PHARMACOLOGIC AND NONPHARMACOLOGIC TREATMENT OPTIONS

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ABSTRACT

Treatment of interstitial cystitis (IC), a chronic inflammatory bladder condition, remains challenging. Whereas the major obstacle to treatment of IC in the past was the absence of effective therapies aimed at the underlying causes of the inflammation, other factors, such as the diverse assortment of treatment approaches and the delay between the onset of symptoms and a confirmed diagnosis of IC, still present a challenge to clinicians. The introduction of intravesical dimethyl sulfoxide in 1978 was an important step forward, providing moderate relief from symptoms and increasing bladder capacity in most patients. The introduction of oral pentosan polysulfate sodium (PPS) in 1996 marked an even greater step forward, providing significant relief from symptoms as well as repair of the damaged urothelium. Oral PPS can also be combined with analgesics and other oral agents to enhance pain relief and resolution of symptoms, as well as with nonpharmacologic interventions such as dietary changes and bladder training to provide additional relief.

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The treatment of interstitial cystitis (IC), a chronic inflammatory condition of the bladder that can adversely affect quality of life, has historically been a major clinical challenge characterized by a wide assortment of treatment approaches, a patient population that is often willing to "try anything" for symptomatic relief, a long delay between the onset of initial symptoms and a confirmed diagnosis of IC, and the absence of a standard therapy and effective treatments that address the underlying pathophysiology of the condition.[1-3] Even today, despite the availability of an approved intravesical agent that provides symptom relief and increases bladder capacity and an approved oral agent that specifically targets and repairs the damaged urothelium, the treatment of IC remains challenging because there is still no single standard therapy or combination of therapies that relieves symptoms in all patients.[1]

In large part, the numerous approaches to therapy reflect the presumed causes of IC, which include a defect in the bladder epithelium that allows irritating substances in the urine to penetrate the bladder wall and cause inflammation[3-5]; inflammatory mast cell release of histamine and other chemicals that promote IC symptoms[3-5]; a substance in the urine that damages the bladder[5]; changes in the nerves that control bladder sensations so that normally pain-free events such as bladder filling become painful[3-5]; autoimmunity following a bladder infection[3,5,6]; and a fastidious microbial agent that is not yet detectable by currently available routine urine culture.[3,7]

Because it is likely that different pathophysiologic processes occur in different subgroups of patients with IC,[5] and because it is also likely that these processes may affect each other[5]—for example, endothelial dysfunction may stimulate mast cells—a treatment regimen that is effective in some patients may not be as effective in others.

The diversity of treatment options, past and present, is amply demonstrated by the findings of the Interstitial Cystitis Data Base (ICDB) study published in 2000.[8] Investigators involved in the ICDB study of nearly 600 women recorded 183 different types of therapy, and further noted that nearly half of these women received a combination of 2 or more of these therapies.

The variety of treatment options, ranging from analgesics and biofeedback to yoga and Zen meditation, is also reflected on the Internet, where numerous websites offer patient and professional information about these options.

Two other important factors that influence the treatment of IC are its frequent misdiagnosis as a urinary

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tract infection, vaginal infection, or endometriosis in women[2,9] or as prostatitis in men,[5] and the delay between symptom onset and a confirmed diagnosis of IC, which is often as long as 5 to 7 years.[1] Thus, many patients with IC may have severe disease by the time IC is correctly diagnosed and appropriate treatment is instituted.[1] As a general rule, the duration of initial pharmacologic therapy is 1.5 months for every year the patient has had IC.[1]

To increase the awareness of IC in the pharmacy community and provide information about current approaches to a historically challenging disorder, this article reviews approved and investigational pharmacologic therapies, addresses various nonpharmacologic treatment options, and describes the use of a multimodal approach for patients with moderate to severe IC.

