

Novel Treatment for Interstitial Cystitis Pilot Study

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Abstract

Background and aims: Use of platelet-rich plasma (PRP) is well established in treatment of orthopedic patients. This pilot study aims to determine the efficacy of using instillation of PRP paired with hydrodistention of the bladder to treat patients with interstitial cystitis (IC).

Methods: Patients with a diagnosis of interstitial cystitis were recruited to this study. Patients completed Pelvic Pain and Urgency/Frequency (PUF) patient symptom scale, which quantified a symptom and bother score. Patients were treated with hydrodistention with instillation of PRP. Patients completed the PUF questionnaire weekly for six weeks following treatment.

Results: 12 patients underwent hydrodistention with instillation of PRP. The patients were all women, ranging in age from 23 to 71. The mean symptom score went from 13.167 to 7.417 and the mean bother score decreased from 6.833 to 4.41, showing a statistically significant reduction in symptom and bother scores.

Conclusions: Hydrodistention with instillation of PRP is an effective treatment of interstitial cystitis.

Keywords: Interstitial cystitis, Platelet-rich plasma, Hydrodistention, Chronic pelvic pain, Urinary incontinence, Painful bladder syndrome, Nocturia

Introduction

Interstitial cystitis (IC) is a bladder disorder with unknown etiology [1]. The most commonly accepted theory is that a defect in the glycosaminoglycan layer of the bladder urothelium allows solutes in the urine to penetrate through the urothelium into the bladder interstitium which causes an inflammatory reaction [1]. This theory is supported by a study which shows increased absorption of lactulose into the bloodstream of patients who have interstitial cystitis compared to controls [2]. A previously published study showed that platelet-rich plasma (PRP) was an effective therapy for interstitial cystitis when injected in multiple areas of the bladder transurethrally with cystoscopic guidance [3]. In accordance with the University of Virginia Ethical Principles for the Protection of Human Subjects of Biomedical Behavioral Research we adhered to the three principles underlying the ethical conduct of research: respect for persons, beneficence, and justice. Consent was obtained from all participants.

Materials & Methods

12 patients with a diagnosis of interstitial cystitis for over one year were recruited to this study. The patients signed informed consents which discussed the risks of the procedure, including the unknown risk of a new procedure and the novel nature of the procedure that was not FDA-approved. Patients were also made aware of similar studies performed in the field of orthopedics. The patients were recruited from a private practice. All patients were women, ranging in age from 23 to 71. All patients had cystoscopy performed which confirmed no foreign bodies or signs of malignancy or abnormalities not associated with interstitial cystitis—such as glomerulations, squamous metaplasia of the trigone, and urethral erythema. The patients had previous unsuccessful treatments with usual interstitial cystitis care, including avoidance of bladder irritants, treatment of comorbid conditions, including anxiety, depression, fibromyalgia, and endometriosis, and use of medications, including amitriptyline, pentosan polysulfate

Please circle the answer that best describes how you feel for each question.

		0	1	2	3	4	SYMPTOM SCORE	BOTHER SCORE
1	How many times do you go to the bathroom during the day?	3-6	7-10	11-14	15-19	20+		
2	a. How many times do you go to the bathroom at night?	0	1	2	3	4+		
	b. If you get up at night to go to the bathroom, does it bother you?	Never Bothers	Occasionally	Usually	Always			
3	a. Do you now or have you ever had pain or symptoms during or after sexual intercourse?	Never	Occasionally	Usually	Always			
	b. Has pain or urgency ever made you avoid sexual intercourse?	Never	Occasionally	Usually	Always			
4	Do you have pain associated with your bladder or in your pelvis (vagina, labia, lower abdomen, urethra, perineum, testes, or scrotum)?	Never	Occasionally	Usually	Always			
5	a. If you have pain, is it usually		Mild	Moderate	Severe			
	b. Does your pain bother you?	Never	Occasionally	Usually	Always			
6	Do you still have urgency after going to the bathroom?	Never	Occasionally	Usually	Always			
7	a. If you have urgency, is it usually		Mild	Moderate	Severe			
	b. Does your urgency bother you?	Never	Occasionally	Usually	Always			
8	Are you sexually active? Yes _____ No _____							
SYMPTOM SCORE = (1, 2a, 3a, 4, 5a, 6, 7a)								
BOTHER SCORE = (2b, 3b, 5b, 7b)								
TOTAL SCORE (Symptom Score + Bother Score) =								

Figure 1. PUF Questionnaire.

sodium, phenazopyridine, and methenamine. During preoperative appointment patients filled out a Pelvic Pain and Urgency/Frequency (PUF) patient symptom scale (Figure 1) [4].

