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Frequency, Urgency, and Pelvic Pain: Treating the Pelvic Floor Versus the Epithelium

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For years the bladder epithelium has been the focus for diagnosing and treating the frequency, urgency, and pelvic pain of interstitial cystitis. However, many patients have not found symptom relief with these therapies. Pelvic floor dysfunction is often present in these patients, yet it is often untreated. Pelvic floor dysfunction may be related to abuse, past surgeries, or other causes. It is important to look outside of the bladder and explore other causes and treatments for this condition. Pelvic floor therapies should be a first line of treatment for those women with chronic pelvic pain related to pelvic floor dysfunction.

Introduction

The key symptoms of interstitial cystitis (IC) are urinary frequency, urgency, and pelvic pain [1]. More than 90 years ago, IC was described as a distinct ulcer seen in the bladder on cystoscopy [2]. This ulcerative form of IC is clearly of bladder origin, and eradicating the ulcer with cautery is often therapeutic. However, only 10% to 20% of patients with the symptoms of IC have ulcers within their bladder. In patients without ulcers, but with symptoms of IC, the bladder epithelium has been the focus of the pathogenesis of IC, and therapy has been directed at treating the "leaky" epithelium. The assumption is that the bladder stores urine that is toxic, and for the bladder to function as a storage organ, it must protect itself from the irritants and toxins in the urine. If the protective layer of the bladder is compromised, the urine will act as an irritant, penetrate into the detrusor, and lead to proliferation of mast cells, nerve upregulation, and ultimately bladder irritation with urinary urgency, frequency, and pain. Despite many studies evaluating compounds directed at treating the epithelium

for IC, few have proven to be effective when studied in a rigorous fashion using a placebo-controlled trial. The lack of compelling clinical evidence to support many therapies directed toward the epithelium may be due to any of the following: 1) an ineffective compound; 2) an epithelium uninvolved in the pathogenesis of IC; or 3) an inclusion of a heterogeneous population in the clinical trials. There has been little solid evidence that proves the causal role of a dysfunctional epithelium in the symptoms of IC, and there are not any consistent histologic features on bladder biopsy that are supportive of inflammatory changes in the bladder. Thus, the term "interstitial cystitis" is a misnomer because this is a histologic description. Several alternative terms for IC have been suggested including painful bladder syndrome (PBS). However, the clinician must first consider the patient to have chronic pelvic pain syndrome (CPPS) and use the term IC or PBS for only those patients whose symptoms clearly are of bladder origin.

Taking the focus away from the bladder may open the door for clinicians to explore other causes and treatments for this syndrome. This is important because IC remains a diagnosis of exclusion. In the past, few patients were diagnosed with IC and went untreated. However, recently, with pharmaceutical company promotion and relying on tests that do not diagnose IC (ie, the potassium sensitivity test), too many patients have been labeled as having IC. Oversimplifying the diagnosis of IC results in initiating therapies directed toward the bladder that are ineffective and risks missing other causes of the symptoms such as urethral diverticulum or transitional cell cancer [3]. A common finding in patients presenting with symptoms of urinary urgency, frequency, pelvic pain, and dyspareunia is pelvic floor dysfunction. It is imperative that the clinician evaluates the pelvic floor and treats this dysfunction before "blaming" the bladder for the patient's symptoms. This is also true in assessing and treating chronic prostatitis, proctalgia, or prostatic dyspareunia in men. The current therapies of antibiotics, anti-inflammatories, and muscle relaxants are not efficacious compared with placebos in randomized, clinical trials, and yet, they continue to be used in treating the majority of these patients [4]. Rather than focusing on the bladder epithelium, this article dis-

