Prostate International 12 (2024) 57–64

Contents lists available at ScienceDirect

Prostate International

journal homepage: https://www.journals.elsevier.com/prostate-international

Review Article

Risks and side effects in the medical management of benign prostatic hyperplasia

Abdulghafour Halawani [a, b], Ryan Paterson [b], Tianshuang Zhong [b], Katie Du [c], Runhan Ren [b], Connor M. Forbes [b, d, *]

[a] Department of Urology, King Abdulaziz University, Jeddah, Saudi Arabia
[b] Department of Urological Sciences, University of British Columbia, Stone Centre at Vancouver General Hospital, Vancouver, British Columbia, Canada
[c] University of Alberta, Edmonton, Alberta, Canada
[d] Vancouver Prostate Centre, Vancouver, British Columbia, Canada

ARTICLE INFO

Article history:
Received 16 October 2023
Received in revised form
14 November 2023
Accepted 30 November 2023
Available online 2 December 2023

Keywords:
Prostatic Hyperplasia
Lower urinary tract symptoms
Alpha-1 antagonists
Medications
Side effects
Treatmetn adverse events

ABSTRACT

Benign prostatic hyperplasia affects up to 80% of men in their lifetime. It causes bladder outflow obstruction, leading to lower urinary tract symptoms, which can have a large impact on quality of life. Lifestyle modifications and pharmacotherapy are often offered as first-line treatments for patients. These include alpha blockers, 5-alpha-reductase inhibitors, phosphodiesterase-5 inhibitors, anticholinergics, B3-agonists, and desmopressin. While often well tolerated, these pharmacotherapies do have significant side effects, which both clinicians and patients should understand and discuss in order to make an informed treatment decision among alternatives. The purpose of this review is to provide a current overview of the risks and side effects of commonly used medications in benign prostatic hyperplasia management.

1. Introduction

Conservative lifestyle changes and pharmacologic therapy are the traditional first-line options for men presenting with lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH).[1–5] This approach is supported by well-designed clinical trials with appropriate follow-up, including the Medical Therapy of Prostatic Symptoms (MTOPS) Study and the Combination of Avodart and Tamsulosin (CombAT) study. These seminal papers show an improvement in multiple endpoints, representing decreased progression of the disease, and were a breakthrough in BPH treatment.[2,6,7] However, the traditional "one size fits all" approach to BPH, which progresses from initial medical management to surgical intervention, does not factor in individual patient preferences. For many patients, these preferences include minimizing unwanted side effects.

While medical therapies for BPH are generally seen as a lower-risk option compared to procedural intervention, clinicians and patients must be aware that this approach is not completely without risk. Medication side effects must be discussed thoroughly with patients when making informed decisions about their healthcare options. This is especially relevant in today's BPH landscape, where minimally invasive surgical techniques (MISTs) are a viable alternative for certain patients. Patients and clinicians should also be aware of the risks associated with delayed intervention, including the potential loss of quality-adjusted life years and changes in bladder function. In this review, we focus on the risks and side effects associated with the medical management of BPH.

2. Alpha-blockers and phosphodiesterase-5 inhibitors

Alpha-1 adrenergic receptor antagonists, also known as alpha-1 blockers, are a first-line medical therapy for male lower urinary tract symptoms secondary to BPH. These medications, not surprisingly, bind to type-1 alpha-adrenergic receptors and inhibit smooth muscle contraction.[8] While both alpha-1A and alpha-1B receptors are distributed in various tissues throughout the body, alpha-1B receptors play a significant role in mediating vascular tone.[8] Meanwhile, alpha-1A receptors do not, and they are present

* Corresponding author. Department of Urological Sciences, University of British Columbia, Stone Centre at Vancouver General Hospital, Vancouver, British Columbia, Canada.
E-mail address: connor.forbes@vch.ca (C.M. Forbes).

https://doi.org/10.1016/j.prnil.2023.11.004

in the smooth muscle of the genitourinary tracts, predominantly in the prostatic stroma.[9] Functionally, blockade of alpha-1A receptors inhibits smooth muscle contraction and reduces the prostate and bladder neck muscle tone.[9,10] This reduces the degree of obstruction at the bladder neck and improves symptoms. Building on this mechanistic understanding, the therapeutic and adverse effects of alpha-1 adrenergic blockers depend in part on their degree of selectivity or nonselectivity for specific receptor subtypes. The selectivity of these agents is aimed at minimizing unwanted systematic adverse effects on blood pressure.

