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Clinical Significance of National Institutes of Health-Chronic Prostatitis Symptom Index Pain Score in Patients with Benign Prostatic Hyperplasia

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Purpose: Many benign prostatic hyperplasia (BPH) patients were accompanied by pelvic pain apart from urinary symptoms. Therefore, we evaluate the treatment outcomes of alpha-blockers via a change of international prostate symptom score (IPSS) according to pain score of the National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI).

Materials and Methods: A total of 356 male patients with BPH from March 2011 to May 2014 were analyzed retrospectively. Prostate specific antigen, prostate volume, IPSS, NIH-CPSI, international index of erectile function (IIEF-5), and uroflowmetry were collected. Patients were categorized according to 2 groups based on the presence and severity of pain and baseline characteristics and treatment outcomes were analyzed.

Results: Two hundred twenty-nine patients (64.3%) reported pain/discomfort on NIH-CPSI. Mean IPSS, mean voiding symptoms, mean storage symptoms on IPSS, and mean IIEF-5 showed a significant difference in groups 1A and 1B. Logistic regression analysis showed that NIH-CPSI pain score was a significant predictive factor for severe IPSS (odds ratio, 2.830; 95% confidence interval, 1.307-6.129). After treatment for 3 months, improvement of IPSS, voiding symptoms, storage symptoms, and quality of life was observed in all groups ($p=0.001$, $p<0.001$, $p=0.026$, $p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$). Group 2B (pain score >5) showed greater improvement of symptoms and statistically significant difference compared with group 2A (pain score ≤ 5) ($p=0.029$, $p=0.026$).

Conclusions: We suggest that the presence and severity of pain score are helpful for therapeutic efficacy in patients with BPH.

Keywords: Prostatic hyperplasia; Lower urinary tract symptoms; Prostatitis

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INTRODUCTION

Recently, with increase in the elderly population, the importance of treatment and interest in lower urinary tract symptoms (LUTS) is increasing as compared to the past. According to the 2002 International Continence Society

definitions, LUTS have three categories: storage, voiding, and postmicturition symptoms. Storage symptoms contain frequency, nocturia, urgency, and incontinence. Voiding symptoms include slow or weak urinary stream, hesitancy, and terminal dribble. Postmicturition symptoms include the sensation of incomplete emptying and postmicturition

dribble. Bladder outlet obstruction, which is represented by benign prostatic hyperplasia (BPH), overactive bladder, neurological disease, aging, and changes in sex hormones are the causes of LUTS [1]. And obstruction due to BPH is the most common cause of LUTS and 8 million people out of the men over 50 years of age in the United States have complained of BPH and LUTS [2].

Prostatitis is an inflammatory disease of the prostate gland which is characterized by pelvic pain and voiding symptoms. National Institutes of Health-Chronic Prostatitis Symptom Index (NIH-CPSI) is in three discrete domains: pain, urinary symptoms, and the impact on quality of life (QoL). The severity of pain may be objectified by using NIH-CPSI pain score and many patients with BPH have complained of pelvic pain in addition to urinary symptoms. Recently, 16% of healthy men reported a history of prostatitis and there was a large overlap with men reporting BPH [3].

Therefore, we evaluated the therapeutic effect of alpha-blockers according to the changes of international prostate symptom score (IPSS) due to NIH-CPSI pain score in patients with BPH.

MATERIALS AND METHODS

Data were collected from 356 patients with BPH who visited the Wonju Severance Christian Hospital between March 2011 and May 2014, retrospectively. As baseline study, medical histories (e.g., the presence of diabetes mellitus), prostate specific antigen (PSA), prostate volume (PV), IPSS, NIH-CPSI, international index of erectile function (IIEF-5) and maximum flow rate on uroflowmetry (Qmax)

were analyzed and the IPSS score was classified in mild ($IPSS \leq 7$), moderate ($8 \leq IPSS \leq 19$) and severe ($IPSS \geq 20$).

We excluded patients with urinary tract infection, hypoechoic lesions on trans-rectal prostate ultrasound, abnormal findings of urinalysis, serum PSA levels at or greater than 4 ng/dl, history of antibiotic treatment in the 6 months preceding initial visit, invasive prostate-related procedures (transurethral resection of the prostate, transurethral incision of the prostate, and transurethral needle ablation), genitourinary cancer, inflammatory bowel disease, active urethral stricture, prostate or bladder surgery, or with neurologic diseases affecting the bladder.

