Sexuality and Management of Benign Prostatic Hyperplasia with Alfuzosin: SAMBA Thailand

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ABSTRACT

Introduction. Benign prostatic hyperplasia (BPH) is a common condition among elderly men. The aim of therapy is to improve lower urinary tract symptoms (LUTS) and quality of life (QoL) and to prevent complications.

Aim. The primary objective was to assess the effect on ejaculatory dysfunction (EjD) of 6 months treatment with alfuzosin (XATRAL) 10 mg once daily (OD) in men with LUTS suggestive of BPH in Thailand. Secondary objectives were to evaluate the efficacy of alfuzosin on LUTS, bother score (International Prostate Symptom Score [IPSS] 8th question), erectile dysfunction (ED), onset of action, and tolerability.

Methods. Overall, 99 men with moderate to severe LUTS suggestive of BPH (mean IPSS 18.9, bother score 4.3) were enrolled in an open-label study. Sexual function was evaluated at baseline and after 6 months treatment, using the International Index of Erectile Function-5 and the Male Sexual Health Questionnaire (MSHQ) ejaculation score, a new validated questionnaire assessing seven EjD symptoms.

Main Outcome Measure. The main outcome measure is mean change from baseline to the end of treatment in the MSHQ Ejaculation score.

Results. MHSQ ejaculation score significantly improved from 23.09 at baseline to 21.54 at 6 months \( (P = 0.022) \). Overall, 70% of patients perceived an improvement in LUTS within 1 week (36.3% within 3 days). IPSS total score significantly improved from 18.93 at baseline to 9.59 at 6 months \( (P < 0.001) \). IPSS voiding and irritative subscores also significantly improved. The percentage of patients with moderate or severe ED decreased from 35.3% at baseline to 21.8% at 6 months. Most adverse events were dizziness (3%) and orthostatic hypotension (1%) with minor intensity. No significant change in blood pressure and heart rate was observed.


Key Words. Alpha-Blocker; Benign Prostatic Hyperplasia; Ejaculation; Lower Urinary Tract Symptoms; LUTS

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Introduction

Benign prostatic hyperplasia (BPH) is a common condition among elderly men. The incidence of BPH is considered as high as 50% in men aged 60 years, rising to 88% in men aged 80 years [1]. It is estimated that nearly half of these men will develop moderate to severe lower urinary tract symptoms (LUTS) [2]. Symptom severity and quality of life (QoL) can be measured using a number of instruments: in accordance with the recommendations of the European Association of Urology on BPH [3]. The most commonly used instruments are based on subjective clinical criteria (International Prostate Symptom Score [IPSS] and bother score). Urinary symptoms of BPH can also affect sexual functioning [4], considered by patients themselves to be one of the most important aspects of the disease [5,6].

The aim of therapy is to improve LUTS and QoL and to prevent complications. There are two main options for the treatment of BPH: medical therapy and surgical management, including minimally invasive procedures. Medical treatment has become the preferred option in patients with symptomatic but uncomplicated BPH [7]. Surgery is indicated in case of bothersome LUTS refractory to medical therapy or in case of serious BPH complications such as refractory urinary retention or renal insufficiency [3].

The efficacy of \( \alpha_1 \)-blockers in patients with LUTS suggestive of BPH is now amply demonstrated by numerous placebo-controlled studies [8]. Alpha-blockers are the most effective monotherapy for LUTS (American Urological Association [AUA] guidelines) and act rapidly. As a result of this, guidelines [3,9] on BPH currently recommend them as a first-line medical treatment in this indication. By reducing sympathetic overstimulation, \( \alpha_1 \)-blockers should also influence the long-term outcome of BPH [10].

Alfuzosin, a quinazoline derivative, is a specific and uroselective postsynaptic \( \alpha_1 \)-blocker showing a preferential tropism for the smooth muscle of the lower urinary tract (trigone, urethra, prostate) compared with its affinity for vessel smooth muscle [11,12]. Immediate-release (2.5 mg three times a day) and sustained-release (5 mg twice a day) formulations and extended release (10 mg once daily [OD]) largely marketed within Europe and other parts of the world confirmed the efficacy of alfuzosin in alleviating symptoms and in improving maximum flow rate in well-designed controlled and open studies [13–19]. Alfuzosin is also the unique alpha-blocker registered in the indication of adjuvant treatment of acute urinary retention (AUR).