All patients in the study underwent hydrodistention of the bladder with intravesical instillation of PRP with anesthesia. 50 ml of peripheral blood was drawn prior to the procedure and separated using centrifugation to obtain the platelet-rich plasma. Under general anesthesia the bladder was distended to a maximum cystometric capacity, which ranged from 200 ml to 750 ml, using a pressure of 80 cm of water. The bladder was distended for three minutes and then drained with the cystoscopic sheath. Then 20 ml of platelet-rich plasma was instilled into the bladder using the cystoscopic sheath and was flushed with 10 ml of saline. The sheath was then removed. The patient was instructed to not void for two hours. The patient was recommended to continue with usual IC care, including avoiding dietary bladder irritants. All patients filled out Pelvic Pain and Urgency/Frequency patient symptom

questionnaires weekly for six weeks after the procedure. A historical control was compared from a previous usual care treatment of hydrodistention in a one to three ratio.

Results

A total of 12 women between the ages of 23 and 71 completed the PUF questionnaires weekly for 6 weeks. The responses were analyzed and showed a statistically significant improvement in the symptom and bother scores from their preoperative responses to the six-week post-procedure responses. Symptom scores before and six weeks after treatment were statistically significant with the average symptom score of 12 before treatment and average symptom score of 5 after treatment, showing with paired t-tests a P-value of 0.001101 (Figure 2).

There was also convincing statistical evidence to conclude that the treatment is effective in reducing patients' bothersome score after six weeks, with a P-value of 0.007 (Figure 3).

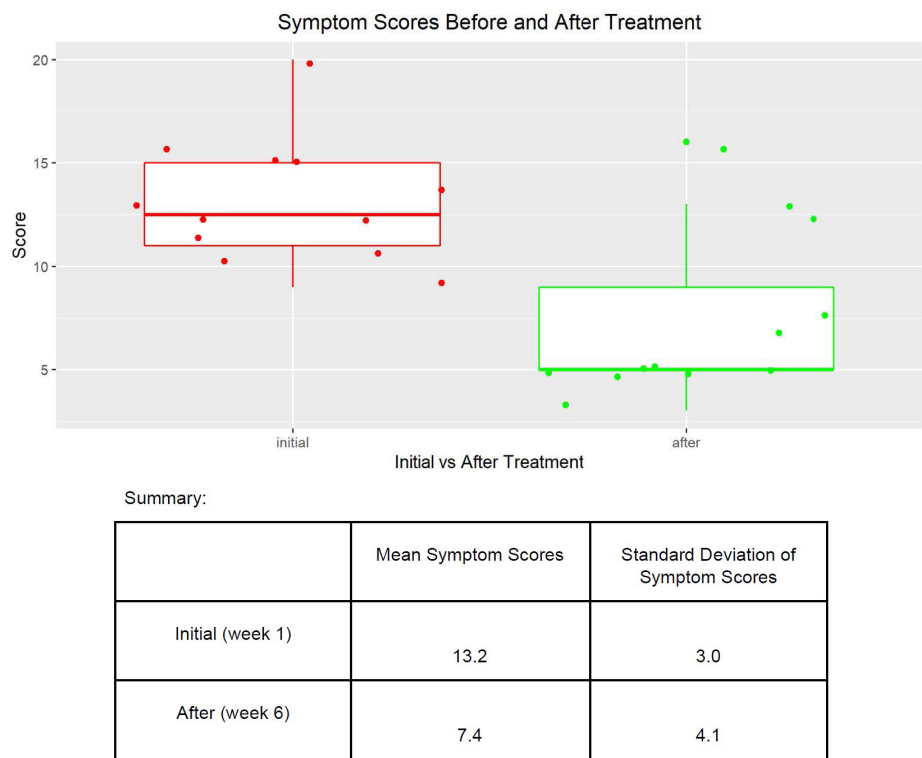


Figure 2. Symptom scores before and after treatment.

