Recovery of Abnormal Ejaculation by Intermittent Tamsulosin Treatment

Serdar Goktas, Yusuf Kibar,* Selim Kilic, Hasret Topac, Hidayet Coban and Bedrettin Seckin

From the Departments of Urology and Public Health (SK), Gülhane Military Medical Academy, Ankara, Turkey

Purpose: We assessed the impact of intermittent tamsulosin treatment on abnormal ejaculation.

Materials and Methods: This prospective study was performed between January 2001 and December 2004. It included 405 patients who were at least 50 years old with lower urinary tract symptoms. This study was divided into 2 phases. In phase 1 patients received a 0.4 mg tamsulosin capsule daily after breakfast for at least 3 months. The second phase of this study was performed in the 30 patients with abnormal ejaculation. In this phase these patients received 0.4 mg tamsulosin once daily every other day. Patients were assessed at study entry and at study week 6.

Results: Abnormal ejaculation was reported as retrograde ejaculation by 18 patients, as decreased volume by 7 and as absent ejaculate by 5. Ejaculatory function recovered during intermittent tamsulosin treatment in 12 patients with retrograde ejaculation and in 7 with decreased volume or absent ejaculate. As a result, 19 of 30 patients (63.3%) with abnormal ejaculation recovered. A significant improvement in retrograde ejaculation was found after intermittent tamsulosin treatment ($p = 0.02$). Although there were improvements in decreased volume or absent ejaculate at week 6 of intermittent treatment, these differences were not statistically significant ($p = 0.42$ and 0.61, respectively).

Conclusions: The results of the current study, which to our knowledge is the first report of the effect of intermittent tamsulosin treatment on abnormal ejaculation, show that this treatment modality is well tolerated and provides comparable improvements for abnormal ejaculation.

Key Words: prostate, prostatic hyperplasia, tamsulosin, ejaculation, semen

α-Blockade continues to be the predominant form of medical therapy for symptomatic bladder outlet obstruction due to BPH. BPH is often associated with BPO. BPO can result in LUTS. LUTS suggestive of BPO can arise through the dynamic component of the sympathetic tone of contractile tissue in the prostate gland. This is mediated via α_1-adrenoceptor stimulation.[1]

Three α_1-adrenoceptors subtypes can be identified in pharmacological studies, namely α_{1A}, α_{1B} and α_{1D}. The α_{1A} subtype predominates in the prostate capsule and is responsible for mediating smooth muscle tone. Although currently available α_1-adrenoceptor antagonists, such as alfuzosin, terazosin and doxazosin, are effective for LUTS suggestive of BPO, they are not selective for any α1-adrenoceptor subtypes.[2]

Tamsulosin is first selective α_{1A}-adrenoceptor antagonist and it has been reported to have 7-38-fold greater selectivity for these receptors.[3] Regardless of the agent used, the current literature advocates continued α-blocker use for their effect to be maintained.[3] We recently reported the results of intermittent tamsulosin treatment in patients with LUTS, in whom 0.4 mg tamsulosin once daily and 0.4 mg once daily every other day provided comparable improvements in urinary flow and symptoms.[4] The 2 treatments were well tolerated.

However, α_1-adrenoceptor antagonists have been associated with ejaculation abnormalities, such as retrograde ejaculation, decreased ejaculate volume and absent ejaculate, in 4% to 11% of patients.[5] Abnormal ejaculation is probably related to α_1-adrenoceptor antagonism in the bladder neck, vas deferens or seminal vesicles with consequent relaxation of these tissues.[5] In this prospective study we investigated whether retrograde ejaculation, the major side effect of tamsulosin, decreases with intermittent treatment. This study is the continuation of our previous series. To our knowledge this is the first report in the literature of abnormal ejaculation in patients with LUTS who received intermittent tamsulosin.

PATIENTS AND METHODS

This prospective study was done between January 2001 and December 2004. It included 405 patients at least 50 years old with LUTS. The study was approved by the local ethics committee and was performed in accordance with the Declaration of Helsinki, updated Hong Kong 1989. Baseline criteria for inclusion were an I-PSS of 8 or more and a Qmax of at least 5 but no more than 15 ml per second for a voided volume of more than 150 ml, post-void residual urine volume lower than 200 ml, a minimum 1 year history of LUTS and patient election of medical therapy. A consistent residual urine volume of more than 400 ml, previous bladder neck, prostate or pelvic region surgery, any coexisting condition

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* Correspondence: Department of Urology, Gülhane Military Medical Academy, 06010 Etlik, Ankara, Turkey (telephone: +90 312 3045613; FAX: +90 312 4341247, +90 312 304 2030 or +90 312 304 2010; or e-mail: yusufkibar@mynet.com, ykibar@gata.edu.tr).

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TABLE 1. *Changes in I-PSS, Qmax, Qave and residual urine in 30 men with abnormal ejaculation*

	Before Intermittent Treatment	Intermittent Treatment Wk 6	p Value (paired samples t test)
Mean I-PSS ± SD	7.6 ± 2.7	7.5 ± 2.4	0.44
Mean Qmax ± SD (ml/sec)	11.7 ± 3.1	11.6 ± 2.9	0.72
Mean Qave ± SD (ml/sec)	5.8 ± 1.9	5.6 ± 1.8	0.16
Mean residual urine ± SD (ml)	73.9 ± 15.8	72.2 ± 16.2	0.33

that might affect micturition, hepatic or renal insufficiency, diabetes mellitus, chronic alcoholism, significant cardiovascular disease, cerebrovascular or central nervous system disease, life threatening diseases or allergic reactions to α-adrenoceptor antagonists, or previous treatment for LUTS were exclusion criteria. Patients were not permitted to receive concomitant drugs that could influence the study outcome, such as other α-adrenoceptor antagonists, combined α/β-adrenoceptor antagonists, α-adrenoceptor agonists, cholinergic or anticholinergic drugs, or calcium antagonists.