Pharmacologic Therapy

At present, there are 2 pharmacologic agents that are approved in the United States for the treatment of IC: dimethyl sulfoxide (DMSO), which is instilled into the bladder, and pentosan polysulfate sodium (PPS; Elmiron; Ortho-McNeil Pharmaceutical, Inc; Raritan, NJ), which is given orally. However, as outlined in Table 1, there are numerous classes of oral agents and 3 other intravesical agents that have been used with some success or are currently being evaluated for treatment of IC.[1]

Intravesical DMSO

Approved by the US Food and Drug Administration (FDA) in 1978, intravesical DMSO was the first drug specifically indicated for the treatment of IC.[1] Data from clinical trials suggest that DMSO, an anti-inflammatory analgesic with muscle-relaxing properties,[1] is safe and moderately effective, providing at least moderate relief from symptoms and an increase in bladder capacity in most patients.[10-13] Specific findings from these studies are outlined in Table 2.

The mechanism by which DMSO exerts its effects is unknown. What is known is that it increases reflex firing of efferent axons, increases bladder capacity, releases nitric oxide from afferent neurons, and inhibits the secretion of mast cells.[10,11,14,15]

Table 1. Overview of Pharmacologic Treatment Options for IC

Approved agents
- Oral PPS
- Intravesical DMSO

Off-label or investigational intravesical agents
- Heparin sulfate
- Hyaluronic acid
- Resiniferatoxin
- Anesthetic solutions (therapeutic cocktails) of PPS or heparin and lidocaine with a sodium bicarbonate buffer

Ancillary oral agents
- Analgesics (aspirin, acetaminophen with or without codeine, nonsteroidal anti-inflammatory drugs if used with caution)
- Antibiotics (if concurrent urinary tract infection is present)
- Anticholinergics (for severe urgency and frequency)
- Antihistamines (hydroxyzine hydrochloride 25-75 mg/day for 3 months)
- Antiepileptics (gabapentin)
- Antispasmodics (hycoscyamine sulfate)
- Hormonal therapy (gonadotrophin analogues or oral contraceptives)
- Antidepressants (especially tricyclics)

Multimodal therapy
- Intravesical DMSO or PPS, anesthetic solutions, and nonpharmacologic therapy
- Oral PPS, ancillary oral agents, and nonpharmacologic therapy

IC = interstitial cystitis; PPS = pentosan polysulfate sodium; DMSO = dimethyl sulfoxide.

Table 2. Clinical Trial Findings for DMSO in Patients with IC

Study	Findings for DMSO
Stewart et al[10] N = 46; severe ulcerative ("classic") IC	75% had satisfactory symptom relief About 80% had increased bladder capacity
Stout et al[11] (3-6 installations at varying intervals) N = 12; strictly diagnosed IC	50% to 77% had symptom relief
Perez-Marrero et al[12]* N = 33; biopsies suggestive of IC	93% had objective improvement (vs 35% for placebo) 53% had subjective improvement (vs 18% for placebo)
Barker et al[13] N = 30; biopsy-proven chronic IC	80% had satisfactory symptom relief No morphologic changes noted on endoscopy

*Patients in this placebo-controlled study received 2 treatments every 2 weeks, for a total of 4 treatments each.
DMSO = dimethyl sulfoxide; IC = interstitial cystitis.
Adapted from Dell et al. Multimodal therapy for interstitial cystitis. *J Reprod Med.* 2004;49(3, suppl):243-252.[1]

Because of its analgesic and muscle-relaxant properties, DMSO was initially studied for use as a topical agent that patients could apply to the suprapubic area to relieve IC symptoms. When this resulted in only minimal improvement, intravesical administration was investigated on the premise that it would allow more direct access to the interstitial tissue and thus prevent the muscle contractions leading to pain and urinary frequency and urgency.

