prostatic hyperplasia from 1990 to 2021 and projection to 2035. BMC Urol. 2025;25(1):34.
2. Xiong Y, Zhang Y, Li X, Qin F, Yuan J. The prevalence and associated factors of lower urinary tract symptoms suggestive of benign prostatic hyperplasia in aging males. Aging Male. 2020;23(5):1432–9.
3. Ng M, Leslie SW, Baradhi KM. Benign Prostatic Hyperplasia. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 [cited 2026 Feb 17]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK558920/.
4. Gravas S, Gacci M, Gratzke C, Herrmann TRW, Karavitakis M, Kyriazis I, et al. Summary Paper on the 2023 European Association of Urology Guidelines on the Management of Non-neurogenic Male Lower Urinary Tract Symptoms. Eur Urol. 2023;84(2):207-22.
5. Haile ES, Sotimehin AE, Gill BC. Medical management of benign prostatic hyperplasia. Cleve Clin J Med. 2024;91(3):16-70.
6. Kapriniotis K, Manolitsis I, Juliebo-Jones P, Pietropaolo A, Tsaturyan A, Tonyali S, et al. The latest in clinical trial results of 5-alpha reductase inhibitors in combination regimens for benign prostatic hyperplasia. Expert Opin Pharmacother. 2025;26(3):301-11.
7. Stamatiou K, Perletti G, Magri V, Trinchieri A. The Role of 5-Phosphodiesterase Inhibitors (PDE-5I) in Current Benign Prostatic Hyperplasia Treatment: A Narrative Review. Medicina (Kaunas). 2024;60(11):1736.
8. Liu P, Li Y, Shi B, Zhang Q, Guo H. Comparison of different types of therapy for overactive bladder: A systematic review and network meta-analysis. Front Med (Lausanne). 2022;9:1014291.
9. Kang TW, Kim SJ, Kim MH, Jung JH. Beta 3 Adrenoreceptor Agonist for the Management of Lower Urinary Tract Symptoms in Men With Benign Prostatic Hyperplasia: A Systematic Review. Int Neurourol J. 2021;25(3):182–91.
10. Csikós E, Horváth A, Ács K, Papp N, Balázs VL, Dolenc MS, et al. Treatment of Benign Prostatic Hyperplasia by Natural Drugs. Molecules. 2021;26(23):7141.
11. Yoosuf BT, Panda AK, Kt MF, Bharti SK, Devana SK, Bansal D. Comparative efficacy and safety of alpha-blockers as monotherapy for benign prostatic hyperplasia: a systematic review and network meta-analysis. Sci Rep. 2024;14(1):11116.
12. Docherty JR. Subtypes of functional alpha1-adrenoceptor. Cell Mol Life Sci. 2010;67(3):405–17.
13. Martin DJ. Preclinical pharmacology of alpha1-adrenoceptor antagonists. Eur Urol. 1999;36 Suppl 1:35–41; discussion 65.
14. Papet J, Cornu JN, Dupuis H. Combination Pharmacotherapy for Benign Prostatic Hyperplasia: Evaluation of Existing Literature on Combination Therapies for Lower Urinary Tract Symptoms Associated with BPH. Drugs Aging. 2025;42(6):527-34.
15. Osman T, Elawady H, Fawaz K, Shabayek M, Essam MD, Osman D, et al. Evaluation of Tamsulosin 0.4 mg versus 0.8 mg in management of lower urinary tract symptoms due to benign prostatic enlargement. Int Urol Nephrol. 2024;56(6):1811-6.
16. Tawfik A, Abo-Elenen M, Gaber M, El-Abd A, Zoeir A, Saad S, et al. Tadalafil versus tamsulosin as combination therapy with 5-alpha reductase inhibitors in benign prostatic hyperplasia, urinary and sexual outcomes. World J Urol. 2024;42(1):70.
17. Lee KS, Yoo JW, Kim DH, Jeon S, Yang J, Chung BH, et al. A prospective, randomized, open-label, parallel trial comparing the efficacy of α-blocker or 5α-reductase inhibitor withdrawal to continued combination therapy on the maintenance of lower urinary tract symptoms in men with benign prostatic hyperplasia. Prostate. 2024;84(4):403-13.