Firstly, we divided the patients into two groups according to the presence of pain (group 1A: pain score ≤ 0 , group 1B: pain score > 0). Baseline characteristics were analyzed between two groups. Secondly, the patients who completed follow up schedule were classified into two groups based on severity of pain scores (group 2A: pain score ≤ 5 , group 2B: pain score > 5) and evaluated the therapeutic effect of alpha-blockers in each group using IPSS and QoL after 3 months alpha blocker monotherapy.

The independent sample t-test was used to compare baseline characteristics between two groups. Paired sample t-test was used to compare the changes of parameters in each group. Multivariate logistic regression analysis was used to determine the potential risk factors of pain score. IBM SPSS Statistics ver. 20.0 (IBM Co., Armonk, NY, USA) was used for all statistical analyses. A p-value of less than 0.05 was considered statistically significant.

Table 1. Baseline characteristics (n=356)

Characteristic	Pain		p-value
	No (n=127)	Yes (n=229)	
Age (y)	65.89 \pm 7.19	66.55 \pm 8.18	0.450
Diabetes mellitus	100 (78.7)	178 (77.7)	0.375
Prostate volume (ml)	32.21 \pm 16.12	29.99 \pm 12.84	0.185
Prostate-specific antigen (ng/dl)	2.53 \pm 7.79	2.14 \pm 5.21	0.699
International prostate symptom score	15.13 \pm 7.96	17.66 \pm 7.90	0.004
Voiding	8.59 \pm 5.31	10.27 \pm 5.22	0.004
Storage	6.53 \pm 4.14	7.39 \pm 3.60	0.041
Quality of life	3.96 \pm 1.45	4.15 \pm 1.42	0.225
International index of erectile function score	11.20 \pm 7.24	9.19 \pm 7.01	0.023
Qmax (ml/s)	10.93 \pm 6.90	11.36 \pm 8.01	0.626

Values are presented as mean \pm standard deviation or number (%). Independent t-test.
Qmax: maximum flow rate on uroflowmetry.

RESULTS

The patients were classified into group 1A (n=229, 64.3%) and into group 1B (n=127, 35.7%) based on pain/discomfort. Table 1 showed baseline characteristics of patients. Mean IPSS were 15.13 ± 7.96 and 17.66 ± 7.90 between 2 groups, respectively. Mean voiding symptoms and storage symptoms on IPSS were 8.59 ± 5.31 , 10.27 ± 5.22 and 6.53 ± 4.14 , 7.39 ± 3.60 in each group, respectively. Mean IIEF-5 were 11.20 ± 7.24 and 9.19 ± 7.01 between 2 groups, respectively. There were statistically significant differences on IPSS and IIEF-5. However, mean age, PSA, PV, QoL, and Qmax did not prove to be significant in this study.

Logistic regression analysis showed that NIH-CPSI pain score were significant predictive factor of severe LUTS on IPSS (odds ratio, 2.830; 95% confidence interval, 1.307-6.129; Table 2).

After made exclusion the patients who were lost, 66 (58%)

patients were reclassified into group 2A (pain score ≤ 5) and 38 (42%) into group 2B (pain score > 5) based on severity of pain scores. Statistically significant improvement of IPSS including voiding symptoms and storage symptoms, and QoL were found in groups (Tables 3, 4). Changes of

Table 2. Risk factor for National Institutes of Health-Chronic Prostatitis Symptom Index pain score

	Odds ratio (95% confidence interval)
Age (y)	
≤ 60	-
$> 60, \leq 70$	0.448 (0.246-0.815)
> 70	1.182 (0.580-2.410)
IPSS	
Mild (IPSS ≤ 7)	-
Moderate ($8 \leq \text{IPSS} \leq 19$)	1.604 (0.793-3.243)
Severe (IPSS ≥ 20)	2.830 (1.307-6.129)
Diabetes mellitus	0.809 (0.459-1.424)

Logistic regression analysis.

IPSS: international prostate symptom score.

Table 3. Comparison of treatment outcomes before and after treatment in each group

