

# Chronic scrotal pain: A variable symptom of interstitial cystitis/bladder pain syndrome

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## Abstract

**Objective:** Treatment of chronic idiopathic scrotal pain is a dilemma and challenge. Many men with this condition undergo multiple therapies and surgeries with no improvement in their symptoms. Patients with interstitial cystitis/bladder pain syndrome (IC/BPS) have a variable clinical presentation and initially complain of only one symptom of urinary urgency, frequency, or pain. We report on patients with chronic idiopathic scrotal pain treated with standard therapy for IC/BPS.

**Patients and Methods:** Patients with chronic idiopathic scrotal content pain were evaluated, determined to have chronic idiopathic scrotal content pain, and were treated with either pentosan polysulfate sodium (PPS) or bladder instillations of alkalinized lidocaine and heparin.

**Results:** Sixteen males were determined to have chronic idiopathic scrotal pain. Eight males received PPS and eight males received a bladder instillation of alkalinized lidocaine and heparin. All patients had improvement of their scrotal pain to a self-reported acceptable level.

**Conclusions:** Chronic idiopathic scrotal pain may be one of the variable presenting symptoms of IC/BPS. This scrotal pain may actually be referred pain from the bladder. Standard therapies for IC/BPS may be a treatment option for chronic idiopathic scrotal pain.

**Keywords:** Bladder instillation, bladder pain syndrome, chronic scrotal pain, idiopathic scrotal pain, interstitial cystitis, orchialgia

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## INTRODUCTION

Chronic pain located in the scrotum is a common, well-described, and challenging clinical condition. Chronic orchialgia is defined as intermittent or constant unilateral or bilateral testicular pain 3 months or longer that significantly interferes with the daily activities of the patient.<sup>[1]</sup> Chronic scrotal pain is a broader description of this condition as it includes pain not only from the testicle but also from the epididymis and/or the spermatic

cord. Chronic scrotal pain is a urological manifestation of a chronic pain syndrome that has a significant social impact including health costs, loss of work, and sexual dysfunction.<sup>[2,3]</sup> Chronic scrotal pain presents a difficult diagnostic and management challenge. Evaluation of patients should include a thorough medical and surgical history, physical examination, and scrotal ultrasound and/or spermatic cord block if indicated. Causes of scrotal pain include orchitis, epididymitis, varicocele,

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postvasectomy pain syndrome or sperm granuloma, and epididymal cyst. Other causes include referred pain to the testicle or spermatic cord by an inguinal hernia or a ureteral calculus. Unfortunately, 25% of patients with chronic scrotal pain have no obvious etiology and are classified as having chronic idiopathic orchialgia.<sup>[1]</sup>

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic, slowly progressive syndrome characterized by variable degrees of urinary urgency, frequency, and bladder pain. However, IC/BPS presents in a variety of ways. Many patients develop insidiously progressive urinary frequency that does not bother the patient until it begins to interfere with their lifestyle. Patients progress to chronic pain cycles that can occur anywhere in the pelvis, including the bladder, urethra, penis, scrotum, vulva, or labia.

In this article, we report our experience with 16 males with chronic idiopathic scrotal pain who had acceptable relief of their pain when treated with standard therapy for IC/BPS.

## PATIENTS AND METHODS

### Ethical practices

For this study, the data were collected under the institutional review board of the University of California San Diego Health System. The study was done in accordance with the ethical principles originating in the Declaration of Helsinki, consistent with good clinical practices and applicable regulatory requirements.

### Patients

We performed a retrospective review of patients who were referred to and evaluated at our urological clinics for chronic scrotal pain between January 2015 and December 2015. Patients were considered to have chronic idiopathic scrotal pain if they had scrotal pain for a minimum of 6 months, had no urologic history as a cause of their pain, and had no findings on physical examination for another diagnosis as a cause for their pain. A spermatic cord block was not performed in these patients as palpation of the scrotal contents did not elicit or exacerbate their pain.

### Interstitial cystitis/bladder pain syndrome therapy

These patients with chronic idiopathic scrotal pain were treated with either pentosan polysulfate sodium (PPS) or therapeutic bladder instillations of alkalized lidocaine and heparin at the discretion of the patients and the authors.

PPS is the only oral Food and Drug Administration approved medication for the treatment of IC/BPS. PPS

is felt to restore the bladder epithelial barrier integrity. The advantage of PPS is that it is taken as an oral medication. However, it may require several months of therapy before patients experience relief of IC/BPS pain symptoms.<sup>[4]</sup> The dose of PPS used was 100 mg, two capsules given three times daily 1 h before meals or 2 h after meals.