This study was divided into 2 phases. In phase 1 patients received a 0.4 mg tamsulosin capsule daily after breakfast for at least 3 months. Patients who noticed a lack of efficacy, did not tolerate side effects and were not followed regularly were excluded from study. The second phase of this study was performed in the 30 patients with abnormal ejaculation. Prior to starting phase 2 tamsulosin was not discontinued. During this phase these patients received 0.4 mg tamsulosin once daily every other day. Patients were assessed at study entry and at study week 6.

Treatment emergent adverse events were defined as any adverse events occurring after the administration of the first dose of study medication that had not previously occurred or had completely resolved and then reemerged after the commencement of treatment.[6] The distinction between retrograde ejaculation and absent ejaculate was made by centrifugation of post-ejaculate urine.

Statistical analysis was performed with SPSS, version 10.0 (SSPS, Chicago, Illinois). Data are expressed as the mean ± SD and percent. Categorical variables were analyzed with the chi-square and Fisher's exact tests. Continuous variables were analyzed with the paired samples t test. Differences were considered significant at 2-tailed $p < 0.05$.

RESULTS

A total of 405 men with a mean age of 62.8 ± 3.5 years who had LUTS were entered into this study. The mean history of symptoms was 14.1 ± 3.2 months. A total of 30 men with abnormal ejaculation were entered into study phase 2.

Before intermittent treatment in the 30 patients with abnormal ejaculation mean I-PSS was 7.6 ± 2.7, mean Qmax was 11.7 ± 3.1 ml per second, mean Qave was 5.8 ± 1.9 ml per second and mean residual urine volume was 73.9 ± 15.8 ml. At study week 6 these values were 7.5 ± 2., 11.6 ± 2.9 ml per second, 5.6 ± 1.8 ml per second and 72.7 ± 16.2 ml, respectively. In these patients the decrease in I-PSS and residual urine, and increase in Qmax and Qave were not statistically significant ($p = 0.44$, 0.72, 0.16 and 0.33, respectively, table 1).

A total of 30 patients (7.3%) had treatment emergent abnormal ejaculation. Abnormal ejaculation was reported as retrograde ejaculation, ie backward ejaculation of semen into the bladder instead of outward through the urethra, by 18 patients (4.4% of 405 cases), and as decreased volume and absent ejaculate by 12 patients (2.9% of 405) (7 or 1.7% and 5 or 1.2%, respectively). In most patients reporting abnormal ejaculation this symptom occurred within the first 2 to 3 weeks of treatment. Ejaculatory function recovered during intermittent tamsulosin treatment, as reported by 12 patients with retrograde ejaculation and by 7 with decreased volume or absent ejaculate. As a result, 19 of 30 cases (63.3%) with abnormal ejaculation recovered. A significant improvement in retrograde ejaculation was found after intermittent tamsulosin treatment ($p = 0.02$). Although there were improvements in decreased volume or absent ejaculate at week 6 of intermittent treatment, these differences were not statistically significant because of the small number of cases in these groups ($p = 0.42$ and 0.61, respectively, table 2).

DISCUSSION

α-Blockers have an increasing role in LUTS. These agents were originally developed for hypertension and adverse events probably related to α1-adrenoceptor blockade in blood vessels, such as asthenia, dizziness and postural hypotension, can limit the usefulness of these agents for LUTS.[6] Although currently available α1-adrenoceptor antagonists, such as alfuzosin, terazosin, prazosin and doxazosin, are effective for LUTS, they are not selective for any α1-adrenoceptor subtypes.[7] Tamsulosin clearly offers advantages over other α_{1A}-adrenoceptor antagonist in terms of the need for a single daily dose only and its low potential for hypotensive effects. Dose titration at the start of treatment is not necessary. Therefore, the drug is a valuable therapeutic option.[7]

Ejaculation necessitates the sequential emission of fluid from the sexual accessory glands and then sperm expulsion along the urethra to the urethral meatus. Closure of the bladder neck to prevent the flow of semen backward into the bladder precedes the secretion of the seminal vesicle, prostate and ampullary vas deferentia contents into the prostatic urethra. Forceful expulsion of semen is caused by rhythmic contractions of the bulbospongiosus muscle. Retrograde ejaculation is caused by failure of bladder neck closure, which in healthy subjects is shown by a dramatic increase in bladder neck pressure at ejaculation (up to 500 cm H_2O).[8] However, anejaculation corresponds primarily to a lack of seminal fluid emission, which accounts for 70% of semen volume. Abnormal ejaculation is probably related to α_1-blockade by tamsulosin at the bladder neck, and in pros-

TABLE 2. *Adverse events related to abnormal ejaculation with tamsulosin before and at week 6 of intermittent treatment*

Treatment Emergent Abnormal Ejaculation	No. Before Treatment (%)	No. 6 Wks (%)	p Value
Retrograde ejaculation	18 (4.4)	6 (1.4)	0.02 (chi-square test)
Decreased ejaculate vol	7 (1.7)	3 (0.7)	0.42 (Fisher's exact test)
Absent ejaculate	5 (1.2)	2 (0.5)	0.61 (Fisher's exact test)
Totals	30 (7.3)	11 (2.6)	