

Treatment outcomes of α -blocker therapy based on Prostate Symptom Score voiding to storage subscore ratio in men with lower urinary tract symptoms

Depolamaya ait semptom skorunun işemeye ait semptom skoruna oranının, alt üriner sistem semptomları nedeniyle alfa bloker kullanan hastalardaki tedavi sonuçlarına etkisi

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Abstract

Aim: We aimed to assess the usability effectiveness of IPSS voiding to storage subscore ratio in men with lower urinary tract symptoms (LUTS) who were treated with α -blockers.

Material and Methods: A total of 356 men with LUTS were included in this study. The voiding symptom score (IPSS-V), storage symptom score (IPSS-S), and the IPSS-V/S ratio was calculated. Alpha-blocker therapy was given to patients with IPSS-V/S >1. The IPSS-T, IPSS-V, IPSS-S, QoL (quality of life) were measured at 1 month and 3 months after treatment. Results were assessed by the changes of QoL.

Results: IPSS-T and IPSS-V values were significantly higher in patients with IPSS-V / S > 1 than IPSS-V / S \leq 1 (p<0,001). Patients with IPSS-V / S > 1 were older than IPSS-V / S \leq 1 (p=0,034). The mean IPSS-T and IPSS-V decreased and the QoL improved significantly at third month (p=0,004, p=0,001, p<0,001, respectively).

Conclusion: IPSS-V/S >1 is a useful tool to define bladder outlet-related LUTD and to predict treatment outcomes in patients with lower urinary tract symptoms.

Key Words: Lower urinary tract symptoms, IPSS-V, IPSS-S, Alpha-blocker therapy

Özet

Amaç: Bu çalışmada depolamaya ait semptom skorunun (IPSS-V) işemeye ait semptom skoruna (IPSS-S) oranının, alt üriner sistem semptomları nedeniyle alfa bloker kullanan hastalardaki tedavi sonuçlarına etkisini saptamayı amaçladık.

Gereç ve Yöntemler: Alt üriner sistem şikayetleri olan 356 hasta çalışmaya dahil edildi. Hastaların depolama semptom skorları (IPSS-V), işeme semptom skorları (IPSS-S) ve IPSS-V/S oranları hesaplandı. IPSS-V/S ORANI >1 olan hastalara alfa bloker tedavi verildi. Tedavi sonrası hastaların 1. ve 3. aylarda toplam IPSS skoru (IPSS-T), IPSS-V, IPSS-S ve yaşam kalitesi hesaplandı. Sonuçlar yaşam kalitesi açısından değerlendirildi.

Bulgular: IPSS-V / S > 1 olan hastalarda IPSS-V / S \leq 1 olanlara göre IPSS-T ve IPSS-V değerleri anlamlı olarak yüksekti (p<0,001). IPSS-V / S > 1 olan hastalar IPSS-V / S \leq 1 olan hastalara göre daha yaşlı idi (p=0,034). Üçüncü aydaki kontrollerde hastaların ortalama IPSS-T (p=0,004) ve IPSS-V (p=0,001) değerlerinin azaldığı ve yaşam kalitesinin (p<0,001) arttığı saptandı.

Sonuç: Alt üriner sistem semptomları ile ilişkili mesane çıkım obstrüksiyonunu göstermek için ve alt üriner sistem semptomları olanlarda tedavi sonuçlarının öngörmek için IPSS-V/S >1 skoru kullanışlı olarak bulunmuştur.