Intravesical therapeutic instillations of alkalized lidocaine and heparin are currently being utilized more frequently for the treatment of IC/BPS. Bladder instillations including heparin and alkalized lidocaine offer the advantage of immediate relief of pain symptoms.<sup>[5,6]</sup> Intravesical instillations of alkalized lidocaine and heparin have provided resolution of external genital pain in women with IC/BPS.<sup>[7]</sup> The bladder instillation patients received a one-time dose containing 200 mg of lidocaine, alkalization with tris buffer, and 50,000 units of heparin. Patients were reassessed 30 min and 1 h after the bladder instillation.

### Evaluation and outcome measurements

The patients who received PPS were evaluated with a participant-reported global assessment. This assessment has been used in previous PPS studies.<sup>[8]</sup> A response of at least moderate or 50% improvement was considered a significant improvement.

The patients who received bladder instillations of alkalized lidocaine and heparin were evaluated with an 11-point analog scale (0–10) for scrotal pain.

## RESULTS

Patients with presenting symptoms of chronic scrotal pain were evaluated, and 16 males were determined to have chronic idiopathic scrotal pain. The authors hypothesized that their scrotal pain may be referred pain from the bladder caused by IC/BPS. The patients were treated with standard therapy for IC/BPS with eight males receiving PPS and eight males receiving a bladder instillation of alkalized lidocaine and heparin. Individual case reports were not described, but their individual history and responses are noted in chart form. It was more understandable and relevant to describe the patients by grouping them by the type of therapy received. The eight patients treated with PPS had a  $\geq 50\%$  improvement in their scrotal pain over follow-up of several months [Table 1]. The eight patients treated with a bladder instillation of alkalized lidocaine and heparin had improvement in their scrotal pain to an acceptable level within 30 min to 1 h [Table 2]. All patients had durable resolution of their scrotal pain during the time frame of this report.

## DISCUSSION

This article presents a series of men with chronic idiopathic scrotal pain who had improvement in scrotal pain to an acceptable level with therapies treating IC/BPS [Table 3]. Chronic idiopathic scrotal pain may be one of the variable presenting symptoms of a male with IC/BPS. IC/BPS is a progressive disorder that classically presents with urinary frequency, urgency, and bladder pain in any combination.<sup>[9]</sup> However, patients with IC/BPS often present initially with

only a single symptom. This disease has an insidious development over many years from mild, intermittent symptoms to more classic and potentially more severe IC/BPS. As the disease develops in patients, they are assigned diagnoses based on their presenting symptoms and their sex and with which specialty they are consulting. With time, there is a progression of symptoms making the IC/BPS diagnosis more likely to be considered and confirmed. The challenge for clinicians is to diagnose IC/BPS early and initiate treatment before there is progression of symptoms and potential further damage to the bladder.

**Table 1: Patients treated with pentosan polysulfate sodium**

Age (years) of patient	Duration of scrotal pain	Resolution of scrotal pain*
36	Over 1 year	4 months of therapy: 75% improvement
30	15 months	6 months of therapy: 50% improvement
43	2 years	6 months of therapy: 50% improvement
50	7-8 months	12 months of therapy: 50% improvement
42	Over 10 years	9 months of therapy: 50% improvement
76	Over 1 year	28 months of therapy: 50% improvement
38	8 months	12 months of therapy: 75% improvement
44	7 months	12 months of therapy: 100% improvement

\*Patients reported global assessment. A response of at least moderate or 50% improvement was considered a significant improvement

**Table 2: Patients treated with bladder instillation of alkalized lidocaine and heparin**

Age (years) of patient	Duration and degree of initial scrotal pain*	Resolution of scrotal pain after bladder instillation*
71	20 years	1 h
99	7/10 pain	5/10 pain
	6 months	30 min
54	5/10 pain	0/10 pain
	8 months	30 min
76	6/10 pain	3/10 pain
	>1 year	30 min
25	4/10 pain	0/10 pain
	>1 year	1 h
36	5/10 pain	1/10 pain
	>6 months	1 h
30	7/10 pain	3/10 pain
	>6 months	1 h
22	8-9/10 pain	3/10 pain
	>6 months	1 h
	9/10 pain	1-2/10 pain

