Original Article

Evaluation of intermittent tamsulosin in treating symptomatic patients with benign prostatic hyperplasia

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Abstract

Purpose: The purpose of this study is to evaluate and assess the effect of intermittent tamsulosin treatment as a trial to increase the drug safety (in terms of reducing the drug side effects, particularly retrograde ejaculation) while maintaining the effect in reducing the symptoms and assess its impact on the patients' quality of life.

Materials and Methods: Patients who enrolled in this study were suffering from lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH) and were using 0.4 mg tamsulosin daily to relieve their symptoms but complained of ejaculatory problems. A baseline assessment involves medical history and evaluation of ejaculatory function abdominopelvic ultrasound, postvoid residual volume (PVR) estimation, the International Prostate Symptom Score (IPSS), quality of life assessed using global satisfaction, vital signs, physical examination including digital rectal examination, and renal function. During the study, patients consented to take 0.4 mg tamsulosin intermittently every other day and to proceed with their sexual activities on the days they did not take the drug in. Baseline assessment was repeated and recorded after 3 months from starting the treatment. The adverse effects and compliance were analyzed in all patients.

Results: Twenty-five patients had a mean baseline IPSS of 6.6 ± 1 and baseline PVR of 87.6 ± 15.1 ml. At the 3rd month, the mean PVR was 100.4 ± 15.1 ml and the mean IPSS was 7.3 ± 1.1. Moreover, 20 out of the total number of 25 patients (80%) reported improvement in their ejaculation. All our 20 patients who showed improvement in their ejaculatory function are either satisfied or very satisfied (4 or 5), in regard to the global satisfaction rate.

Conclusion: Intermittent tamsulosin therapy (0.4 mg/every other day) is well-tolerated and shows a potential advantage in recovery in patients who suffer from LUTS/BPH and complaining from abnormal ejaculation, especially absent ejaculate. Although there was a significant change in PVR and IPSS after using intermittent tamsulosin therapy. Most patients show a higher overall satisfaction with the treatment compared to the standard dose (0.4 mg/daily). A study on a larger scale is still needed to confirm our results.

Keywords: Benign prostatic hyperplasia, ejaculation, erectile dysfunction, lower urinary tract symptoms, prostate, tamsulosin

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Received: 13.08.2021, **Accepted:** 19.04.2022, **Published:** 08.11.2022.

Access this article online	
Quick Response Code:	**Website:** www.urologyannals.com
	DOI: 10.4103/ua.ua_143_21

How to cite this article: Soliman MG, Al-Ghadeer MR, Al-Shabaan HR, Al-Hamrani AH, AlGhadeer HA. Evaluation of intermittent tamsulosin in treating symptomatic patients with benign prostatic hyperplasia. Urol Ann 2023;15:43-7.

INTRODUCTION

Benign prostatic hyperplasia (BPH) describes a common condition in old age in which there is a benign enlargement of the prostate gland.[1] BPH may lead to bladder outlet obstruction, initially inducing lower urinary tract symptoms (LUTS).[1,2] About 70% of men under the age of 80 years are affected by LUTS.[3] LUTS include storage and voiding, the severity of which can be assessed using the International Prostate Symptom Score (IPSS).[4,5] BPH can be treated using surgical therapies, for example, transurethral resection of the prostate or medical therapies (e.g., α1-Adrenoceptor antagonists [α-blockers], 5α-reductase inhibitors, or a combination).[6] However, α-blockers are the drugs of choice for LUTS secondary to BPH (LUTS/BPH).[7] Alpha 1-adrenoceptor is additionally divided into three subtypes α 1a, α 1b, and α 1d, α 1a being the most predominant in patient with BPH (up to 85%).[8,9] Alpha-blockers relax prostatic smooth muscles thus relieving LUTS/BPH.[8]

Uroselective drugs, such as tamsulosin, that specifically target α 1a-receptors have an advantage over the other less selective α-blockers, especially in reducing serious side effects such as hypotension. Due to their high selectivity, these drugs have low-cardiovascular side effects and virtually no intervention with the activity of antihypertensive agents. Tamsulosin (0.4 mg) daily proved to be favorably safe, effective, and well-tolerated.[8,10-15] However, tamsulosin is known to cause ejaculatory dysfunction.[16,17] This side effect has a significant impact on the patients' quality of life.[18-21] Several studies were conducted to assess the efficacy of modified dosage of tamsulosin into either lowering the dose (0.2 mg) or using it intermittently to alleviate ejaculatory issues, showed a potential improvement for the medication's overall effectiveness.[18, 22-24]

The aim of this study is to assess the influence of using full dose of tamsulosin (0.4 mg) every other day in reducing LUTS secondary to BPH on patients living in Eastern province in Saudi Arabia as a trial to increase the drug safety (in terms of reducing the drug side effects, especially retrograde ejaculation) while maintaining the efficacy in relieving the patients' symptoms and its impact on the patients' quality of life.