Hence, McNeill [20] showed in a double-blind, randomized, placebo-controlled study that a successful trial without catheter after two doses was observed in 62% of AUR patients treated with XATRAL 10 mg OD, compared to 48% in the placebo treatment group (\( P = 0.012 \)).

In recent large real-life practice studies [21–23] in BPH men with LUTS, alfuzosin have been shown to be effective in improving LUTS and QoL, to be well tolerated from a cardiovascular standpoint, and to have no deleterious effect on both erectile and ejaculatory dysfunction (EjD).

All the results highlight the clinical importance of evaluating LUTS in patients with sexual dysfunction and the need to consider sexual issues in the choice of treatment for managing patients with BPH.

The aims of this study were to assess the sexual function improvement with alfuzosin 10 mg given once a day (XATRAL 10 mg OD) administered during 24 weeks using a new validated questionnaire, the Male Sexual Health Questionnaire (MSHQ), and to confirm its efficacy including the onset of action and its safety profile.

Patients and Methods

The study was an open, noncomparative, multicenter study. Patients with BPH who were attending 13 urology clinics in Thailand were included in the study. Patients received XATRAL 10 mg OD at the end of evening meal for 24 weeks.

The eligible patients were male aged 50 years or more who were suffering from moderate to severe LUTS, suggestive of symptomatic BPH, with an IPSS total score ≥8, sexually active, and have given their written informed consent. Patients were excluded if they had one of the following criteria: a history of hepatic or severe renal insufficiency, unstable angina pectoris, concomitant life-threatening condition, previous prostate surgery, a minimally invasive procedure within 6 months prior to inclusion, planned prostate biopsy, prostate surgery or minimally invasive procedure during the whole study period, acute symptomatic urinary tract infection or prostatitis, neuropathic bladder defined as a spinal injury consequence or related to a neurological disorder or a known residual volume ≥350 mL, a diagnosed prostate cancer, have received 5\( \alpha \)-reductase inhibitors or LUTS-related phytotherapy within 6
months prior to inclusion or α1-blockers within 30 days, or SSRI (Zoloft, Prozac) within 30 days prior to inclusion, are receiving any treatment for erectile dysfunction (ED) (i.e., phosphodiesterase type 5 [PDE5] inhibitors) at inclusion, a history of postural hypotension or syncope, known hypersensitivity to alfuzosin, illiterate patients or patients who are unable to understand or to complete the questionnaires, and patients who participated in any clinical study in the past month.

Data were collected anonymously and recorded on a Data Collection Form at visit 1 (baseline), visit 2 (week 1 ± 2 days), visit 3 (week 4 ± 3 days), visit 4 (week 12 ± 7 days), and visit 5 (week 24 ± 7 days).

At baseline, the following variables were recorded: the patients’ demographic data, physical examination and vital signs, concomitant diseases, concomitant treatments, and laboratory investigations (prostate specific antigen [PSA], creatinine, and urinary analysis).

All patients suggestive of BPH were asked to complete the IPSS, the International Index of Erectile Function-5 (IIEF-5), the MSHQ and Bother score (IPSS 8th question).

The IPSS is the internationally accepted standard questionnaire for assessing LUTS. It is a validated 8-item scale which assesses the severity of incomplete emptying, urinary frequency, intermittency, urgency, weak stream, and nocturia in every visit. The first seven items have an ordered categorical response that can be scored 0–5, with an overall score of 0–35. The severity of symptoms is classified as none (IPSS 0) or symptomatic and mild (≤7), moderate (8–19), or severe (≥20). The eighth question (bother score) assesses the degree of bother and dissatisfaction associated with the symptoms, with responses scored from 0–6.

Sexual function was assessed using two independent questionnaires, the IIEF-5 and MSHQ. The IIEF-5 questionnaire (also referred to as the Sexual Health Inventory of Men), is an abridged 5-item version of the IIEF-15 questionnaire. It is a validated, multidimensional questionnaire that is a sensitive indicator of changes in erectile function and treatment outcomes being used in visit 1 and visit 5. It is scored from 1 to 5, where 1 = never/occasionally; 2 = less than half of the time; 3 = sometimes/half of the time; 4 = more than half of the time; and 5 = almost always. The total IIEF-5 score, calculated by totaling the response to all five questions, is interpreted as: normal, 22–25; mild ED, 17–21; moderate ED, 12–16; and severe ED; 5–11.