2.1. Nonselective versus selective alpha-1 adrenoceptor antagonists

Initially, only nonselective alpha-1 adrenoceptor antagonists (also called "alpha-blockers") such as prazosin, terazosin, doxazosin, and alfuzosin were available for use in the medical management of BPH/bladder outlet obstruction (BOO). Prazosin suffers from requiring multiple daily doses, whereas terazosin and doxazosin benefit from a daily dosing schedule due to their longer half-lives. Due to their effects on peripheral vasodilation, nonselective alpha-1 blockers have, in general, more systemic side effects (Table 1). An early meta-analysis of doxazosin showed a 47% rate of side effects in doxazosin-treated patients compared to 37% in placebo.[11,12] Notably, this included a 17% rate of dizziness versus 6% in placebo and 4% versus 0% rate of hypotension. Trends among terazosin are similar. Interestingly, in BPH patients, both terazosin and doxazosin demonstrate a decrease in the blood pressure of hypertensive men with BPH; however, no change in blood pressure in normotensive cohorts was found.[13–15] The lack of change in baseline blood pressure, however, may be different from the hypotensive episodes reported in BPH trials.

Like the others, alfuzosin is a slow-release, single daily dose alpha-1 blocker that exhibits no selectivity for alpha-1 receptor subtypes.[10] Interestingly, alfuzosin appears to have a better side-effect profile compared to other nonselective alpha blockers, with lower incidences of ejaculatory dysfunction, dizziness, and asthenia compared to terazosin and doxazosin (Table 1).[16–18] Perhaps for this reason, it is sometimes characterized as a clinically selective alpha-receptor antagonist but does not display pharmacologic selectivity for the alpha-1 subtype.[19] However, on meta-analysis,[20] patients on alfuzosin do still have a higher incidence of hypotension, dizziness, or syncope than those on placebo or tamsulosin. Terazosin and doxazosin's incidence, however, is higher.[21] International Prostate Symptom Score (IPSS) improvement may be less with alfuzosin compared to terazosin/doxazosin based on outcomes from initial pivotal trials,[16] although meta-analyses are conflicting.

2.2. Selective alpha-1 adrenoceptor antagonists

Selective "alpha-blockers" have relative specificity for the 1A subtype in order to maximize prostate symptom improvement and minimize systemic side effects. Tamsulosin was introduced as the first subtype of selective alpha-1 antagonists; however, it actually has a fairly modest receptor selectivity of less than 10-fold.[10] Tamsulosin quickly gained popularity over terazosin and doxazosin, in part because it does not require titration for most men unlike doxazosin and terazosin, starting at a straightforward 0.4 mg dose.[22] Despite only minimal selectivity, tamsulosin does also have the advantage of less cardiovascular impact.[21] This, however, is thought to be due to the extended release formulation rather than the modest receptor selectivity. However, there is more ejaculatory dysfunction (Table 1).[23–26] This has been

Table 1
Comparison of treatment-emergent adverse events (TEAEs) related to different alpha-1 blockers use for treatment of BPH.

