Urological Science 24 (2013) 10–13

Contents lists available at SciVerse ScienceDirect

Urological Science

journal homepage: www.urol-sci.com

Original article

# Long-term treatment outcomes in patients with interstitial cystitis/painful bladder syndrome: 10-year experience in NCKUH

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ARTICLE INFO

*Article history:*
Received 29 February 2012
Received in revised form
11 April 2012
Accepted 10 May 2012
Available online 15 March 2013

*Keywords:*
bladder
hydrodistention
interstitial cystitis
pelvic pain

ABSTRACT

*Objective:* A retrospective review of long-term treatment outcomes for patients diagnosed with interstitial cystitis/painful bladder syndrome (IC/PBS) over a 10-year period.
*Materials and Methods:* Patients who were diagnosed with IC/PBS based on cystoscopic hydrodistention from 2001 to 2010 and thereafter received regular follow-up treatments were enrolled in this study. Clinical information was collected via a retrospective chart review. The following aspects were evaluated: treatment modalities and outcomes; symptom manifestation before and after treatments; and patients' perception on treatment effectiveness. The O'Leary–Sant Interstitial Cystitis Symptom Index (ICSI) and Interstitial Cystitis Problem Index (ICPI), and the Global Response Assessment Questionnaire were used as evaluation tools.
*Results:* A total of 54 patients with adequate clinical information were included for analysis in this study. The mean age was 38.11 ± 12.71 years and the female-to-male ratio was 3.15:1. The average follow-up duration was 30.61 ± 25.54 months. All patients had bladder or pelvic pain. Pretreatment urinary frequency and nocturia were 13.43 ± 5.09 times per day and 3.74 ± 2.18 times per night, respectively. Functional bladder capacity recorded from urinary diary was 228.1 ± 116.5 mL. Under anesthesia, bladder capacity at the start of a 10-minute therapeutic hydrodistention was 422.0 ± 197.5 mL, which increased to 542.9 ± 220.1 mL at the end of hydrodistention. No major complications were reported during and after the procedure. Additional treatments including oral medications and bladder instillation therapies were instituted in 98.1% of patients. Compared with pretreatment condition, the O'Leary–Sant ICSI and ICPI were decreased by 24% and 15.5%, respectively, after treatments. The subjective improvement rate, which was evaluated by the Global Response Assessment Questionnaire, was 81.6%.
*Conclusion:* Long-term continual treatments for IC/PBS are appreciated by most patients even though combinations of modalities are required and the improvements in symptoms and problems are only moderate.


## 1. Introduction

Interstitial cystitis/painful bladder syndrome (IC/PBS) is a disease of bladder pain characterized by urgency to urinate, frequent urination, nocturia, and dysuria. The disease causes serious impairment to quality of life in the affected patients. Clinically, the patients present with a wide spectrum of symptoms, physical examination findings, and clinical test responses.[1] According to the diagnostic inclusion and exclusion criteria established by the National Institute of Diabetes, Digestive and Kidney Diseases (NIDDK), bladder hydrodistention is a recommended test for the diagnosis of IC/PBS. Besides, a clinical guideline for IC/PBS developed by a group of East Asian urologists indicates that performing cystoscopy with hydrodistention is crucial and should be recommended for definitive diagnosis.[2] In contrast, according to the latest American Urological Association (AUA) guideline for IC/PBS, cystoscopy is not necessary for making the diagnosis in uncomplicated presentations. However, the procedure is still listed as a third-line treatment option for IC/PBS.[3]

Etiologies of IC/PBS are multifactorial and complicated. It has been postulated that interactions among urothelial, nervous, immunological, and endocrinological factors form a vicious cycle, provocating and maintaining inflammatory reactions in the bladder.[2] In accordance, a myriad of therapeutic modalities are developed based on the pathophysiological processes. According to the AUA guideline, the following six lines of treatment are

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1879-5226 
http://dx.doi.org/10.1016/j.urols.2013.01.005

suggested: (1) education, behavior modification; (2) pain management, oral medication (amitriptyline, cimetidine, hydroxyzine, or pentosan polysulfate), bladder instillation therapy (dimethyl sulfoxide, heparin, lidocaine); (3) cystoscopy/hydrodistention, ulcer fulguration; (4) neurostimulation; (5) cyclosporine, botulinum toxin A; and (6) major surgery (cystoplasty, diversion).[3]

Baseline and regular symptom severity assessments are essential to monitor clinical progress in patients with IC/PBS. Questionnaires for the evaluation of IC/PBS symptoms and patient well-being are widely used. Commonly used assessment tools are Global Response Index; O'Leary–Sant Interstitial Cystitis Symptom Index (ICSI), and Interstitial Cystitis Problem Index (ICPI) as well as Pain, Urgency, Frequency Symptom Scale. Kushner et al demonstrated that the Pain, Urgency, Frequency Symptom Scale and the O'Leary–Sant ICSI and ICPI were useful as both a screening tool and a treatment evaluation tool for IC/PBS.[3]

This study was aimed to report our experience with IC/PBS patients who had been diagnosed by cystoscopic hydrodistention and received long-term regular treatments. The O'Leary–Sant ICSI and ICPI, and the Global Response Assessment Questionnaire were used as evaluation tools.