\*11-point analog scale (0–10) for scrotal pain

**Table 3: Summary of treatment of idiopathic orchialgia with standard therapy for IC/BPS**

Characteristic, median (IQR)	Pentosan polysulfate sodium (n=8)	Bladder instillation with alkalized lidocaine and heparin (n=8)	P*
Age (yr)	43 (37-47)	45 (28-74)	P=0.6
Duration of scrotal pain (yr)	1 (.7-1.6)	0.6 (.6-1)	P=0.7
Time to acceptable pain relief	11 (6-12) months	60 (30-60) min	
Improvement in pain (%)	50 (50-75)	74 (47-95)	P=0.5

IQR=Interquartile range, \*2-Sample t-test

Women with IC/BPS often present with suprapubic, bladder pain. However, multiple pain sites including the external genitalia are common.<sup>[10]</sup> Women with IC/BPS present with genital pain of either vulvodynia or dyspareunia.<sup>[11,12]</sup> Women with IC/BPS who have vulvodynia complain of pain, burning, irritation, or rawness in the vulvar area, but on examination, no identifiable source for the discomfort is identified. This vulvodynia appears to be referred pain from the bladder. If women with IC/BPS have external genital discomfort, it follows that men with IC/BPS would also present with external genital discomfort.

More male patients are now being diagnosed with IC/BPS.<sup>[13,14]</sup> Scrotal or testicular pain, not related to bladder fullness, was recognized as a predominant symptom. Back, perineal, or scrotal pain was the initial symptom in 7% of male IC/BPS patients and progressed to be a predominant symptom in 45% of patients.<sup>[14]</sup> There was a delay in diagnosis of IC/BPS in men between 2.5 and 4 years due to initial unsuccessful treatment for benign prostatic hypertrophy and chronic prostatitis. Men with perineal pain attributed to the prostate, now called chronic pelvic pain syndrome, may actually have IC/BPS with the perineal pain being referred from the bladder.<sup>[15-17]</sup>

Patients with IC/BPS treated with PPS have shown a greater reduction in pain compared to placebo.<sup>[18]</sup> The benefit of treatment with PPS is that it is taken as an oral medication and can have long-term responses. However, it may take several months for patients to improve.

Intravesical therapeutic solutions of alkalized lidocaine and heparin have provided immediate relief of pain

and urgency in patients with IC/BPS.<sup>[5,6]</sup> Henry *et al.*<sup>[19]</sup> demonstrated that patients with IC/BPS experienced a significant pain reduction durable for 2 days with alkalinized intravesical lidocaine. Intravesical instillations of heparin attained clinical remission in over 50% of patients with IC/BPS.<sup>[20]</sup> Combination of intravesical alkalinized lidocaine and heparin successfully attained immediate and sustained relief of pain in patients with IC/BPS refractory to conventional therapy.<sup>[21]</sup> The benefits of treatment with intravesical instillations of alkalinized lidocaine and heparin are rapid relief of symptoms and obtaining a presumed diagnosis of IC/BPS. However, the procedure does require catheterization.

Chronic idiopathic scrotal pain is a frustrating urological condition for both the patient and the clinician. Many men with this condition undergo multiple therapies and surgeries with no improvement in their symptoms.<sup>[2]</sup> Significant voiding symptoms were recognized in these males with chronic orchialgia. Based on our experience with women with IC/BPS presenting with vulvodynia, we extrapolated this clinical presentation to males with chronic idiopathic scrotal content pain. Focused questioning and/or a voiding diary may elicit abnormal urinary symptoms supportive of the diagnosis of IC/BPS. Treatment of our patients with chronic idiopathic scrotal content pain using standard therapies for IC/BPS resulted in improvement of their scrotal pain to acceptable levels.

Chronic idiopathic scrotal pain may be a presenting symptom of IC/BPS. External genitalia pain may be referred pain from the bladder in patients with IC/BPS. PPS therapy may offer relief of scrotal pain for males with IC/BPS. Intravesical instillations of alkalinized lidocaine and heparin can be both a diagnostic tool and therapeutic option for scrotal pain in males with IC/BPS.

### Limitations of this study

Small sample size and nonrandomized nature were the limitations of this study. Long term follow-up would be interesting as patients continued on therapy for their chronic IC/BPS.

### CONCLUSIONS

Chronic idiopathic scrotal content pain may be one of the variable symptoms of IC/BPS in males. This scrotal pain is referred bladder-generated pain. Standard therapy for IC/BPS with either PPS or intravesical instillations of alkalinized lidocaine and heparin may offer relief for these patients. Early diagnosis and treatment of IC/BPS

may alleviate both progression of symptoms and further damage to the bladder.

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### Conflict of interest

There are no conflicts of interest.

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