Adverse events	Alpha-1 blocker									
	Terazosin		Doxazosin		Tamsulosin		Alfuzosin		Silodosin	
	Treated patients *n* (%)	Placebo *n* (%)	Treated patients *n* (%)	Placebo *n* (%)	Treated patients *n* (%)	Placebo *n* (%)	Treated patients *n* (%)	Placebo *n* (%)	Treated patients *n* (%)	Placebo *n* (%)
Orthostatic hypotension	57/1655 (3.4%)	8/1487 (<1%)	23/1400 (2.3%)	6/643 (<1%)	1/248 (<1%)	2/239 (1.0%)	10/469 (2.1%)	8/478 (1.7%)	12/466 (2.6%)	7/457 (1.5%)
Dizziness	252/1802 (14.0%)	98/1586 (6.2%)	136/1450 (11.2%)	49/693 (7.1%)	176/1474 (11.9%)	56/714 (7.8%)	68/1298 (5.2%)	25/1000 (2.5)	24/641 (3.7%)	9/546 (1.6%)
Asthenia/Fatigue/Headache	153/1736 (8.8%)	62/1566 (4.0%)	93/1450 (6.4%)	17/693 (2.5%)	89/1474 (6.0%)	31/714 (5.5%)	18/1090 (1.7%)	18/792 (2.3%)	11/466 (2.4%)	4/457 (<1%)
Erectile dysfunction	24/386 (6.2%)	15/384 (3.9%)	15/275 (5.8%)	9/269 (3.3%)	5/502 (1.0%)	6/493 (1.2%)	9/896 (1.0%)	9/596 (1.5%)		
Ejaculatory dysfunction	15/1053 (1.4%)	2/1031 (<1%)	56/696 (8.0%)	40/672 (6.0%)	148/1376 (8.4%)	3/686 (<1%)	2/186 (1%)	2/186 (1%)	224/1022 (21.9%)	6/736 (<1%)
Withdrawals due to TEAEs	229/1817 (12.6%)	140/1607 (8.7%)	108/1282 (8.4%)	39/640 (6.1%)	71/982 (7.2%)	32/475 (6.7%)	53/907 (5.8%)	43/742 (5.8%)	56/1022 (5.4%)	17/736 (2.3%)

TEAEs associated with terazosin,[13,15] doxazosin,[11,12] alfuzosin,[17,18] tamsulosin,[23–26] and silodosin.[29]
BPH, benign prostatic hyperplasia.

historically characterized as "retrograde ejaculation" due to an open bladder neck; however, it is likely to include at least a component of anejaculation from smooth muscle inhibition, which prevents seminal fluid propulsion. Thankfully, alpha blockers are not associated with an increase in erectile dysfunction compared to placebo on meta-analysis.[27]

Silodosin is the only commercially available alpha-1 blocker with a high degree of adrenoceptor subtype selectivity.[28] Silodosin has a high affinity for alpha-1A with more potency ($\approx$200-fold) for blocking alpha-mediated prostate smooth muscle contraction. This higher degree of receptor selectivity, however, does come at the expense of a highly reported ejaculatory dysfunction.[29] Interestingly, experiencing ejaculatory dysfunction as a silodosin side effect was associated with the most significant degree of improvement in LUTS and peak flow rate.[30] This phenomenon has also been noted in other alpha blockers and has been hypothesized to explain why there has been little trial drop-out from anejaculation.[19] Even with pharmacologically or clinically selective alpha-blockers, however, postural hypotension, dizziness, and headache still do occur. Even selective alpha blockers are associated with a small but statistically significantly increased risk of emergency room visits for falls, fractures, and hypotension.[31]

2.2.1. Associations between alpha blockers and systemic diseases

Epidemiologic studies have found an association between systemic diseases and alpha blockers. The new onset of diabetes was found to be associated with pharmacologic treatment for BPH. While this was higher for 5-alpha-reductase inhibitors (5ARIs), the effect was still present for alpha blockers.[32] A similar study also found an association between alpha blockers and congestive heart failure.[33] This risk was higher for men on alpha blockers than 5ARIs. While confounders abound in these types of associative studies, they do raise concern for at-risk men and should be discussed with patients.

2.2.2. Intraoperative floppy iris syndrome

Intraoperative floppy iris syndrome (IFIS) occurs during ophthalmologic surgery, usually seen during "phacoemulsification," which is an ultrasonic step during cataract surgery. Intraoperative movements of the iris increase the chance of complications for patients undergoing these surgeries.[34] Tamsulosin is the main cause of IFIS due to its widespread use; however, silodosin has an even higher odds ratio for IFIS.[34] The nonselective alpha blockers alone, including alfuzosin, were not found to increase the risk of IFIS. IFIS does not appear to be associated with the length of tamsulosin use and may persist for years after alpha blocker cessation.[35] Interestingly, finasteride was associated with IFIS in a meta-analysis at a lower rate than tamsulosin, although this may suffer from confounders.[34] For men with ophthalmologic conditions who may have surgery in the future, clinicians may wish to consider deferring alpha blocker use or using a nonselective alpha blocker.

