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Original Article

Urinary and psychological outcomes in women with interstitial cystitis/bladder pain syndrome following hyaluronic acid treatment

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ABSTRACT

Objective: To investigate urinary and psychological symptoms in patients with interstitial cystitis/bladder pain syndrome (IC/BPS) after intravesical hyaluronic acid (HA) treatment.
Materials and methods: Thirty patients with newly diagnosed with IC/BPS undergoing 4 weekly intravesical HA instillations followed by 5 monthly instillations were recruited. Pre-treatment evaluation included a urinalysis and urinary culture, a 3-day voiding diary, and cystoscopy with hydrodistention of the bladder. Questionnaires containing hospital anxiety and depression scale (HADS), O'Leary-Sant score, Pelvic Organ Prolapse/Urinary Incontinence Sexual Function Questionnaire (PISQ-12), and a pain visual analog scale were completed before and after treatment. Thirty age-matched, asymptomatic women were recruited as controls for assessing HADS scores, and comparison of urinary and psychological symptoms in patients before and after HA treatment.
Results: The mean age (range 25–71 years old) and symptomatic duration (range 1–11 years) were 47 and 4.5, respectively. When compared with the control group, patients with IC/BPS had a significant increase in HADS depression subscale score and total score. Frequency, nocturia, bladder capacity, IC symptom and problem index scores, and pain score improved after 6 months of intravesical HA treatment. After HA treatment, 73% (n = 22) of patients showed improvement in their urological symptoms, but no significant changes were found in their HADS and PISQ-12 scores.
Conclusions: Bladder pain and lower urinary tract symptoms in patients with IC/BPS may improve after a 6-month intravesical HA treatment. However, no significant changes in their psychological and sexual functional scores were found.

Introduction

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic bladder condition characterized by urinary frequency, urgency and bladder pain in the absence of urinary tract infection or other identifiable pathology [1,2]. The diagnosis of IC/BPS is made based on clinical symptoms, cystoscopic findings, and exclusion of other bladder diseases [2–4]. The prevalence of IC/BPS is estimated to range from 0.01% to 2.3%, with the wide variation as a result of different study populations and various IC/BPS definitions [5–7]. The differences in definition also accounts for the difficulty in comparison of clinical studies and results.

In spite of unclear etiology, the pathogenesis of IC/BPS was discovered to involve the glycosaminoglycan layer of the bladder urothelium [8]. Hyaluronic acid (HA) is an important component of glycosaminoglycan [9], which has been used to treat IC/BPS for reconstruction of glycosaminoglycan in bladder mucosal defects.

The response of patients with IC/BPS to intravesical administration of HA was reported to be satisfactory [10–13]. Although IC/BPS is not a life-threatening disease, it may have a negative impact on patients' life qualities due to urological symptoms, sexual dysfunction [14,15], and psychological disorders [16–21]. Previous studies have demonstrated that many patients with IC/BPS experience depression and anxiety [16]; however, the therapeutic efficacy of intravesical therapy for symptoms of depression and anxiety in IC/BPS patients has rarely been reported. The present study was conducted to investigate urinary and psychological symptoms in patients with IC/BPS after intravesical HA treatment.

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Materials and methods

This was a prospective study conducted from August 2014 to July 2015 at a tertiary hospital. Institutional Review Board of the hospital approved this study protocol (No. 103-4793B). A written informed consent was obtained from every patient before participating in the study. Thirty consecutive patients newly diagnosed with IC/BPS according to the diagnostic criteria described in the European Society for the Study of Interstitial Cystitis guidelines were recruited [2]. A bladder biopsy was not routinely carried out but only performed for ruling out suspicious bladder pathology. Patients with urinary tract infection, chronic urinary retention, stress urinary incontinence and pelvic organ prolapse were excluded. None took any antidepressant or anti-anxiety drugs during the period of clinical and psychological evaluation. For a better evaluation of baseline mental health of all recruited subjects, a hospital anxiety and depression scale (HADS), an instrument for detecting states of depression and anxiety, was used for psychological evaluation before HA treatment [22]. All patients underwent a 6-month intravesical HA treatment regimen. The protocol of treatment included 4 weekly intravesical instillations of 40 mg/50 mL of HA solution (Cystistat®, Bioniche Teo., Inverin, Co. Galway, Ireland) followed by 5 monthly HA instillations. Patients were instructed to retain HA solution in the bladder for 60 min before voiding. The complete treatment duration was 6 months. Thirty age-matched asymptomatic women without any history of chronic inflammatory or pain conditions, chronic urinary disorders including IC/BPS, anxiety, depression or anti-inflammatory medication were recruited at out-patient department and used to serve as controls.