The 25-item MSHQ is a validated, self-administered instrument for assessing the primary domains of erection, ejaculation, and sexual satisfaction in aging men (see Appendix 1) in visit 1, 3, 4, and 5. This new instrument has excellent psychometric properties and is well suited for use in clinical and research settings [24].

Statistical Analysis
Analysis utilized paired t-test, using the SPSS statistical program (version 11.5 for Windows, SPSS Inc., Chicago, IL, USA). Statistical significance was set at a P value of 0.05 or less. In case of missing data or early termination from the study, the analysis of the intent to treat (ITT) population was based on the Last Observation Carried Forward method. In case of missing items in the MSHQ scale, the mean of this item was imputed.

Primary Efficacy Analysis
The primary analysis evaluated the impact of treatment on sexual function based on the mean change in MSHQ Ejaculation score from baseline to study end (week 24 or premature withdrawal). The proportion of patients presenting an improvement in MSHQ Ejaculation score of at least 20% at study end (week 24 or withdrawal) was to be presented with its 95% confidence interval. The analysis was done for the ITT population. Summary tables were given for the per-protocol population and on an observed case basis.

Secondary Efficacy Analysis
Descriptive statistics for the percentage change and raw differences from baseline in MSHQ Ejaculation score and questions and other subscores were performed after 4, 12, and 24 weeks of treatment.

Safety Analysis
Analyses on laboratory parameters and vital signs were based on the definitions of potential clinically significant abnormalities.

Results
Eligible patients were enrolled between June 2006 and December 2007 from 13 centers throughout Thailand.

Demographics and Baseline Characteristics
A total of 99 patients were consecutively recruited into the study with the mean age 62.26 years old.
Mean serum PSA and creatinine at baseline were 1.77 ng/mL and 1.18 mg/dL, respectively. The most common concomitant cardiovascular comorbidities were hypertension (31.3%), dyslipidemia (14.1%), diabetes mellitus (7.1%), and ischemic heart disease (2%). Of the patients with hypertension, the patients were treated with calcium channel blocker 9.09%, beta-blocker 8.08%, diuretic 7.07%, ACE-Inhibitors 5.05%, angiotensin receptor blocker 2.02%, and nitrate derivatives 1.01%. In most patients (86.87%), BPH had never been treated previously (Table 1).

### Table 1  General characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>All patients (n = 99)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General characteristic</strong></td>
<td></td>
</tr>
<tr>
<td>Age, mean ± SD, years</td>
<td>62.26 ± 7.06</td>
</tr>
<tr>
<td>Height, mean ± SD, cm</td>
<td>165.78 ± 6.23</td>
</tr>
<tr>
<td>Weight, mean ± SD, kg</td>
<td>66.00 ± 9.72</td>
</tr>
<tr>
<td>SBP, mean ± SD, mm Hg</td>
<td>130.39 ± 16.00</td>
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<tr>
<td>DBP, mean ± SD, mm Hg</td>
<td>81.84 ± 10.95</td>
</tr>
<tr>
<td>Heart rate, mean ± SD, bpm</td>
<td>76.66 ± 10.90</td>
</tr>
<tr>
<td><strong>Associated disease</strong></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>31 (31.3%)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>14 (14.1%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>7 (7.1%)</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>2 (2%)</td>
</tr>
<tr>
<td><strong>Concomitant treatments</strong></td>
<td></td>
</tr>
<tr>
<td>CCB</td>
<td>9 (9.09%)</td>
</tr>
<tr>
<td>ß-blocker</td>
<td>8 (8.08%)</td>
</tr>
<tr>
<td>Diuretic</td>
<td>7 (7.07%)</td>
</tr>
<tr>
<td>ACE-I</td>
<td>5 (5.05%)</td>
</tr>
<tr>
<td>ARB</td>
<td>2 (2.02%)</td>
</tr>
<tr>
<td>Nitrate derivatives</td>
<td>2 (2.02%)</td>
</tr>
<tr>
<td><strong>History of BPH treatment at baseline</strong></td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td>13 (13.13%)</td>
</tr>
<tr>
<td>Alpha-1 blocker</td>
<td>13 (13.13%)</td>
</tr>
<tr>
<td>Doxazosin</td>
<td>6 (6.06%)</td>
</tr>
<tr>
<td>• Alfuzosin</td>
<td>3 (3.03%)</td>
</tr>
<tr>
<td>• Tamsulosin</td>
<td>1 (1.01%)</td>
</tr>
<tr>
<td>• Prazosin</td>
<td>3 (3.03%)</td>
</tr>
<tr>
<td>5-alpha reductase inhibitor</td>
<td>2 (2.02%)</td>
</tr>
<tr>
<td>No treatment</td>
<td>86 (86.87%)</td>
</tr>
</tbody>
</table>

