

PATIENT EDUCATION AND SELF-ADVOCACY: QUESTIONS AND RESPONSES ON PAIN MANAGEMENT

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Interstitial Cystitis

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ABSTRACT

Questions from patients about analgesic pharmacotherapy and responses from authors are presented to help educate patients and make them more effective self-advocates. The topic addressed in this issue is interstitial cystitis and a discussion on pathology, genetics, course of disease, symptoms, and treatments.

KEYWORDS Biofeedback, bladder pain syndrome, gene FZD8, hydrodistension, IC, interstitial cystitis, painful urination, pelvic PT, phenylacetylglutamine, sacral stimulation, UCPPS

QUESTION FROM A PATIENT

I was diagnosed with interstitial cystitis over 10 years ago. I have been home for 6 years dealing with this awful illness. I have no social life, had to give up many foods/alcohol and must rely on pain medication. I find there are so many people who have never heard of it or don't believe how serious it can be. My daughter was diagnosed with it last year. Can you tell me about new treatments for it? Is it hereditary?

ANSWER

Interstitial cystitis, also known as bladder pain syndrome (BPS/IC) or urologic chronic pelvic pain syndromes (UCPPS), is a disease of the bladder linked with pain, painful urination, increased frequency of urination, urination at night, urgency and hesitancy (1). Other complaints may include bladder and pelvic floor pressure, pain with sexual intercourse, and pain in doing activities of daily living (ADLs) such as driving, working and traveling. BPS/IC affects men and

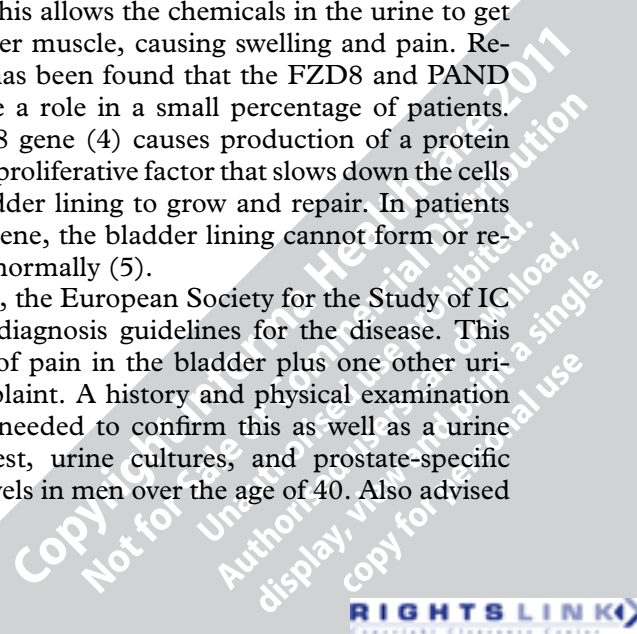
women of all cultures, ages, and social and economic backgrounds. Growing numbers of men and women are being diagnosed in their 20s and younger. BPS/IC is more common in women than in men. BPS/IC affects 1 in 100,000 to 5 in 1000 of the general population (2).

The pathology of interstitial cystitis is not known, although several theories have been suggested, including autoimmune disorder (the body attacking itself), genetic factors, allergy mechanisms, and neurologic mechanisms (3). Despite the cause, it is found that most people with BPS/IC suffer with a damaged bladder lining, often following several bladder infections, excess caffeine and soda intake, or past bladder injuries. This allows the chemicals in the urine to get into bladder muscle, causing swelling and pain. Recently, it has been found that the FZD8 and PAND genes have a role in a small percentage of patients. The FZD8 gene (4) causes production of a protein called antiproliferative factor that slows down the cells of the bladder lining to grow and repair. In patients with this gene, the bladder lining cannot form or repair itself normally (5).