2.2.3. Adherence

Two-thirds of men discontinue alpha-1 blocker therapy, with overall adherence around 38.8% at 6 months, and 31.0% of men were adherent to the treatment at 12 months.[36] However, 20% subsequently restart alpha-1 blocker or switch to another BPH therapy.[36] As the medication adherence is low, careful education of the patients is necessary to maximize the benefits.

2.3. Phosphodiesterase-5 inhibitors

Currently, preclinical and clinical trials demonstrate that phosphodiesterase-5 inhibitors (PDE5-Is) can also improve male.[37] A systematic review and meta-analysis by Gacci et al showed that PDE5-Is significantly improved LUTS and erectile dysfunction (ED) in men with BPH.[38] Adverse events related to PDE5-Is use include back pain, pyrosis, headache, flushing, and nasal congestion. Furthermore, the combination of alpha-1 blockers and PDE5-Is may increase the incidence of symptomatic hypotension[39] and other symptoms as well, such as headache and dizziness.[38,40] Although some concerns have been raised regarding the cardiac impact of PDE5-Is alone or in combined therapy (with alpha-1 blockers), several RCTs and meta-analysis prove their safety and well tolerability.[41–43]

3. 5ARIs

5ARIs are recommended for the primary medical management of BPH, for prostates greater than 30 cc, in the 2022 CUA Guidelines.[44] It has been shown to improve both symptoms and alter the natural course of disease progression, especially in combination with alpha-blockers.[5,45]

5-Alpha-reductase (5AR) converts testosterone to dihydrotestosterone. There are three isoenzymes: type I is mainly expressed in the skin and liver; type II is predominately expressed in the prostate, seminal vesicles, and epididymis; and type III is ubiquitously expressed.[46] Dutasteride inhibits both types I and II, while finasteride inhibits only type I, although clinically major differences in outcomes have not been observed between these two 5ARIs. However, these medications do have side effects that can be significant and bothersome to patients and are in some cases irreversible (Table 2).

3.1. Sexual adverse effects

Sexual side effects are the most common and concerning for men on 5ARIs, ranging from 0.9% to 38% of patients.[47,48] The rates are similar between dutasteride and finasteride[5,49] and not found to be different between normal and low-dose finasteride.[50] The Proscar Long-Term Efficacy and Safety Study (PLESS) did show improvement in these adverse effects over time.[51] However, some studies show possible sexual dysfunction even after treatment has been stopped.[52]

5ARIs are also associated with gynecomastia, with the risk being higher for dutasteride compared to finasteride.[53] The Prostate Cancer Prevention Trial (PCPT) reported rates of gynecomastia in 4.5% of patients on finasteride compared to 2.8% placebo.[54] The risk is present regardless of duration and timing.[55] It is more commonly seen in patients undergoing androgen deprivation therapy in prostate cancer. Management is usually conservative but may involve tamoxifen, aromatase inhibitors, radiotherapy, and mastectomy. Medical therapy is typically reserved for symptomatic, acute, idiopathic gynecomastia. Tamoxifen, perhaps the most studied, in a randomized trial had a 78% complete resolution rate compared to 40% with danazol in patients with idiopathic gynecomastia, however, with a higher relapse rate.[56] Surgical options can be considered for chronic cases or concern for malignancy. There is no association between 5ARI and male breast cancer.[57]

3.2. Psychiatric adverse effects

Recently, psychiatric side effects are becoming more recognized and brought to the forefront. During the initial clinical trials, depression was rarely reported and was not listed on the initial medication packaging.[58] Since then, post-finasteride syndrome has been used to describe prolonged and persistent sexual and psychological effects and reports of suicidality, even after discontinuing the medication.[59] It is proposed that allopregnanolone, a

Table 2
Comparison of adverse effects of 5-alpha-reductase inhibitors (5ARIs).