SBP = systolic blood pressure; DBP = diastolic blood pressure; CCB = calcium channel blocker; ACE-I = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; SD = standard deviation.

Effect of Alfuzosin on MSHQ

After 6 months treatment with alfuzosin, significant improvements in MSHQ erection score (9.51 vs. 8.54 at baseline; $P = 0.003$; Figure 1), erection bother score (4.09 vs. 3.65 at baseline; $P = 0.002$; Figure 2), and ejaculation score (23.09 vs. 21.54 at baseline; $P = 0.022$; Figure 3) were observed. In addition, the proportions of patients presenting with improvement in MSHQ ejaculation score of at least 20% at study end (week 24 or premature withdrawal) was 28.43% (95% confidence interval: 19.63–37.23). Ejaculation bother score (Figure 4), satisfaction score (Figure 5), and sexual activity (Figure 6) tended to improve, although the difference from baseline was not statistically significant.
Effect of Alfuzosin on IPSS

At baseline, 58.6% of patients reported the severity of their urinary symptoms as moderate (IPSS 8–19) and 41.4% as severe (20–35). Figure 7 showed the changes in IPSS total, IPSS obstructive, and IPSS irritative. After 24 weeks treatment with alfuzosin, IPSS total score markedly decreased from 18.93 at baseline to 9.59 ($P < 0.001$). Significant improvements in IPSS Obstructive score; (from 11.63 to 5.12 $P < 0.001$) and IPSS Irritative score (from 7.30 to 4.36 $P < 0.001$) were also observed. A significant LUTS improvement was reported from the first week of treatment and was maintained until the end of the study.

There was also a significant improvement in nocturia (from 2.74 to 2.01, $P < 0.001$) and bother score (from 4.32 to 2.38, $P < 0.001$) with alfuzosin treatment. Nocturia significantly decreased from the first month of treatment ($P < 0.001$) with maintenance of a significant improvement until the end of the study (Figure 8). Bother score was significantly improved from the first week of treatment (Figure 9). Based on a patient questionnaire, which was evaluable in 91 patients, an improvement in LUTS was perceived from the first week of treatment in 70 patients (70.70%) and within the first 3 days of treatment in 36 patients (36.36%).

**Figure 4** Ejaculation Bother Score evaluated from baseline to 24th week. ITT = intent to treat.

**Figure 5** Satisfaction Score evaluated from baseline to 24th week. ITT = intent to treat.

**Figure 6** Sexual activity evaluated from baseline to 24th week. ITT = intent to treat.

**Figure 7** International Prostate Symptom Score (IPSS) score including I-PSS Total, I-PSS Obstructive, and IPSS Irritative. ITT = intent to treat.

**Figure 8** Nocturia evaluated from baseline to 24th week. ITT = intent to treat.
After 24 weeks administration, the percentage of patients with mild LUTS increased from 0 at baseline to 44% with a decrease in the percentages of patients with moderate LUTS (58% vs. 45%) and severe LUTS (41% vs. 10%).

**Effect of Alfuzosin on IIEF-5**

The percentage of patients without ED according to IIEF increased from 7% at baseline to 17% after 6 months treatment with alfuzosin. A decrease in the percentage of patients with moderate ED with treatment was also observed (from 22.22% at baseline to 8.8%), while other categories remained stable (Figure 10). The result of IIEF score shows very good correlation with MSHQ score (Figure 11) indicating that MSHQ is not only a good questionnaire for the ejaculatory function but also reliable for erectile function, compared with IIEF-5.