Intravesical DMSO is usually administered in the physician's office, but it can be administered by intermittent self-catheterization at home in motivated patients.[1,16] Once the catheter is inserted, DMSO is instilled into the bladder, retained for approximately 15 minutes, and then expelled. Treatments are given once a week or every other week for 6 to 8 weeks, and a response to therapy is usually seen within 3 to 4 weeks after the first 6- to 8-week cycle.[1]

Studies have shown that DMSO produces at least partial remission, but rarely complete remission,[17] and that the majority of patients need more than 1 treatment course.[18] Multiple treatment courses, however, can reduce the duration of remissions.[1] Nevertheless, the beneficial effects of DMSO can be enhanced by the addition of heparin and/or lidocaine,[19,20] as described later in this article.

Although DMSO has a good safety profile, it can leave a garlic-like taste in the mouth and/or odor on the breath or skin for up to 72 hours after it has been administered.[21] Semi-annual blood testing, including kidney and liver function tests, is recommended for all patients receiving DMSO.[1]

Oral PPS

PPS, the first and only oral agent approved by the FDA for the relief of bladder pain and discomfort associated with IC, has been available since 1996.[1-3] Because it coats the damaged bladder epithelium and soothes the inflammation,[1,3] and because it is administered orally, it represents a major advance in the treatment of IC.

A heparin-like compound that is structurally and chemically similar to the naturally occurring glycosaminoglycans (GAGs) produced in the urothelium,[22] PPS is thought to replenish the defective GAG (mucous) layer and inhibit inflammatory processes. Thus, PPS serves as a barrier that reduces cell permeability and prevents irritating solutes in the urine from reaching epithelial cells.[1] Other reports suggest that PPS may have anti-inflammatory properties[23] and a stabilizing effect on mast cells.[24]

The current FDA-recommended dosage of oral PPS is 100 mg (in capsule form) 3 times daily. However, higher (off-label) doses may be needed to relieve symptoms in some patients.[25] One higher-dose regimen of 200 mg twice daily is currently being studied.[3]

While oral PPS may provide pain relief in as little as 6 to 8 weeks in patients who have had an early diagnosis of IC, those diagnosed later in the disease course—usually with moderate disease or worse—usually require 2 to 4 or more months of treatment before experiencing improvement.[1] Patients with severe disease or increased urinary frequency typically require treatment for 6 to 12 months, an observation that accounts for the general recommendation that patients receive oral PPS for at least 6 months.[1-3]

Oral PPS is safe and well tolerated, and it does not interact with other drugs. Side effects, which include headache, nausea, and gastrointestinal discomfort, occur infrequently, and are mild and transient. Although PPS is a heparin-like compound, it has no effect on coagulation profiles when used at recommended doses. Minor liver function abnormalities occur in about 1% of patients, but they are not associated with jaundice or other signs and symptoms of liver dysfunction, and they resolve spontaneously. Therefore, routine liver function tests are not necessary in patients receiving PPS.[1-3]

Several double-blind studies have shown that oral PPS is significantly more effective than placebo in producing subjective improvement (>50%) with regard to pain reduction, urgency, frequency, and nocturia (Table 3).[26-28] It is worth noting that one of the studies, reported by Mulholland et al, included patients who had IC for at least 1 year and who failed to respond to other treatments such as intravesical DMSO or sodium oxychlorosene.[27]

In another double-blind study, 38% of patients receiving oral PPS reported a reduction in pain of over 50% after 3 months of treatment compared with 18% of patients receiving placebo, a statistically significant difference ($P = .005$).[29]

A randomized, double-blind, optimal-dose trial evaluating the efficacy of 3 dosages of oral PPS (300, 600, or 900 mg/day) for 32 weeks in 377 patients at 28 centers found that pain and urinary urgency were significantly lower at study completion than at study entry with all dosages, although differences among the 3 dosage groups at the end of the study were minimal.[30]