Adverse events	Dutasteride	Placebo	Finasteride	Placebo
Any drug-related event	22.0%[49]	14.6%[49]	36.0%[7]	34.9%[7]
Leading to discontinuation	4.3%[49]	2.0%[49]		
Erectile dysfunction	9.0%[49]	5.7%[49]	8.1%[7]	3.7%[7]
Decreased libido	3.3%[49]	1.6%[49]	6.4%[7]	3.4%[7]
Loss of libido	1.9%[49]	1.3%[49]	–	–
Decreased semen volume	1.4%[49]	0.2%[49]	3.7%	0.8%[7]
New type 2 diabetes	(any 5ARI) 14.15%[32]	10.74%[32]	–	–
Gynaecomastia	2.3%	0.7%[5]	0.5%	0.1%[7]
Cardiac failure	(any 5ARI) 0.7%[49]	0.4% ($P = 0.03$)[49]	–	–
Psychiatric	(any 5ARI)	0.04% ($P > 0.10$)[97]	–	–
	Suicide 0.04%[97]	0.14% ($P < 0.01$)[97]		
	Self-harm 0.18%[97]	1.37% ($P < 0.01$)[97]		
	Depression 1.95%[97]			
Prostate cancer	22.8% relative risk reduction incidence of prostate cancer over 4 years.[49]		24.8% relative risk reduction over 7 years.[54]	
	High risk: increased risk at 3-4y (0.5% vs. 0.1%).[49]		High risk: increased risk (6.4% vs. 5.1%).[54]	

neurosteroid produced by 5AR, is decreased in patients with depression and altered by 5ARIs.[60] A review of VigiBase, the World Health Organization's global database of case safety reports, found increased signals of suicidality, depression, and anxiety in young patients, aged less than 45 years, taking low-dose finasteride.[59] In 2011, a post-market report was sent to the FDA, and warnings have been added since then.[59]

3.3. Metabolic syndrome

Although both BPH and metabolic syndrome are common in the aging male, there is emerging evidence linking metabolic syndrome to 5ARIs.[33,47,61] 5AR type 1 does play a role in glucose utilization in metabolically active organs such as the liver and adipose tissue.[62] Studies have shown an association with altered metabolic function, lower testosterone levels, increased A1c, and altered lipid profiles.[47]

A population-based study using the UK Clinical Practice Research Datalink, evaluated over 55,000 men, showed an increased risk of Diabetes mellitus (DM) in dutasteride (HR 1.32) and finasteride (HR 1.26) compared to tamsulosin alone.[63] Recently, a retrospective cohort study of 130,000 patients in Ontario[32] found men receiving any medical therapy for BPH were at increased risk for DM, and this was highest in men on 5ARIs.[32]

Cardiovascular risk is closely associated with metabolic syndrome. The Reduction by Dutasteride of Prostate Cancer Events (REDUCE) study found a higher incidence of cardiac failure in men on 5ARIs (0.7% vs. 0.4%), although this was not the primary endpoint.[49] There was a higher incidence of composite events; however, no difference in overall incidence or mortality. Lusty et al completed a study of 175,000 men with BPH to focus on 5ARIs and the development of new cardiac adverse events.[33] Cardiac failure was highest for a-blocker alone (HR 1.22), intermediate for combination therapy (HR 1.16), and lowest for 5ARIs (HR 1.09), while still higher than no medications.[33]

3.4. Prostate cancer

Studies of 5ARIs for chemoprevention have been controversial, mainly investigated in two large clinical trials: PCPT and REDUCE. They both showed a decreased incidence of prostate cancer with 5ARI; however, there was an increased risk of higher-grade prostate cancer.[54,64] No significant difference in prostate cancer mortality or overall survival has been found.[65]

There has been much debate on whether these results represent a true biologic difference in prostate cancer risk or if they are a result of unknown confounders. PCPT included only 42–46% of finasteride and placebo groups in the final analysis.[66] Almost a quarter of patients declined end-of-study biopsy, with significantly more declining in the finasteride group.[54] Studies have attempted to use mathematical models to predict the true incidence of prostate cancer and 5ARI.[67]

