Investigating the effect of tamsulosin on the measurement of bladder wall thickness and International Prostate Symptom Score in benign prostatic hyperplasia

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Abstract

Introduction: According to previous studies, aging, gender, bladder volume and pathological states, such as bladder outflow obstruction, affect bladder wall thickness (BWT). The aim of this study was to evaluate the correlation between BWT and the International Prostatic Symptom Score (IPSS) in patients with benign prostatic hyperplasia (BPH) before and after tamsulosin treatment.

Methods: In this study, 60 BPH patients were included. After obtaining informed consent, data were gathered using questionnaires to determine IPSS. After that, prostate-specific antigen was measured and a clinical examination, including a digital rectal examination, was performed for all patients. BWT was determined by transabdominal ultrasound. Finally, all patients were treated with tamsulosin (0.4 mg/day) for 2 months. After completing treatment, the IPSS and BWT were measured again and compared with the initial findings.

Results: In total, 44 patients completed treatment. Patients aged 61.7 ± 9.2 years old. The mean ± standard deviation of IPSS and BWT were 14.6 ± 5.0 and 5.36 ± 1.28 mm before treatment, while they significantly ($p < 0.0001$) decreased to 8.2 ± 4.7 and 4.69 ± 1.23 mm, respectively, after treatment. Chi-square test showed that the decrease in BWT was significantly correlated with the improvement in IPSS ($p = 0.002$; r = 0.449).

Conclusion: After treatment with tamsulosin, patients experienced a reduction in their BWT which was significantly correlated with improvement in their IPSS. We conclude that transabdominal evaluation of BWT could be included in the follow-up assessment in BPH.

Introduction

The incidence of benign prostatis hyperplasia (BPH) increases with age; it affects 50% of men in their 60s.[1] Additionally, about 28% of men over 70 years old have moderate-to-severe lower urinary tract symptoms (LUTS).[2,3] Bladder outflow obstruction (BOO) is found in 60% of symptomatic patients, and in 52% of asymptomatic patients.[4,5] Previous studies have demonstrated that BOO causes smooth muscle hypertrophy, fibrocyte hyperplasia and collagen deposition in the bladder wall.[6,7]

The contraction of smooth muscles of prostate, urethra and bladder neck is mediated by alpha1A-adrenoceptor subtype which is the target for tamsulosin (a selective alpha1A-adrenoceptor blocking agent).[8,9] Currently, alpha1A-receptor blockers have been one the most important therapies to relieve LUTS in BPH by decreasing bladder outlet resistance at the bladder neck and improving urine flow rates, which result in the reduction of voiding and storage bladder symptoms.[10]

The International Prostatic Symptom Score (IPSS) is used to assess the severity of LUTS in BPH patients.[11] In addition, measuring BWT by transabdominal ultrasound is a simple, non-invasive method to assess BOO in BPH patients.[12]

In this study, we evaluated the BWT (as measured by transabdominal ultrasound) and IPSS of patients with BPH before and after treatment with tamsulosin. Ultrasonic evaluation of BWT can be a diagnostic or outcome assessment tool.

Methods

This prospective study was done according to the Declaration of Helsinki (as revised in Tokyo 2008) and was approved by the institutional review board and ethics committee of Azad University of Medical Sciences–Mashhad Branch, Iran.

We obtained history and clinical data, including digital rectal examination (DRE) and IPSS of previously diagnosed BPH patients with LUTS. We included patients over 40 years old. The IPSS is calculated as the sum of 7 individual scores related to voiding (sensation of incomplete emptying, intermittency, weak urine stream and straining) and storage (nocturia, urgency and frequency) symptoms.

Prostate-specific antigen (PSA) was assessed using Roche Elecsys total PSA assay (Roche Diagnostic Corporation, Basel, Switzerland) by electrochemiluminescence. We

excluded patients with suspected cancer in DRE, a PSA >4 ng/mL, a history of taking finasteride, urethral stricture, neurogenic bladder, diabetes mellitus, urinary retention, bladder tumour, infection or stone and history of pelvic surgery or lower urinary tract operation.