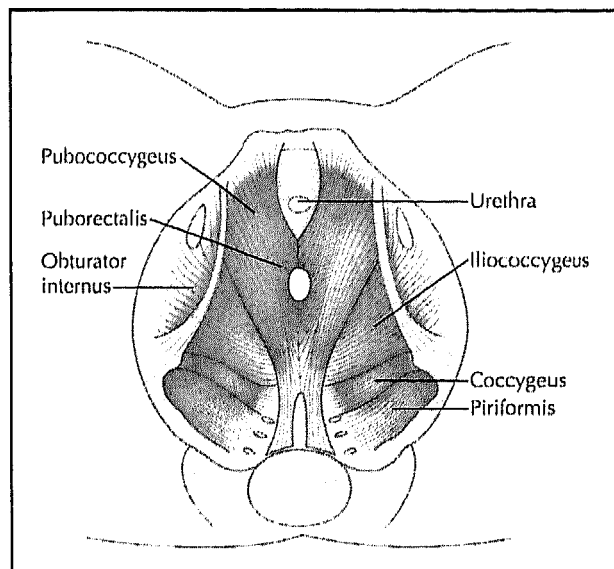


Figure 1. Diagram of the pelvic floor muscles.

cusses the management of CPPS (primarily in women) in terms of treating the pelvic floor.

The Pelvic Floor

It is important to remember that pelvic floor dysfunction may derive from the muscles (Fig. 1), the nerves, or the connective tissue [5]. Innervation of the pelvic floor muscles is from the second, third, or fourth sacral nerve root through the pudendal nerve [6], and direct innervation of the levator ani muscles is from the third or fourth sacral motor nerve root by the pudendal nerve. In addition, the pelvic floor is also supported by the endopelvic fascia, a group of tissues including collagen, elastin, smooth muscle, ligaments, blood vessels, and nerves [7].

Pelvic floor dysfunction

Myofascial pain and hypertonic pelvic floor dysfunction are present in as many as 85% of patients with IC and/or chronic pain syndromes. A noxious stimulus may trigger the release of nerve growth factor and substance P in the periphery causing the mast cells in the bladder to release proinflammatory substances, causing neurogenic inflammation of the bladder wall. This can result in painful bladder symptoms (IC) or vulvar or vaginal pain. There may also be a visceromuscular reflex resulting in the pelvic floor muscles being in a hypertonic contracted state. This hypertonic state results in decreased muscle function, increased myofascial pain, and myofascial trigger points. The pelvic floor muscles then become a source of pain even if the bladder is treated [8]. In addition, neural cross-talk may explain the interface of many chronic pelvic pain conditions including IC and irritable bowel syndrome. Neural pathways coordinating smooth and striated muscle activity of the pelvic organs may respond

to ongoing, long-term stimulation by negatively impacting the nonirritated pelvic organs. This may lead to neurogenic inflammation and sensitization through the release of neurotrophic factors [9•].

Pelvic pain from levator ani myalgia may occur with sexual intercourse. Dyspareunia, vulvodynia, and vaginismus can be the result of contracted pelvic floor muscles. Sixty percent of IC sufferers complain of pain with sexual intercourse, many so severe that they abstain altogether [10–12].

The resulting sexual dysfunction may affect the woman's self-esteem and her relationship with her partner. It may also potentiate the pain/pelvic floor muscle contraction cycle. Usually the woman with IC will also have an increase in her painful bladder symptoms of frequency, urgency, or pain with pelvic floor dysfunction [13].

Abuse: A potential trigger of pelvic floor dysfunction

A search of the English literature found no articles on IC and abuse and only one article on abuse and pelvic floor dysfunction related to gastrointestinal disorders [14]. To our knowledge no one has reported on the prevalence of abuse in women with IC and pelvic floor dysfunction. In the United States, the National Clearinghouse on Child Abuse [15] reports that almost 18% of children are physically abused, 10% are sexually abused, and 7% are emotionally maltreated. Approximately one in five female high school students reports being physically and/or sexually abused by a dating partner [16]. In 16 cross-sectional, community sample surveys of adult women, a 16.8% prevalence of childhood sexual abuse was calculated [17]. In addition, nearly one third of American women (31%) report being physically or sexually abused by a husband or boyfriend at some point in their lives [18].