**Adverse Events**

Among 99 patients, 15 adverse events (14.7%) were reported in 13 patients. Adverse events potentially related to study drug included three cases of dizziness and one case of orthostatic hypotension. One patient developed AUR. There was no significant change in blood pressure and heart rate comparing at baseline to the end of the study. There was no treatment discontinuation because of adverse event. No serious adverse event was observed.

**Discussion**

In spite of the adverse effects of pharmacological treatment for BPH on sexual function, recent studies reported significant correlation between LUTS and ED and also an improvement in erectile function with alpha-blockers taken for LUTS caused by BPH [21,22,25,26,35]. Recently, Rosen et al. reported significant improvement in the mean change from baseline in erectile function after the treatment with alfuzosin on day 29 compared with placebo. However, no significant difference was observed between these two groups in the mean change from baseline in ejaculatory function [36]. In a 3-year real-life practice study to evaluate the effects of alfuzosin in patients with LUTS suggestive of BPH, using the IPSS and the Danish Prostate Symptom Score sexual function domain, alfuzosin significantly improved IPSS (−6.4 [−33%]; \( P < 0.001 \)) compared with baseline at the study end point. Moreover, the sexual symptoms (stiffness of erection −0.7, reduced ejaculation −0.5, painful ejaculation −1.3; all \( P < 0.001 \)) were also significantly improved in men with sexual dysfunction [39].
In addition, there is also evidence to suggest that successful medical treatment for ED appears to improve LUTS [27]. In a pilot randomized study in men with previously untreated LUTS suggestive of BPH and ED to evaluate the efficacy and safety of alfuzosin 10 mg once daily (OD), sildenafil 25 mg OD, and combination of both using IPSS and IIEF scores, men aged 50–76 years were randomized to receive alfuzosin (n = 20), sildenafil (n = 21), or the combination of both (n = 21) for 12 weeks [26]. Improvement of IPSS was significant with all the treatments, although was greatest with the combination of alfuzosin and sildenafil (−24.1%) compared with alfuzosin (−15.6%) and sildenafil (−16.9%) alone (P < 0.03), confirming that PDE5 inhibitor has a beneficial effect on LUTS. However, the combination is more effective than monotherapy. Furthermore, Giuliano et al. also demonstrated that combination of alfuzosin and tadalafil showed an additive effect of inhibiting adrenergic smooth muscle tone of prostatic tissue and electrical field stimulation-induced detrusor contractions in an organ bath study [28], consistent with either in vivo or in vitro studies for the combination effect of alfuzosin and tadalafil [29,30]. Moreover, not only alfuzosin but also combination treatment between tamsulosin 0.4 mg/day and tadalafil 20 mg/day was shown to be more effective than tamsulosin 0.4 mg/day alone to improve LUTS and ED [31].

In the past, ED has been mainly attributed to increased sympathetic vasoconstrictor tone to the helicine arteries supplying the lacunar spaces of the penile corpora cavernosa [21]. Alpha-1 adrenoceptors are functionally important for controlling the contractile tone of cavernosal smooth muscle in the flaccid stage. For this reason, alpha-1 blockers may facilitate penile erection by counteracting the contraction (detumescence) of corpus cavernosum smooth muscle fibers when there is sexual stimulation. However, currently, the relationship between LUTS and ED is supported not only by the sympathetic overactivity idea but also by several theories, which include (i) metabolic syndrome hypothesis; (ii) changing in the nitric oxide synthetase/nitric oxide (NOS/NO) cyclic-guanine monophosphate pathway in the prostate and corpus cavernosa; (iii) the Rho-kinase activation/endothelin pathway; and (iv) the physiopathologic consequences of pelvic atherosclerosis [32,33,41]. Furthermore, the relationship between LUTS and ED is also supported by the result from the epidemiological study called multinational survey of the aging male study which was designed to investigate the relationship between LUTS and sexual problems in aging men. The result suggests that the presence and severity of LUTS are independent risk factors for sexual dysfunction in older men [40].

