



Review

# Sexual Dysfunctions Related to Drugs Used in the Management of Lower Urinary Tract Symptoms Due to Benign Prostatic Hyperplasia: A Narrative Review on $\alpha$ -Blockers and 5-Alpha Reductase Inhibitors

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**Abstract:** This is a critical review of the current literature data about sexual dysfunction as a potential side effect related to drugs commonly used for the treatment of Benign Prostatic Hyperplasia and Lower Urinary Tract Symptoms. In this narrative review, we analyzed data from the literature related to the development of sexual dysfunctions during the treatment of BPH or LUTS. Both  $\alpha$ -blockers and 5-alpha reductase inhibitors (5-ARIs) can induce erectile dysfunction, ejaculatory disorders and a reduction in sexual desire. The sexual side effect profile of these drugs is different. Among the  $\alpha$ -blockers, silodosin appears to have the highest incidence of ejaculatory disorders. Persistent sexual side effects after the discontinuation of finasteride have been recently reported; however, further studies are needed to clarify the true incidence and the significance of this finding. However, most of the published studies are affected by a weak methodology and other important limitations, with only a few RCTs available. Therefore, it is desirable that future studies will include validated tools to assess and diagnose the sexual dysfunction induced by these medications, especially for ejaculation and sexual desire disorders.

**Keywords:**  $\alpha$ -blockers; 5-alpha reductase inhibitors; Benign Prostatic Hyperplasia (BPH); LUTS (Lower Urinary Tract Symptoms); sexual side effects



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## 1. Introduction

Sexual dysfunctions are common in elderly men [1–5], even if they could be adverse drug reactions (ADRs) of antidepressants, antipsychotics and anti-hypertensive drugs [6–12]. Moreover,  $\alpha$ -blockers and 5-alpha reductase inhibitors (5-ARIs) can induce erectile dysfunction and ejaculatory disorders [5,9,13–19], despite these drugs being used to treat Benign Prostatic Hyperplasia (BPH) and Lower Urinary Tract Symptoms (LUTS) that induce sexual dysfunction [20–24]. In this manuscript we reviewed data from the literature related to the development of sexual dysfunctions during the treatment of BPH or LUTS.

## 2. Materials and Methods

The PubMed, Embase and Cochrane library databases were searched for articles published before 15 February 2021. Secondary search included articles cited in reference lists identified by the primary search. Records were first screened by title/abstract, before full-text articles were retrieved for eligibility evaluation. Remaining articles were then subject to a citation search before a final hand-search of all reference lists. Papers were deemed eligible if they included any form of the following words: “sexual dysfunction”, “drugs”, “carotid atherosclerosis”, “ $\alpha$ -blocker”, “5-alpha reductase inhibitors”, “phosphodiesterase type 5 inhibitors”, Benign Prostatic Hyperplasia (BPH), LUTS (Lower Urinary Tract Symptoms), “sexual side effects” and “treatment-emergent sexual dysfunction”. All citations were downloaded in Mendeley Ltd. software (Elsevier, London, UK), and duplicates were deleted. A.L.T. and C.P. screened all articles by title/abstract to determine their eligibility and L.G. reviewed a random sample of 20% in order to evaluate the reliability of the selection process. In order to avoid a bias of exclusion, the full text articles were retrieved following first round exclusions and were also subject to two independent eligibility reviews (T.C. 100%, G.D.S. 20%), this time with perfect agreement. The studies evaluated as eligible are enclosed in the present narrative review.

## 3. Results

All the reviewed articles are listed in Tables 1 and 2. In Table 1, we indicated the articles on sexual dysfunction related to the drugs used in the treatment of LUTS and/or BPH, while in Table 2 the articles on phosphodiesterase type 5 inhibitors (PDE5i) used in LUTS and/or BPH are listed.