We recently completed a study of women diagnosed with IC by cystoscopy and hydrodistension and having complaints of ongoing pelvic pain who were referred to the Beaumont Women's Initiative for Pelvic Pain and Sexual Health program (the WISH Program). These women had been evaluated and treated by gynecologists, gastroenterologists, or various specialists without resolution of their pain. A comprehensive history (including assessment of abuse history) was taken, and a pelvic examination was performed by a certified women's health nurse practitioner. The pelvic examination included assessment of levator pain on the right and left sides at the ischial spines. Pain was quantified on a 10-point visual analog scale (VAS) by the patient. A retrospective chart review was done to gather additional data. A total of 66 women with IC and pelvic pain were evaluated. The mean age was 45 with standard deviation of 12 years, and 65% were married. More than half of the women had more than 12 years of education (54%), were menopausal (55%), or were not working outside of the home (52%).

Thirty-two women, almost half the sample (49%), reported a history of abuse. The vast majority of the women (85%) had levator pain. Of those reporting abuse,

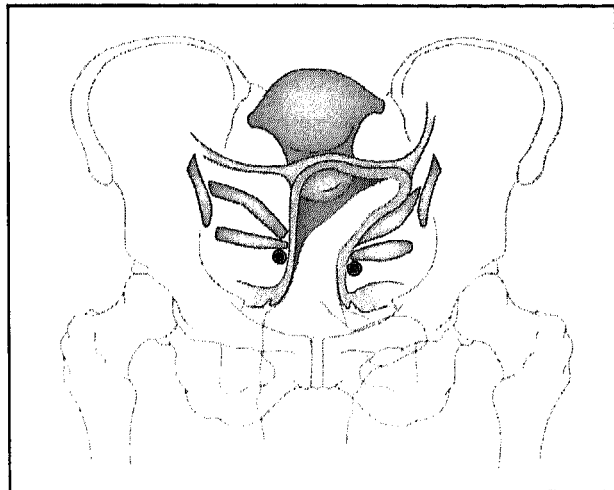


Figure 2. Illustration of levator assessment for pain.

91% reported emotional abuse, 78% reported physical abuse, 66% reported sexual abuse, and almost half (47%) were victims of domestic violence.

In this study, almost one out of every two women with refractory IC and pelvic pain reported a history of abuse. This is a much higher prevalence of abuse than reported in the general population. Our data do not allow us to determine if abuse may have impacted the pelvic floor or contributed to the pathogenesis of IC. However, it seems reasonable to hypothesize that abuse may increase the likelihood of pelvic floor guarding and the inability to contract and relax the pelvic floor musculature. This pelvic floor dysfunction may lead to voiding difficulties and ultimately urinary urgency, frequency, and pelvic pain. Other triggers of pelvic floor dysfunction could be pelvic trauma, pelvic surgery, or an acute, severe life-stressor. The literature does note that post-traumatic stress disorder, which includes abuse, is associated with irritable bowel syndrome, chronic pelvic pain, genitourinary conditions, and myalgias [19]. It is important to screen all patients for a history of abuse, especially those with CPPS, and then refer for psychological services to address any unresolved issues related to the patient's history of abuse.

Clinical evaluation for pelvic floor dysfunction

First, a complete history should be taken including past surgeries, procedures, and medications that may impact the pelvic muscles or organs. Include an assessment for sexual dysfunction, history of any type of abuse, and psychosocial alterations in health. Note any traditional or complementary therapies that have been used to treat the IC/CPPS. A cotton swab test for vulvodynia should be done. This involves touching the vestibule with the cotton swab at the 2, 4, 6, 8, and 10 o'clock positions [20]. Response to touch is rated on a VAS of 0 to 10 (no pain–worst pain ever).

