

Complementary and alternative medical therapies for interstitial cystitis: an update from the United States

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Abstract: The diagnosis and treatment of interstitial cystitis/bladder pain syndrome (IC/BPS) has shifted from organ-specific to a multifactorial, multidisciplinary and individualized approach. Patients with refractory and debilitating symptoms may respond to complementary and alternative medical treatments (CAM). Through CAM therapies, practitioners assist the patient to be at the center of their care, empowering them to be emotionally and physically involved. Multi-disciplinary care, including urology, gynecology, gastroenterology, neurology, psychology, physiotherapy and pain medicine, is also identified to be the crux of adequate management of patients with chronic pelvic pain because of its variable etiology. The purpose of this review is to emphasize these changes and discuss management strategies.

Keywords: Interstitial cystitis (IC); bladder pain syndrome (BPS); percutaneous tibial nerve stimulation; complementary and alternative medicine

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Introduction

The scientific committee of the International Consultation on Incontinence voted to use the term “bladder pain syndrome (BPS)” for the disorder that has been commonly referred to as “interstitial cystitis (IC)” (1). IC implies an inflammatory process within the bladder urothelium, involving gaps or spaces in the bladder tissue. BPS focuses on the symptom complex rather than what appears to be a specific pathologic diagnosis of IC. Patients with IC have significantly higher comorbidities including chronic fatigue syndrome, irritable bowel syndrome, and fibromyalgia resulting in greater symptomatic impact in the patient’s life (2). BPS is defined as chronic pelvic pain (>6 months), pressure or discomfort perceived to be related to the urinary

bladder accompanied by at least one other urinary symptom, such as persistent urge to void or frequency. Other diseases with similar symptoms must be excluded. Findings at cystoscopy with hydrodistention and morphological findings in bladder biopsies may influence the categorization of BPS as per the ESSIC criteria (3). The presence of other organ symptoms, cognitive, behavioral, emotional, and sexual symptoms should also be addressed (1).

IC/BPS treatment options

IC diet

Dietary modification has become standard IC therapy and has been incorporated into the American Urological

Association (AUA) clinical guidelines (4). It is considered first line therapy and listed as: “avoidance of certain foods known to be common bladder irritants for IC/BPS patients such as coffee or citrus products and use of an elimination diet to determine which foods or fluids may contribute to symptoms” (4). Based on patient ratings, there were no remarkable therapies other than dietary modification. Dietary changes controlled symptoms “pretty well” or “completely” for 50% or more of these patients. The diet research implies that IC patients’ sensitivities vary considerably, outside of a few common symptom triggers (5).

Unfortunately, the data in this study showed that almost one-third of patients did not take advantage of diet and physical therapy in the first year after diagnosis (4). For example, an elimination diet of bladder irritants, decreasing dietary acid load, and urinary alkalinization with baking soda or potassium citrate has been an effective treatment for many IC patients. Also, a steady intake of water helps to dilute urine and reduce constipation (6). Patients have reported that their bladder symptoms have lasted anywhere from days to weeks following ingestion of offending items. It would be beneficial for the patient if healthcare providers consult a nutritionist or a registered dietitian to educate patients regarding self-care for dietary needs, and elimination of certain beverages and food items to deter symptoms. Through clinical experience, Shorter and Gordon [2015] recommend for the patient to have a dedicated hour for their first patient appointment to assess the patient’s food/beverage consumption, and also to evaluate for adequate nutrient intake. A food/symptom/voiding diary is essential in assessing patients, their symptoms, to discover potential triggers, and formulate an appropriate elimination diet (7). Also, a steady intake of water helps to dilute urine and reduce constipation (6). At times, patients will report a decrease in fluid intake in relation to frequency. It is important to emphasize adequate hydration, and find the perfect balance to prevent frequency (7).