Some authors suggest that 5ARIs and decreased prostate volumes increase the sensitivity and specificity of subsequent biopsies.[68] In REDUCE, the dutasteride group decreased prostate volume from 45.7 to 39.0 ml, while placebo increased from 45.8 to 56.2 ml at four years. Subsequent publications have attempted to evaluate the relationship with logistic regression models, showing no difference in high-grade disease after volume adjustment.[67,69,70] However, it should be noted that 5ARIs do induce clear biologic changes in prostate tissue. In one of many examples, our group previously found increased levels of glucocorticoids in BPH tissue compared to normal prostate tissue, with this increase most pronounced in patients on 5ARIs.[71] Meanwhile, the glucocorticoid receptor may play a role in driving the growth of castrate-resistant prostate.[72] While a definitive biological mechanism linking 5ARI to high-grade prostate cancer development has not been elucidated, there are biologically possible mechanisms that require further investigation.

4. Urgency and nocturia treatments (anticholinergics, beta-3 agonist, desmopressin)

Anticholinergics block M2 and M3 muscarinic receptors, thereby suppressing detrusor smooth muscle activity and decreasing storage symptoms.[73] This can translate to patient-reported improvement in lower urinary tract bother scores in patients with BPH/LUTS.[74] However, as with other pharmacologic therapies, there are side effects that affect patient adherence and overall quality of life.

The most commonly reported side effect in anticholinergics for BPH is dry mouth, also called xerostomia, which occurs at a high rate of between 3.7% and 15.9% of patients. In 2% of patients, this was severe enough to cause trial withdrawal.[74] Acute urinary retention can occur in up to 0.8% of patients, although this is fairly similar to placebo in patients who are well-selected.[74] Of note, patients in many trials of anticholinergics were included only if they had low PVRs at baseline, with many urologists consequently

avoiding their use in patients with PVRs>200 cc. In a meta-analysis comparing antimuscarinics combined with alpha-blockers to alpha-blockers alone, there was an increased risk of AUR with the use of antimuscarinics in combination with alpha blockers.[75] Patients who start on an anticholinergic should have an assessment of their PVR to ensure that they are not at risk of going into retention both before and after starting therapy. Additional reversible side effects, such as constipation in 10–20% of patients and blurry vision in 1–2% of patients, can also be bothersome.[76]

There is a known risk of cognitive decline associated with anticholinergic exposure among older patients.[77,78] In a prospective study, a dose-dependent association between total anticholinergic exposure and a new diagnosis of Alzheimer's/dementia was found, controlling for demographics and comorbidities.[79] The hazard ratios ranged from 0.92 to 1.54, depending on the total dose/duration. While there is a modest increase in the hazard ratio, cognitive impairment is a serious side effect that gives many patients pause when treating a predominantly quality-of-life disease.

Beta-3 agonists are a relatively new medication class that stimulates beta-3 adrenoreceptors, thereby leading to detrusor muscle relaxation and improvement of storage symptoms.[80] Although beta-3 agonists are safe and effective in the short term for treating LUTS/BPH, long-term safety and efficacy data are still maturing.[81] In an evaluation of the safety and efficacy of mirabegron using pooled data from three randomized controlled trials and two other phase III studies, the most frequently reported side effect from both the pooled studies and one of the other phase III trials was arterial hypertension. However, the reported rate of hypertension among mirabegron-treated groups (10.9% and 12.4%) was comparable to placebo- or antimuscarinic-treated groups (9.3% and 11.8%).[82] This finding offers interesting insight into current practice guidelines that advise against the use of mirabegron among patients with severe uncontrolled hypertension.[83] Interestingly, preliminary retrospective data suggest the median time to discontinuation with mirabegron (169 days) was more than double that of tolterodine (56 days) and significantly longer than that of other antimuscarinics (range, 30–78 days).[84]

Desmopressin acetate is a synthetic analog of vasopressin shown to improve nocturia frequency, IPSS, and quality of life scores among LUTS/BPH patients[85]; however, desmopressin acetate–treated patients were more likely to experience side effects such as headache, 20% versus 2.44%, nausea, 4.71% versus 0%, dizziness, 5.88% versus 0%, and hyponatremia, 4.74% versus 0%, in the short term compared to the control group. Preliminary evidence suggests the incidence of long-term side effects is similar between desmopressin acetate–treated patients and the control group, 28.1% versus 32.8%. This is consistent with the fact that the two groups had comparable drug withdrawal and lost follow-up.