Data related to BWT were obtained and recorded in questionnaires just before treatment. Similar to previous studies, the BWT remained almost stable for bladder volume >250 ml.[13] However, because some patients suffered from overactive bladder and could not tolerate a high bladder volume without discomfort, we chose 200 mL as the target bladder capacity for BWT measurement. We also measured and compared each patient's BWT when bladder capacity was the same before and after treatment. In addition, changes in BWT were less than 5% when bladder volume was between 200 and 400 mL;[14] changes were negligible for bladder volume less than 200 mL.[15] Therefore, we evaluated bladders which contained at least 200 mL of urine. Since our goal was to measure BWT in bladders with more than 50% of their urine capacity, we asked patients to drink water and then we repeatedly measured bladder volume by ultrasonography until we were certain that the bladders contained at least 200 mL of urine. The bladder wall was then assessed using a suprapubic sonography (Medison SonoAce X8 Ultrasound System, Korea) by a 7.5-MHz Probe in 3 points, each with 1 cm distance from the midline, finally the average BWT was calculated and recorded.

Immediately after clinical and laboratory evaluations, patients were treated with tamsulosin (0.4 mg). Capsules were taken once a day for 2 months. After patients completed their treatment, their IPSS and BWT were measured and recorded again using the aforementioned methods and devices.

Clinical and laboratory data were analyzed with SPSS version 18 (IBM Corporation, New York, NY) and Statistica (Version 8; StatSoft Inc.; Oklahoma City, OK). Data were displayed as mean ± standard deviation (SD). For all variables, the Kolmogorov-Smirnov test was applied to test for normal distribution. Student paired t-test was performed to evaluate parametric data. To compare non-parametric data, Wilcoxon Signed Ranks Test was used. To assess the correlation between variables, we performed the Pearson's chi-square test, Spearman's Rank Correlation Test, linear regression and One-Way ANOVA. A p value less than 0.05 was considered significant.

Results

Before treatment started, we chose 60 patients. During the first 2 months, 6 patients refused to continue treatment and 10 patients did not take the drugs in timely manner. In the end, 44 patients with BPH, who properly complied with the regimen, were included in this study. Patients' ages ranged from 44 to 80, mean 61.7 ± 9.2 years. All data related to BWT and IPSS, including voiding and storage symptom scores, followed normal distribution.

Student paired t-test showed that IPSS and BWT were reduced significantly from 14.6 ± 5.0 to 8.2 ± 4.7 and from 5.36 ± 1.28 mm to 4.69 ± 1.23 mm respectively (Table 1) ($p < 0.0001$). Of the 44 patients, 42 (95.5%) experienced a decrease in their IPSS following treatment with tamsulosin. The remaining 2 patients (4.5%) experienced no change in their symptom score. After treatment, the BWT decreased in 29 (65.9%) patients. However, it increased in 3 (6.8%) patients and remained unchanged in 12 (27.3%) (Table 1).

Pearson's chi-square test showed no correlation between initial IPSS and BWT in 44 patients (Fig. 1) ($p = 0.976$). According to the IPSS, 34 (77.3%) patients had moderate and 9 (20.5%) had severe symptoms. Only one (2.3%) patient was mildly symptomatic. In the severe and moderate groups, their BWT was 5.4 ± 1.3 mm and 5.4 ± 1.2 mm, respectively. Student paired t-test showed no significant difference in BWT between the moderate and severe groups ($p = 0.961$).

On the other hand, Pearson's chi-square test showed a positive correlation ($p = 0.002$; $r = 0.449$) between changes in IPSS and BWT after treatment with tamsulosin (Fig. 2).

Table 1. Comparison of bladder wall thickness and IPSS before and after treatment with tamsulosin

Variable		Before	After	Diff%	*p* value
Bladder wall thickness		5.36±1.28	4.69±1.23	11.44±15.43	*0.0001>
IPSS	Nocturia	2.1±1.5	1.2±1.1	N/A	*0.0001>
	Straining	1.4±1.7	0.6±1.1	N/A	*0.0001>
	Weak stream	3.5±1.6	1.6±1.5	N/A	*0.0001>
	Urgency	1.0±1.5	0.9±1.3	N/A	0.299
	Intermittency	2.5±1.8	1.3±1.5	N/A	*0.0001>
	Frequency	1.6±1.5	1.0±1.3	N/A	*0.0001>
	Incomplete emptying	2.5±2.1	1.6±1.8	N/A	*0.0001>
	Total score	14.6 ± 5.0	8.2 ± 4.7	46.1 ± 21.9	*0.0001>
	Quality of life	3.5 ± 1.1	2.1 ± 1.2	N/A	0.0001

IPSS: International Prostatic Symptom Score. The percentage change is also calculated (Diff% = (before – After) / before × 100) and displayed in a separate column. Data are shown as Mean ± SD. *Significant.