Three-day food and voiding diaries revealed that the intake of foods and fluids that exacerbate IC symptoms increased painful bladder symptoms within 2 to 4 hours of ingestion. The symptoms were reduced with the elimination, among others, of the following: alcoholic beverages, carbonated drinks, caffeine, spicy foods, tomatoes, citrus fruits, and vinegar (8). Arylalkylamine-containing foods (tryptophan, tyrosine, tyramine, and phenylalanine) can also exacerbate IC symptoms and include the following: bananas, beer, cheese, mayonnaise, aspartame, nuts, onions, raisins, sour cream, wine and

yogurt (9). In addition to dietary modifications, urinary alkalinization with potassium citrate may be useful in maintaining a urinary pH of 6.0-6.5 (6). Studies have shown a relationship between acidic, urine-producing foods or liquids and an increase in IC symptoms, as well as an alleviation of these symptoms with the restriction of such foods. The most commonly implicated foods and beverages are coffee, chocolate, alcohol, carbonated drinks, citrus fruits, and tomato based products (10).

Alternative over the counter medication options

CystoProtek[®]

CystoProtek[®] is a multi-agent dietary supplement formulated as soft gel capsules and constitutes of glucosamine sulfate (120 mg), chondroitin sulfate (150 mg), hyaluronate sodium (10 mg), quercetin dehydrate (150 mg), rutin (20 mg), olive kernel extract (45%), produced by a GMP certified company (Tischon Corporation, Westbury, NY, for Alaven Pharmaceutical, LLC, Marietta, GA, USA). *CystoProtek*[®] contains multiple components similar to bladder surface glycosaminoglycans (GAGs) to help reduce bladder wall dysfunction and inflammation by its combination of naturally occurring molecules and its function of addressing multiple pathogenic pathways in IC/BPS. It is thought that the mucopolysaccharide GAG bladder surface layer is composed primarily of chondroitin sulfate and sodium hyaluronate, with glucosamine sulfate serving as the synthetic building block. In a study by Theoharides [2008], patients aged 18 to 69 years with IC/BPS who had failed other treatment options took two capsules of *CystoProtek*[®] twice a day with food. In the 252 patients who participated in this study, 50% had an overall positive response to *CystoProtek*[®]. Twenty-five of the men had an overall symptom reduction of 51.8% in their visual analog scale (VAS) scores related to their IC/BPS symptoms, whereas women experienced a 48.5% reduction in their VAS scores. With *CystoProtek*[®], isoflavonoids are present to decrease bladder inflammation and multiple mucopolysaccharides to replenish the bladder lining (11).

Prelief[®]

Some patients respond to urinary alkalinization provided by an antacid such as *Prelief*[®] (AkPharma, Pleasantville, NJ, USA). *Prelief*[®], or calcium glycerophosphate (CGP), is the main supplement rated helpful in one study performed by

Bologna [2001] in which patients kept a 4-week food diary and recorded food-related flares, an IC symptom index, and an SF-12 quality of life (QOL) survey. Patients then took two tablets of CGP prior to each meal for a total of 4 weeks. The specific foods evaluated in the patient's diets were coffee, pizza, carbonated drinks, acidic fruits and juices, chocolate, pizza, alcohol, tomato-based products, and spicy foods. Surveys were repeated after the 4 weeks and symptom severity had decreased by over 40% in participants with the use of CGP. A 20-30% reduction was seen in the participants' exacerbations of symptoms with alcohol, chocolate and carbonated drinks, therefore showing that CGP can improve QOL and symptom management in IC patients (12). Other nutraceutical and oral antacids are also available (13). Researchers found that while patients with IC/BPS were more likely to be food sensitive than patients with chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS), both had similar symptom exacerbations with grapefruit juice, spicy foods, alcohol, and caffeinated coffee. Both groups also had symptom improvements with other comestibles, in particular water and Preliet® (14).

Bladder retraining/biofeedback

Through bladder training, the patient focuses on inhibiting the urge to urinate in an effort to extend the voiding interval (6). A decrease in frequency, nocturia, and urgency was seen in 15 (71%) of 21 IC/BPS patients in one study in which patients progressively increased voiding intervals of 15 to 30 minutes every 3 to 4 weeks (15). Biofeedback is another aspect of pelvic floor physical therapy that can provide beneficial results for the urologic chronic pelvic pain syndrome (UCPPS) patient. Through biofeedback, the patient can learn to control the pelvic floor muscles by visualizing the activity of the muscle on the computer and using visual feedback to achieve conscious control over contraction of the pelvic floor muscle, thus breaking the cycle of spasm (13). Of note this should be done in conjunction with a home exercise program, and decreasing the resting tone should be emphasized.