Anahtar Kelimeler: Alt üriner sistem semptomları, IPSS-V, IPSS-S, Alfa bloker tedavi

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Introduction

Lower urinary tract symptoms (LUTS) including voiding, storage and post-micturition symptoms significantly affect the urinary system by causing voiding dysfunction and worsen the quality of life (QoL). Although LUTS are considered synonymous with benign prostatic hyperplasia (BPH), it is estimated that only 25-50% of men with BPH have LUTS and only 50% of men with LUTS have urodynamically proven bladder outlet obstruction (BOO) [1,2]. Treatments for LUTS/BPH traditionally target the prostate, despite the important role of the bladder in the pathogenesis of the most bothersome LUTS [3]. It is difficult to distinguish the causes of male LUTS solely based on their clinical symptoms [4]. Storage symptoms that often persist after medical or surgical therapy are most important issue that should be considered for treatment outcomes. So detailed urological investigations are essential for determining the correct interpretation of LUTS [1].

The International Prostate Symptom Score (IPSS) was developed to assess the severity of LUTS in men with bladder outlet obstruction or bladder dysfunction and to evaluate the response to medical or surgical therapy for benign prostatic obstruction [5,6]. Symptom score, urine flow rate and prostate volume are poorly predictive of BOO when used alone, and elevated postvoiding residual volume (PVR) is only weakly associated with BOO [4,7]. Liao et al previously reported that measuring IPSS subscores and calculating the IPSS voiding-to-storage subscore ratio (IPSS-V/S) is a simple and useful method for differentiating between failure to voiding lower urinary tract dysfunction (LUTD) and failure to storage LUTD [8]. Patients with predominantly voiding LUTD have greater voiding subscores (IPSS-V), whereas those with predominantly storage LUTD have greater storage subscores (IPSS-S) [1]. The IPSS/V can serve as a guide for initial treatment of male patients with LUTS [8].

Voiding and storage symptoms are usually seen together in patients admitted with LUTS. The distinction of predominant symptoms by using IPSS-V/S ratio may be useful in deciding convenient medical therapy. Therefore the success of targeted medical therapy increases and we may prevent patients from unnecessary drug use. We aimed to assess the usability and effectiveness of Pros-

tate Symptom Score voiding to storage subscore ratio in men with lower urinary tract symptoms who were treated with α -blockers in present study.

Methods

A total of 356 men (≥ 45 years old) who were admitted to the hospital with LUTS were enrolled from September 2013 to October 2014. Men with a history of prostatic surgery, urethral stricture, acute or chronic urinary retention, genitourinary cancer, neurologic disorders, urinary tract infection, diabetes mellitus and needing further cancer evaluation for abnormal digital rectal examination or elevated serum PSA levels were excluded from the study. After full medical history was obtained, digital rectal examination, urine analysis, serum prostate-specific antigen (PSA) and creatinine measurement, and ultrasonography (USG) were done to all patients. USG was performed to evaluate the urinary system and also used for residual urine measurement (PVR). The total IPSS score (IPSS-T) was defined to indicate the severity of LUTS as mild (IPSS ≤ 7), moderate ($8 \leq$ IPSS ≤ 19) or severe (IPSS ≥ 20). Patients had IPSS-T score 8 or more, a total prostate volume (TPV) of 30 ml or more, a maximum flow rate (Qmax) of 15 ml/s or less at a minimum voided volume (VV) of 150 ml. After the results of IPSS questionnaire were evaluated, the voiding symptom score (IPSS-V), storage symptom score (IPSS-S), and the IPSS-V/S ratio was calculated. Patients with an IPSS-V/S >1 at baseline were considered to have bladder outlet dysfunction and those with an IPSS-V/S ≤ 1 were considered to have bladder dysfunction.

After IPSS subscore, medical treatment consisting of an α -blockers (tamsulosin, alfuzosin or doxazosin) was given to patients with IPSS-V/S >1 who were not candidates for surgical treatment. The IPSS-T, IPSS-V, IPSS-S, QoL, Qmax, voided volume and postvoiding residue (PVR) were measured at 1 month and 3 months after treatment. Therapeutic results were assessed by the changes of quality of life index (QoL-I) adapted from the IPSS questionnaire as effective (QoL-I improved by ≥ 2) or failure (QoL-I improved < 2)

Statistical analyses were performed with SPSS version 21.0 (Chicago,IL) statistical software package. Student t