18. Yamanishi T, Asakura H, Seki N, Tokunaga S. Triple Therapy with Tamsulosin, Dutasteride, and Imidafenacin for Benign Prostatic Hyperplasia in Patients with Overactive Bladder Symptoms Refractory to Tamsulosin: Subgroup Analyses of the DIrecT Study. Urol Int. 2021;105(9–10):817-25.

19. El-Shaer W, Abd-Allah AR, El-Shafie MF, Salama IM, El Shaer A. Evaluation of the Therapeutic Potential of Garcinia cambogia Alone or in Combination With Silodosin in the Management of LUTS/BPH: A Prospective Randomized Controlled Study. Urology. 2025;200:198-205.
20. AbdelRazek M, Abolyosr A, Mhammed O, Fathi A, Talaat M, Hassan A. Prospective comparison of tadalafil 5 mg alone, silodosin 8 mg alone, and the combination of both in treatment of lower urinary tract symptoms related to benign prostatic hyperplasia. World J Urol. 2022;40(8):2063-70.
21. Fung KW, Baye F, Baik SH, McDonald CJ. Tamsulosin use in benign prostatic hyperplasia and risks of Parkinson's disease, Alzheimer's disease and mortality: An observational cohort study of elderly Medicare enrollees. PLoS One. 2024;19(8):e0309222.
22. Samajdar SS, Mukherjee S, Gupta S, Saha D, Kayal A, Begum SA, et al. Effect of α-blockers on Handgrip Test Response of Diastolic Blood Pressure in Hypertensive, Benign Hypertrophy of Prostate Patients in a Therapeutics Clinic, Kolkata: A Cross-sectional Study. J Assoc Physicians India. 2024;72(4):2-3.
23. Rathi A, Nayyar R, Rathi N, Jain S, Seth A, Ghorai RP, et al. Outcomes of transurethral resection of prostate for benign prostatic obstruction stratified as per duration of prior medical therapy. World J Urol. 2025;43(1):251.
24. Zerafatjou N, Amirzargar M, Biglarkhani M, Shobeirian F, Zoghi G. Pumpkin seed oil (Cucurbita pepo) versus tamsulosin for benign prostatic hyperplasia symptom relief: a single-blind randomized clinical trial. BMC Urol. 2021;21(1):147.
25. Baldev NR, Baldev RR. Impact of Combination Therapy with Tamsulosin and Finasteride on Lower Urinary Tract Symptoms in BPH Patients: A Randomized Controlled Trial. European Journal of Cardiovascular Medicine. 2025;15(5):669-72.
26. Kim HJ, Sun HY, Choi H, Park JY, Bae JH, Doo SW, et al. Efficacy and Safety of Initial Combination Treatment of an Alpha Blocker with an Anticholinergic Medication in Benign Prostatic Hyperplasia Patients with Lower Urinary Tract Symptoms: Updated Meta-Analysis. PLoS One. 2017;12(1):e0169248.
27. Yu ZJ, Yan HL, Xu FH, Chao HC, Deng LH, Xu XD, et al. Efficacy and Side Effects of Drugs Commonly Used for the Treatment of Lower Urinary Tract Symptoms Associated With Benign Prostatic Hyperplasia. Front Pharmacol. 2020;11:658.
28. Zhu Y, Zhao YR, Zhong P, et al. Detrusor underactivity influences the efficacy of TURP in patients with BPO. Int Urol Nephrol. 2021;53(5):835-41.
29. Franco JVA, Trivisonno LF, Sgarbossa N, et al. Serenoa repens for the Treatment of Lower Urinary Tract Symptoms Due to Benign Prostatic Enlargement: An Updated Cochrane Review. World J Mens Health. 2024;42(3):518-30.
30. Jackson EM, Khooblall P, Lundy SD, Bajic P. A Review of Combined Phosphodiesterase-5-Inhibitors and α-Blockers versus Phosphodiesterase-5-Inhibitors Alone for Lower Urinary Tract Symptoms due to Benign Prostatic Hyperplasia. Arab J Urol. 2024;22(1):13-23.
31. Jiang YH, Lee J, Kuo HC, Wu YH. Urinary Inflammatory and Oxidative Stress Biomarkers as Indicators for the Clinical Management of Benign Prostatic Hyperplasia. Int J Mol Sci. 2025;26(13):6516.