Original Article

Predictive value of the immediate effect of first dose of tamsulosin on lower urinary tract symptoms improvement in benign prostatic hyperplasia patients

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Abstract

Objectives: The objective is to study the effect of tamsulosin within hours after the first dose and its prediction of the future improvement of LUTS.

Materials and Methods: From May 2016 until August 2017, 340 patients aged over 40 years with benign prostatic hyperplasia (BPH)-related symptoms were prospectively enrolled; 0.4 mg tamsulosin for 3 months was given. The first visit was before beginning of tamsulosin; uroflowmetry (UFM), postvoid residual urine volume (PVR), international prostate symptom score (IPSS), and quality of life (QoL) were measured. The second visit was after 6 h from the administration of tamsulosin. UFM and PVR were measured. The third visit was after 1 month and the fourth visit was after 3 months, on which UFM, PVR, IPSS, and QoL were also measured.

Results: The mean patients' age was 63 ± 6.18 and the mean prostate volume was 52.23 ± 24.59 cc. The mean Q_{max} at 1st, 2nd, 3rd, and 4th visits was 10.28 ± 3.06 s, 14.58 ± 4.84 s, 14.46 ± 4.94 s, and 14.28 ± 5.07 s, respectively, $P = 0.04$. The mean voiding time at 1st, 2nd, 3rd, and 4th visits was 41.24 ± 27.18 s, 33.84 ± 18.14 s, 31.96 ± 22.02 s, and 30.14 ± 17.52 s, respectively, $P = 0.03$. The mean PVR at 1st, 2nd, 3rd, and 4th visits was 46.40 ± 22.14 ml, 27.76 ± 26.10 ml, 25.16 ± 28.36 ml, and 25.58 ± 28.10 ml, respectively, $P = 0.001$. The first dose of tamsulosin significantly increases Q_{max} and decreases voiding time and residual urine (RU); there was no statistical significant difference between 1st dose, 1 and 3 months in Q_{max}, voiding time, and RU. QOL and IPSS were significantly improved after 1 and 3 months, $P < 0.001$.

Conclusion: The first dose of tamsulosin improves UFM and predicts the mid-term change in UFM as well as IPSS and QoL indices in the treatment of BPH-related LUTS.

Keywords: Benign prostatic hyperplasia, lower urinary tract symptom, tamsulosin, uroflowmetry

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Received: 05.05.2018, **Accepted:** 16.04.2019

INTRODUCTION AND OBJECTIVES

Lower urinary tract symptoms (LUTSs) caused by benign prostatic hyperplasia (BPH) occur in 23% of men aged 50 years, with moderate-to-severe LUTS being occurred in up to 50% of men with BPH.[1,2] El-Gilany *et al.* claimed that no community-based studies on the magnitude of the problem of BPH symptoms among elderly men in Egypt

Access this article online	
Quick Response Code:	Website: www.urologyannals.com
	DOI: 10.4103/UA.UA_57_18

How to cite this article: Moussa AS, Ibrahim RM, ElAdawy MS, Ragheb AM, El-Dessoukey AA, Abdelbary AM, *et al*. Predictive value of the immediate effect of first dose of tamsulosin on lower urinary tract symptoms improvement in benign prostatic hyperplasia patients. Urol Ann 2019;11:294-7.

are available.[3] LUTSs influence the quality of life (QoL) and hence require treatment. Pharmacological therapy with alpha blockers is the first step of the treatment in patients with BPH,[4] which gives a strong recommendation to have a method for response prediction. Tamsulosin HCl is the most widely used drug in the treatment of LUTS associated with BPH.[5] Tamsulosin is a highly selective alpha-1A and alpha-1D-adrenergic receptors blocker affecting prostate, bladder neck, and urethra. Thus, tamsulosin provides comfortable micturition which improves QoL.[6] The predictive value of the change in flowmetry parameters at the first dose of tamsulosin on the improvement of LUTS in BPH patients has been studied by Akin *et al*.[7] We aimed to reevaluate this predictive value of the changes in flowmetry parameters at the first dose of tamsulosin on the improvement of LUTS in Egyptian BPH patients.