**Table 1.** Sexual dysfunction related to drugs used in the treatments of LUTS and/or BPH.

Manuscripts	References
Reviews and meta-analysis: 58	[9,13–15,17,18,20–72]
RCTs (Randomized Clinical Trials): 21	[73–93]
Clinical trials, Case Control, Retrospective studies, Surveys and “Case reports”: 41	[1,2,5,18,64,94–129]
Others: 57	[3,6–11,16,19,48,130–171]

**Table 2.** Manuscripts on PDE-5i used to treat LUTS and/or BPH.

Manuscripts	References
Reviews and meta-analysis: 30	[92,172–201]
RCTs: Randomized Clinical Trials: 24	[78,202–224]
Others (non RCTs): 9	[126,189,225–231]

As reported in Table 1, most of the articles (58; 36.9%) are reviews and meta-analyses, while only 21 (12.7%) are randomized studies (RCTs: Randomized Clinical Studies, such as randomized, double-blind, placebo-controlled studies) and only 2 of these [82,85] used a specific and validated rating scale to measure sexual function. In contrast, among the 41 non-RCT studies (24.8%) (Table 1), 32 (78%) used a specific questionnaire (mainly IIEF) to detect sexual dysfunction, while 9 (22%) [96,97,106,110,112,114,115,120,129] did not use any validated rating scale.

Both  $\alpha$ -blockers and 5-ARIs can cause erectile dysfunction, ejaculatory disorders and a reduced sexual desire [35,232] (we have sorted the pharmacologic effects by sexuality as “excitatory” (+), “inhibitory” (–) or “no effect” (+/–); we also defined as “uncertain” (?) the results that were difficult to interpret).

### 3.1. $\alpha$ -Blocker

Both silodosin and tamsulosin induce ejaculatory disorders (up to 28.1%) [91] (Tables 3–5). The different sexual side effect profile of  $\alpha$ -blockers may be related to the following several factors: (1) the chemical structure; (2) the binding affinity/selectivity for  $\alpha$ 1-adrenergic receptor subtypes; (3) binding to other receptor-mediated mechanisms; and (4) the different volume of distribution. Alfuzosin, doxazosin and terazosin show equal binding with the three subtypes of  $\alpha$ 1-adrenergic receptors, while tamsulosin and silodosin show a super-selective binding with the  $\alpha$ 1-A receptor [4,14,43]. The most uroselective alpha-blocker is silodosin and has the most marked effect on ejaculation [23,113]. The sexual side effect profile of dutasteride appears to be similar to that of finasteride with regards to erectile dysfunction (ED), ejaculatory dysfunction (EjD) and decreased libido [72,123,140]; both drugs appear to be associated with a higher risk of ED, EjD and reduced libido than a placebo [30,131,233]. Recently, Corona et al. [125] found that 5-ARIs are associated with decreased libido and spontaneous nocturnal erection, while no relationship was found with ED or EjD.

**Table 3.** Effects of  $\alpha$ -blockers on erectile functions.

Silodosin	Tamsulosin (¶) (♥)	Alfuzosin (¶)	Terazosin	Doxazosin (¶)
(+/-) [82]	(+/-) [16,19,53,90,98,121,122,140] (+) [101,103,107,116]	(+/-) [16,19,53,75,86,90,140] (+) [31,64,79,98,101,102,111,118,119, 122,128,234]	(+/-) [16,19,53,140] (+) [107]	(+/-) [16,19,53,98,140] (+) [33,77,105,107,127,235]

(¶) There are, apparently, conflicting data on the effects of alfuzosin, doxazosin and tamsulosin on sexual function: some authors suggest a placebo-like effect, while others an improvement. The methodological problems concerning the various studies are detailed in a review by van Dijk et al. [50]. Methodological problems are likely responsible for some of the contradictory findings on sexual side effects [31]. (♥) Hellstrom and Sikka [87] reported that in about 90% of health volunteers treated with tamsulosin (0.8 mg/day) a significant decrease (20%) in the volume of ejaculation was recorded. Liefefeld et al. [108] failed to report the effect of  $\alpha$ -blockers. Several authors considered gynecomastia as a sexual dysfunction. This side effect has been reported in some manuscripts on  $\alpha$ -blockers [72,115].