A speculum examination, vaginal pH test (normal = 4.5), and wet mount slide should be done to check for vaginitis. Vaginal cultures should be done if indicated. If atrophic vaginitis is present, hormone therapy may be ordered or adjusted. Vaginal examination should assess for vaginismus, cervical motion tenderness (if cervix is intact), uterus and ovaries (if present), and note any bladder/urethral pain upon touch. To assess for levator pain, press laterally on the levator at the ischial spines (Fig. 2). It is helpful to quantify any pain with a VAS. Normally there would be no pain. Assess both the right and left sides because there is often discordance in the pelvic floor tension bilaterally. It is helpful to record the patient's pain responses and also the clinician's evaluation of muscle tension by palpation.

Consideration must be given to other disorders that may contribute to the pelvic pain. Appropriate referrals for evaluation and treatment should be made to gynecologists, gastroenterologists, psychologists, physical therapists, etc.

Treatment of CPPS: screen and treat pelvic floor dysfunction first

When evaluating a patient with urinary urgency, frequency, and pelvic pain, it is imperative to not only focus on the bladder as a cause of the syndrome but also the pelvic floor. If palpation of the levator muscles reproduces their pain or "bladder pressure," then it is reasonable to consider pelvic floor therapy as a first-line treatment before any invasive testing or medications are used. If pelvic floor involvement is identified, treatment by a therapist knowledgeable in myofascial release may markedly improve symptoms and often is the only treatment needed. If no levator spasm or tenderness is identified on initial evaluation or if after completing pelvic floor therapy the patient continues to have urinary symptoms, then it is reasonable to evaluate and treat them further with standard therapies for IC.

Pelvic Floor Therapy

Physical therapy has been reported to be helpful in managing pelvic pain and relaxing the pelvic floor [21•]; however, there are not any published randomized, controlled trials to support this in IC [22]. Weiss [23] utilized manual therapy for the pelvic floor trigger points and myofascial release in IC patients and found that 70% had marked or moderate improvement in symptoms after treatment. He found that pelvic floor therapy decreased the neurogenic triggers and central nervous system sensitivity and alleviated pain. The use of trigger point release, stretching, or strumming the muscles is often effective in relieving this dysfunction.

The goal of these stretching exercises is to lengthen the anterior contracted muscles by decreasing periurethral tension, release trigger points in the levator muscles, reeducate the muscles to a normal range of motion, and improve patient awareness of muscle tension. Treatment should con-

tinue until tenderness and tightness has been minimized or disappears, which requires one or two visits weekly for 8 to 12 weeks depending on the duration and severity of symptoms. As symptoms decrease in severity, the frequency of therapy is decreased, and the patient continues with home pelvic muscle stretches and relaxation techniques.

Similar techniques utilized myofascial trigger point release and paradoxical relaxation training in 138 men with chronic prostatitis and CPPS. The premise of this study was that chronic pelvic pain is due to tension in the pelvic floor that is a cycle perpetuated by anxiety and pain leading to more tension, more anxiety, and more pain. The results of this study showed a 72% moderate/marked improvement in symptoms when the men were treated for at least 1 month. More than half of these men had at least a 25% decrease in pain and urinary symptoms [24].

Biofeedback

Significant pain improvement was found in a prospective study treating 16 patients with levator ani syndrome with biofeedback [25]. Electrical vaginal or rectal stimulation has been used with variable reported success in patients with high-tone pelvic floor dysfunction [26]. IC patients with long-term intravaginal or transcutaneous nerve stimulation with continuous, daily use eventually had a decrease in pain and frequency [27].

Neuromodulation

Neuromodulation is approved for the treatment of urinary urgency, frequency, and idiopathic retention. Its exact mechanism of action is unknown, but it may have a beneficial effect on relaxing the pelvic floor muscles and working centrally at the micturition center.

Sacral nerve stimulation

Sacral nerve stimulation (SNS) shows promise for the treatment of refractory IC symptoms (InterStim[®]; Medtronic, Inc., Minneapolis, MN). This technology is approved by the US Food and Drug Administration for urinary urgency, frequency, urge incontinence, and idiopathic urinary retention. The benefit of SNS is that a test can be performed before placing a permanent implant. The response to the test is assessed, and if a patient experiences at least a 50% improvement in their symptoms and desires a permanent implant, the neurogenerator can be placed permanently in a subcutaneous pocket in the upper buttock. The device can be adjusted via an external programmer similar to a cardiac pacemaker, and the patient has his or her own external programmer to control the degree of stimulation. Early evidence suggested that temporary SNS may be effective in treating refractory IC [28,29].