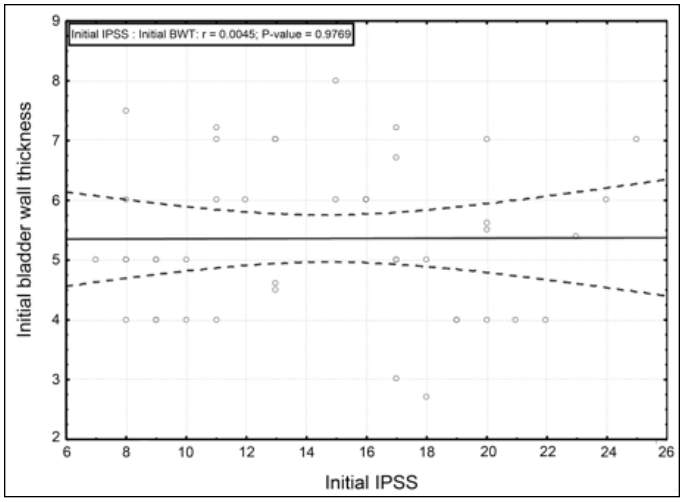

Fig. 1. This scatter plot shows the correlation between initial International Prostatic Symptom Score (IPSS) and bladder wall thickness among 44 patients with benign prostatic hypertrophy.

Further analysis by Pearson's chi-square test revealed that only BWT changes were significantly ($p = 0.002$; r = 0.512) correlated with voiding symptoms (Table 1). There was no significant correlation between changes in BWT and alterations in storage symptoms ($p = 0.103$). Based on the final IPSS question related to quality of life, patient bother improved significantly ($p < 0.0001$) from 3.5 ± 1.1 to 2.1 ± 1.2 after treatment with tamsulosin. In addition, there was a significant ($p = 0.0004$; $r^2 = 0.263$) correlation between changes in patient bother and BWT (Table 1).

Discussion

Aging, gender, bladder volume and pathological states, such as BOO, affect BWT. For example, a small increase in BWT with age is seen in both genders, and BWT tends to be greater in men.[15] In patients with a mean bladder volume of 400 mL and in those with volume 50% more than their bladder capacity, the BWT remains constant.[14,16] In addition, with ultrasonic measurement methods, for every milliliter increase in bladder volume, the BWT is reduced by 0.00108 mm.[15] Therefore, a 50-mL increase in bladder volume changes the BWT by 0.054 mm, which means BWT measurements were not taken in patients with a bladder volume significantly below 250 mL.

In our study, we evaluated patients' BWT when bladder volume was at least 200 mL, as estimated by ultrasonography. Kuhn and colleagues showed dissimilarities in values of BWT between different methods of ultrasonography, such as vaginal, perineal and abdominal measures.[17] We suggest that, as an easy, quick and non-invasive test, transabdominal ultrasonography could be regarded as a paraclinical test in the diagnosis or follow-up of patients with BPH.

In common clinical practice, history, physical examination, urinalysis, and symptom assessment are helpful for the initial evaluation and diagnosis of BPH. Urodynamic tests and measurement of post-void residual volume may be needed in patients with complex medical history, such as neurogenic bladder, and in those desiring invasive therapies (i.e., surgery).[18] Although urodynamic tests are considered more reliable, they are time-consuming and expensive.[19,20]

Although IPSS is a useful test, it has some drawbacks which limit its use to diagnose and assess the severity of BPH. IPSS lacks objective parameters. Although it is used in the initial evaluation of BPH, other alternatives to assess treatment outcome in BPH should be sought. Both subjective and objective components are important.[21] In addition to the subjective parameters, transabdominal ultrasound could be included in the assessment of follow-up in patients with BPH.