MATERIALS AND METHODS

This prospective study was conducted in King Faisal University's Health Care Center between January 2015 and April 2015. Patients who participated in this study were suffering from LUTS due to BPH and were using 0.4 mg tamsulosin daily to relieve their symptoms but complained from no ejaculate or low-volume ejaculate. Exclusion criteria involved IPSS ≥18, postvoid residual volume (PVR) >400 ml, and any conditions affecting the function of the bladder neck either medical or surgical, renal or hepatic impairment, significant cardiovascular disease, central nervous or cerebrovascular system disease, diabetes mellitus, or allergic reactions to α-adrenoceptor blockers. The baseline assessment involves medical history and evaluation of ejaculatory function, IPSS, quality of life assessed using global satisfaction, vital signs, physical examination including digital rectal examination, renal function, abdominopelvic ultrasound, and PVR estimation.

During the study, patients consented to take 0.4 mg tamsulosin intermittently every other day, and to proceed with their sexual activities on the days they did not take the drug in. The baseline assessment was repeated and recorded after 3 months from starting the treatment. The adverse event and patients' compliance with the drug were analyzed. Patients who developed aggravation of their symptoms were excluded and returned to their standard dose.

RESULTS

In the beginning, 30 patients were enrolled in the study with the mean age of 55.5 ± 6.4 years. Out of these 30 patients, a total of 5 (16.7%) were excluded from the study due to the following reasons: incomplete follow-up in the clinic in three patients and worsening of the symptoms of BPH in the remaining two patients. Ultimately, 25 patients remaining matched the predefined criteria and carried on the intermittent dose of tamsulosin, 0.4 mg every other day.

In the start of our study, the mean baseline IPSS for the 25 patients was 6.6 ± 1 and the baseline PVR was 87.6 ± 15.1 ml. Then, after 3 months of follow-up, the mean IPSS increased to 7.3 ± 1.1, and the mean PVR increased to 100.4 ± 15.1 ml. Statistical analysis for these two parameters showed a statistically significant difference ($P = 0.0001$) [Table 1].

Before our study, 17 out of the 25 patients (68%) have reported symptoms of no ejaculate at all, and the rest of eight patients (32%) have reported low-volume ejaculate. All of these, 17 patients have shown either dissatisfaction with these symptoms or neutral satisfactions (2 or 3 respectively) as per the global satisfaction rate.

After the trial of the intermittent dose of tamsulosin, in the 17 patients who had no ejaculation, all of them (100%) plus 3 out of the 8 (37.5%) who had low-volume ejaculation have reported improvements in their ejaculatory volume. Hence overall, 20 out of the total number of 25 patients (80%) reported improvement in their ejaculation. Analysis

with the Chi-square test of independence has revealed a significant relationship between the intermittent dosing and the recovery of abnormal ejaculation ($P = 0.0001$). Moreover, in regard to the global satisfaction rate, all of the 20 patients showing improvement in their ejaculatory volume have stated that they are either satisfied or very satisfied with their conditions (4 or 5, respectively) [Figures 1 and 2].

DISCUSSION

Alpha-blockers are the first line of medical treatments for LUTS/BPH. Drugs, such as tamsulosin, are highly selective blockers to α 1a-receptors in the prostate gland. Tamsulosin is advantageous over the other less selective α-blockers in terms of cardiovascular side effects reduction such as decreased hypotension. And therefore, it is the drug of choice in the treatment of LUTS/BPH.[8,10-12] However, tamsulosin has been noted to impact ejaculation negatively and can cause low-volume ejaculate or no ejaculate.[13-15] This side effect has been found to be dose-dependent, i.e., more prevalent with higher doses.[16] To reduce this side effect while maintaining the drug's safety and efficacy, tamsulosin dose manipulation studies were conducted. Dose adjustment was in terms of either dose reduction (0.2 mg) or intermittent dosing.

