Interstitial Cystitis: Understanding the Syndrome

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Abstract

Interstitial cystitis (IC) is a chronic pain syndrome that affects close to a million people in the United States. The syndrome presents differently in many individuals, with the unifying factor being chronic pelvic pain and disruption of daily life activities. Many etiologies have been proposed as causative factors for IC, although it is likely triggered by more than one process. Treatment for many individuals revolves around symptom management and improving quality of life; however, it is imperative to remove aggravating factors such as food and daily stressors. Treatment will vary for individuals, as symptoms and etiology will differ. This article discusses nutritional and other non-toxic approaches to treating IC.

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Introduction

Interstitial cystitis is a chronic, debilitating, multifactorial syndrome characterized by pelvic and/or perineal pain, urinary urgency and frequency, and nocturia. This symptom complex has also been called painful bladder syndrome, leaky bladder syndrome, and irritative bladder syndrome. Individuals diagnosed with this syndrome typically fit no other pathologic picture, including urinary tract infections, carcinoma, or cystitis induced by radiation or medication.[1]

Interstitial cystitis was first described by Hunner in 1915, in patients who presented with fibrotic, contracted bladders and the presence of distinctive ulcers of the bladder epithelium.[2,3] At the time, IC was considered extremely rare. Today, epidemiological studies reveal quite different numbers. In a Finnish study in 1990, the annual incidence of new cases was estimated at 1.2 per 100,000 and the prevalence at 10-11 per 100,000.[4] By 2002, a similar Finnish study revealed the prevalence jumped to 450 per 100,000.[5] In 1997, Jones and Nyberg reported an incidence of 500,000-1,000,000 cases of IC in the United States.[6] A more recent population-based study revealed the incidence of IC to be as high as 52-67 per 100,000 cases, more than 50-percent greater than previously reported.[7]

IC has no single, definable presentation, but is best viewed as a continuum extending across decades of an individual's life, beginning with mild, intermittent symptoms. Ultimately, after years of remissions and relapses, symptoms become more severe and more constant. Most IC patients suffer from urgency and frequency in the early stages of disease. As the disease progresses, pain increases in severity and becomes the most dominating and debilitating symptom. For many, the pain becomes so severe it significantly impacts their personal and professional life.

Levels of pain not only correlate to stage of disease, but also vary with fluctuating factors that can provoke symptom flare-up, such as allergies and hormonal cycles. Although not well documented, it has been observed by many clinicians that IC symptoms are exacerbated the week before menses. In addition, both women and men with this condition may experience the most severe pain during or following sexual intercourse.

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This can be extremely psychologically damaging, as it places significant burden on relationships and often results in severe depression.

Pathophysiology

Several etiologic factors have been proposed for IC, involving structural, neurological, autoimmune, lymphatic, infectious, and psychological factors. These etiologies remain largely hypothetical, as insufficient data is available to definitively establish their roles in the pathology of IC. However, in any given patient, a combination of factors likely plays a role in causing insult to the bladder epithelium.

Normal bladder epithelium possesses an anionic, hydrophilic, sulfated glycosaminoglycan (GAG) surface layer that, when healthy, protects the bladder from noxious elements including microorganisms, toxins, carcinogens, and hyperosmolar, acidic and potassium-rich urine. Through the resulting formation of a water barrier of ionic hydrogen-sulfate bonds, the GAG layer has been found experimentally to prevent proteins, ionic substances, and non-ionic entities from contacting the luminal surface of the bladder (Figure 1).[8,9] Parsons et al have suggested breakdown of this "bladder protective layer" leads to changes in permeability, stimulation of pain receptors, and inflammatory/hyperalgesic symptoms.[10] Further investigations by Parsons using the potassium sensitivity test confirmed this theory.

Neurological up-regulation is likely an important component in the pathogenesis of IC. Neurogenic inflammation is a process by which sensory nerves may secrete inflammatory mediators, resulting in hyperalgesia and inflammation. Substance P, a short chain peptide, is a central component of this process. Substance P is an inflammatory mediator that functions as a nociceptive neurotransmitter in the central and peripheral nervous system. When released by peripheral nerves, substance P causes an inflammatory cascade to occur, resulting in such processes as mast cell degranulation and activation of nearby nerve terminals. Several studies support this theory, having found increased numbers of substance P-containing nerves in patients with IC.[11,12] In addition, substance P has been found in the urine of women with IC, with increased concentrations dependent on the severity of pain.[13]