All patients underwent the intravesical potassium sensitivity test (PST), an indicator of epithelial permeability, at study entry and completion to determine

whether treatment with oral PPS produced any change in PST results, and all patients rated their symptoms before and after treatment using the Patient Overall Rating of Improvement in Symptoms (PORIS) scale.[30] Of the 198 patients who completed the study, 158 (80%) had a positive PST at study entry, and 92 (58.2%) of these patients reported clinical improvement at study completion, with highly significant improvement in PST pain and urgency scores (P <.0001). In addition, 71% of patients completing the study reported a 50% or greater improvement on the PORIS scale.[30]

The reduction in potassium sensitivity as measured by the PST after PPS treatment demonstrated the efficacy of PPS and also confirmed that the PST is a valid indicator of abnormalities in epithelial permeability and a reliable test for the diagnosis of IC. The PST results and PORIS scale findings also demonstrated that improvement continues as the duration of PPS therapy increases.[30] As shown in the Figure, the percentage of study completers who reported a greater than 50% improvement on the PORIS/Interstitial Cystitis Symptom Index with PPS 300 mg/day increased as the duration of treatment increased.[31]

Other Pharmacologic Interventions

Numerous other pharmacologic agents have been used alone or in combination to treat IC. These include off-label or investigational intravesical drugs, as well as a host of oral agents to relieve pain and treat allergies and other conditions associated with IC (Table 1). Many of these agents have been found to work synergistically with intravesical DMSO and PPS.[1]

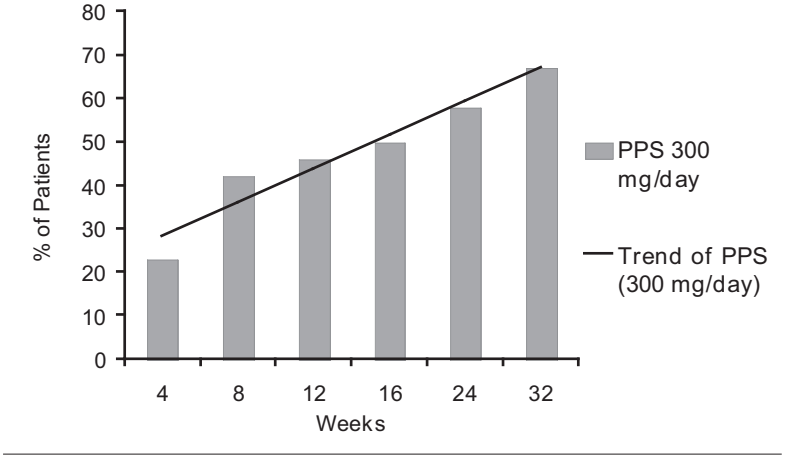
Intravesical agents. Although not specifically indicated for IC, intravesical heparin sulfate has been used off-label for some time, with generally favorable results.[1] Heparin, a normal component of the bladder epithelium, appears to have beneficial antiadherence properties that protect the bladder against bacterial invasion.[32] Intravesical heparin sulfate is believed to correct the mucosal defect in the bladder that promotes irritative bladder symptoms. It can be used as monotherapy or combination therapy for acute management and long-term prophylaxis.[1]

Table 3. Double-Blind Trial Findings for Oral PPS in Patients with IC

Study (dose/duration)	Findings for Oral PPS
Parsons and Mulholland[26] (100 mg 3 times daily x 4 mo) N = 62; IC	Significant increase in subjective improvement vs placebo regarding pain, urgency, frequency, nocturia Significant increase in subjective improvement vs placebo in average voided volumes No significant difference vs placebo in average number of daily voids Responders showed improvement starting with week 5
Mulholland et al[27] (100 mg 3 times daily x 3 mo) N = 110; recalcitrant IC	Greater subjective decrease in pain vs placebo (27% vs 14%) Greater subjective improvement in pressure to urinate vs placebo (22% vs 11%) Greater increase in bladder capacity vs placebo
Hanno[28] (100 mg 3 times daily; open label) N = >2800; IC (1600 continued in open-label phase for >3 to >90 mo)	Significant overall improvement vs placebo Half reported increase in moderate improvement/ pain relief Benefits continued with duration of use