Table 1. Baseline parameters between IPSS-V/S > 1 and IPSS-V/S ≤1

	IPSS-V / S > 1 N:186	IPSS-V/S ≤1 N:170	P
Age (years)	63,2±8,4	61,1±9,5	0,034
PSA (ng/ml)	2,6±0,8	2,7±0,9	0,737
IPSS-T	19,6±7,2	11,7±4,9	0,000
IPSS-V	13,5±5,2	5,1±2,6	0,000
IPSS-S	6,1±2,6	6,5±2,7	0,200
QoL	3,6±1,1	2,7±0,9	0,000
Prostate volume (ml)	53,5±19	52,0±16	0,424
Qmax (ml/s)	10,1±1,6	11,8±2,3	0,000
Volume (ml)	254,9±86,4	241,6±70,9	0,117

Student t test

test test and chi-square test were used. Statistical significance was set as a p value of <0.05.

Results

Table 1 shows baseline parameters between IPSS-V /S > 1 and IPSS-V/S ≤1. The mean age was 62,2±9,0 years (range, 45-84 years) and mean PSA value was 2,6±0,9 ng/ml (range 0,6-3,9 ng/ml). While IPSS-T and IPSS-V values were significantly higher in patients with IPSS-V/S > 1 than IPSS-V/S ≤1 (p<0,001), IPSS-S value was similar between two groups (p=0,200). Patients with IPSS-V /S > 1 were older than IPSS-V /S ≤1(p=0,034). There were no significant differences between two groups in terms of PSA values, prostate volume and bladder capacity. Alpha-1 blocker therapy was given to the patients with IPSS-V /S > 1. Parameters changes of patients with IPSS-V/S > 1 after alpha

Table 2. Parameters' changes after alpha blocker treatment for 3 months

	Baseline	3 rd month	P
IPSS-V	13,5±5,2	11,6±5,6	0,001
IPSS-S	6,1±2,6	5,8±2,5	0,341
IPSS-T	19,6±7,2	17,4±7,4	0,004
QoL	3,6±1,1	1,9±0,7	0,000
Qmax (ml/s)	10,1±1,6	12,0±1,7	0,000
Volume (ml)	254,9±86,4	269,6±82,1	0,093

Student t test

blocker treatment for 3 months were given in table 2. The mean IPSS-T and IPSS-V decreased and the QoL improved significantly at third month (p=0,004, p=0,001, p<0,001, respectively). On the other hand, the bladder capacity and IPSS-S values remained the same. When we subgrouped the patients by IPSS severity; QoL increased ≥2 points in 111 (59,6%) patients (p<0,05) and Qmax increased more than 2 ml/s in 115 (61,8%) patients (p<0,05). The comparison of QoL and Qmax due to IPSS severity was given in table 3.

Discussion

Despite its limitations, the IPSS is internationally recognized as a validated 1-mo recall assessment of LUTS/BPH 9,10. A potential criticism of the IPSS is that it fails to emphasize the differential bothersomeness of storage compared with voiding symptoms 11. The IPSS can be performed multiple times to compare the progression of symptoms and their severity over months and years 1. But IPSS-T correlates poorly with bladder outlet obstruction (BOO) and overactive bladder and is unreliable for establishing an accurate diagnosis in men with LUTS 12. In order to provide maximum information from the score system and to direct patients to more efficient treatment, clinicians admitted to IPSS- subscores. This study was designed to evaluate the efficiency of IPSS-subscores in our group of patients. When we evaluated our patients according to IPSS subscores, 186 (52,2 %) had IPSS- V/S >1 and 170 (47,8 %) had IPSS- V/S ≤1. While the patients with IPSS- V/S >1 were treated by alpha blocker therapy to correct the obstruction, the patients with IPSS-V/S ≤1 had antimuscarinic therapy to relieve storage symptoms. In the current study, we targeted to evaluate the patients with IPSS-V/S >1 and presented the outcomes of α-blocker therapy in this group of patients. Alpha-blockers are the most commonly used first-line medication for male LUTS and result in an improvement of around 30-45% in IPSS-T 13. In their series, Liao et al have found 40% decrease in IPSS-T and 2.2 ml/s mean increase in Qmax after first-line doxazosin monotherapy for men with IPSS-V/S >1 14. In open-label studies (without a run-in period), an IPSS improvement of up to 50% and Qmax increase of up to 40% were documented 15,16. In the comparison of the baseline parameters with third