This study was aimed to assess the sexual function improvement with alfuzosin 10 mg given once a day administered during 6 months using MSHQ and IIEF-5, and to confirm its efficacy including the onset of action and its safety profile. The 7-item ejaculatory function domain of the MSHQ (see Appendix 1), with items assessing frequency of ejaculation, strength/force of ejaculation, volume of ejaculation, delay of ejaculation, dry ejaculation, pleasure when ejaculating, and pain when ejaculating, provides a more in-depth assessment of ejaculatory function which are not focused in the standard IIEF-15.

The results from our study demonstrated that 36.36% of our patients got LUTS improvement after day 3, 70.71% after 1 week, and 91.92% after 4 weeks, indicating that majority of BPH patients who had taken alfuzosin would get response within 4 weeks. Moreover, the onset of action can be manifested rapidly, with 36.35% having shown an improvement within 3 days.

Therefore, the result from our study confirms that alfuzosin administered for 6 months improves both erectile and EjD consistent with the theories mentioned earlier. Moreover, the result of this study demonstrated that alfuzosin did not only cause ejaculatory disorder but actually improved the ejaculation. In the past, we thought that tamsulosin caused dry ejaculation or decreased ejaculated volume due to retrograde ejaculation. However, an animal model study to see the effects of alfuzosin and tamsulosin on seminal vesicle and bladder neck in anesthetized rats demonstrated that tamsulosin decreased the seminal vesicle and bladder neck pressure significantly compared with control group and alfuzosin, consistent with the result of this study [34]. Hellstrom et al. reported the effects of 5-day treatment with 0.8 mg tamsulosin and 10 mg alfuzosin compared with placebo on ejaculatory function in normal volunteers [42]. The results demonstrated that ejaculate volume in tamsulosin group decreased in almost 90% of subjects and anejaculation was reported in approximately 35% of the participants, which was not observed in any subjects in the alfuzosin or placebo groups. The authors also reported the acute effects of alfuzosin and tamsulosin on sperm parameters in a similar study design in 48 healthy men [42]. In this study, the percentage of motile sperm...
decreased 13.8% from baseline to day 5 of treatment with tamsulosin compared with decreases of 2.3% with placebo and 0.4% with alfuzosin, suggesting a negative effect on sperm parameter from tamsulosin [43]. Nonetheless, a recent clinical study in three healthy men taking silodosin, which exhibits 40-fold greater alpha 1A selectivity compared with tamsulosin and showed high incidence of ejaculatory disorder (22.3%), demonstrated that the mechanism of EjD as observed from color Doppler ultrasonography is intricately related to retrograde ejaculation, insufficient contraction of the seminal vesicles, and insufficient rhythmic contraction of pelvic floor muscles [37]. In this study, ejaculation was induced 2 hours after the intake of silodosin for 3 days under audiovisual sexual stimulation and by manual stimulation of the penis. Another study demonstrated that 15 volunteers on silodosin had anejaculation and did not show post-ejaculate sperm in their urine, suggesting that the mechanism of EjD caused by silodosin is a loss of seminal emission [38]. Therefore, the reasons why some alpha-blockers cause ejaculatory disorder could be demonstrated from both in vitro and in vivo studies. However, the reasons why alfuzosin can improve the ejaculation score significantly still need more investigations.

Conclusion
The results of the study have shown that within 6 months administration, alfuzosin 10 mg OD demonstrated early improvement of LUTS (within 1 week in two out of three patients) which was maintained during the overall treatment period. It significantly decreased bother associated with LUTS and improved both erectile and EjD compared to baseline in these patients suffering from BPH and sexual dysfunction. Moreover, the results of this study proved that alfuzosin did not only cause ejaculatory disorder but actually improved the ejaculation.

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References

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33 Kaplan SA, Gonzalez RR, Te AE. Combination of alfuzosin and sildenafil is superior to monotherapy in treating lower urinary tract symptoms and erectile dysfunction. Eur Urol 2007;51:1717–23.


Appendix 1: Male Sexual Health Questionnaire (MSHQ)

INTRODUCTION: The following questions concern various aspects of your ability to have sex. In answering these questions, please think about all aspects of the sexual activity you have had with your main partner, with other partners, or masturbating. By sexual activity, we mean any type of sex you may have had, including intercourse, oral sex or other sexual activities that could lead to ejaculation.