In 2006, the European Society for the Study of IC proposed diagnosis guidelines for the disease. This consisted of pain in the bladder plus one other urinary complaint. A history and physical examination would be needed to confirm this as well as a urine dipstick test, urine cultures, and prostate-specific antigen levels in men over the age of 40. Also advised

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were urine flow study and ultrasound scanning of posturination bladder volume. If these tests pointed to interstitial cystitis, then the gold standard of cystoscopy (inserting a fiber optic camera into the bladder via the urethra) and hydrodistension (filling the bladder with saline) with biopsy would be used to confirm the diagnosis (6). There is also a “potassium chloride sensitivity” test in which the bladder lining is exposed to potassium chloride (KCl) via a catheter placed in the bladder causing pain in patients with interstitial cystitis (7). In 2009, Japanese researchers found a marker chemical called phenylacetylglutamine that could be used for early diagnosis (8).

As with most pain syndromes, there are multiple factors involved in the cause of it. Therefore multiple different approaches are usually necessary for controlling the symptoms. These are discussed in the following sections.

Medication

Pentosan polysulphate (Elmiron) (PPS) is an oral bladder coating medication that has been helpful in some patients to provide relief of pain. PPS remains the medication choice for most patients. Although the exact way PPS works on the bladder is not completely clear, it is believed to function by coating the bladder lining and reducing potassium leak into the bladder muscle. Patients using PPS need to be aware that the full effect may not be seen for 6 to 9 months, but they can be reassured that many patients see improvement in as little as 4 weeks (9). Intravesicular (in the bladder) installation of other coating medications such as Uracyst and Cystistat also have been found to be helpful. There is a lot of excitement about the use of bladder instillations via a catheter for acute attacks that consist of Elmiron, heparin lidocaine, and sodium bicarbonate. This provides great pain relief for acute attacks in 90% of patients (10).

Medications such as amitriptyline have proved successful in 46% of patients taking this medication. They work by affecting the chemicals in nerve endings. This is thought to reduce nerve firing, irritation, and inflammation that cause pain. It may help with urinary urgency and frequency (11). If a patient cannot tolerate the side effects of amitriptyline, alternatives such as nortriptyline, doxepine, and trazodone have been used. There are no placebo-controlled trials for the use of selective serotonin inhibitors in IC. If there is nerve involvement at the spinal or brain level, as often occurs in longstanding pain, then adding gabapentin (Neurontin), a medication that affects nerve transmission in the brain and spine, may be necessary (12).

Antihistamine medications also are used to stop cells that cause inflammation and pain. Hydroxyzine hydrochloride remains the most effective medication for the management of this inflammation (13).

Traditional pain medications—opioids and synthetic opioids like tramadol—are used to treat the severe pain often associated with this condition (1). Inadequate pain treatment can lead to whole-body pain and amplification of the pain syndrome.

Pelvic Physical Therapy

There are theories that IC is part of a myofascial pain syndrome in which muscles of the pelvic floor are wound up to the point where they are hypersensitive. These knots, called trigger points, are painful if pressed and cause shooting pain. Therapy is often focused to stretch and loosen these wound-up loops of muscle causing them to relax and become less hypersensitive. Most IC clinics will refer to a physical therapist for pelvic PT. This consists of stretching and lengthening the pelvic floor muscles to relax and is done externally as well as internally. The therapist will also teach exercises to the individual to do at home to maintain looseness of the pelvic muscles (14). Muscle relaxation audiotapes, stress reduction, and anxiety management on a daily basis are also needed. Transvaginal manual therapy of the pelvic floor muscles (Thiele massage) has shown promise in relieving the pain associated with IC in at least one open, clinical pilot study (15).

Diet

The foundation of therapy is changing the diet to help patients avoid foods that can further irritate the damaged bladder wall. Common offenders are highly spiced or acidic foods and include alcohol, coffees, teas, all sodas (particularly diet), fruit juices, chocolate, potassium-rich foods such as bananas, tomatoes, citrus fruit, cranberries, the B vitamins, vitamin C, and monosodium glutamate (16,17). The problem with diet triggers is that they vary from person to person; the best way for a person to discover his or her own triggers is to use an elimination diet. Most IC support groups and many urology clinics have diet lists available. One study does show chronic pelvic pain caused by celiac disease in a woman who was able to benefit from a gluten-free diet (18).