Cognitive behavioral therapy/psychotherapy

Patients can develop better coping strategies and alter their pain beliefs for their chronic pain through cognitive behavioral therapy. Studies have shown that these changes can predict positive treatment outcomes by reducing helplessness, increasing perceived control, and decreasing

pain catastrophization (16). Through recent advances in research, a newly created interdisciplinary treatment for chronic pain, referred to as contextual cognitive behavioral therapy (CCBT) has been formulated. It appears to be effective in patients suffering longstanding and complex chronic pain conditions and may be particularly suited for multi-problem cases characterized by change-resistant behavior patterns (17). During this treatment, both the standard and highly disabled patients attended treatment for 3 weeks. The total time of exposure for patients to treatment was approximately 80 hours. Treatment processes incorporated principles of exposure, acceptance, cognitive de-fusion, mindfulness, and value based methods. The primary goals of treatment were not to reduce or control pain, but rather to increase patients' psychological flexibility for dealing with unwanted experiences and improve their engagement in activities that are important to them (17,18). The psychological component of treatment was designed to increase patients' willingness to face uncomfortable thoughts and feelings, and to focus their efforts on behaviors that improve functioning in the long run rather than serving some momentary urge or feeling. There was a physical exercise component and a cognitive component addressing healthy habits and choosing a path in life that was meaningful (17). The study showed a statistically significant reduction in the patient's rating of pain distress even though there was not a significant decrease in pain during treatment. They also showed significant changes towards a healthy direction of the seven remaining measures of functioning including physical and psychosocial disability, depression, pain-related anxiety, acceptance of pain, daily rest related to pain, and their sit-to-stand performance. Of the sample, close to half (47.6%) showed a reliable change in their improvement related to disability, a large majority showed improvement in their acceptance of pain (92.9%), over half showed improvement for depression (61.9%), a large majority showed improvement in their acceptance of pain (92.9%), and a smaller minority of patients showed reliable improvement for pain-related anxiety (32.5%). Through interdisciplinary pain management treatment, this study demonstrates that highly disabled patients with chronic pain can experience significant symptom improvement. Nickels *et al.* [2010] also carried a similar study using questionnaires completed by 207 patients who had been diagnosed with IC/PBS and 117 controls. These 207 patients compared with controls reported significantly higher pain, depression, increased sleep dysfunction, worse physical QOL, anxiety, stress, moderately increased sexual/

social function problems, and catastrophizing. Stress, anxiety, depression, and catastrophizing further correlated with the degree of the patient's general pain and IC specific symptoms, and with their overall decreased QOL. This study concluded that patients who suffer with IC/PBS have a higher degree of considerable cognitive and psychosocial changes within their life versus the control patients (19).

Physical therapy

With its inclusion in the AUA clinical guidelines, myofascial physical therapy has become well accepted (5). The NIDDK-sponsored trial of myofascial physical therapy gained level 1 evidence (20). The Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network along with Fitzgerald *et al.* found that one study suggested myofascial physical therapy might also be effective for patients suffering with IC/BPS. An increase in pelvic floor muscle tone occurs during bladder filling via a guarding reflex, accompanied by bombardment by unmyelinated C-fiber afferents with an increased somatic efferent stimulation of the pelvic floor muscles during vesical distention. In IC patients, the result is high-tone pelvic floor muscle dysfunction (HTPFD). HTPFD has also been known as coccygodynia, tension myalgia, levator ani spasm, and levator syndrome (19). Short, hypertonic pelvic floor has also been implicated in patients who experience pelvic pain (21). Nociceptive, afferent C-fibers become active in response to bladder inflammation or irritation, resulting in pain and reflex voiding (22). Neuromodulation therapy attempts to ablate the sustained guarding reflex. Treatment of HTPFD involves physical therapy of the outer and inner pelvis followed by biofeedback and functional electrical stimulation of the pelvic floor muscles (6). Realignment of the sacrum and ilium aids in restoring normal tension to the pelvic floor musculature. In a pilot study of 16 IC patients with HTPFD and sacroiliac dysfunction, 94% had significant improvement in irritative voiding symptoms and dyspareunia following manual therapy, myofascial massage, and muscle-energy techniques, along with a home exercise regimen that included stretch and strengthening exercises (23).