Some of these questions might be difficult to answer. Please answer as many as possible, and be as honest as you can when answering them. Please remember that all of your answers are confidential.

The first questions concern your erections, which some people refer to as “hard-ons”.

In the last month have you taken Viagra or any similar drugs for problems with your erection?  
1 □ Yes  2 □ No

Male Sexual Health Questionnaire

1. In the last month, without using drugs like Viagra, how often have you been able to get an erection when you wanted to? (Check only one)  
   5 □ All of the time  
   4 □ Most of the time  
   3 □ About half of the time  
   2 □ Less than half of the time  
   1 □ None of the time  
   0 □ Used Viagra or similar drug with every sexual encounter

2. In the last month, if you were able to get an erection without using drugs like Viagra, how often were you able to stay hard as long as you wanted to? (Check only one)  
   5 □ All of the time  
   4 □ Most of the time  
   3 □ About half of the time  
   2 □ Less than half of the time  
   1 □ None of the time  
   0 □ Used Viagra or similar drug with every sexual encounter

3. In the last month, if you were able to get an erection, without using drugs like Viagra, how would you rate the hardness of your erection? (Check only one)  
   5 □ Completely hard  
   4 □ Almost completely hard

4. In the last month, if you have had difficulty getting hard or staying hard without using drugs like Viagra, have you been bothered by this problem? . . . (Check only one)  
   5 □ Not at all bothered/Did not have a problem with erection  
   4 □ A little bit bothered  
   3 □ Moderately bothered  
   2 □ Very bothered  
   1 □ Extremely bothered

5. In the last month, how often have you been able to ejaculate when having sexual activity? (Check only one)  
   5 □ All of the time  
   4 □ Most of the time  
   3 □ About half of the time  
   2 □ Less than half of the time  
   1 □ None of the time/Could not ejaculate

6. In the last month, when having sexual activity, how often did you feel that you took too long to ejaculate or “cum”? (Check only one)  
   5 □ None of the time  
   4 □ Less than half of the time  
   3 □ About half of the time  
   2 □ Most of the time  
   1 □ All of the time  
   0 □ Could not ejaculate

7. In the last month, when having sexual activity, how often have you felt like you were ejaculating (“cumming”), but no fluid came out?  
   5 □ None of the time  
   4 □ Less than half of the time  
   3 □ About half of the time  
   2 □ Most of the time  
   1 □ All of the time  
   0 □ Could not ejaculate
8. In the last month, how would you rate the strength or force of your ejaculation?
   5 □ As strong as it always was
   4 □ A little less strong than it used to be
   3 □ Somewhat less strong than it used to be
   2 □ Much less strong than it used to be
   1 □ Very much less strong than it used to be
   0 □ Could not ejaculate

9. In the last month, how would you rate the amount or volume of semen when you ejaculate?
   5 □ As much as it always was
   4 □ A little less than it used to be
   3 □ Somewhat less than it used to be
   2 □ Much less than it used to be
   1 □ Very much less than it used to be
   0 □ Could not ejaculate

10. Compared to ONE month ago, would you say the physical pleasure you feel when you ejaculate has . . .
    5 □ Increased a lot
    4 □ Increased moderately
    3 □ Neither increased nor decreased
    2 □ Decreased moderately
    1 □ Decreased a lot
    0 □ Could not ejaculate

11. In the last month, have you experienced any physical pain or discomfort when you ejaculated? Would you say you have . . .
    5 □ No pain at all
    4 □ Slight amount of pain or discomfort
    3 □ Moderate amount of pain or discomfort
    2 □ Strong amount of pain or discomfort
    1 □ Extreme amount of pain or discomfort
    0 □ Could not ejaculate

12. In the last month, if you have had any ejaculation difficulties or have been unable to ejaculate, have you been bothered by this?
    5 □ Not at all bothered
    4 □ A little bit bothered
    3 □ Moderately bothered
    2 □ Very bothered
    1 □ Extremely bothered

These next few questions ask about your relationship with your main partner over the last month. Some of these questions concern your sexual relationship, while others are about your overall relationship.