**Table 4.**  $\alpha$ -blockers: Effects on ejaculator function.

Silodosin	Tamsulosin	Alfuzosin	Terazosin	Doxazosin
(-) (1**) [14,43,73,74,80,82,83,88,89,91,106, 110,112–114]	(-) (2**) [14,75,87,96,116,117,120,236]	(+/-) [53,75,79] (+) [64,118,119,122,128]	(+/-) [14,53]	(+/-) [14,53] (+) [105]

(1\*\*) The prevalence of silodosin-induced ejaculation dysfunction (EjD) is between 5 and 28.1%, with an average value of about 20% [159]; silodosin appears to be the drug with the highest risk of EjD [14,23]; these data are also confirmed by Capogrosso et al. [113], who report 48% of cases of anejaculation. The efficacy of silodosin appears to be increased in patients with “abnormal ejaculation” [112]. (2\*\*) The prevalence of tamsulosin-induced ejaculation dysfunction ranges from 3 to 11% [53,236]; tamsulosin is associated with a significantly lower risk of ejaculatory disorders than silodosin [14]. In studies by Hellstrom and Sikka [87] and Hisasue et al. [96], ejaculation disorders due to tamsulosin (decreased ejaculate volume and anejaculation) were not attributed to retrograde ejaculation.

**Table 5.** Effects of  $\alpha$ -blockers on sexual desire.

Silodosin	Tamsulosin	Alfuzosin	Terazosin	Doxazosin
(-) [113]	(+) [116] (+/-) [53,54,121]	(+) [64,122] (+/-) [53,54]	(+/-) [53,54]	(+) [105] (+/-) [53,54,92]

### 3.2. 5-ARI

The sexual ADRs of 5-ARIs are comparable to placebos after a 2-year treatment [27,72,81,115]. Kaplan et al. [104] reported that a chronic treatment (5 years) with dutasteride induces a higher incidence of erectile dysfunction and gynecomastia than finasteride. Cases of persistent sexual dysfunction have been recently reported after the discontinuation of finasteride [32,60,97,99,100,129,131,134,141,147,149,166,170]. Irwig and

Kolukula [99], using the Arizona Sexual Experience Scale (ASEX) validated questionnaire, interviewed 71 healthy male (21–46 years) finasteride-users, finding a high incidence of sexual dysfunction (Tables 6 and 7). In particular, 69–94% of those interviewed described “low libido” (94%), “erectile dysfunction” (92%), “decreased arousal” (92%) and “problem with orgasm” (69%). The same authors acknowledged the limitations of their study, stating that “the true incidence of these events is unknown as it is a post-hoc approach” and that, in previous randomized, placebo-controlled trials, the incidence of ADR on sexual function was 8% lower in the finasteride group and less than 3% in the control group. “Assuming the vast majority of these events have resolved, the incidence of persistent sexual side effects in patients receiving finasteride was less than 1%” [99]. Indeed, some methodological “biases”, such as the following, could limit these results: (i) the study was conducted only through “standardized telephone or Skype interviews”; (ii) the study was conducted on a sample of patients recruited from a website for people complaining of sexual dysfunction; and (iii) the study was an observational survey (with no control groups) and involved only a small number of patients. The pathophysiological mechanisms responsible for 5-ARI-induced sexual dysfunction may be related to the decrease in dihydrotestosterone levels and possibly other neurosteroids, such as progesterone metabolites [32,47,133]. Psychological factors (“nocebo effect”) have also been implicated as responsible for sexual dysfunction in patients treated with 5-ARIs [144]. However, to date, little is known about the exact mechanisms underlying the sexual dysfunctions related to 5-ARIs [61,71]. There is a cumulative risk of sexual ADRs with  $\alpha$ -blockers vs. monotherapy or a placebo [40,65,85,92,112]: Gacci and co-authors [14] found that combination therapy with  $\alpha$ -blockers and 5-ARIs resulted in a three-fold increased risk of ejaculation disorders vs. monotherapy.