		Baseline	3 month later	p-value
Pain score ≤ 5 (n=66)	IPSS	15.30 ± 6.53	11.95 ± 7.13	0.001
	Voiding	9.09 ± 4.63	6.82 ± 4.71	0.000
	Storage	6.21 ± 3.64	5.12 ± 3.32	0.026
	QoL	3.86 ± 1.28	2.95 ± 1.54	0.000
	Pain score	1.55 ± 1.96	1.67 ± 2.55	0.735
	IIEF-5 score	12.12 ± 6.69	9.51 ± 7.42	0.009
	Qmax (ml/s)	9.54 ± 6.04	10.91 ± 5.50	0.083
Pain score > 5 (n=38)	IPSS	18.26 ± 6.93	11.34 ± 6.80	0.000
	Voiding	11.03 ± 4.77	6.82 ± 4.45	0.000
	Storage	7.24 ± 3.41	4.53 ± 3.00	0.000
	QoL	4.53 ± 1.25	2.87 ± 1.32	0.000
	Pain score	9.53 ± 2.69	3.45 ± 3.29	0.000
	IIEF-5 score	10.64 ± 6.28	10.86 ± 7.07	0.881
	Qmax (ml/s)	11.53 ± 6.69	13.20 ± 8.11	0.054

Values are presented as mean \pm standard deviation. Paired t-test.

IPSS: international prostate symptom score, QoL: quality of life, IIEF-5 score: international index of erectile function score, Qmax: maximum flow rate on uroflowmetry.

Table 4. The changes of subjective and objective parameters between 2 groups

Changes of parameters	Pain score ≤ 5 (n=66)	Pain score > 5 (n=38)	p-value
IPSS	-3.35 ± 7.69	-6.92 ± 8.34	0.029
Voiding	-2.27 ± 4.80	-4.21 ± 5.82	0.070
Storage	-1.09 ± 3.89	-2.71 ± 3.73	0.041
QoL	-0.91 ± 1.62	-1.65 ± 1.63	0.026
NIH-CPSI pain score	0.12 ± 2.90	-6.08 ± 3.79	0.000
IIEF-5 score	-2.60 ± 6.28	0.22 ± 7.04	0.104
Qmax (ml/s)	1.36 ± 5.16	1.67 ± 4.70	0.796

Values are presented as mean \pm standard deviation. Paired t-test.

IPSS: international prostate symptom score, QoL: quality of life, NIH-CPSI pain score: National Institutes of Health Chronic Prostatitis Symptom Index pain score, IIEF-5 score: international index of erectile function score, Qmax: maximum flow rate on uroflowmetry.

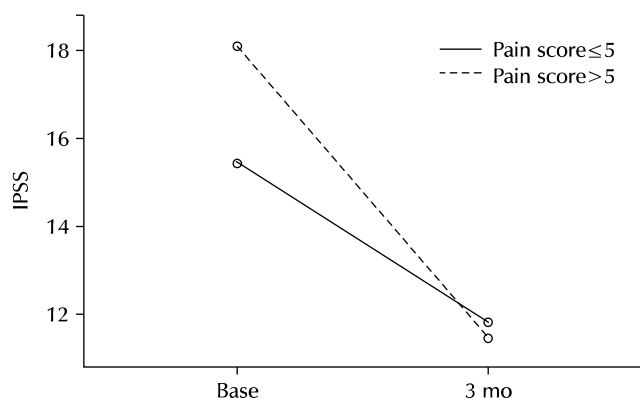


Fig. 1. Changes of international prostate symptom score (IPSS) between 2 groups.

IPSS and QoL were -3.35 ± 7.69 , -6.92 ± 8.34 , and -0.91 ± 1.62 , -1.65 ± 1.63 between 2 groups, respectively group 2B presented greater symptom improvements compared with group 2A and showed a statistically significant difference ($p=0.029$, $p=0.026$; Fig. 1, 2).

DISCUSSION

BPH represents the most commonly diagnosed urological disease in men after the fifth decade [4]. In fact, the histological prevalence of BPH, which has been examined in several autopsy studies around the world, is approximately 10% for men in their 30s, 20% for men in their 40s, reaches 50% to 60% for men in their 60s, and is 80% to 90% for men in their 70s and 80s. Aging is risk factor of the development of BPH [5].

Recently, the role of chronic inflammation is emerging as an important factor in BPH development and progression [6]. De Nunzio et al. [5] suggested that chronic prostatic inflammation has an important role in the development of chronic prostatic diseases such as BPH and prostate cancer. Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS), is characterized by chronic pelvic pain symptoms with the absence of urinary tract infection. The symptoms include characteristic urogenital pains, voiding discomfort and sexual dysfunction that reduce patients' QoL [7]. Men reporting a history of BPH had an eight fold greater odds of a history of prostatitis [8]. Furthermore, there is an evidence of a relationship between the degree of LUTS and the degree of chronic inflammation [9]. In addition, Nickel et al. [10] reported that 20% of sexually active men