Oelke and colleagues proposed that BWT measurement is more suggestive for the diagnosis of BOO compared to uroflowmetry and for the assessment of post-void residual volume.[16,22] In another study, BWT was significantly correlated with parameters of pressure-flow study.[23] According to Casado and colleagues, although no association was found between BWT and other diagnostic tests, including urodynamic tests and post-void residual volume, there was a significant correlation between BWT and IPSS in patients with BPH.[24] These studies suggest an association between the morphology alterations and physiologic functions of urinary system in BPH.

While Manieri and colleagues suggested that a 5-mm thickness of bladder wall could be considered the best cutoff point for the diagnosis of BPH,[23] Kessler and colleagues suggested that a ≥2.9-mm cutoff point for detrusor muscle thickness has a high predictive value for the diagnosis of BOO.[25] In addition to the disagreements in the cutoff point, Yilmaz and colleagues found no correlation between BWT and IPSS.[26] Similarly, in our study, there was no correlation between initial BWT and IPSS. These discrepancies in results indicate that the definite role of ultrasonic measurement of BWT in the diagnosis of BPH is still controversial. Furthermore, various ultrasound frequencies, such as 3.5, 5, 7.5 and 8 MHz, are applied in different studies.[15,16,20,23,25,27] These varieties cause inaccuracies in the comparison of different study results. Bright and colleagues argued that higher frequency ultrasounds are more valid compared to low frequency measures, since the former is able to penetrate deeper tissues in muscular or overweight individuals; therefore, a better resolution and superior image quality are available.[28] It is for these reasons that we used 7.5 MHz ultrasound to measure BWT in patients with BPH. Moreover, a single operator performed these measurements.

Currently, treatment outcome can be usually evaluated by questionnaires and tests, such as IPSS, American Urological Association (AUA) Symptom Score, symptom problem index,

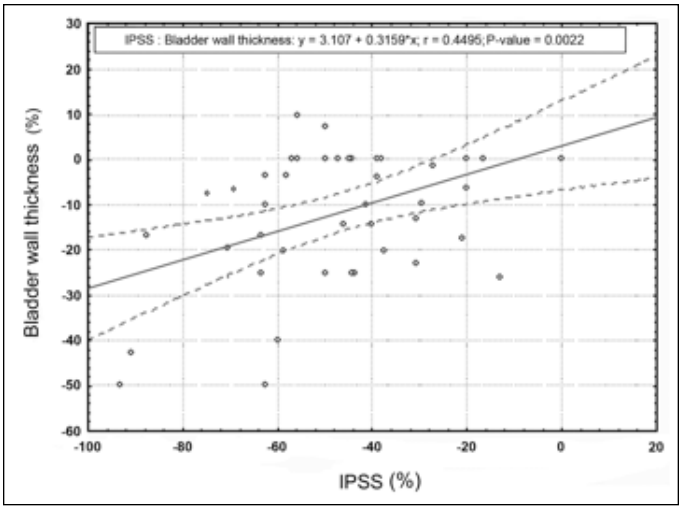

Fig. 2. This scatter plot shows the correlation between changes in International Prostatic Symptom Score and bladder wall thickness following 2-month treatment with 0.4 mg tamsulosin among 44 patients with benign prostatic hypertrophy.

Bother Score and BPH Impact Index.[29,30] All of these tests assess subjective complaints and the results are uncertain. Therefore, Weiss and colleagues developed and validated the LUTS outcome score (LOS) as a new treatment outcome tool by adding objective components to previous assessment systems.[31]

Conclusion

In this study, we found that improvements in voiding symptoms and decreases in BWT after tamsulosin treatment indicated that ultrasound measurements of BWT, with flow-rate studies and IPSS, could be considered an outcome assessment tool in the pharmacologic treatment of BPH. However, longer, large population-based studies with a specific transabdominal ultrasound frequency are required to confirm this. In future studies, objective measurements of symptoms, such as urodynamic tests, are suggested to obtain more accurate results. Uroflowmetry and residual post-void measurements are also necessary to evaluate bladder detrusor muscle function. They could provide more accurate results alongside BWT changes, which are due to BPH-induced BOO. However, as mentioned these tests are more expensive and time-consuming. As previously mentioned, we chose 200 mL as the target bladder capacity for the BWT measurement because some patients were intolerant of high bladder volume. This study could be improved if patients with bladder volumes ≥250 mL were included.

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