Neuromodulation

In this treatment, nerve signals causing pain are changed and reduced (modulated) into nonpainful sensations by the use of small electrical impulses. This

can be done outside the body, e.g., a transcutaneous electrical nerve stimulation (TENS) unit that uses electric current to stimulate the nerves for therapeutic purposes (19). This same process can be done more permanently inside the spine by implanting electrode wires into the lower lumbar or sacral epidural space with a pulse generator implanted into the buttock pocket area that causes continuous stimulation. This is called a spinal cord stimulator implant. Sacral nerve root stimulation (20) has proven to be effective in trial studies. This method is usually kept for patients who have not benefited from other treatments and have undergone a trial placement of the spinal cord stimulator electrodes (usually 1 week), with greater than 50% reduction in their pain scores and increases in activities of daily living.

Surgery

Surgical procedures are rarely used for IC. Even after complete cystectomy (removal of the bladder), many patients continue to experience chronic pelvic pain (21). Surgical interventions for IC include transurethral fulguration and resection of ulcers, using electricity/laser; bladder denervation, in which some of the nerves to the bladder are cut (modified Ingelman-Sundberg procedure) and bladder augmentation. Effectiveness of these procedures is lacking. There are some patients who have had implantation of an intrathecal (spinal) medication infusion device for uncontrolled pain from IC, usually because they are on increasing doses of opioids, which cause them intolerable side effects such as sedation, constipation, confusion, nausea, and itching.

Psychology

Most patients suffering from pain have resulting psychological issues that worsen the pain experience. One of the more beneficial therapies for pain control includes cognitive-behavioral therapy; the patient is taught how to respond to their painful condition in a nondefeating, positive, and constructive way. They are also taught how to recognize errors in their cognition (understanding) about the condition they have and about how this impacts their daily lives and the lives of the people around them. Biofeedback (22) is also used; this therapy trains a person to control their pulse, blood pressure, and breathing in response to pain, therefore altering their pain experience. It is also important to identify other psychological conditions, e.g., anxiety and depression, that might occur with IC and treat it appropriately (23). In a 19-patient study using breathing techniques, relaxation techniques, sitz baths, and diazepam, there was a sig-

nificant reduction in pain in patients over a 3-month period. The doses for antidepressants used to treat pain are usually lower than the doses of antidepressants used to treat depression.

Acupuncture

Affecting nerve transmission through acupuncture occurs by reestablishing a balanced flow of energy, termed Yin and Yang, throughout the body via 12 meridians and multiple acupoints. Stimulation of these points leads to release of various chemicals in the body that change pain transmission and chemistry. A study reported the results of 14 patients with pelvic pain who had 6 to 8 weeks of acupuncture therapy twice a week. Eleven patients had a greater than 50% reduction in pain. This suggests a role for acupuncture in association with other therapies. Many IC clinics offer this treatment (24).

CONCLUSION

There is no evidence that IC is hereditary. Our understanding of this disease has improved greatly over the last 15 years. With new treatment options becoming available, the cornerstone of therapy is multidisciplinary management. The aim is to make the person function at an acceptable level in their life while controlling their symptoms. There is no one single cure for this syndrome and treatment is focused on increasing functional goals and activities of daily living.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

REFERENCES

- [1] Moldwin RM. The Interstitial Cystitis Survival Guide: Your Guide to the Latest Treatment Options and Coping Strategies. Oakland, CA: New Harbinger Publications; 2000.
- [2] Jones CA, Nyberg L. Epidemiology of interstitial cystitis. *Urology*. 1997;49(Suppl 5A):2-9.
- [3] Rosenberg MT, Newman DK, Page, SA. Interstitial cystitis/painful bladder syndrome: symptom recognition is key to early identification, treatment. *Cleve Clin J Med*. 2007;74(Suppl 3):S54-S62.
- [4] National Center for Biotechnology Information Gene Database. FZD8 frizzled homolog 8 (*Drosophila*). Available at: http://www.ncbi.nlm.nih.gov/sites/pubmed?Db=gene&Cmd=retrieve&dopt=full_report&list_uids=8325. Accessed October 10, 2010.