month results after alpha blocker therapy, there were significant increase in IPSS-V, IPSS-T, Qmax and improvement in QoL in our patients. Interestingly, there was no significant change in IPSS-T. Our results revealed that IPSS-V/S >1 is a more powerful tool to define bladder outlet -related LUTD.

In the past, LUTS in elderly men were traditionally attributed to the enlarging prostate and treatment modalities depended on reducing prostate volume. The IPSS questionnaire has been used for decades to evaluate the severity of LUTS/BPH, but it is well-known that LUTS can be found with many other conditions causing LUTS. Uroflowmetry and PVR are simple tests in urology for evaluating LUTS in men. But impaired detrusor contractility or BOO can both cause to decreased urinary volume or increased PVR. To distinguish the underlying pathology, invasive pressure-flow studies are the referred test 17. Although IPSS-V/S could not replace pressure-flow studies in the aspect of confirmed diagnosis of BOO or the role of pre-operative evaluation, it could elevate the initial diagnostic rate in differentiating bladder outlet-related LUTD from bladder-related LUTD and guide the initial treatment 18.

The diagnostic value of IPSS subscores was shown in many studies 8,19. Liao et al found that IPSS-V/S was a better predictor than IPSS-T, IPSS-V, IPSS-S, Qmax, PVR or TPV and IPSS-V/S with 1 as a cut-off value had a high sensitivity and acceptable specificity for differentiating LUTD 8. This finding is utmost important in BPH treatment which carries paradoxes to clinicians for selecting a treatment modality between non-invasive and invasive therapies. Jhang et al revealed that patients with BPH and mild LUTS have more bladder storage dysfunction component, whereas patients with BPH and severe LUTS had higher grade of bladder outlet disorders in associated with storage symptoms 1. And they concluded that IPSS-V/S ratio provided a guide for initial treatment, especially for patients with mild-to- moderate LUTS, but not severe LUTS. They found that after treatment with alpha-blocker the men with mild LUTS and IPSS-V/S>1 subscores had the highest success rate (84%) after completion of medical therapy based on the IPSS-V/S ratio than did the moderate LUTS (63.8%) or the severe LUTS (33.3%). Our study also showed that alpha blocker therapy was more

Table 3. The comparison of QoL and Q max values due to the IPSS severity

	IPSS≤7	7<IPSS<20	IPSS≥20	P
QoL-I ≥2	28 (15%)	67 (36%)	16 (8,6%)	<0,05
QoL-I <2	11 (5,9%)	41 (22%)	23 (12,3%)	
Qmax> 2 ml/s	31 (16,6%)	71 (38,6%)	13(6,9%)	<0,05
Qmax≤ 2ml/s	8(4,7%)	37(19,8%)	26 (13,9%)	

Chi-Square test

useful in patients with mild-to-moderate LUTS. While mean IPSS-T decreased, Q max and QoL were significantly improved after treatment. A total of 115 patients had increased Qmax values (Qmax>2ml/s) and 111 patients had improvement in QoL. Of these, patients with moderate IPSS had significantly higher successful treatment results. Alpha blockers are often considered the first-line drug treatment of moderate to severe LUTS 20. On the other hand, men with mild to moderate uncomplicated LUTS (causing no serious health threat), who are not too bothered by their symptoms, are suitable for a trial of watchful waiting 13. Approximately 85% of men will be stable on watchful waiting at 1 year, deteriorating progressively to 65% at 5 years 20,21. In this respect, IPSS subscore ratio can be beneficial to select proper treatment and to predict treatment results. It is non-invasive and simple, useful method that can be applied in out-patient procedure. In addition to, patient selection by using IPSS subscore ratio provides a guide for the initial treatment, especially for differentiating the patients with voiding and storage symptoms.

