

Original Article

## Hydrodistention plus bladder training versus hydrodistention for the treatment of interstitial cystitis

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Accepted 14 September 2012

### Abstract

**Objective:** To assess the efficacy of hydrodistention (HD) followed by bladder training (BT) versus HD alone in patients with interstitial cystitis (IC).

**Methods:** A total of 70 patients with IC were included and randomly assigned to two groups: one treated with HD (HD group) and the other treated with HD plus BT (HD plus BT group). Each patient was followed up using a weekly diary for 8 weeks after HD and monthly thereafter for 6 months after HD. Evaluation parameters included age, duration of IC in years, how many doctors visited before treatment, urgency, bladder pain, daytime voided volume per void, nocturnal volume per void, daytime voids per day, and nocturia per day.

**Results:** Age, duration of IC in years, doctors visited before treatment, and voiding profiles of patients before treatments between the two groups did not show statistical significance. However, at 24 weeks after HD, the proportions of urgency, and bladder pain of the HD group versus the HD plus BT group were 43.48% versus 10.71% ( $p = 0.008$ ), and 34.78% versus 14.29% ( $p = 0.086$ ), respectively. Concurrently, the mean  $\pm$  standard deviation of daytime voided volume per void, nocturnal volume per void, daytime voids per day, and nocturia per day of the HD group and HD plus BT group are  $212.2 \pm 114.2$  mL and  $300.1 \pm 90.2$  mL ( $p = 0.005$ ),  $276.8 \pm 113.0$  mL and  $360.0 \pm 129.6$  mL ( $p = 0.018$ ),  $8.2 \pm 3.2$  and  $6.2 \pm 1.4$  ( $p = 0.010$ ), and  $2.2 \pm 1.2$  and  $1.5 \pm 0.7$  ( $p = 0.019$ ), respectively.

**Conclusion:** HD followed by BT produced a statistically significantly better effect than HD alone in the treatment of patients with IC.

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**Keywords:** bladder training; hydrodistention; interstitial cystitis; lower urinary tract symptoms; nocturia; painful bladder syndrome; urgency urinary frequency

### Introduction

Interstitial cystitis (IC) had been described as a chronic multifactorial bladder disease of unknown etiology. It is characterized by suprapubic pain, urinary frequency, urgency, and nocturia. The consensus on the best available treatment for

this disease is lacking [1]. Treatment of IC is currently based on empiricism. There are multiple forms of therapy available for the treatment of IC, including self-care, behavior therapies, oral medication, intravesical therapy, hydrodistention (HD), sacral neuromodulation, and surgery.

Normal bladder capacity is usually stated as 400–600 mL. Larsson and Victor [2] reported the mean of largest voided volume was 460 mL in a study of 151 healthy women over 2 days. Patients with IC usually have a bladder with a reduced capacity of 350 mL or less, which is caused partially by sensory urgency and also frequent voiding of low volumes.

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These two factors result in the bladder entering a state of disuse and atrophy [3]. The famous words “use or disuse” by French biologist La March (1744–1829) may help to explain the reduced bladder capacity in patients with IC.

The efficacy of HD of the bladder for the treatment of IC has been known since 1930 [4]. In that study, Bumpus [4] reported that bladder HD improved the symptoms of IC and, as a result, this procedure has been a mainstay of IC patient therapy ever since. However, there is little evidence of HD's long-term efficacy despite most doctors relying on this therapy. Most studies of HD for patients with IC revealed a short-term effect. Therefore, HD is an efficient therapy that can enlarge a patient's bladder, although not for an extended period of time [5–7]. However, none of these studies show patient education on bladder therapy (BT), neither before HD nor during outpatient department (OPD) follow-up after HD treatment. Nevertheless, Hsieh et al [8] showed that HD followed by BT, when there was good patient compliance, was able to produce outcomes with both a good efficacy and long-term benefits. Hence, the hypothesis of this study is that treatment with HD followed by BT with good patient compliance may have a long-term efficacy in the treatment of patients with IC. This study tries to evaluate whether post-HD BT is able to restore functional bladders in patients with IC and reverse their problems with small-capacity bladders.