13. Generally, how satisfied are you with the overall sexual relationship you have with your main partner? (Check only one)
    5 □ Extremely Satisfied
    4 □ Moderately Satisfied
    3 □ Neither Satisfied nor Unsatisfied
    2 □ Moderately Unsatisfied
    1 □ Extremely Unsatisfied

14. Generally, how satisfied are you with the quality of the sex life you have with your main partner?
    5 □ Extremely Satisfied
    4 □ Moderately Satisfied
    3 □ Neither Satisfied nor Unsatisfied
    2 □ Moderately Unsatisfied
    1 □ Extremely Unsatisfied

15. Generally, how satisfied are you with the number of times you and your main partner have sex?
    5 □ Extremely Satisfied
    4 □ Moderately Satisfied
    3 □ Neither Satisfied nor Unsatisfied
    2 □ Moderately Unsatisfied
    1 □ Extremely Unsatisfied

16. Generally, how satisfied are you with the way you and your main partner show affection during sex?
    5 □ Extremely Satisfied
    4 □ Moderately Satisfied
    3 □ Neither Satisfied nor Unsatisfied
    2 □ Moderately Unsatisfied
    1 □ Extremely Unsatisfied

17. Generally, how satisfied are you with the way you and your main partner communicate about sex?
    5 □ Extremely Satisfied
    4 □ Moderately Satisfied
    3 □ Neither Satisfied nor Unsatisfied
    2 □ Moderately Unsatisfied
    1 □ Extremely Unsatisfied

18. Aside from your sexual relationship, how satisfied are you with all other aspects of the relationship you have with your main partner?
    5 □ Extremely Satisfied
    4 □ Moderately Satisfied
    3 □ Neither Satisfied nor Unsatisfied
    2 □ Moderately Unsatisfied
    1 □ Extremely Unsatisfied
INTRODUCTION: The next set of questions concern the sexual activity you have had in the last month. In answering these questions, we want to know about all of the sexual activity you have had with your main partner, with other partners, or masturbating. By sexual activity, we mean any type of sex you may have had, including intercourse, oral sex, or any other sexual activities that could lead to ejaculation.

19. In the last month, how often have you had sexual activity, including masturbating, intercourse, oral sex, or any other type of sex? (Check only one)
   5 Daily or almost daily
   4 More than 6 times per month
   3 4–6 times per month
   2 1–3 times per month
   1 0 times per month

If your answer is “0” for item 5, please answer the following questions:
A. When was the last time you had sex? (Check only one)
   5 1–3 months ago
   4 4–6 months ago
   3 7–12 months ago
   2 13–24 months ago
   1 More than 24 months ago

B. What are the reasons you have not had sex?
   I could not have sex because I could not get an erection: □ Yes □ No
   I could not have sex because I could not ejaculate or “cum”: □ Yes □ No
   I had no partner: □ Yes □ No
   Other (specify): _____________________

20. Compared to ONE month ago, has the number of times you have had sexual activity increased or decreased?
   5 □ Increased a lot
   4 □ Increased moderately
   3 □ Neither increased nor decreased
   2 □ Decreased moderately
   1 □ Decreased a lot

21. In the last month, have you been bothered by these changes in the number of times you have had sexual activity?
   5 □ Not at all bothered
   4 □ A little bit bothered
   3 □ Moderately bothered
   2 □ Very bothered
   1 □ Extremely bothered

INTRODUCTION: These next questions ask about your urge or desire to have sex with your main partner. Some people refer to this as “feeling horny”. These questions concern the sexual urges you have felt toward your main partner, and not whether you actually had sex.

22. In the last month, how often have you felt an urge or desire to have sex with your main partner?
   5 □ All of the time
   4 □ Most of the time
   3 □ About half of the time
   2 □ Less than half of the time
   1 □ None of the time

23. In the last month, how would you rate your urge or desire to have sex with your main partner?
   5 □ Very high
   4 □ High
   3 □ Moderate
   2 □ Low
   1 □ Very low or none at all

24. In the last month, have you been bothered by your level of sexual desire? Have you been . . .
   5 □ Not at all bothered
   4 □ A little bit bothered
   3 □ Moderately bothered
   2 □ Very bothered
   1 □ Extremely bothered

25. Compared to ONE month ago, has your urge or desire for sex with your main partner increased or decreased?
   5 □ Increased a lot
   4 □ Increased moderately
   3 □ Neither increased nor decreased
   2 □ Decreased moderately
   1 □ Decreased a lot