MATERIALS AND METHODS

A prospective study from May 2016 until August 2017 was designed; after approval by the ethical committee of Beni-Suef University, written informed consent was obtained from all patients participated in the study. All patients over 40 years old presented to the urology outpatient clinic at Beni-Suef University with BPH-related symptoms were enrolled. Patients with previous medical or surgical treatment of the prostate, post-void residual urine volume (PVR) >150 ml, and symptoms suggesting neurogenic bladder, urinary tract stones, suspected prostate cancer (prostate-specific antigen [PSA] >4 ng/dl), and/or abnormal digital rectal examination (DRE) were excluded. Physical examination included DRE. PSA, creatinine, urine analysis, urine culture, and sensitivity were done to exclude patients with urinary tract infection, uroflowmetry (UFM) (Solar Uroflow, Medical Measurement Systems), and PVR, international prostate symptom score (IPSS), QoL index, and transrectal ultrasonography of prostate (TRUS) were performed.

Three hundred and ninety patients were enrolled into the study, but only 340 patients were included and completed the four visits; all patients instructed to take 0.4 mg tamsulosin after breakfast for 3 months; the first visit was the baseline before beginning of tamsulosin including UFM, PVR, IPSS, QoL, PSA, creatinine, urine analysis, urine culture and sensitivity, DRE, and history-taking. The second visit was after about 6 h from administration of tamsulosin in which UFM and PVR were measured. The third visit was after 1 month and the fourth visit was after 3 months from administration of tamsulosin; in these visits, UFM, PVR, IPSS, and QoL were measured and compared to baseline.

Statistical analysis

Data were checked for normality using the Shapiro–Wilk test. Data with a normal distribution were analyzed with parametric tests; data without a normal distribution were analyzed with nonparametric tests. To analyze the data from more than two independent groups, one-way analysis of variance (ANOVA) and Kruskal–Wallis variance analysis were used. Data from two different periods in the same group were analyzed with paired *t*-test and Wilcoxon signed-ranks test. Multiple comparisons after one-way ANOVA and Kruskal–Wallis variance analysis were performed with Tukey HSD test within SPSS 19.0 software (SPSS Inc., Chicago, Illinois, USA). Repeated-measures ANOVA with a Greenhouse–Geisser correction were used for repeated measures of different points of times of follow-up. Statistical significance level was 0.05.

RESULTS

The study included 340 patients with a mean age of 63 ± 6.18 years, mean PSA level 2.63 ± 0.89 ng/dl, and mean prostate volume 52.23 ± 24.59 cc using TRUS and mean PSA density 0.06 ± 0.02 (ng/ml/cc) [Table 1].

The mean Q_{max} at 1st, 2nd, 3rd, and 4th visits was 10.28 ± 3.06 s, 14.58 ± 4.84 s, 14.46 ± 4.94 s, and 14.28 ± 5.07 s, respectively ($P = 0.04$). The mean voiding time at 1st, 2nd, 3rd, and 4th visits was 41.24 ± 27.18 s, 33.84 ± 18.14 s, 31.96 ± 22.02 s, and 30.14 ± 17.52 s, respectively ($P = 0.03$). The mean PVR at 1st, 2nd, 3rd, and 4th visits was 46.40 ± 22.14 ml, 27.76 ± 26.10 ml, 25.16 ± 28.36 ml, and 25.58 ± 28.10 ml, respectively ($P = 0.001$). The effect of first dose of tamsulosin after 6 h significantly increase Q_{max} and decrease voiding time and residual urine (RU) comparable to the 1st and 3rd months; there was no statistical significant difference between 1st dose, 1 and 3months in Q_{max}, voiding time, and RU.

QOL was significantly improved after 1 and 3 months, $P < 0.001$. IPSS was significantly improved after 1 and 3 months with $P < 0.001$. No statistical significant difference between 1 and 3 months in QOL and IPSS [Table 2].

Multivariate analysis was done between improvement of IPSS and other parameters in the study group that

Table 1: Patient criteria

Parameter	Mean	Median	SD	Maximum	Minimum
Age (years)	63	61.5	6.18	77	52
PSA (ng/ml)	2.63	2.90	0.89	4.00	0.84
Creatinine (ml)	1.03	1.00	0.17	1.30	0.60
Size of prostate (cc)	52.2	45	24.5	172	30
PSA density (ng/ml/cc)	0.06	0.05	0.02	0.10	0.01

PSA: Prostate-specific antigen, SD: Standard deviation

Table 2: Parameters at baseline, 6th h, 30th day, and 90th day

Parameter	Baseline	6th h	30th day	90th day	*P*
Q_{max}	10.28±3.06	14.58±4.84	14.46±4.94	14.28±5.07	<0.04*
PVR	46.40±22.14	27.76±26.10	25.16±28.36	25.5±28.10	0.001*
Voiding time	41.24±27.18	33.84±18.14	31.96±22.02	30.14±17.52	<0.001*
IPSS	20.62±4.02		11.48±7.87	11.34±7.9	0.001*
QoL	4.30±0.89		1.92±1.81	1.92±1.81	<0.001*

*Statistically significant. IPSS: International prostate symptom score, PVR: Postvoid residual, QoL: Quality of life

showed there is no relationship between prostate size, PSA, age, PVR, baseline IPSS, baseline QoL, and response to tamsulosin with ($P > 0.05$).