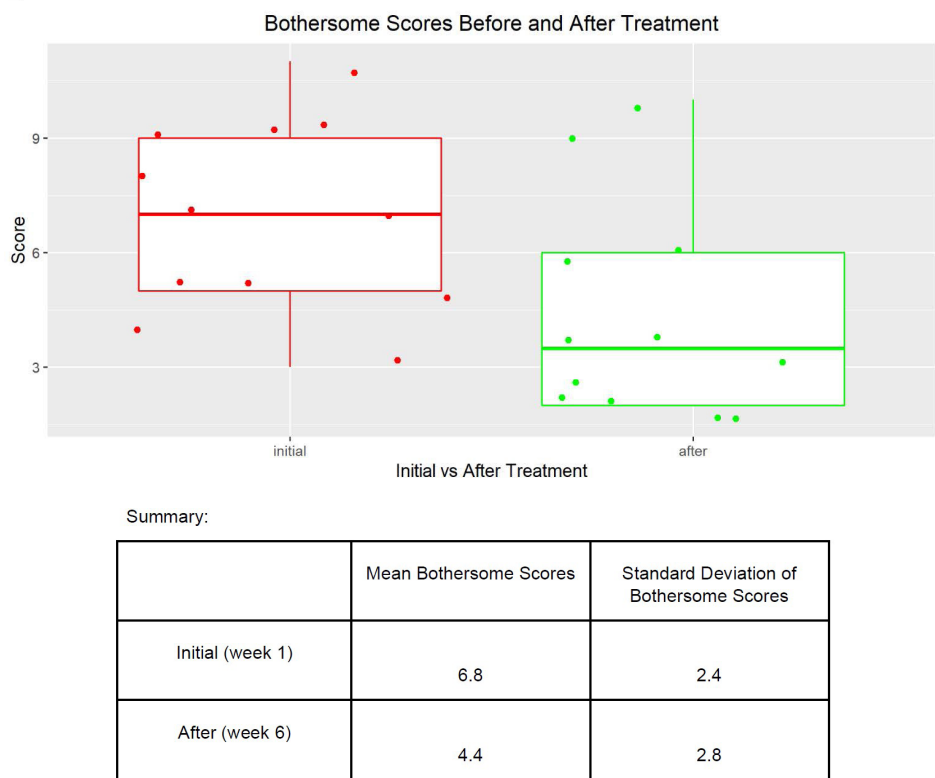
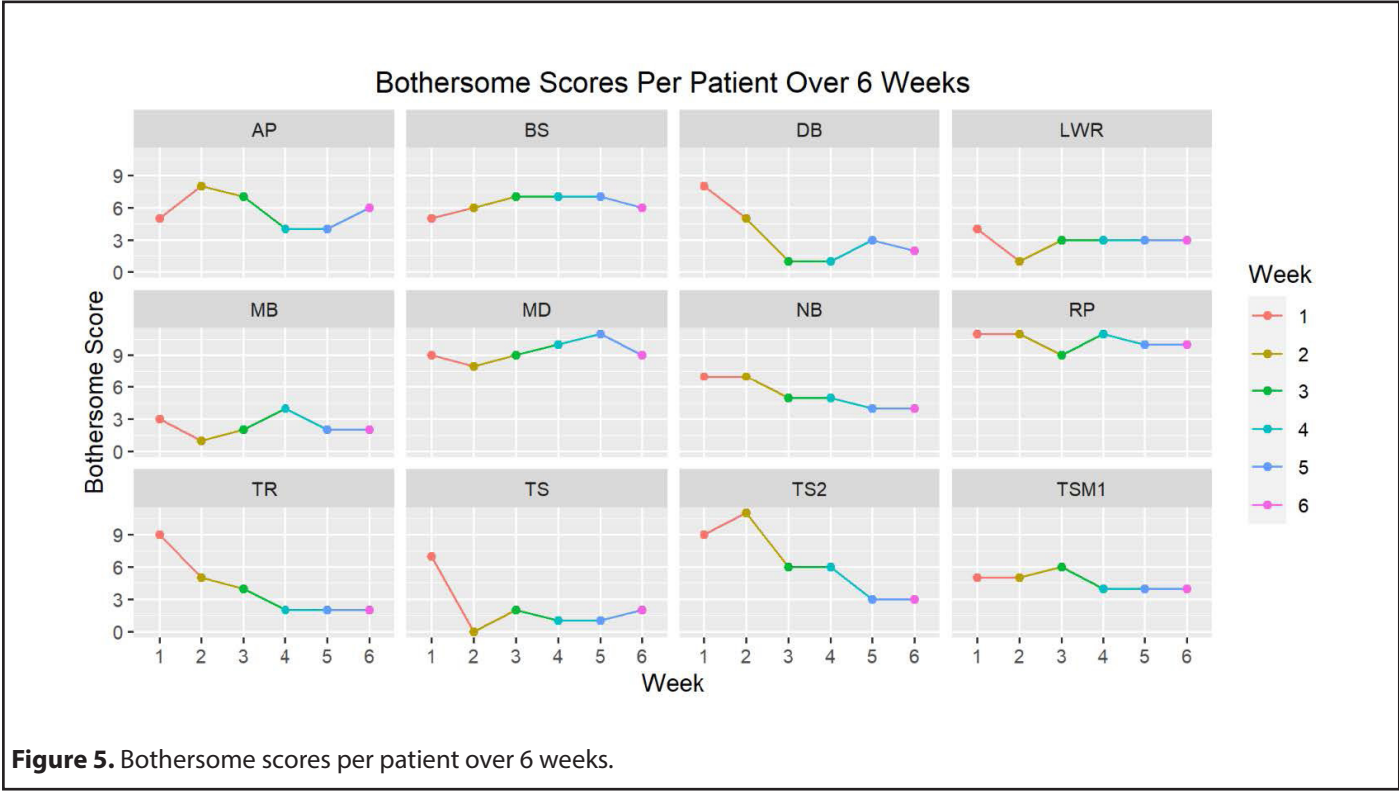