PPS = pentosan polysulfate sodium; IC = interstitial cystitis.
Adapted from Dell et al. Multimodal therapy for interstitial cystitis. *J Reprod Med.* 2004;49 (3, suppl):243-252.[1]

Figure. Percentage of Patients* Reporting a Greater than 50% Improvement† with Ongoing Use of PPS



*Completers.
†Patient Overall Rating of Improvement in Symptoms/Interstitial Cystitis Symptom Index
PPS = pentosan polysulfate sodium. (PORIS/ICSI) assessing pain, urgency, frequency, and nocturia.
Reproduced with permission from Nickel et al. Randomized, double-blind dose-ranging study of pentosan polysulfate sodium (PPS) for interstitial cystitis (IC). *J Urol.* 2001;165(suppl):67.[31]

Studies have shown that intravesical heparin sulfate given 2 or 3 times a week for 3 months can produce clinical remissions and significant improvement in symptom scores in the majority of patients,[33,34] while extended therapy for an additional 3 to 9 months can maintain remission.[33] Other studies have shown that intravesical heparin in combination with DMSO augments symptomatic improvement, reduces the relapse rate, and promotes extended remissions.[14,35]

Hyaluronic acid and resiniferatoxin have recently been under study for the treatment of IC, with the former believed to provide temporary replacement of the defective mucosal lining of the bladder, and the latter providing desensitization of sensory nerve fibers in the bladder. Because the active ingredient in resiniferatoxin is capsaicin, a pepper derivative, an anesthetic solution should be instilled into the bladder first to prevent discomfort.[1]

Anesthetic intravesical solutions, also referred to as "therapeutic cocktails," are used to provide immediate relief of pain and urgency in patients with IC, and may also be especially helpful in patients who are starting therapy with oral PPS and in those with severe disease.[1,25,36] Anesthetic solutions utilize either heparin (10 000-40 000 units) or PPS (100-200 mg, with each 100-mg capsule dissolved in 10 mL buffered normal saline) as the active ingredient, which is then combined with 3 mL 8.4% sodium bicarbonate and 10 mL 1% lidocaine or 16 mL 2% lidocaine.[19,33,36] The solution is then instilled into an empty bladder, where it is retained for approximately 30 minutes or until the patient needs to void. Each instillation can relieve IC symptoms for several hours to several days.[1,3]

Ancillary oral agents. As summarized in Table 1, numerous classes of oral medications are used as adjunctive therapy in the management of IC. Analgesics such as aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs), which inhibit prostaglandin synthesis, can be used to alleviate mild discomfort. Because NSAIDs are associated with increased histamine release, which can worsen IC symptoms, they should be recommended with caution.[1] For patients with severe pain, short-term narcotic therapy may be necessary.

Antihistamines can be used to alleviate nocturia and reduce IC symptoms, especially in patients with a history of allergy,[37] and antibiotics are frequently prescribed for patients with concurrent urinary tract infections.[1-3]

Antidepressants, particularly amitriptyline and other tricyclic agents, are useful in enhancing pain relief and facilitating sleep. Tricyclic antidepressants enhance pain relief by inhibiting histamine release from mast cells and decreasing the reuptake of norepinephrine and serotonin in the central and peripheral nervous systems.[1-3] Amitriptyline, which has anticholinergic properties, appears to modulate mild to moderate pain and reduce nocturia and urinary frequency.[38] Patients who receive a prescription for an antidepressant should be assured that it is being prescribed to provide additional relief from pain and nocturia rather than for psychiatric reasons.

Other ancillary oral medications used in the treatment of IC include antispasmodic agents such as hycoscyamine, the antiepileptic drug gabapentin, gonadotropin analogues or oral contraceptives, and, for patients with severe urgency and frequency, anticholinergic agents such as oxybutinin.[1-3]

Nonpharmacologic Therapy

As with pharmacologic therapy, there are numerous nonpharmacologic modalities that have been used to treat IC (Table 4). Although nonpharmacologic therapies rarely provide sufficient relief from IC symptoms when used as monotherapy, they often enhance the effects of pharmacologic therapy.