Several studies have investigated the safety and efficacy of using daily 0.2 mg dose for relieving LUTS with less side effects. Kim *et al*.[18] studied 138 male patients over 50 years of age with LUTS and found that the use of low-dose treatment of tamsulosin for 3 months showed significant improvement in both IPSS and quality of life. However, the study revealed an incidence of *de novo* ejaculatory discomfort of 10.2% at 1 month and 6.0% at 3 months and thereafter concluded that low-dose tamsulosin did not show any significant impact on ejaculatory function. On the other hand, Park *et al*.[24] studied 146 patients who were administered tamsulosin 0.2 mg daily over the course of 1 year. The study found significant improvement in all efficacy parameters, including reduction in total IPSS mean by 41.1% and a mean increase of Qmax by 4.56 mL/s. Only 0.6% of the 146 patients showed ejaculatory dysfunction and adverse events occurred in 6.2%. The study concluded that low dosing was well-tolerated and effective in improving LUTS and urinary flow. Finally, Kim *et al*.[25] conducted a large cross-sectional study with a total sample of 2574 patients to evaluate efficacy and treatment satisfaction with low-dose tamsulosin. However, despite the improvement with low-dose tamsulosin in IPSS and satisfaction in 63.4% of the patients that the study showed, dissatisfaction was reported in 36.5% of the patients. The reasons for dissatisfaction included efficacy problems (84.66%) and side effects (3.72%). Compared to these studies, our study revealed that the patients who recovered from ejaculatory dysfunction were more satisfied with using an intermittent dose of tamsulosin than with the standard dose.

In the other forms of dose manipulation, and in concordance with our study, two studies from Turkey investigated the safety and efficacy of using intermittent tamsulosin therapy. In the first study, Goktas *et al*.[22] included 405 patients with LUTS, of which 30 patients had abnormal ejaculation and were studied subsequently in another phase. The study reported that intermittent dosing provided comparable improvements for abnormal ejaculation. Of the 30 patients, 19 (63.3%) have recovered from abnormal ejaculation expressed as retrograde ejaculation, low-volume ejaculate, and no ejaculate. Of importance note that the

Table 1: Analysis of intermittent tamsulosin therapy before and after

Variable	Baseline	After 3 months	*P* value
IPSS	6.6 ± 1	7.3 ± 1.1	0.0001
PVR	87.6 ± 15.1 ml	100.4 ± 15.1	0.0001