Figure 1. *A Depiction of Normal and Abnormal Bladder Epithelium*

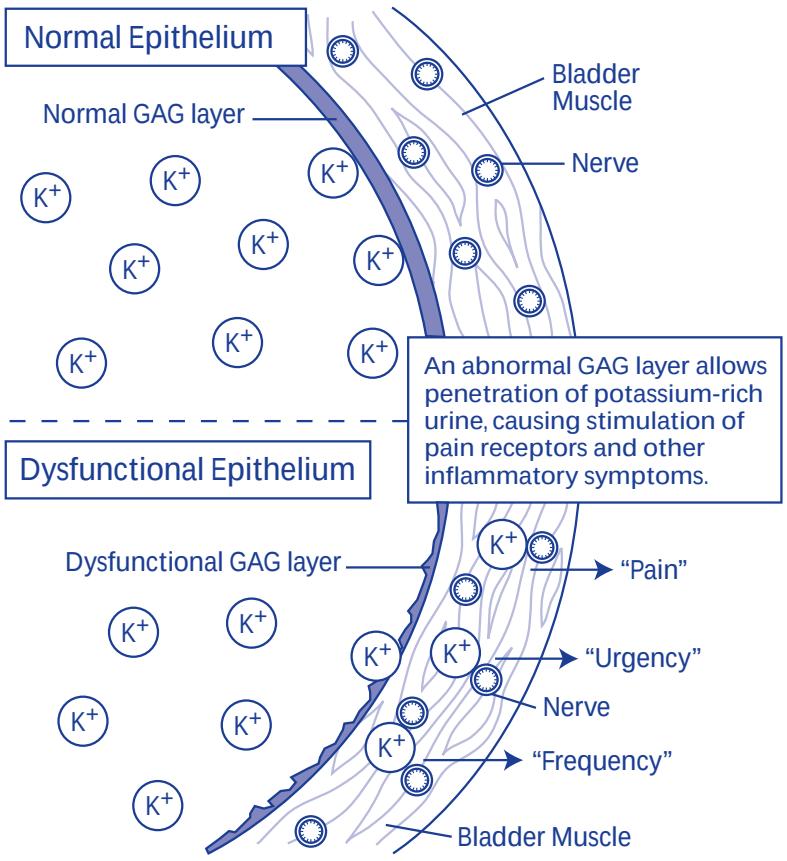


Table 1. *Potential Role of Estrogens in Interstitial Cystitis*

- The syndrome exists almost exclusively among women
- Symptoms are often worse premenopausally or during ovulation
- Estrogens exacerbate many autoimmune conditions
- Estrogens worsen atopic disease
- Estrogens augment mast cell activation
- Estrogens induce mast cell proliferation

One recent study revealed no significant increase in substance P in women with IC when compared to a control group;[14] however, the control group consisted of women who suffered from symptoms of stress incontinence.

As many as 40 percent of female IC patients report symptoms worsen premenstrually, particularly around the time of ovulation, although symptoms often improve during pregnancy.[15] Sensory afferent nerve fibers for pelvic organs, including the bladder, are found within the hypogastric and pelvic nerves.[16] In female rats the threshold of the hypogastric and pelvic nerves for recognition of mechanical stimuli applied to the reproductive organs was found to vary with phases of the estrous cycle. This observation also appeared to correlate with fluctuations observed in pain sensation associated with bladder disorders during the menstrual cycle. Ultimately, it can be presumed that estrogen may play a role in determining the intensity of the response to neurogenic inflammation within the bladder (Table 1).

There is considerable research suggesting mast cells play a significant role in the pathology of IC; whether causative or secondary is not yet known. As a causative agent, mast cells could produce the symptoms of IC simply by degranulating. It is also possible mast cells are responding to an irritating factor in IC, such as leaky epithelium. If the latter is true, then the mast cell response may simply contribute to and compound the severity of an epithelial leak.[17] Mastocytosis has been reported in the bladders of 30-65 percent of patients with IC.[18,19] The validity of this data is called into question, however, as it is technically difficult to measure mast cells that have already degranulated. Further evidence of mast cell involvement comes from increased levels of histamine in the walls of bladder epithelium in patients with IC[20] and increased urinary excretion of 1,4-methylimidazole-acetic acid, a histamine metabolite, by these same patients.[21]

Interstitial cystitis has the classic picture of an autoimmune disease: symptom chronicity with exacerbations and remissions, frequent organ-specific mononuclear cell infiltrates, the lack of a clearly defined pathogen, and occasional response to steroids or other immunosuppressants.[22,23] Studies investigating autoimmunity as a possible etiology have been inconclusive and conflicting. Some literature suggests the presence of specific bladder auto-antigens is an indirect response to local cellular damage.[24]

Interstitial cystitis presents a similar clinical picture to bacterial cystitis; however, urinalyses and urine cultures routinely demonstrate no evidence of infection. There is significant debate as to whether IC is associated with latent bacterial infection, as documented urinary tract infections often precede chronic bladder symptoms.[25] To date, no consistent organism has been isolated in urine or bladder biopsy specimens. Schillings et al describe the possibility of an occult *E.coli* infection within the underlying epithelium.[26] They describe the host defense system as being able to effectively eradicate 99 percent of the acute bacterial infection, with a small percentage of organisms persisting in the bladder tissue – intracellular, but persistent nonetheless.

