Sexual Side Effects of Medical and Surgical Benign Prostatic Hyperplasia Treatments

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KEYWORDS

• Benign prostatic hyperplasia • Lower urinary tract symptoms • Erectile dysfunction
• Ejaculatory dysfunction • Erectile function • Adverse events

KEY POINTS

- Sexual dysfunction in the cohort of men who seek treatment of lower urinary tract symptoms is common.
- Alpha blocker use frequently has effects on ejaculatory function with large difference in dysfunction rates based on medication selectivity.
- 5-alpha reductase inhibitor use may precipitate a variety of sexual adverse events with a complicated and layered pathophysiologic process.
- Surgical treatments frequently cause retrograde ejaculation with variation in incidence rates depending on the surgical treatment or technique.

INTRODUCTION

Lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH) are a common consultation for most practicing urologists. Although treatment rightly focuses on relief of urinary symptoms, the offered medical and surgical treatments frequently have unwanted effects that provoke sexual dysfunction in the forms of erectile dysfunction (ED) or ejaculatory dysfunction (EjD).

Despite the high prevalence of sexual dysfunction in the cohort of men who frequently require treatment of LUTS due to BPH,[1–6] sexual adverse events (AEs) of treatments are often inadequately assessed. These endpoints are often recorded by sporadic patient report and not by validated questionnaires. As a result, the true incidence and severity of ED or EjD with many of these treatments is only partially understood. Additionally, the effects of LUTS and increasing age on sexual dysfunction[1–6] makes interpretation of changes during the study period more challenging because new onset dysfunction may be related to treatment or natural age-related decline.

This article considers potential pathophysiologic causes of dysfunction with treatment of LUTS due to BPH and attempts to critically review the available data to assess sexually related AEs.

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MEDICATIONS

Alpha Blockers

Alpha receptors are found throughout the human body, mostly as part of vascular smooth muscle and stromal tissue. In humans, there are 3 subtypes of alpha1 receptors: 1a, 1b, and 1d. Alpha1a receptor subtype comprises approximately 70% of prostatic alpha1 adrenergic receptors, with alpha1b generally found in systemic vasculature, although it has also been identified in the prostate.[7] Alpha1d receptors are found in the bladder and in the central nervous system where they may play role in central regulation of voiding.[8]

Alpha blockers (ABs) act by reversibly inhibiting receptor activation and are considered a first-line treatment of LUTS experienced secondary to BPH.[7] Having a firm understanding of receptor subtype and location helps explain the efficacy and side-effect profile of these commonly used drugs. The alpha1a subtype offers a promising target for lower urinary tract relaxation and obstruction relief, whereas action at 1b and 1d can produce systemic effects of vasodilation, including orthostatic hypotension and syncope. The different ABs are equally efficacious in reducing symptoms of BPH but differ in their side-effect profiles.[9,10]

AB medications can be roughly divided into selective and nonselective types. Third-generation ABs such as silodosin and tamsulosin have selective blockade, with silodosin acting specifically at alpha1a receptors and tamsulosin acting at both 1a and 1d. Nonselective ABs such as doxazosin and terazosin are not subtype specific and thus lead to more systemic side effects (headache, nasal congestion, syncope, orthostatic hypotension). These 2 medications produce fewer sexual AEs but must be titrated to mitigate their effects on orthostatic hypotension and syncope. The exception to this is alfuzosin, which is a nonselective AB that produces fewer first-dose systemic effects and does not need to be dose-titrated.[11]

The most common side effect of the ABs is EjD because alpha receptors are widely distributed in organs involved in the emission phase of ejaculation.[12] However, the previously held notion that EjD was due to relaxation of the bladder neck leading to retrograde ejaculation has been challenged. Although there are studies that still support the paradigm of retrograde movement of seminal fluid into the bladder with AB use, increasing evidence points towards anejaculation as the root cause.[13–15] Specifically, in vitro work on human vas deferens demonstrates alpha 1a receptor antagonism eliminates electrically induced contractions.[16,17]

As outlined in the American Urologic Association (AUA) guidelines for the treatment of BPH, sexual function is irregularly reported in most large AB studies.[9] A few studies to date have attempted to measure changes in sexual function beyond EjD in men taking ABs. See later discussion of nonselective and selective ABs as separate groups, and of studies comparing adverse effects between ABs.

Nonselective alpha blockers

The nonselective ABs include alfuzosin, terazosin, and doxazosin, and have a relatively low incidence of overall sexual dysfunction and EjD.[9,10]

One of the most rigorous examinations of the effects of a nonselective AB on various aspects of sexual function comes from the Medical Therapy of Prostatic Symptoms (MTOPS) trial data.[18] Five different domains of sexual function were examined using a validated questionnaire that was state of the art at that time. Doxasozin was the AB examined and minimal effects on sexual function were seen in subjects. In another trial looking at doxasozin in a randomized, controlled fashion, the incidence of EjD, decreased libido, and ED was not different between study and control groups with both reporting incidence of roughly 1%.[19]

In an uncontrolled study, 10 mg alfuzosin taken once daily for 1 year displayed improved ejaculatory function when compared with baseline measurements.[20] A study from the ALFORTI study group was a double-blind, controlled study that showed no significant difference in EjD, decreased libido, or ED between groups, adding further evidence to the low incidence of sexual side effects with nonselective ABs.[11] Another open-label study of 538 men taking 10 mg alfuzosin once daily over 2 years showed a small improvement in international index of erectile function (IIEF) score with no statistically significant difference in EjD or ED.[21]

Selective alpha blockers

More selective ABs, such as tamsulosin and silodosin, produce fewer systemic side effects but have a greater incidence of EjD. Multiple studies have demonstrated a subjective incidence of reported EjD between 4.5% to 11% with the 0.4 mg tamsulosin dose. However, there is no change in erectile function between treatment and placebo groups.[22–24] Slight improvements were noted in sexual desire, although differences in overall sexual satisfaction were not seen.[24]

There does seem to be a dose-EjD correlation in patients taking tamsulosin.[23] This was verified in a 2003 Cochrane review that found EjD in 18% of patients taking 0.8 mg dose tamsulosin, 6% in