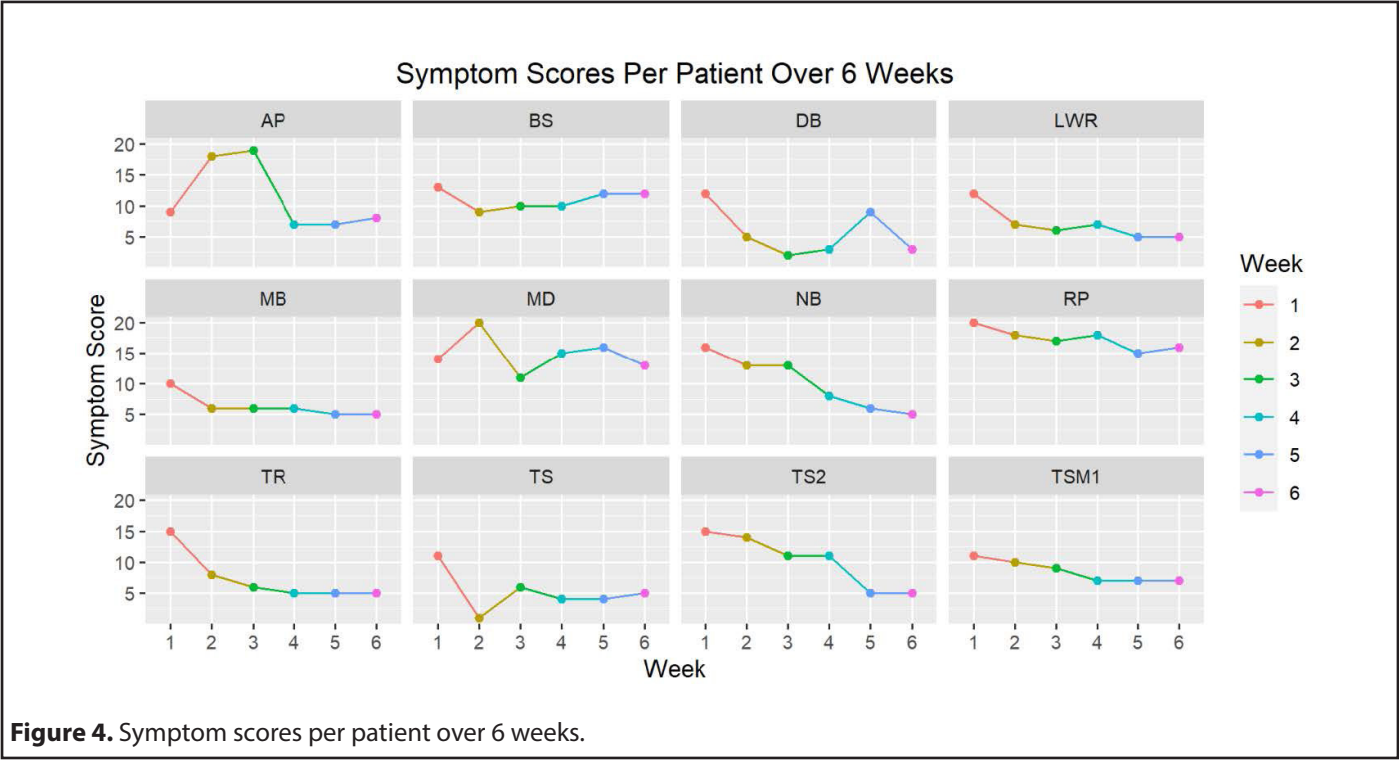