In most patients, IPSS storage and voiding subscores appear together and usually expressed with mixed symptoms. Storage symptoms interfere more with QoL than voiding symptoms do and exhibit tighter correlations with QoL across all treatment modalities 22-24. Storage symptoms also have a negative effect on disease-specific QoL accompanying with LUTS. It is very important to distinguish voiding symptoms from storage symptoms. Beyond that many men have both voiding and storage symptoms that require the use of alpha blockers and antimuscarinics together. To use IPSS-V/S subscores helps to guide the initial treatment for male LUTS. While alpha blocker treatment is suitable for men with IPSS-V/S>1, antimuscarinic monotherapy can be initiated for those with IPSS-V/S≤1, regardless of their prostate volume,

PSA levels or Qmax. We believe that appropriate IPSS subscore of our patients lead favorable contribution to improvements in QoL.

Conclusion

The patients with IPSS subscore IPSS- V/S >1 had better response to alpha blocker therapy, had significant decreases in IPSS and significant increases in Qmax. IPSS- V/S >1 is a useful tool to define bladder outlet-related LUTD and to predict treatment outcomes in patients with lower urinary tract symptoms.

References

1. Jhang JF, Liao CH, Kuo HC. Severity of lower urinary tract symptoms reflects different composition of bladder storage dysfunction and bladder outlet obstruction in men with symptomatic benign prostatic hyperplasia. *Int J Clin Pract* 2014;68:743-748.
2. Milson I, Abrams P, Cardoza L, Roberts RG, Thüroff J, Wein AJ. How widespread are the symptoms of an overactive bladder and how are they managed? A population based prevalence study. *BJU Int* 2001;87:760-6.
3. Chapple CR, Roehrborn CG. A shifted paradigm for the further understanding, evaluation, and treatment of lower urinary tract symptoms in men: focus on the bladder. *Eur Urol* 2006;49:651-658.
4. Madersbacher S, Pycha A, Kingler CH, Shatzl G, Marberger M. The International Prostate Symptom score in both sexes: a urodynamics-based comparison. *Neurol Urodyn* 1999;18:173-182.
5. Barry MJ, Fowler FJ, O'Leary MP, Bruskewitz RC, Holtgrewe HL, Mebust WK, et al. The symptom index for benign prostatic hyperplasia. The Measurement Committee of American Urologic Association. *J Urol* 1992;148:1549-1557.
6. Roehrborn CG. BPH progression: concept and key learning from MTOPS, ALTESS, COMBAT, and ALF-ONE. *BJU Int* 2008;101:17-21.
7. Steele GS, Sullivan MP, Sleep DJ, Yalla SV. Combination of symptom score, flow rate and prostate volume for predicting bladder outflow obstruction in men with lower urinary tract symptoms. *J Urol* 2000;164:344-8.
8. Liao CH, Chung SD, Kuo HC. Diagnostic value of International Prostate Symptom Score voiding-to-storage subscore ratio in male lower urinary tract symptoms. *Int J Clin Pract* 2011;65:552-558.
9. McVary KT, Roehrborn CG, Avins AL, Barry MJ, Bruskewitz RC, Donnell RE, et al. Update on AUA guideline on the management of benign prostatic hyperplasia. *J Urol* 2011;185:1793-1803.
10. Lepor H. Phase III multicenter placebo-controlled study of tamsulosin in benign prostatic hyperplasia. Tamsulosin Investigator Group. *Urology* 1998;51:892-900.