- [5] Keay SK, Zhang CO, Shoenfelt J, et al. Sensitivity and specificity of antiproliferative factor, heparin-binding epidermal growth factor-like growth factor and epidermal growth factor as unique markers for interstitial cystitis. *Urology*. 2001;57(6 Suppl 1):9–14.
- [6] Nordling J, Anjum FH, Bade JJ, et al. Primary evaluation of patients suspected of having interstitial cystitis (IC). *Eur Urol*. 2004;45:662–669.
- [7] Parsons CL, Zupkas P, Parsons JK. Intravesical potassium sensitivity in patients with interstitial cystitis and urethral syndrome. *Urology*. 2001;57:428–432.
- [8] Fukui Y, Kato M, Inoue Y, et al. A metabonomic approach identifies human urinary phenylacetylglutamine as a novel marker of interstitial cystitis. *J Chromatogr B Anal Technol Biomed Life Sci*. 2009;877:3806–3812.
- [9] Parsons CL, Benson G, Childs SJ, et al. A quantitatively controlled method to prospectively study interstitial cystitis and demonstrate the efficacy of pentosan polysulfate. *J Urol*. 1993;150:845–848.
- [10] Parsons CL. Successful downregulation of bladder sensory nerves with combination of heparin and alkalized lidocaine in patients with interstitial cystitis. *Urology* 2005;65:45–48.
- [11] Watson CPN. Antidepressants as adjunctive analgesics. *J Pain Symptom Manage*. 1994;9:392–415.
- [12] Brookoff D. The causes and treatment and pain in interstitial cystitis. In: Sant GR, ed. *Interstitial Cystitis*. Philadelphia: Lippincott-Raven; 1997:177–192.
- [13] Theoharides TC, Sant GR. Hydroxyzine therapy for interstitial cystitis. *Urol*. 1997;49(Suppl 5A):108–109.
- [14] Lukban JC, Whitmore K, Kellogg-Spadt S, et al. The effect of manual physical therapy in patients diagnosed with interstitial cystitis, high-tone pelvic floor dysfunction, and sacroiliac dysfunction. *Urology*. 2001; 57(6 Suppl 1):121–122.
- [15] Mendelowitz F, Moldwin R. Complementary therapies in the management of interstitial cystitis. In: Sant G, ed. *Interstitial Cystitis*. Philadelphia: Lippincott-Raven; 1997:235–239.
- [16] Whitmore KE. Self-care regimens for patients with interstitial cystitis. *Urol Clin North Am*. 1994;21:121–130.
- [17] Rovner E. Treatments used in women with interstitial cystitis: the Interstitial Cystitis Data Base (ICDB) study experience. *Urology*. 2000;56:940–945.
- [18] Porpora MG, Picarelli A, Prosperi Porta R, et al. Celiac disease as a cause of chronic pelvic pain, dysmenorrhea, and deep dyspareunia. *Obstet Gynecol*. 2002;99(5 Pt 2):937–939.
- [19] Fall M, Lindström S. Transcutaneous electrical nerve stimulation in classic and nonulcer interstitial cystitis. *Urol Clin North Am*. 1994;21:131–139.
- [20] Whitmore KE, Payne CK, Diokno AC, Lukban JC. Sacral Neuromodulation in patients with interstitial cystitis: a multicenter clinical trial. *Int Urogynecol J Pelvic Floor Dysfunct*. 2003;14:305–308; discussion 308–309.
- [21] Baskin LS, Tanagho EA. Pelvic pain without pelvic organs. *J Urol*. 1992;147:683–686.
- [22] Dell JR, Parsons CL. Multimodal therapy for interstitial cystitis. *J Reprod Med*. 2004;49(3 Suppl):243–252.
- [23] Magni G, Moreschi C, Rigatti-Luchini S, Merskey H. Prospective study on the relationship between depressive symptoms and chronic musculoskeletal pain. *Pain*. 1994;56:287–297.
- [24] Rapkin AJ, Kames LD. The pain management approach to chronic pelvic pain. *J Reprod Med*. 1987;32:323–327.