Percutaneous nerve stimulation (PTNS)/acupuncture

PTNS can also be used for treatment of IC/BPS. PTNS is used twice weekly in a study with a group of female Chinese patients (18 patients, mean age of 60 years old) who

presented with IC symptoms of frequency, urgency, perineal pain or suprapubic pain. The patients experienced the IC symptoms of frequency, urgency, perineal pain or suprapubic pain for 3.4 years. The patients were part of a prospective study and participated in twice weekly 30-minute sessions for a total of ten sessions. In order to gauge their response to treatment, patients were given a VAS for pain, voiding diary, O'Leary/Saint IC symptom and problem index, and a 36-item short-form health survey QOL questionnaire. At the end of their treatment, patients were then allowed to self evaluate with a rating of no effect, some effect, and significant effect. The end of treatment evaluation rating was completed using a self-evaluation table by answering yes or no questions. Very rare complications occurred with the PTNS procedure including localized tenderness or temporary pain at the needle insertion site, and minor bleeding immediately upon removal of the needle. Even though these minor complications were experienced, none of the 18 patients chose to discontinue treatment if they experienced this, and 4 of the 18 patients chose to continue further treatment courses after completion of the trial.

The patients all completed the ten treatment sessions with no complications. There were no statically significant changes in the VAS pain scores except for improvement among nighttime voiding with bladder volume, IC Problem Index, O'Leary/Saint IC Symptom Index, and health status scales scores on the 36-item short-form health survey. Of the 18 patients, ten patients reported that the trial had no effect, whereas the other eight patients reported the trial as having some effect, especially in improvement related to bladder volume. Therefore, this trial was important in showing the PTNS might be an alternative treatment for patients with IC symptoms (24). Success rates in the United States and Europe regarding PTNS therapy have shown approximately 60% to 80% improvement in evaluation of a decrease in leakage episodes, nocturia, daytime frequency, volume voided, and the amount of pads used per patient (25,26).

Neuromodulation through acupuncture occurs by re-establishing a balanced flow of energy, termed Yin and Yang, throughout the body through 12 meridians and 1,000 acupoints. A rebalance of energy flow is thought to occur by increasing endorphin production and pain ablation by stimulating A delta, large-diameter myelinated sensory nerve fibers with the inhibition of unmyelinated sensory C-fibers (6).

Our experiences

Patients with severe symptoms in our practice tend to

respond favorably to multimodal management. Once we focus on involving our patients at every decision in their care within our practice, they have improved response to each part of their therapy, especially when the care is individualized to the patient's specific needs. In regards to referring patients for physical therapy and biofeedback, most of our patients pursue based on financial availability, and third-party coverage which we often see a lack of, or an inadequacy in full coverage benefits for our patients. We discuss first line therapies as recommended by the AUA guidelines and our patients tend to respond well to dietary modifications. We provide bladder friendly information packets and counseling, discuss Cystoprotek[®], Prelief[®], and Javacid[®] for coffee-drinkers. We also discuss the importance of stress relief, physical therapy, and other types of treatment including acupuncture and myofascial massage. Additionally, we may use these complementary and alternative medical (CAM) therapies as an adjunct to further medical or surgical therapies pending patients' responses. The elimination diet is emphasized among patients, with education provided on an individualized basis. However, we have noted that some food triggers cause severe symptoms, many patients do not adhere to the diet as it is difficult, and eliminates many of their favorite foods and beverages. When these patients have co-morbidities of HTPFD, we encourage myofascial therapy and pelvic floor physical therapy as an adjunct to the IC/BPS tier 1 treatments. By discussing treatments in detail and helping the patient to understand the disease process of IC/BPS, we find patients have improved symptomatology and pain scores.

Conclusions

Patients used a 5-point scale survey to rate CAM therapies. They reported that their interest in CAM therapies is due to the side effects experienced with traditional therapies, lack of efficacy, and frustration with providers. Through this survey's open-ended questions, respondents reported that CAM therapies were most frequently recommended by the patient's physicians; thus showing physicians' acceptance of diet and physical therapy as mainstream IC treatments (5). This further supports the use of CAM therapies either as a first line treatment option or as an adjunct to facilitate medical and/or surgical therapies.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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