## 2. Materials and methods

From January 2001 to March 2011, patients who were diagnosed with IC/PBS after hydrodistention and received regular follow-up treatments in the National Cheng Kung University Hospital (NCKUH) were retrospectively enrolled in this study. The diagnosis of IC/PBS was made according to the NIDDK criteria.[4] The cystoscopic criteria for diagnosis included presence of Hunner's ulcer or diffuse glomerulations over three quadrants of the bladder after hydrodistention. Under spinal or general anesthesia, diagnostic hydrodistention was performed under a hydrostatic pressure of 80 $cmH_2O$ for 2 minutes. Therapeutic hydrodistention was then performed under the same pressure for another 10 minutes if the cystoscopic findings were compatible with IC/PBS. Besides hydrodistention, combination treatments with oral analgesics, pentosan polysulfate, and bladder instillation with heparin or hyaluronic acid were administered on a case-by-case basis.

The study was conducted and completed in July 2011. The clinical information was collected via a chart review and included a detailed evaluation of history, results of physical examination, urinalysis, urine cytology, and 48-hour frequency–volume chart (FVC) before treatment. Numbers of frequency, nocturia, and functional bladder capacity were measured from the FVC. The O'Leary–Sant ICSI and ICPI were used to assess the treatment outcomes. IC symptom and problem severities before and after treatment were compared. In addition, the Global Response Assessment Questionnaire was used to evaluate the overall treatment perception.

Statistical analysis was performed by Student's $t$ test for comparisons between the two groups. A probability $p < 0.05$ was considered statistically significant.

## 3. Results

During the study period, a total of 73 patients were diagnosed with IC based on hydrodistention in NCKUH, and 19 patients were excluded due to incomplete clinical data. Fifty-four patients were enrolled in this study and the basic clinical information was showed in Table 1. In the study group, 41 patients were female, which gave a female-to-male ratio of 3.15:1. Average daytime frequency and nocturia were 13.43 and 3.74 times per day. Mean functional bladder capacity was 228.1 mL. Combination treatments after hydrodistention were needed in 98.1% patients (Table 2). Oral pentosan polysulfate (Elmiron 100 mg tid), bladder instillation of heparin (25,000 units in 30 mL of normal saline), and bladder instillation of hyaluronic acid (Cystistat 50 mL) were given in 81.5%, 59.3%, and 46.3% patients, respectively. More than one form of combination treatment modalities were needed in the majority of patients.

**Table 1**
Basic information of patients and voiding diary before treatment ($n = 54$).

| | Mean | Median | SD | Range |
|---|---|---|---|---|
| Age (y) | 38.11 | 35.50 | 12.71 | 17–72 |
| Follow-up duration (mo) | 30.61 | 26.50 | 25.54 | 3–122 |
| Functional bladder capacity (mL) | 228.1 | 220.0 | 116.5 | 30–500 |
| Daytime frequency | 13.43 | 12.0 | 5.09 | 6–40 |
| Nocturia | 3.74 | 3.0 | 2.18 | 1–10 |

mo = months; y = years.

The immediate effect of the 10-minute therapeutic hydrodistention on bladder capacity is shown in Table 3. Average bladder capacity at the start of the 10-minute hydrodistention was 422 mL, which gradually increased by 120.9 mL during the course of therapeutic hydrodistention. No major adverse event such as bladder rupture occurred. Mild gross hematuria was noted in almost all patients and they generally recovered within 1 day.

Questionnaire information was obtained from 38 patients. The average O'Leary–Sant ICSI and ICPI scores before treatment were 16.95 and 14.29, respectively. After treatments, both scores were significantly reduced by 24% and 15.5%, respectively (Table 4). In contrast, 31 patients reported slight or moderate improvements in Global Response Assessment scores, giving an overall positive perception rate of 81.6% for long-term treatments (Fig. 1).

## 4. Discussion

IC/PBS is a chronic, debilitating disease mainly affecting women, while there are reports that the disease affects men and children as well. Characteristic clinical presentations are urinary urgency and frequency as well as chronic bladder pain but without any evidence of bacterial infection. Many patients with IC/PBS have a very poor quality of life for many years. However, IC is an enigmatic disorder surrounded by controversies. The etiology is unknown, the pathophysiology remains uncertain, and the efficacy of treatment regimens is questionable.[5] One current issue of debate concerning IC is the need of diagnostic hydrodistention. In the early 20$^{th}$ century, it was considered mandatory to see the typical Hunner's ulcers for diagnosing IC. Although urologists are no longer seeking Hunner's ulcers, petechial hemorrhages or glomerulations in the bladder after hydrodistention have become the hallmark of diagnosis. However, evidence has cast doubts on the specificity of glomerulations in the diagnosis of IC. Waxman et al assessed 20 asymptomatic women undergoing tubal ligation and showed similar hydrodistention findings as in patients with IC.[6] In the NIDDK

**Table 2**
Additional treatment modalities after hydrodistention ($n = 54$).

| | Patients | Percentage |
|---|---|---|
| Treatments | | |
| Pentosan polysulfate | 44 | 81.5% |
| Heparin | 32 | 59.3% |
| Hyaluronic acid | 25 | 46.3% |
| Number of treatments | | |
| 0 | 1 | 1.9% |
| 1 | 20 | 37.0% |
| 2 | 18 | 33.3% |
| 3 | 15 | 27.8% |