5. Phytotherapies

Phytotherapy, also known as plant-based herbal preparation, has purported benefits in men with LUTS, but there is limited evidence. Common phytotherapeutic agents include *Serenoa repens* (saw palmetto), *Pygeum africanum* (African plum bark), *Cucurbita pepo*, and *Urtica dioica*.[86] Due to conflicting evidence, phytotherapy is not considered a standard treatment for LUTS/BPH and is not recommended by CUA (Canadian Urological Association).[87] Similarly, the American Urological Association (AUA) guidelines note that Saw Palmetto fails to provide a clinically meaningful effect on LUTS secondary to BPH.[3,88]

Saw palmetto is the most studied of the BPH phytotherapies. According to the systematic review of adverse events of saw palmetto, 14 randomized controlled and placebo-controlled trials reported numerous adverse events occurring in 4.6% of patients overall. These include common pharmacologic side effects such as headache, diarrhea, and other gastrointestinal disorders, fatigue, nausea, vomiting, and vertigo, cardiovascular complaints, common cold, gastrointestinal bleeding, and urinary problems.[89] Furthermore, there have been a few reported cases of liver damage and pancreatitis linked to the use of saw palmetto.[90,91] Serious adverse events requiring hospitalization from the saw palmetto are acute urinary retention, abdominal pain, cardiovascular event, elective orthopedic surgery, gastrointestinal bleeding, and melanoma.[91] However, quantification of side effects from phytotherapy in aggregate is difficult, in part because there are discrepancies in the levels of active ingredient among the trials as well as differences in methodology.[3,92]

6. Opportunity cost: QALY, bladder function changes, and cost

A final effect that patients should be aware of when making decisions about their treatment for BPH is the opportunity cost of proceeding with medical management. Certain patients who are apprehensive about procedures for BPH may experience years of reduced urinary and overall quality of life due to suboptimal voiding or side effects during medical management. Of course, these considerations must be carefully balanced against the risks of side effects from procedures and individualized for every patient. However, with the advent of MISTs, the traditional treatment paradigm of “escalation of care”[93] is no longer suitable for all patients. Select patients may benefit instead from earlier or upfront MIST or surgery if medications are either not tolerated, not preferred, or under-effective.[94] Evidence is lacking in this area; however; one trial that randomized patients to TURP or watchful waiting showed that patients who received delayed intervention in the watchful waiting group had less improvement in symptoms compared to upfront TURP.[95] Furthermore, a cost-utility analysis demonstrated that initial treatment with water vapor thermal therapy is superior to pharmacotherapy and subsequent water vapor thermal therapy in terms of lifetime Quality adjusted life year (QALYs) but not cost, 15.50 versus 15.35 QALYs and $14,626 versus $11,795.[96] Initial treatment with prostatic urethral left (PUL), an alternative MIST, was equivalent in lifetime QALYs to pharmacotherapy and subsequent PUL at 15.29 QALYs; however, upfront PUL was a much more costly option at $19,151 versus $13,582. While there are many possible confounders in this trial given the self-selective nature of crossover to TURP, clinicians should counsel patients in the context of their goals when they are deciding between medical management or procedural intervention.

7. Conclusions

This review provides a contemporary overview of risks and side effects in the medical management of BPH. Medical management options for BPH can be effective in alleviating symptoms and are deemed relatively low-risk first-line modalities appropriate for many patients or patients who prefer nonsurgical management of BPH. However, it is crucial to discuss the potential risks and side effects associated with pharmacologic therapy for BPH with patients. These detailed conversations are critical to ensure that patients understand their options in order to proceed with treatments that are most aligned with their individual goals.

Authors' contributions

Drafting of the manuscript: Abdulghafour Halawani, Tianshuang Zhong, Katie Du, and Runhan Ren and Connor M. Forbes; Critical revision of the manuscript and supervision: Connor M. Forbes; and Approval of the final manuscript: Abdulghafour Halawani, Ryan

Paterson, Tianshuang Zhong, Katie Du, Runhan Ren, and Connor M. Forbes.

Conflicts of interest

None of the authors have conflicts of interest to declare.

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