11. Chapple CR, Roehrborn CG, McVary K, Barry MJ, Bruskewitz RC, Donnell RE, et al. Effect of tadalafil on male lower urinary tract symptoms: an integrated analysis of storage and voiding international prostate symptom subscores from four randomised controlled trials. *Eur Urol* 2015 ;67:114-22.
12. de la Rosette JJ, Witjes WP, Schäfer W, Abrams P, Donovan JL, Peters TJ, et al. Relationships between lower urinary tract symptoms and bladder outlet obstruction: results from the ICS-"BPH" study. *Neurol Urodyn* 1998;17:99-108.
13. Oelke M, Bachmann A, Descazeaud A, Emberton M, Gravas S, Michel MC, et al. EAU guidelines on the treatment and follow-up of non-neurogenic male lower urinary tract symptoms including benign prostatic obstruction. *Eur Urol* 2013 ;64:118-40.
14. Liao CH, Lin VC, Chung SD, Kuo HC. Therapeutic effect of α -blockers and antimuscarinics in male lower urinary tract symptoms based on the International Prostate Symptom Score subscore ratio. *Int J Clin Pract* 2012;66:139-145.
15. Djavan B, Chapple C, Milani S, Marberger M. State of the art on the efficacy and tolerability of alpha1-adrenoceptor antagonists in patients with lower urinary tract symptoms suggestive of benign prostatic hyperplasia. *Urology* 2004;64:1081-8.
16. Michel MC, Mehlburger L, Bressel HU, Goepel M. Comparison of tamsulosin efficacy in subgroups of patients with lower urinary tract symptoms. *Prostate Cancer Prostatic Dis* 1998;1:332-335.
17. Abrams P, Chapple C, Khoury S, Roehrborn C, de la Rosette C. Evaluation and treatment of lower urinary tract symptoms in older men. *J Urol* 2013;189:93-101.
18. Jiang YH, Lin VCH, Liao CH, Kuo HC. International Prostate Symptom Score voiding-to-storage subscore ratio in association with total prostatic volume and maximum flow rate is diagnostic of bladder outlet-related lower urinary tract dysfunction in men with lower urinary tract symptoms. *PLOS ONE* 2013;8:59176.
19. Lee JY, Lee SH, Kim SJ, Kim CS, Lee HM, Kim CI, et al. Change in International Prostate Symptom storage subscore after long-term medical therapy in BPH patients: finasteride and alpha-blocker combination therapy in men with moderate-to-severe LUTS/BPH in Korea. *Urology* 2011;77:171-6.

20. Wasson JH, Reda DJ, Bruskewitz RC, Elinson J, Keller AM, Henderson WG. A comparison of transurethral surgery with watchful waiting for moderate symptoms of benign prostatic hyperplasia. The Veterans Affairs Cooperative Study Group on Transurethral Resection of the Prostate. *N Engl J Med* 1995;332:75-9.
21. Netto NR Jr, de Lima ML, Netto MR, D'Ancona CA. Evaluation of patients with bladder outlet obstruction and mild international prostate symptom score followed up by watchful waiting. *Urology* 1999;53:314-316.
22. Kingery L, Martin ML, Naegeli AN, Khan S, Viktrup L. Content validity of the Benign Prostatic Hyperplasia Impact Index (BII); a measure of how urinary trouble and problems associated with BPH may impact the patient. *Int J Clin Pract* 2012;66:883-90.
23. Peters TJ, Donovan JL, Kay HE, Abrams P, de la Rosette JJ, Porru D, et al. The International Continence Society "Benign Prostatic Hyperplasia" Study: the bothersomeness of urinary symptoms. *J Urol* 1997;157:885-9.
24. Sountoulides P, van Dijk MM, Wijkstra H, de la Rosette JJ, Michel MC. Role of voiding and storage symptoms for the quality of life before and after treatment in men with voiding dysfunction. *World J Urol* 2010;28:3-8.