## Methods

From January 2009 to December 2011, 70 patients with IC according to the criteria of the National Institute of Diabetes, Digestive and Kidney Disease were prospectively included and randomly assigned to two groups after HD treatment: HD only (HD group) or HD plus BT (HD plus BT group). The diagnosis of IC was made based on clinical symptoms, a complete history, physical examination, routine laboratory tests of urine, 3 days of voiding diary entries, and urodynamic study. Furthermore, cystoscopy with HD under intravenous general anesthesia and a bladder biopsy were performed. During HD, the patient's bladder was filled with normal saline to maximal capacity at the pressure of 80 H<sub>2</sub>O. The full bladder was then drained and emptied immediately. HD was not repeated after the bladder had been drained. The bladder was inspected during the course of cystoscopy to check for any abnormalities and the presence of glomerulations. The procedures were performed and completed in the OPD and all patients then went home after HD.

This study does not include a statement regarding institutional review board approval because HD and BT are well-recognized and effective short-term treatment modules for IC. However, all patients were informed of the nature and purpose of this study and each had to provide oral and written informed consent before enrollment. Those who did not provide informed consent were excluded from the study, but they were still treated with HD plus BT.

All patients were asked to complete voiding diaries during weekly follow-up during the 8 weeks after the HD treatment. Thereafter, they came back to the OPD for follow-up once a month and this process also included a diary. At the OPD, both before and after HD, all patients and their accompanying family members were educated by the same physician about the characteristics of IC and the details of how to create the voiding diary. The HD plus BT group also received education on the details of how to conduct BT. The BT guidelines involved asking the patient to drink water or other fluids gradually, at a speed of 150–200 mL/hour except during mealtimes and at night. They underwent self-scheduled voiding BT, aiming to increase the time interval between two voids and also to increase each voided volume. At the first OPD education session following HD, the patients were recommended to start the average time interval between voids for at least 2 hours. Once they have achieved this interval successfully for most of the voids, they were recommended to increase this interval by 15 minutes weekly. However, patients were allowed to use the toilet if the sensation of urgency became intolerable. The aim was to eventually be able to have at least 3 hours between voids at 2 months post-HD. The exclusion criterion of this study was nonadherence to diary keeping. Those who could not come back for OPD follow-up or could not provide the diaries were excluded from this study. There were 12 and 7 patients who were dropped from the study from the HD group and HD plus BT group, respectively.

The International Continence Society (ICS) in 2002 promulgated widely accepted definitions for urgency, bladder pain, urethral pain, vaginal pain, daytime frequency, and nocturia [9]. The lower urinary tract symptoms evaluated and mentioned in this study adopt the ICS definition. The clinical symptoms and voiding profiles of all patients were compared to evaluate the efficacy of treatment between the HD group and the HD plus BT group. Both *t*-statistic and *z*-statistic are used to test the differences of the two group means and group proportions respectively. For continuous quantitative data, normal distributions are assumed and *t*-statistic is used to test the mean difference. For binary response variables, the

Table 1  
Age, years suffered from IC and doctors visited of the patients of the two groups.

Parameter	Mean (SD) of the group		<i>t</i> -Statistic	df	<i>p</i>	95% CI of mean (CS + HD) – mean (CS + HD + BT)
	CS + HD ( <i>n</i> = 35)	CS + HD + B T ( <i>n</i> = 35)				
Age (y)	46.1 (7.6)	45.9 (7.8)	0.1086	67	0.914	(–3.474, 3.874)
Years with IC	3.5 (1.6)	3.8 (1.4)	–0.8348	66	0.407	(–1.017, 0.417)
Doctors visited	2.8 (1.9)	2.9 (1.7)	–0.232	67	0.817	(–0.96, 0.76)

BT = bladder training; CI = confidence interval; CS = cystoscopy; df = degrees of freedom; HD = hydrodistention; SD = standard deviation.

Table 2  
Urgency and pain among IC patients of the two groups before HD.

Symptom	Number (%) of the group		z-Statistic	p	95% CI of proportion (CS + HD) – proportion (CS + HD + BT)
	CS + HD (n = 35)	CS + HD + BT (n = 35)			
Urgency	24 (68.57)	26 (74.29)	−0.5292	0.597	(−0.268, 0.154)
Pain as bladder is full	31 (88.57)	29 (82.86)	0.6831	0.495	(−0.106, 0.221)
Bladder	15 (42.86)	16 (45.71)	−0.2406	0.810	(−0.261, 0.204)
Urethra	10 (28.57)	8 (22.86)	0.5469	0.584	(−0.147, 0.261)
Vagina	4* (11.43)	4* (11.43)	0	1	(−0.149, 0.149)

BT = bladder training; CI = confidence interval; CS = cystoscopy; HD = hydrodistention.