**Table 6.** 5-ARI: Effects on sexual function.

	Dutasteride (A), (B), (C)	Finasteride (A), (B), (C), (D)
Effects on erectile function	(–) [27,34,40,48,49,71,76,93,112,123,140] (+/-) [125]	(–) [34,48,49,71,77,81,85,92,140] (+/-) [125] (?) [59]
Effects on ejaculatory function.	(–) [14,27,48,49,61,71,76,84,123,140] (+/-) 125	(–) [14,48,49,59,71,77,81,85,92,140] (+/-) 125
Effects on sexual desire.	(–) [27,40,48,49,76,84,93,123,125,140]	(–) [48,49,77,81,85,92,125,140]

(A) Both finasteride and dutasteride exhibit comparable sexual effects and side effects [72,140]. A study by Lee et al. [34], however, reports a doubled risk of ED with finasteride. (B) The rates of these adverse effects become comparable to placebo after treatment has continued for more than 2 or more years [115,140]. Contrary to these data, recently Kaplan et al. [104] found that, over the long term (5 years), dutasteride causes significantly more sexual side effects and breast complications (gynecomastia) than finasteride. (C) In a review of clinical trials by Anitha et al. [59], the authors concluded that there was no clear evidence that finasteride (5 mg or 1 mg/die) had an adverse effect on erectile function. Similar conclusions were also reached by Canguven and Burnett, [26] and Haber et al. [95]. Anitha et al. [59] found that older uncontrolled studies reported high rates of erectile dysfunction during treatment with finasteride (0.8–33%), while randomized controlled trials reported rates of erectile dysfunction between 0.8–15.8%. However, the results of these clinical trials were not considered reliable because they neither assessed baseline sexual function nor used a validated questionnaire. Probably for similar reasons, Erdemir et al. [71] reported high rates of sexual dysfunction with 5-ARIs (between 2.1–38%); however, they conclude that the rate of erectile dysfunction in clinical trials with 5-ARIs ranges from 5 to 9%. Similar conclusions were also reached by Ponholzer et al. [39]: “5 $\alpha$ -reductase inhibitors are associated with ED, loss of libido and decreased ejaculate volume by up to 10%”. Regarding 5ARIs, Gacci et al. [14] found “an overall prevalence of ejaculation disorder equal to 3%, although about 3 times higher than placebo”. In a review by Trost et al. [49], slightly higher rates than placebo for reduced libido (1.5%), erectile dysfunction (1.6%) and ejaculatory dysfunction (3.4%) were indicated for 5-ARIs. A recent review by Traish et al. [48] shows slightly different rates of sexual dysfunction. Gur et al. [30] report instead that the true prevalence of sexual side effects with 5-ARI treatment is currently unknown. (D) There have been recent reports of persistent sexual dysfunction after discontinuation of finasteride treatment [32,56,60,97,99,100,129,131,134,141,147,149,166,170,237]. Several authors have considered gynecomastia as a sexual dysfunction. This side effect has been reported in a lot of research on 5-ARIs [37,47,49,66,72,76,93,104,115].

**Table 7.** 5-ARI: Rates (minimum and maximum percentages) of sexual dysfunction in double-blind, randomized, placebo-controlled clinical trials for benign prostatic hyperplasia.

	Finasteride	Dutasteride
ED (Erectile Dysfunction)	3.4–15.8% (1.7–6.3%)	1.7–11% (1.2–3%)
EjD (Ejaculatory Dysfunction)	0.2–7.7% (0.1–1.7%)	0.5–2% (0.1–1%)
Decrease in sexual desire	2.4–13% (1.4–2%)	0.6–4% (0.3–2%)

The effects of placebo are reported in parenthesis. Data by Gur et al. 2013 [30].