Pre-treatment evaluation included general and obstetric histories, urinalysis and urine culture, a 3-day voiding diary to assess functional bladder capacity, pelvic examination and cystoscopy. Cystoscopic hydrodistension was routinely performed at an intravesical pressure of 80 cm of water under anesthesia. Symptomatic and psychological changes at baseline and 1, 6 and 9 months after HA treatments were assessed by a single research nurse at out-patient department using several face-to-face questionnaires, which contained the HADS, the O'Leary-Sant index [23], the Pelvic Organ Prolapse/Urinary Incontinence Sexual Function Questionnaire (PISQ-12) [24], and a 10-point pain visual analog scale (VAS).

The HADS involves 2 subscales of anxiety (HADS-A) and depression (HADS-D). Each subscale contains 7 questions rated on a severity scale of 0–3. The 2 subscales can be summed to provide a total anxiety and depression score. O'Leary-Sant IC symptom index (ICSI) and problem index (ICPI) both include 4 questions that assess the severity of urgency, frequency of urination, nocturia and level of bladder pain in the previous 4 weeks. Each of the questions was rated on a severity scale of 0–5. The total scores for symptom and problem score were then calculated. The PISQ-12 contains 12 questions for assessment of sexual function rated on a severity scale of 0–5. Total scores of these questions were calculated at the same time. Treatment efficacy was analyzed based on the global response assessment [12,25]. At the timing of complete treatment (at 6 months) and 3 months after complete treatment (at 9 months), all patients were requested to rate their bladder symptoms compared with pre-treatment on a severity scale of 0–5 as worse, no change, slightly, moderately or markedly improved. Successful treatment outcomes were defined as moderately and markedly improved results after treatment. The terminology used in this study conforms to the recommendations by the International Continence Society [1].

Clinical data are presented as mean ± standard deviation or percentage according to the variables. Fisher's exact test was used to evaluate categorical data, and Wilcoxon rank-sum test was applied for continuous variables. Repeated measurement analysis was used for analysis of variables at different time-points. Statistical assessments were performed using SPSS version 20 for Windows (SPSS, Inc, Chicago, IL, USA). A p value of <0.05 was considered statistically significant.

Results

All 30 patients completed all the questionnaires before and after HA treatment, which were included for data analysis. Characteristics of patients are presented in Table 1. The mean age of 30 patients with IC/BPS at the start of treatment was 47 years (range 25–71). The mean of symptomatic duration was 4.5 years (range 1–11). There were no significant differences in variables between patients of IC/BPS and normal controls. However, patients with IC/BPS had a significant increase in HADS-D score and total HADS score, in comparison with the control group (Table 2). In Table 3, when compared with pre-treatment, frequency, nocturia, bladder capacity, VAS pain score, ICSI and ICPI were improved 6 months after HA treatment. Improvement of these symptoms may sustain up to 9 months after HA treatment. Patients with IC/BPS had a decrease in HADS scores and an increase in PISQ-12 score after HA treatment, but there were no significant differences in both scores between pre-treatment and post-treatment. Table 4 shows moderately or markedly improved responses in 22 (73.3%) patients at 6 months and 21 (70%) patients at 9 months after HA treatment.

Discussion

The American Urological Association guideline on IC/BPS suggests that treatment strategies should proceed by using conservative therapies first, which includes behavior modifications, physiotherapy techniques and oral medications [4]. Modifying certain behaviors may improve IC/BPS symptoms in some patients but no single behavior treatment has been found effective for the majority of patients with IC/BPS [4]. A randomized trial showed that although myofascial physiotherapy can provide pelvic muscular pain relief, it does not significantly improve frequency, urgency, the O'Leary-Sant and sexual function index [26]. Second-

Table 1
Patients' demographics.

	IC/BPS group (n = 30)	Control group (n = 30)	p value
	Mean ± SD	Mean ± SD	
Age	47.0 ± 10.5	46.4 ± 7.5	0.421
BH (cm)	156.6 ± 5.8	158.1 ± 5.6	0.324
BW (kg)	55.8 ± 9.5	58.6 ± 11.4	0.171
BMI	22.6 ± 3.3	23.7 ± 3.7	0.237
Parity	1.6 ± 1.2	1.7 ± 1.3	0.802
Menopause	40.0% (n = 12)	33.3% (n = 10)	0.566
Symptoms duration (y)	4.5 ± 5.6		

IC/BPS = interstitial cystitis/bladder pain syndrome; BH = body height; BW = body weight; BMI = body mass index.