\* The fact that the expected cell counts less than 5 may inflate the chance of wrong decision.

asymptotic z-statistic is used to test population proportions between groups. All statistical analyses were made using Excel. A *p* value <0.05 is considered to be statistically significant.

## Results

The mean ages of the HD group and the HD plus BT group were  $46.1 \pm 7.6$  and  $45.9 \pm 7.8$  years, respectively (Table 1). There was no statistically significant difference between the mean ages of these two groups. Neither were there significant differences regarding how many years the patients had IC and how many doctors they had visited before treatment between the HD group and the HD plus BT group.

Table 2 shows that full bladder pain, including bladder, urethral, and vaginal pain, was approximately 85% among the patients with IC before treatment, and there was no statistically significant difference between the two groups. In addition, at 24 weeks after HD, bladder pain as full still did not show a statistically significant difference between these two groups, although improvement of pain was more effective in the HD plus BT group as compared to the other (Table 3). Even though there is not a statistically significant difference regarding urgency between the HD plus BT group versus the HD group before HD (Table 2), HD plus BT demonstrated a significant improvement in urgency compared to HD in the treatment of IC at 24 weeks after HD (Table 3).

Similarly, there were no statistically significant differences in voided volumes (neither daytime nor nocturnal), urinary frequency, or nocturia observed between these two groups prior to treatment (Table 4). However, combining HD with BT was followed by a significant increase in both daytime and

nocturnal voided volumes, and a significant reduction in both daytime voiding frequency and nocturia compared with the HD group (Table 5).

## Discussion

The cause of IC is not well-understood, although it is thought to be a long-standing and chronic progressive inflammatory bladder disease that results in a bladder with small capacity. Patients in this study had persistent symptoms for a mean of more than 3.5 years in duration despite having visited about three doctors before treatment. Most patients in this study had already undergone a number of therapies, including antibiotics, analgesic agents, antimuscarinic agents, and intravesical instillations. However, their IC symptoms still persisted and deteriorated. Hence, public health education to make the patient aware of this disease in order to make earlier diagnoses of IC is crucially important to improving treatment outcomes.

There were 12 patients in the HD group and seven patients in the HD plus BT group who could not return for OPD follow-up or could not provide the urinary diaries. The main reasons patients dropped out of this study were inability to create a diary due to poor education, subjectively symptomatic improvement a few weeks after OPD follow-up, unwillingness to follow up due to transportation issues, the “annoyance factor” of BT, misunderstandings regarding IC, and lack of time.

A type of disuse/atrophy effect seems to happen with the bladders of patients with IC and this effect results in the bladders of the patients having small capacities. Hence, this suggests that “use or disuse” is likely to be one of the

Table 3  
Urgency and pain among patients with IC of the two groups at 24 weeks after HD.

Symptom	No (%) of the group		z-Statistic	p	95% CI of proportion (CS + HD) – proportion (CS + HD + BT)
	CS + HD (n = 23)	CS + HD + BT (n = 28)			
Urgency	10 (43.48)	3 (10.71)	2.6715	0.008	(0.095, 0.56)
Pain as bladder is full	8 (34.78)	4* (14.29)	1.7171	0.086	(−0.029, 0.439)
Bladder	4* (17.39)	1* (3.57)	1.6515	0.099	(−0.031, 0.308)
Urethra	3* (13.04)	1* (3.57)	1.252	0.211	(−0.059, 0.249)
Vagina	1* (4.35)	0* (0.00)	1.1143	0.265	(−0.04, 0.127)

BT = bladder training; CI = confidence interval; CS = cystoscopy; HD = hydrodistention.

\* The fact that the expected cell counts less than 5 may inflate the chance of wrong decision.

Table 4  
Voiding profiles of patients with IC of the two groups before HD.