In addition, there is a decrease in antiproliferative factor and normalization of heparin-binding EGF-like growth factor levels in patients with successful test stimulation [30]. Peters et al. [31] reported sustained improvement in refractory IC subjects with permanent implantation, and

the success rate was increased with a staged test using a permanent lead rather than a percutaneous office test. Comiter [32] reported that 17 of 25 patients with IC/PBS had a successful test stimulation, and at a mean follow-up of 14 months, 16 of 17 patients maintained their improvement. Finally, Peters and Konstant [33] demonstrated that long-term SNS significantly improved pain levels and resulted in a reduction in long-term opiate use. Further studies are needed to assess the utility of this technology for treating IC and to use these findings to study the pathophysiology of this disease.

Posterior tibial nerve stimulation

Posterior tibial nerve stimulation had a positive effect in 39% of 33 pelvic pain patients who were refractory to all other previous treatments [34]. Stimulation is applied for 30 minutes on a weekly basis for 12 weeks, and an attempt to wean treatments to once per month is tried. Unfortunately, there are not any sham studies done on posterior tibial nerve stimulation for voiding dysfunction so its use remains in question.

Botulinum toxin type A

Botulinum toxin type A has been used with some success in treating chronic pelvic pain associated with levator ani muscle spasms as well as chronic perineal pain [35,36,37]. Twelve women with pelvic floor spasm [35] who received botulinum toxin type A injections in their puborectalis and pubococcygeus muscles had decreased pain scores and improved quality of life and sexual function scores. The studies to date have been of limited size and are not well-controlled. More research is needed on the use of botulinum toxin type A for CPPS before it becomes a first-line therapy.

Conclusions

IC has been a difficult disease to recognize and treat for many years. Part of the problem is that there is not an absolute diagnostic test to identify who has IC, and our treatment has focused solely on the bladder as the cause of symptoms. It is now clear that many patients diagnosed with IC have significant pelvic floor dysfunction. This levator spasm often is the major contributor to voiding dysfunction and pelvic pain. We do not know what causes this levator spasm; however, with one out of five women reportedly abused as children and one out of six women being the victim of domestic violence in the United States today, it is reasonable to extrapolate that abuse may be a precursor to this pelvic floor dysfunction in some patients. In our study almost half of the women with IC and pelvic floor dysfunction reported abuse. Conversely then, not all women with IC and pelvic floor dysfunction have been abused. After ruling out significant causes of their symptoms, such as urinary infection, bladder cancer, or urethral diverticulum, the pelvic floor should be evaluated. If the pelvic floor is a source of pain and the muscles are in spasm, treating the pelvic floor first before other invasive testing,

such as a bladder hydrodistension or potassium sensitivity test, would be appropriate. Many patients find a marked improvement in symptoms by treating the pelvic floor, and epithelial-based therapy may not be required. It is important for urologists and all health care providers to assess their patients for abuse and make appropriate referrals.

Until recently, IC/CPPS was believed to be a disease predominantly of women; however, more men are now being diagnosed with this disease. Men presenting with symptoms of genital pain, perineal pain, frequency, or dysuria account for more than 2 million office visits per year and are often labeled as having chronic, abacterial prostatitis [38]. In fact, many of these men have characteristic findings of IC/CPPS upon cystoscopy and hydrodistension and will respond to standard IC/CPPS therapies [39–42]. IC/CPPS is more prevalent in men than previously thought, and it is imperative that the health care provider has a high index of suspicion for IC/CPPS in the man with chronic prostatitis symptoms.

We must look “outside the bladder” when evaluating patients with CPPS and be open-minded regarding the underlying cause and potential treatments to improve their quality of life.

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