DISCUSSION

To determine the alpha-blocker treatment effect, a 1-month trial is generally preferred, and if an improvement in IPSS and/or QoL with UFM parameters is obtained, the treatment is continued until failure of treatment or patient's desire for another therapy.

In our study, we used standard dose of 0.4 mg tamsulosin, once daily orally administered after breakfast for 340 patients for 3 months, we aimed to investigate whether the first dose of oral tamsulosin 0.4 mg is effective in terms of UFM parameters and whether the first change of UFM parameters could predict the mid-term results in terms of UFM parameters and IPSS and QoL indices.

In our series, we used a selected population that suffers from "moderate-to-severe LUTS" (mean IPSS of 20.62 ± 4.02) and the mean age of patients was 63 ± 6.18 years. This was an ideal population for treatment with alpha blockade.[8]

We preferred to study the UFM at the 6th h of the first dose since the peak serum level of tamsulosin occurs at 6 h. However, the tissue level occurs at the 7.6–10.9 days with continuous medication. In our study, we used 0.4 mg of tamsulosin because tamsulosin 0.4 mg was proved to be effective than tamsulosin 0.2 mg in a study by Chung *et al*.,[9] which included 116 patients from three urology centers. The trial demonstrated that tamsulosin 0.4 mg has favorable efficacy and tolerability in patients with symptomatic BPH refractory to tamsulosin 0.2 mg.

Korstanje *et al*. had done a study that contains 41 patients with BPH scheduled for open prostatectomy; they were given tamsulosin 0.4 mg for 6–21 days to reach steady-state plasma pharmacokinetic. Patients were randomized over four groups to allow collection of plasma and tissue samples at different time points after last dose administration. Samples were collected during surgery and assayed for tamsulosin. The free fraction of tamsulosin was determined by ultracentrifugation of plasma and prostate tissue spiked with 14 C-tamsulosin.

They showed that maximum concentration of tamsulosin in the plasma was at 4.4 h for total tamsulosin, while for prostate, the maximum concentration was at 11.4 h postdose. These data indicate that in patients with confirmed BPH, the amount of tamsulosin freely available in the target tissue (prostate) is much higher than in the plasma.[8]

In our series, we used a selected population that suffers from "moderate-to-severe LUTS" and larger prostate volume. Akin *et al*. in a similar work to ours selected 40 patients with moderate symptoms; the mean IPSS was 16.46 ± 5.77 and mean prostate volume was 35.77 ± 3.86 cc in TRUS; we selected more patients with larger prostate volume (52.23 ± 24.59) and higher mean IPSS (20.62 ± 4.02) to confirm the result of Akin *et al*. in a large group of Middle Eastern patients.

There was a statistically significant increase in Q_{max} and decrease in RU for about 326 patients (96%) from baseline at the first dose of tamsulosin as well as 1st and 3rd months of the treatment; there was no significant difference in Q_{max} and RU between the first dose of tamsulosin as well as the 1st and 3rd months of the treatment. This means that first dose might predict the improvement of LUTS at the 3rd month. Moreover, according to our results, prostate volume, age, PSA, baseline IPSS, and baseline UFM parameters such as Q_{max}, voiding time, and RU are not predictors of tamsulosin response. These findings are parallel with Kang *et al*.[10] and Akin *et al*.[7]

There was statistically significant decrease in IPSS and QoL scores from baseline at 1st and 3rd months of treatment. These results are similar to the report of Djavan *et al*.[11] and Akin *et al*.[7] There was insignificant difference between results of IPSS and QOL in the 1st and 3rd months.

In our community, patients with BPH tend to change the medication frequently since even family doctors can prescribe alpha-blockers or other drugs such as phytotherapy and 5 a-reductase inhibitors. Our limitations are (1) not long term due to patient compliance

problems, (2) validated Arabic version of IPSS and QOL, and (3) no placebo control.

CONCLUSION

Our prospective study presents that the first dose of tamsulosin 0.4 mg is effective to improve UFM parameters immediately and can predict the mid-term change in UFM parameters as well as IPSS and QoL indices in the treatment of BPH-related LUTS, so we can predict if this treatment will be enough from first dose or will need another line of treatment.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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