PVR: Postvoid residual, IPSS: International prostate symptom score

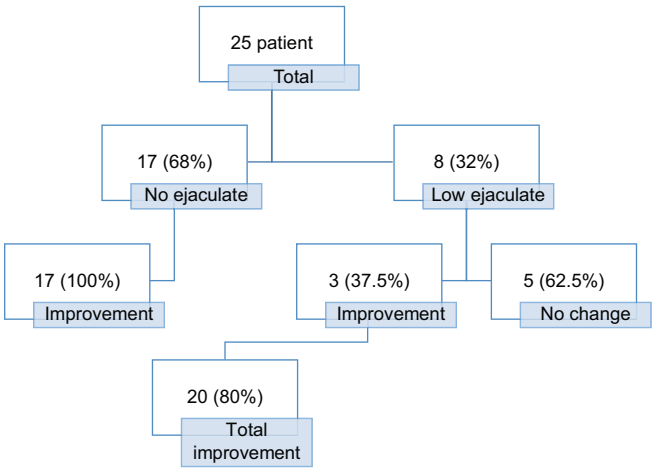

Figure 1: Summary of the trial

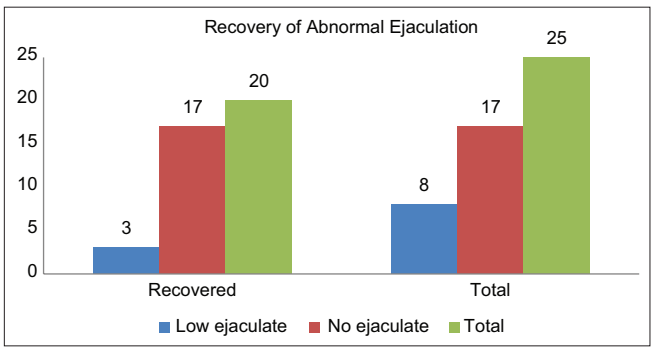

Figure 2: Before and after the trial

majority of recovery in ejaculatory function was observed in the patients with retrograde ejaculation. Namely, 12 out of the 19 (63%) who recovered had retrograde ejaculation. These patients have reported a significant improvement in their ejaculation after intermittent tamsulosin dosing. In the second study, Yanardag *et al*.[23] studied 140 patients for intermittent tamsulosin therapy in two phases. In the first phase, patients received 0.4 mg of tamsulosin daily for 3 months. Moreover, in the second phase, the responders to tamsulosin were divided randomly into three groups – Group 1 continued the standard dose of 0.4 mg tamsulosin daily, Group 2 was given intermittent tamsulosin dose, i.e., 0.4 mg every other day, and Group 3 discontinued tamsulosin. For patients in Groups 1 and 2, there were no statistically significant differences among them at 6 months for IPSS, maximum or average urine flow, or residual urine. Nevertheless, it was noted that 9.6% of patients in the standard dosing group (Group 1) have suffered from retrograde ejaculation and only 2.9% of patients in the intermittent dosing group (Group 2). These two studies go in agreement with our study, where recovery of ejaculatory dysfunction was in 17 (100%) patients that reported no ejaculate, and in 3 out of 8 (37.5%) patients that reported low ejaculate.

In our study, we explored the safety and efficacy of using intermittent doses of tamsulosin (0.4 mg every other day) in patients with LUTS who were also suffering from abnormal ejaculation. In all 25 patients, after 3 months of intermittent therapy, mean IPSS and mean PVR have increased and showed a statistically significant difference compared to the initial baseline. However, out of the 25 patients studied, 20 patients (80%) expressed improvement in ejaculatory function and were more satisfied with the intermittent therapy than with the standard dose as shown by their global satisfaction and improved quality of life, and despite their significant increase in IPSS and PVR. In those 20 patients, recovery was in all 17 (100%) patients with no ejaculate and in 3 out of 8 (37.5%) patients with low ejaculate. According to these results, we can conclude that the intermittent therapy is more effective in patients complaining from absent ejaculation.

CONCLUSION

In patients suffering from LUTS/BPH and complaining from abnormal ejaculation, especially absent ejaculate, intermittent tamsulosin therapy (0.4 mg/every other day) is well-tolerated and shows a potential advantage in their recovery. Even with the significant change in IPSS and PVR after applying the intermittent tamsulosin therapy, most patients show a higher overall satisfaction with the treatment compared to the standard dose (0.4 mg/daily). A study on a larger scale is still needed to confirm our results.

Informed consent

Written and oral informed consent was obtained from all individual participants included in this study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

Acknowledgment

We would like to thank the participants who were all contributed samples to the study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Schwinn DA, Roehrborn CG. Alpha1-adrenoceptor subtypes and lower urinary tract symptoms. Int J Urol 2008;15:193-9.
2. Yamanishi T, Mizuno T, Kamai T, Yoshida K, Sakakibara R, Uchiyama T. Management of benign prostatic hyperplasia with silodosin. Open Access J Urol 2009;1:1-7.
3. Parsons JK, Bergstrom J, Silberstein J, Barrett-Connor E. Prevalence and characteristics of lower urinary tract symptoms in men aged>or=80 years. Urology 2008;72:318-21.
4. Park HJ, Won JE, Sorsaburu S, Rivera PD, Lee SW. Urinary Tract Symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) and LUTS/BPH with erectile dysfunction in Asian men: A systematic review focusing on tadalafil. World J Mens Health 2013;31:193-207.
5. Barry MJ, Fowler FJ Jr., O'Leary MP, Bruskewitz RC, Holtgrewe HL, Mebust WK, *et al*. The American Urological Association symptom index for benign prostatic hyperplasia. The Measurement Committee of the American Urological Association. J Urol 1992;148:1549-57.
6. McVary KT, Roehrborn CG, Avins AL, Barry MJ, Bruskewitz RC, Donnell RF, *et al*. Update on AUA guideline on the management of benign prostatic hyperplasia. J Urol 2011;185:1793-803. doi:10.1016/j.juro.2011.01.074.
7. Nordling J. Efficacy and safety of two doses (10 and 15 mg) of alfuzosin or tamsulosin (0.4 mg) once daily for treating symptomatic benign prostatic hyperplasia. BJU Int 2005;95:1006-12.
8. Narayan P, Tunuguntla HS. Long-term efficacy and safety of tamsulosin for benign prostatic hyperplasia. Rev Urol 2005;7 Suppl 4:S42-8.
9. Nasu K, Moriyama N, Kawabe K, Tsujimoto G, Murai M, Tanaka T, *et al*. Quantification and distribution of alpha 1-adrenoceptor subtype mRNAs in human prostate: Comparison of benign hypertrophied tissue and non-hypertrophied tissue. Br J Pharmacol 1996;119:797-803.
10. Kim JJ, Han DH, Sung HH, Choo SH, Lee SW. Efficacy and tolerability of tamsulosin 0.4 mg in Asian patients with lower urinary tract symptoms secondary to benign prostatic hyperplasia refractory to tamsulosin 0.2 mg: A randomized placebo controlled trial. Int J Urol 2014;21:677-82.
11. Bird ST, Delaney JA, Brophy JM, Etminan M, Skeldon SC, Hartzema AG. Tamsulosin treatment for benign prostatic hyperplasia and risk of severe hypotension in men aged 40-85 years in the United