### 3.3. $\alpha$ -Blocker and PDE5i Combination

Several clinical studies seem to confirm that the combination of  $\alpha$ -blockers and PDE5i is more effective in improving both LUTS and erectile dysfunction than treatment with  $\alpha$ -blockers alone [28,186,205,222,226]. The results from a combination treatment with  $\alpha$ -blockers and PDE5i in men with ED and BPH suggested a synergistic effect on both erectile dysfunction and LUTS [23,40,146,177,222].

### 3.4. PDE5i

In this review, among the studies on treatment in combination with  $\alpha$ -blockers or 5-ARIs and PDE5i, 17 RCTs were performed on tadalafil [40,192,202–206,208–210,213,215,217–219,221], 3 RCTs on sildenafil [207,214,216], 2 RCTs on vardenafil [209,222] and 2 RCTs on UK-369.003 [179,212].

PDE5i is used alone or as an add on to  $\alpha$ -blockers, alfuzosin or tamsulosin, or finasteride [180,203,219]. Oelke et al. [206] reported a significant increase in Qmax (“maximum urinary flow rate”, which is the urodynamic parameter for the evaluation of LUTS), even if other studies must be performed to validate this result [169]. The link between erectile dysfunction and LUTS is based on the following four hypotheses: (1) a decrease in or alteration of the endothelial nitroxide synthetase levels in the prostate and in the smooth muscle of the penis; (2) effects related to autonomic hyperactivity; (3) the increased activation of Rho-kinase; (4) pelvic atherosclerosis [33,38,112]. As recently reported, all these mechanisms could be countered by PDE5i [183]. Moreover, PDE5 inhibition has been shown to affect several pathogenic pathways contributing to LUTS, although the exact mechanism of action remains to be elucidated [222]. However, PDE5i use is well tolerated in patients with LUTS and/or BPH (Table 2).

## 4. Discussion

In the present review we found different and apparently conflicting epidemiological data on  $\alpha$ -blocker- and 5-ARI-induced sexual ADRs (Table 8). Several problems make it difficult to quantify and qualify  $\alpha$ -blocker- and 5-ARI-induced sexual dysfunction. These problems mainly concern the diagnostic criteria of ejaculatory disorders. None of the reviewed studies used the diagnostic criteria for sexual dysfunction proposed by ICD-10 (WHO, ICD) DSM-IV-TR (American Psychiatric Association, 2000 and DSM5 (American Psychiatric Association, 2013) [153,164,238]. Other proposed classifications, such as that of NIH (National Institutes of Health), are rarely used. There is no clear consensus on the classification of “non-premature ejaculatory dysfunction” [152]. There are no clear and shared diagnoses for delayed ejaculation [143]. Previously, Hartmann and Waldinger [138] wrote that “a big problem we should solve is finding consensus on the operational definitions of ejaculatory disorders”. As far as we know, the classification of delayed ejaculatory dysfunction is still far from precise. Delayed ejaculation, inadequate ejaculation, inhibited ejaculation, idiopathic ejaculation, (primary) ejaculation and psychogenic ejaculation and psychogenic anejaculation have been used interchangeably to describe a delay or an absence of male orgasmic response [143]. Furthermore, some authors included orgasmic disorders in ejaculatory disorders [139], while others considered ejaculatory dysfunction as orgasm dysfunction [53] due to the lack of consensus on the diagnostic criteria of ejaculatory disorders. We think that it is also important to distinguish anejaculation from retrograde



ejaculation. Jannini and Lenzi [139] argued that “it is important not to confuse the classification of anejaculation with that of retrograde ejaculation. In the latter case, orgasm is usually present, even if attenuated, while anejaculation always coincides with anorgasmia (even if the opposite is not true)”. Hellstrom et al. [21] and Rosen and Seftel [150] defined “severe ejaculatory dysfunction as ejaculation with reduced sperm count or ejaculation loss”. Retrograde ejaculation (or dry ejaculation) occurs when semen enters the bladder instead of emerging through the penis [152]. Despite this important difference, many studies do not distinguish between anejaculation and retrograde ejaculation.