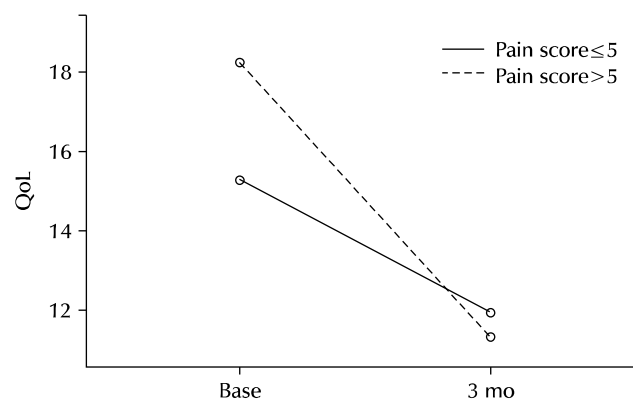


Fig. 2. Changes of quality of life (QoL) between 2 groups.

with LUTS suggestive of BPH complained of the specific prostatitis-like symptom of pain/discomfort on ejaculation. Cologne Male Survey reported a prevalence of LUTS of 72% in men with erectile dysfunction, vs. 38% in men with normal erections in a sample of 8000 men aged 30-80 years [11]. In addition, the severity of sexual dysfunction is positively associated with increasing severity of LUTS, irrespective of age and comorbidities [12-14]. Men with BPH and painful ejaculation have more severe LUTS and reported greater bother, and had a higher prevalence of erectile dysfunction and reduced ejaculation, than men with LUTS only [10].

Current medical treatment of LUTS is mainly based on $\alpha 1$ -adrenergic receptor blockers (ABs) and 5 α -reductase inhibitors (5-ARIs), alone or in combination [11]. ABs relieves BPH symptoms by inhibiting the ABs in smooth muscle, which results in the relaxation of prostatic, and bladder neck smooth muscle and mitigation of LUTS [15]. 5-ARIs reduce the prostate size by blocking that testosterone is converted to dihydrotestosterone to induce apoptosis of prostate epithelial cells [16-18]. Several randomized placebo-controlled studies showed that ABs can reduce the pain symptoms in CP/CPPS patients [19-21]. Kwon et al. [22] evaluated the relationship between chronic intra-prostatic inflammation and the response to BPH medical treatment. They reported that patients with BPH not responding to medical treatment might be considered at higher risk of chronic, significant and intra-prostatic inflammation. Cantoro et al. [23] reported that there are no correlations between initial IIEF-5 score and NIH-CPSI score, statistically. However after α -blocker treatment, erectile dysfunction

could be improved by reducing the spasm of prostate smooth muscle, the associated inflammation and improving prostate and penis blood flow. And there is statistically significant increase in IIEF-5.

Abs has been shown to provide symptomatic relief for some patients with CP/CPPS [24-26]. The mechanisms for relief of pain associated with CP/CPPS are unclear, but researchers thought that substance P is a significant mediator and α -blocker antagonizes the local and spinal α 1A and α 1D receptors, probably [21,27]. The spinal cord contains many α 1A and α 1D-adrenergic receptor subtypes, and a recent study showed that selective ABs inhibits up-regulation of substance P after pain stimulation of the rat's prostate. It is possible substance P is released in the spinal cord in response to stimulation of pain receptors in the prostate, and may be attenuated by ABs [27]. Nickel et al. [21] found that α -blocker improved symptomatic relief in men with CP/CPPS, particularly in those with more severe symptoms. We also found similar results. Depending on the presence of pain score, baseline IPSS were different between the two groups. Higher pain score group showed greater symptom improvements compared with lower group. As a result, we believe that the presence and severity of pain score are independent risk factors in patients with LUTS, and pain score can help physicians to predict therapeutic efficacy in patients with LUTS.

There were limitations to this study. The first limitation pertains to the retrospective study design. Second the follow-up period might not have been long enough, so it was not sufficient to evaluate the long term therapeutic efficacy. Third, follow-up loss was present including an incomplete completion of Questionnaire and potential interviewer bias. A prospective randomized trial and long-term follow-up are needed.

CONCLUSIONS

BPH is a progressive disease that requires long term treatment and periodic assessment of therapeutic efficacy. Because the goal of BPH treatment is not only symptom improvement but also increase of the patient's QoL by relieving the disturbance of LUTS. Many studies show that chronic inflammation is an important factor of disease progression and development of chronic prostate diseases such as BPH or CPPS. In addition, ABs treatment relieves

the symptoms of the promised in patients with BPH or CPPS, particularly shows the increase in QoL by reducing pain.

Our study provides that presence and severity of pain score may be helpful for therapeutic efficacy in patients with BPH.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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