Figure 3. Bothersome scores before and after treatment.

Figures 4 and 5 demonstrates the change in symptom and bother scores over the six-week study period. Individual patients experienced improvement in symptom and bother scores. Of note the patient labeled MD was not able to comply with the posttreatment course of avoiding alcohol.

Discussion

The treatment of 12 patients with longstanding interstitial cystitis with hydrodistention with instillation of platelet-rich plasma shows statistically significant evidence of efficacy in



relieving symptoms of IC over a six week course. The previously published case study by the author suggested people who have anxiety or high stress are in a constant “fight or flight” mode which prevents adequate perfusion of the bladder and decreases growth factors [5]. This deferred maintenance could be the etiology of the defect in the glycosaminoglycan layer of the urothelium in patients with IC. This therapy is supported by articles in the medical literature which shows the role of serotonin in the function of the gastrointestinal and genitourinary organ systems. High levels of stress decreases serotonin in the central nervous system and in the peripheral nervous system [6]. With increased stress, blood flow is diverted away from organs such as the bladder. Women who have anxiety or high stress and low levels of serotonin perceive the pain as more intense [6]. Intravesical instillation of platelet-rich plasma provides growth factors to the urothelium and encourages healing and repair of the defects in the

umbrella cells of the urothelium and the glycosaminoglycan layer. Once the layer is repaired and barrier integrity is restored, the inflammation decreases and the pain decreases. The procedure is done by first performing hydrodistention, which many times leads to terminal hematuria from the defective urothelium. The bladder is then drained, and the platelet-rich plasma is instilled in the bladder. After the procedure is performed, the patients are instructed to avoid bladder irritants strictly for two weeks to encourage complete healing of the urothelium.

In previous studies hydrodistention showed that stretching of the bladder increased urinary heparin-binding epidermal growth factor and reduced antiproliferative factor in patients with interstitial cystitis [7]. Normal bladder stretch of detrusor smooth muscle cells is known to stimulate heparin-binding epidermal growth factor. However, an antiproliferative factor in patients with IC inhibits urothelial proliferation. Patients with IC also have decreased levels of heparin-binding epidermal growth factor [8].

Unfortunately, this procedure is not permanent. It has been shown to be effective in some patients for up to one year. This initial study requires further study and, eventually, a randomized control study comparing a control group to a treatment group receiving hydrodistention with PRP.

Conclusions

This pilot study concludes that hydrodistention with intravesical instillation of PRP is an effective treatment for female patients with longstanding interstitial cystitis symptoms. Randomized controlled study is needed to confirm these initial findings.

Conflict of Interest

The author has no conflicts of interest.

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