States: Risk window analyses using between and within patient methodology. BMJ 2013;347:f6320.
12. Wilt TJ, MacDonald R, Nelson D. Tamsulosin for treating lower urinary tract symptoms compatible with benign prostatic obstruction: A systematic review of efficacy and adverse effects. J Urol 2002;167:177-83.
13. Schulman CC, Lock TM, Buzelin JM, Boeminghaus F, Stephenson TP, Talja M, *et al*. Long-term use of tamsulosin to treat lower urinary tract symptoms/benign prostatic hyperplasia. J Urol 2001;166:1358-63.
14. Abrams P, Speakman M, Stott M, Arkell D, Pocock R. A dose-ranging study of the efficacy and safety of tamsulosin, the first prostate-selective alpha 1A-adrenoceptor antagonist, in patients with benign prostatic obstruction (symptomatic benign prostatic hyperplasia). Br J Urol 1997;80:587-96.
15. Chapple CR, Wyndaele JJ, Nordling J, Boeminghaus F, Ypma AF, Abrams P. Tamsulosin, the first prostate-selective alpha 1A-adrenoceptor antagonist. A meta-analysis of two randomized, placebo-controlled, multicentre studies in patients with benign prostatic obstruction (symptomatic BPH). European Tamsulosin Study Group. Eur Urol 1996;29:155-67.
16. Rosen RC, Giuliano F, Carson CC. Sexual dysfunction and lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH). Eur Urol 2005;47:824-37.
17. van Dijk MM, de la Rosette JJ, Michel MC. Effects of alpha (1)-adrenoceptor antagonists on male sexual function. Drugs 2006;66:287-301.
18. Kim SW, Lee WC, Kim MT, Ko K, Lee WK, Lee CH, *et al*. Effects of low-dose tamsulosin on sexual function in patients with lower urinary tract symptoms suggestive of benign prostatic hyperplasia. Korean J Urol 2013;54:697-702.
19. Descazeaud A, de La Taille A, Giuliano F, Desgrandchamps F, Doridot G. Negative effects on sexual function of medications for the treatment of lower urinary tract symptoms related to benign prostatic hyperplasia. Prog Urol 2015;25:115-27.
20. Yoshimura K, Kadoyama K, Sakaeda T, Sugino Y, Ogawa O, Okuno Y. A survey of the FAERS database concerning the adverse event profiles of α1-adrenoreceptor blockers for lower urinary tract symptoms. Int J Med Sci 2013;10:864-9.
21. Pietrzyk B, Olszanecka-Glinianowicz M, Owczarek A, Gabryelewicz T, Almgren-Rachtan A, Prajsner A, *et al*. Depressive symptoms in patients diagnosed with benign prostatic hyperplasia. Int Urol Nephrol 2015;47:431-40.
22. Goktas S, Kibar Y, Kilic S, Topac H, Coban H, Seckin B. Recovery of abnormal ejaculation by intermittent tamsulosin treatment. J Urol 2006;175:650-2.
23. Yanardag H, Goktas S, Kibar Y, Kilic S, Erduran D. Intermittent tamsulosin therapy in men with lower urinary tract symptoms. J Urol 2005;173:155-7.
24. Park CH, Chang HS, Oh BR, Kim HJ, Sul CK, Chung SK, *et al*. Efficacy of low-dose tamsulosin on lower urinary tract symptoms suggestive of benign prostatic hyperplasia: A nonblind multicentre Korean study. Clin Drug Investig 2004;24:41-7.
25. Kim JH, Park JY, Oh MM, Lee JG, Kwon SS, Bae JH. Treatment satisfaction with low-dose tamsulosin for symptomatic benign prostatic hyperplasia: Results from a multicentre cross-sectional survey. Int J Clin Pract 2012;66:1209-15.