**Table 8.** Summary of the main conclusions on sexual dysfunction in patients treated with  $\alpha$ -blockers and 5-ARIs (table modified by La Torre et al., 2016) [9].

Tamsulosin is associated with a significantly lower risk of EjD than silodosin (OR: 0.09; $p < 0.00001$ ) [14]
Alfuzosin, doxazosin and terazosin are associated with a lower risk of EjD compared to a placebo.
Both finasteride and dutasteride have a significantly higher risk of EjD than a placebo.
EjD is significantly more common with combination therapy than with $\alpha$ -blockers alone or 5 ARI alone [14].
A-blockers (alfuzosin, doxazosin, tamsulosin, terazosin) show an incidence of decreased libido and erectile dysfunction (ED) very similar to a placebo [72,107].
5-ARIs (finasteride and dutasteride) are associated with an increased risk of erectile dysfunction (ED), ejaculatory dysfunction (EjD) and decreased libido compared to a placebo [72].
The ED rate in 5-ARI clinical trials ranged from 5 to 9% [71].

The examination of the “post-ejaculate urine semen concentration” serves as a reliable indicator of retrograde ejaculation, but only a few studies considered these data [87,89,96]. Other methodological issues include the definition of reduced ejaculatory volume. Numerous physiological factors can cause a reduction in semen volume, e.g., a short period of sexual abstinence (<2 days) or frequent ejaculations before semen collection [167].

In many studies, the abstinence period before semen analysis was not specified. Another possible methodological “bias” is the absence of an objective measurement of semen volume leading to an underestimation of EjD [87]. A further methodological limitation depends on the lack of definition of the reduction in sperm volume. For example, the WHO indicated that the lower reference limit for semen volume is 1.5 mL, but none of the studies reviewed and reported in this study indicated a reference point for the definition of reduced ejaculate volume, except Hellstrom and Sikka [87], who defined a “decrease in ejaculate volume” as “a greater than 20% decrease from baseline”. The Danish Prostatic Symptom Score (DAN-PSS) is a questionnaire used for the detection of ejaculatory disorders [137]. It includes 12 questions related to voiding problems and the perceived disturbance of each individual symptom and 3 questions related to sexuality (erection, volume of ejaculation, pain/discomfort during ejaculation). This questionnaire has been validated and used in numerous epidemiological surveys and clinical studies [130,135,137,158]. However, to the best of our knowledge, the DAN-PSS has only been validated for the evaluation of urinary symptoms and not for sexual function [171]. This could be a potential limitation of the studies using DAN-PSS, as it may have led to an overestimation (or underestimation) of ejaculatory disorders. Rosen and Fitzpatrick [5] reported that the DAN-PSS and ICS questionnaire evaluate only two ejaculatory dysfunctions, i.e., a reduced amount of semen and pain and discomfort during ejaculation. Rosen et al. [3] proposed the use of the MSHQ questionnaire, but few studies used it. As previously pointed out, among the RCTs examined on  $\alpha$ -blockers and 5-ARIs, only two [82,85] of these used a specific and validated rating scale to measure sexual functioning. In studies that did not use a self-administered questionnaire or that did not directly ask the patient about sexual function, the identification of sexual dysfunction often relies on spontaneous disclosure by patients, but previous research has shown that patients rarely spontaneously report side effects concerning the sexual sphere [140]. Therefore, failure to use the rating scales compromises the true rate