Dietary Modification

Numerous case reports have suggested that eliminating foods high in potassium or acid—tomatoes, citrus fruits, coffee, tea, chocolate, alcohol, and spices—can minimize IC symptoms.[1-3] Many patients find that dietary modification, with or without supplements that reduce acid levels in the blood, urine, and saliva, is helpful. Patients who use this approach should also be advised to eliminate or reduce the use of bladder irritants such as artificial sweeteners and cigarette smoking to avoid exacerbation of symptoms.[1-3]

Stress Reduction and Physical Therapy

Many patients find that stress reduction modalities and/or physical therapy are helpful. One recent report, for example, noted that yoga has been extremely useful in relieving pain and improving quality of life in patients with IC and other chronic urologic conditions.[39]

Similarly, 2 recent studies reported the benefits of manual massage of the pelvic floor musculature (Thiele massage).[40,41] One study noted that twice-weekly massage for 5 weeks was very helpful in relieving irritative bladder symptoms and decreasing pelvic

Table 4. Overview of Nonpharmacologic Treatment Options for IC

Dietary modification and supplements
- No caffeine, alcohol, spices, and foods high in acid, particularly citric acid
- Acid-reducing supplements

Stress reduction techniques and physical therapy
- Yoga
- Pelvic floor muscle massage
- Pelvic floor relaxation exercises (biofeedback)
- Exercises and hot and cold packs to relieve pain
- Other techniques

Bladder training/behavioral modification
- Timed voiding (often used in conjunction with biofeedback)

Cystoscopy with hydrodistention under anesthesia

Electrical nerve stimulation
- Transcutaneous
- Sacral root

Surgery
- Used only as a last resort

IC = interstitial cystitis.

floor muscle tone in women with documented IC and high-tone pelvic floor dysfunction.[40] The other study, which included men and women with IC and urge-frequency syndrome, demonstrated that twice-weekly massage for 8 to 12 weeks effectively ameliorates the symptoms of both conditions.[41]

Other stress reduction and physical therapy techniques that have been used, with varying degrees of success, include pelvic floor relaxation exercises (with or without biofeedback), gentle stretching exercises, warm sitz baths, and applications of heat (hot pack or heating pad) or cold.[1-3]

Bladder Training and Behavioral Modification

Bladder training, which involves behavioral modification and is often used in conjunction with pelvic floor relaxation exercises and biofeedback, is an important nonpharmacologic approach to managing patients with IC.[1-3]

Bladder training, which is also referred to as bladder retraining, is best suited for patients with mild to moderate pain.[42] It is based on the premise that patients with IC, who void an average of 16.5 times a day compared with an average of 6.5 times a day among healthy subjects,[42] can be taught to void at designated times, gradually increasing the time between voids to 3 to 4 hours. Patients are also taught relaxation and distraction techniques to help maintain the schedule.[1-3]

Cystoscopy with Hydrodistention

In addition to being used to confirm a diagnosis of IC and assess a patient's maximum bladder capacity, cystoscopy with hydrodistention under anesthesia is used as a therapeutic procedure. A recent study has found that it lessens symptoms in 30% to 60% of patients, particularly if they have less severe disease.[43] However, improvement is typically delayed because symptoms temporarily worsen in the initial period after hydrodistention.

Electrical Nerve Stimulation

Both transcutaneous and sacral root electrical nerve stimulation, which have been used to treat patients with various pain syndromes, have been investigated as a treatment option for patients with IC and other dysfunctional bladder conditions. As noted in a report of a literature search to ascertain the benefits of transcutaneous electrical nerve stimulation (TENS) in patients with IC, detrusor overactivity, and stress incontinence, results were difficult to assess because of differences in patient selection criteria, small study samples, and deficient reporting of objective and subjective outcomes.[44] Nevertheless, TENS produced a beneficial effect in some studies of patients with IC and detrusor overactivity, prompting the investigators to conclude that further studies of TENS in these patients were justified.