	Mean (SD) of the group		<i>t</i> -Statistic	df	<i>p</i>	95% CI of mean (CS + HD) – mean (CS + HD + BT)
	CS + HD ( <i>n</i> = 35)	CS + HD + BT ( <i>n</i> = 35)				
Voided volumes (ml)						
Daytime	112.1 (46.5)	110.5 (47.0)	0.1432	67	0.887	(–20.706, 23.906)
Nocturnal	173.0 (91.7)	172.4 (92.3)	0.0273	67	0.978	(–43.297, 44.497)
Number of voids						
Daytime frequency	14.5 (10.0)	14.2 (11.0)	0.1194	67	0.905	(–4.716, 5.316)
Nocturia	2.8 (1.7)	2.9 (1.6)	–0.2534	67	0.801	(–0.888, 0.688)

BT = bladder training; CI = confidence interval; CS = cystoscopy; df = degrees of freedom; HD = hydrodistention; SD = standard deviation.

mechanisms of IC pathophysiology. Therefore, the treatment strategy for IC in this study was to help patients cope with their IC symptoms by means of reversing the bladder from a state of disuse/atrophy into a functional state, and then subsequently training them to increase the duration of the time between voids to obtain a long-term effect. The theory about HD plus BT for the treatment of IC patients is similar to that of correcting patients with hunchbacks: the patient has to maintain a straight and upright posture continuously after treatment/rehabilitation at hospital. Hence, the implementation of BT is seen to be important for long-term remission of symptoms for patients with IC undergoing treatment.

Parsons and Koprowski [10] reported successful management of IC by progressively increasing urinary voiding intervals. Within 3 months, 71% of patients with IC who were able to retrain their voiding patterns experienced successful management of their symptoms, reporting a 50% decrease in their symptoms of urinary urgency, frequency, and nocturia, as well as a significant increase in bladder capacity and decrease in average daily voids. In addition, another study confirmed the efficacy of behavior therapy in selected patients with IC, including increasing the intervoiding interval, after a mean of 12 weeks [11]. Both of the studies revealed that behavioral therapy, including BT, improved symptoms in more than one half of the patients with IC.

Because the etiology of IC is thought to be multifactorial, multimodal therapies might be performed once an individual treatment does not result in significant remission of the symptoms. Both HD and BT have been shown to obtain a short-term effect in the treatment of IC. However, the long-term effect of BT after HD was still not clear before this study even though Hsieh et al [8] had reported a long-term effect of HD followed by BT for the treatment of IC. During this study,

the authors found it was more complicated and difficult to properly educate patients about BT and how to create a voiding diary than to simply perform HD in the outpatient setting.

Micturition patterns are usually based on common beliefs and education, and a woman tends to use her own voiding pattern as a standard. However, a behavior therapy such as BT involves providing information on how the bladder works, and learning new patterns of response to urine storage and new patterns of voids, or reestablishing previously learned voiding patterns to match normal patterns. Furthermore, BT is a method in which patients can become aware of voiding patterns, correct and modify bad voiding habits, and learn voluntary control of their bladder, which then makes it possible to help patients with IC to cope with the disease. Hence, it is crucially important for the physician to help patients with IC understand that the efficacy of this treatment depends on their own willpower and compliance with the physician's advice. Therefore, treatment of IC by BT depends on motivated and compliant patients, and thus may need time to regain normal bladder function.

The advantage of BT is that it does not have any side effects and it may result in long-term efficacy. Therefore, therapeutic intervention by BT after HD for IC will be efficacious if the pathophysiology of IC is similar to that of hunchback. Indeed, this study does show that adequate HD combined with subjective BT would be able to reverse the bladder from a state of disuse/atrophy into a functional state. In addition, the implementation of HD and BT is crucial for long-term remission among patients with IC. Thus, HD of the bladder and subsequent BT should be recommended as the first choice of treatment for patients with IC because it provides significant remission and it is a simple and conservative therapy, and it avoids the need for extirpative surgery.

Table 5  
Voiding profiles of patients with IC of the two groups at 24 weeks after HD.

	Mean (SD) of the group		<i>t</i> -Statistic	df	<i>p</i>	95% CI of mean (CS + HD) – mean (CS + HD + BT)
	CS + HD ( <i>n</i> = 23)	CS + HD + BT ( <i>n</i> = 28)				
Voided volumes (mL)						
Daytime	212.2 (114.2)	300.1 (90.2)	–3.0016	41	0.005	(–147.042, –28.758)
Nocturnal	276.8 (113.0)	360.0 (129.6)	–2.4481	48	0.018	(–151.533, –14.867)
Number of voids						
Daytime frequency	8.2 (3.2)	6.2 (1.4)	2.7863	28	0.010	(0.53, 3.47)
Nocturia	2.2 (1.2)	1.5 (0.7)	2.4732	33	0.019	(0.124, 1.276)

BT = bladder training; CI = confidence interval; CS = cystoscopy; df = degrees of freedom; HD = hydrodistention; SD = standard deviation.

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