of sexual dysfunction. Most researchers used the term “libido,” which does not indicate which stage (desire, arousal, orgasm) of the human sexual response is affected by sexual dysfunction. Indeed, the term “libido” does not discriminate between the various phases of the sexual response cycle [145]. In the literature, we have found the use of the following, apparently similar, expressions of sexual function, which, however, have probably been interpreted with different meanings: “loss of sexual desire”, “Hypoactive Sexual Desire (HSD)”, “Hypoactive Sexual Desire Disorder (HSDD)”, “Low sexual desire”, “reduced sexual desire (libido)”, “loss of libido (sexual desire)”, “reduced libido”. Roehrborn et al. [40] distinguished between “altered (decreased) libido” and “loss of libido”, but did not explain the difference between these. Skolarus and Wei, [46] described “erectile function” as defined in terms of (1) “Quality of erection”, (2) “Libido/sexual desire” and (3) “Satisfaction”. However, defining erectile function in terms of “libido/sexual desire” can be confusing and difficult for the patient to understand.

## 5. Conclusions

Few rigorous studies have been conducted using both control groups and validated questionnaires to evaluate the sexual side effects of  $\alpha$ -blockers and 5-ARIs [53]. It is desirable that future studies include validated tools to assess and diagnose drug-induced sexual dysfunction, particularly for ejaculation and sexual desire disorder. Failure to use these assessment questionnaires reduces the possibility of detecting the exact incidence of sexual dysfunction and the likelihood of accurately diagnosing the specific type of sexual dysfunction involved, as well as hindering the objective monitoring of the improvement or worsening of symptoms during drug treatment. The MSHQ is a validated questionnaire for the assessment of sexual dysfunction, in particular for the assessment of strength, delay and pleasure in ejaculation [5,150]. Other specific rating scales, such as ASEX [142] or CSFQ [154], could also be used for patients with LUTS/BPH. Only a small amount of research has intentionally initiated the study of sexual dysfunction caused by  $\alpha$ -blockers and 5-ARIs. Therefore, studies that specifically evaluate the sexual dysfunction induced by these drugs are needed. Further studies are needed to determine the pathophysiological mechanisms involved in the link between LUTS and sexual dysfunction (particularly ejaculation disorders) and the optimal management strategies for men with these concomitant conditions [5,21]. The sexual side effect profile of these drugs is different. Among the  $\alpha$ -blockers, silodosin (followed by tamsulosin) shows the highest incidence of ejaculatory disorders. Alfuzosin has no deleterious effects on sexual function and is well tolerated when used in combination with a low dose of PD5i for the treatment of erectile dysfunction. Several authors have documented that the  $\alpha$ -blocker/PD5i combination may act synergistically to improve both LUTS and sexual function [23,40,146,222]. With the exceptions of only silodosin and, to a lesser extent, tamsulosin, the effect of  $\alpha$ -blockers on sexual function appears similar to a placebo. The sexual adverse event profile of dutasteride appears to be similar to that of finasteride. There have been recent reports of persistent sexual dysfunction after the discontinuation of finasteride treatment, but further studies are required to evaluate a causal relationship [49]. Further studies are also needed to evaluate the long-term role of a combination therapy of PD5i and  $\alpha$ -blockers or 5-ARIs in LUTS/BPH treatment [184,222]. Several studies show that sexual dysfunction has a high prevalence in sexually active men with LUTS [4], which must be carefully evaluated and diagnosed before treating LUTS, as some treatments may further aggravate it. Despite this, Giona et al. [132] documented that there is a significant discrepancy in the attitude of urologists in advising patients with LUTS-related erectile dysfunction: in particular, a significant minority of urologists do not discuss either erectile dysfunction or ejaculatory disorders with patients before the treatment; moreover, they do not discuss an alternative treatment [132]. The tendency of urologists to not investigate the sex life of patients could negatively affect their quality of life to the extent that effective treatments are not proposed [58]. The importance of both sexological history and clinical evaluation is evident:

this procedure is essential for the objective monitoring of the improvement or worsening of symptoms during drug treatment.

## 6. Patents

Male sexual dysfunction could be the result of inaccurate sexual history and clinical assessment in patients with urological diseases. In this sense, the evaluation of all drug-related side effects on male sexual function is essential to improve a patients' overall quality of life.

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