A study of long-term treatment with TENS found that it produced remission in patients with IC, with overall results being better in those with classic IC than in those with nonulcer IC.[45] A prospective study of 23 patients with classic IC found that TENS reduced pain in 18 and returned urinary frequency to normal in 8.[46] However, a study comparing traditional acupuncture with TENS in patients with chronic IC found that both modalities had a very limited effect on voiding frequency, mean and maximal voiding volumes, and symptom scores.[47]

Data for sacral root electrical nerve stimulation are more positive. In a study of 6 consecutive patients with IC, percutaneous neurostimulation of the sacral third nerve root significantly reduced symptoms and normalized urinary factors that are specifically altered in IC.[48] Another study found that a permanently implanted nerve stimulator produced moderate or marked improvement in urinary frequency, urgency, pelvic pain,

pelvic pressure, incontinence, and overall quality of life in more than two thirds of 26 patients with refractory IC.[49] Moreover, a multicenter clinical trial found that percutaneous sacral nerve root stimulation produced statistically significant reductions in frequency, pain, and average and maximum voided volumes in women with refractory IC.[50]

Surgery

Surgery is reserved as a last resort. There are 4 options, and none of them ensures success. Hunner's ulcers can be burned or fulgurated with electricity or a laser, or they can be resected and removed. In many cases, there is a dramatic initial improvement, but ulcers and pain tend to recur within 1 to 2 years.[1,2]

Bladder augmentation, which involves attaching a small segment of the large intestine to the bladder to enlarge it or replace badly ulcerated portions, reduces urinary frequency but does not necessarily reduce pain. Ironically, IC may recur in the bowel segment used to enlarge the bladder, and frequency and urgency may remain or return after surgery.[1,2]

Cystectomy, or removal of the bladder, is reserved for those rare patients in whom all other therapies have failed.[1,2]

Multimodal Therapy

A multimodal therapeutic approach, which combines oral PPS with ancillary oral agents, adjunctive intravesical therapy, and nonpharmacologic options, may be necessary for patients with moderate to severe disease.[1,3] Given the delay between initial symptom onset and a confirmed diagnosis of IC, many patients may already have moderate to severe disease by the time IC is diagnosed and treatment is initiated.

Oral PPS is the foundation of multimodal therapy. While PPS resurfaces the GAG layer on the bladder epithelium, individualized therapy with ancillary oral agents—antihistamines for patients with allergic flares, for example, or anticholinergics for patients with severe frequency and urgency—can be used to supplement its healing effects. If necessary, adjunctive treatment with intravesical anesthetic solutions can be instituted to speed the response to therapy. Nonpharmacologic treatments can be integrated into the multimodal therapy plan as appropriate.[1,3]

Also integral to the multimodal approach are a clinical assessment after 3 months of therapy, when medications can be adjusted as needed, and regular assessments at 3- to 6-month intervals. Patients who are symptom-free at any of these visits can be weaned, 1 medication at a time.[1,3]

As with all chronic pain syndromes, patients with IC need current and accurate information, ongoing support, and understanding.

Conclusions

With the availability of 2 approved pharmacologic agents, the treatment of IC is less challenging and more effective than it was in the past. Nonetheless, it still presents a challenge because of the wide assortment of off-label pharmacologic and supplementary pharmacologic and nonpharmacologic options. Because there is no single standard treatment, the need to individualize therapy is essential.

Multimodal therapy, using oral PPS as the foundation, provides patients, particularly those with moderate to severe IC, with effective treatment options and a treatment plan that can be individualized and modified as necessary. Together with patient education, ongoing support, counseling, and sensitivity to the chronic and painful nature of IC, the multimodal approach increases the chances of enhanced symptom relief and improved quality of life.

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