Diagnostic Criteria

In 1987 and 1988, the National Institutes of Health (NIH) convened workshops to develop diagnostic criteria for a research definition of IC (Table 2).[27] When used as guidelines for clinical diagnosis, however, these criteria tend to miss all but advanced-stage IC. Data from two recent studies indicate the National Institute of Diabetes, Digestive, and Kidney Diseases criteria miss approximately two-thirds of IC cases when strictly applied,[28,29] and, in fact, likely miss more than these estimates demonstrate.

Interstitial cystitis patients frequently have overlapping symptoms related to other pelvic organs. Diseases with a symptom picture similar to IC that need to be ruled out include urinary tract and genital tract infections, tumors of the urogenital and gastrointestinal tract, certain gynecological tumors, previous pelvic irradiation, carcinoma in situ, previous exposure to toxins such as chemotherapeutic agents, and a history of endometriosis.[6] IC often becomes a diagnosis of exclusion.

Many patients with IC are treated with repeated courses of antibiotics before being definitively diagnosed, ultimately creating digestive disturbances. IC should be considered in the differential diagnosis of patients with symptoms of cystitis who are unresponsive to antibiotics, especially if urine cultures are negative. Up to 70 percent of men with symptoms of nonbacterial prostatitis and prostatodynia have the cystoscopic appearance of IC when observed under anesthesia, suggesting chronic prostatitis/prostatodynia and IC may be the same syndrome.[30,31]

Table 2. *National Institutes of Health Diagnostic Criteria for Interstitial Cystitis*

Category A: At least one of the following cystoscopic findings:
1. Diffuse glomerulations (≥10 per quadrant) in at least 3 quadrants of the bladder
2. A classic Hunner's ulcer

Category B: At least one of the following symptoms:
1. Pain associated with the bladder
2. Urinary urgency

In addition, a patient must not have any of the following conditions, symptoms, or history:
- Age <18 years
- Urination frequency while awake < 8 times per day
- Nocturia < twice per night
- Maximal bladder capacity >350 cc while patient is awake
- Absence of an intense urge to void with bladder filled to 100 cc of gas or 150 cc of water, with medium filling rate during cystoscopy
- Involuntary bladder contractions
- Symptoms persistent < 9 months
- Symptoms relieved by microbial agents, anticholinergics, or antispasmodics
- Urinary tract or prostate infection in the past three months
- Active genital herpes or vaginitis
- Urethral diverticulum
- Uterine, cervical, vaginal, or urethral cancer within the past five years
- History of cyclophosphamide, chemical, tuberculous, or radiation cystitis
- History of bladder tumors

Diagnostic evaluation should begin with urinalysis, urine microscopy, cytology and culture, and cystoscopy. Bladder biopsy may be performed if clinically warranted. The presence of submucosal hemorrhage after bladder distension in an anesthetized patient,[32] or the presence of Hunner's ulcer, is considered to be diagnostic in patients who have the symptom complex.

Because IC mimics many gynecological conditions, it is important to perform a complete pelvic exam, including inspection of the vestibule to Hart's line and assessment of the levator ani muscles and utero-sacral ligaments. The uterus, cervix, and adnexa should also be assessed for any abnormalities and/or pain. A wet prep of vaginal discharge should be performed to assess for chronic recurrent infections or atrophy. In addition, a pelvic ultrasound should be considered.

The intravesical potassium sensitivity test, also known as Parson's Test, was first introduced in 1994.[33] In a later investigation on a large group, 75 percent of patients with IC had a positive potassium sensitivity test.[34] In the test, a dilute solution of potassium (40 mEq in 100 mL of water) is left in the bladder for five minutes. The patient then rates the degree of provocation with urgency and frequency on a scale of zero (no provocation) to five (marked provocation). A positive test is defined by a change in score of greater or equal to two. The potassium sensitivity test has been advocated as a minimally invasive, office diagnostic test for IC. Presumably, the hyperalgesia effect elicited by this test is due to enhanced absorption of the potassium salt through the "defective" GAG layer. If a dysfunctional epithelium allows for deposition of potassium into the bladder muscularis, potassium is allowed to depolarize nerves and muscles, leading to tissue injury. As this test may only define a subgroup of IC patients with epithelial permeability dysfunction, it is not considered definitive. A recent study also suggests the potassium sensitivity test may predict responsiveness to the pharmaceutical agent sodium pentosan polysulfate.[35]

In an effort to search for noninvasive techniques for the diagnosis of IC, a series of urinary markers is being evaluated. A subgroup of IC patients have an increased number and activation of mast cells, paralleled by increased levels of urinary histamine and histamine metabolites (such as methylhistamine) and tryptase (a specific mast cell enzyme).[36] Other suggested urinary markers include urinary nitric oxide, glycosaminoglycans, epinephrine, nitric oxide synthase, cyclic guanosine monophosphate, and interleukin-1β.[37] Most recently, urinary antiproliferative factor (APF)[38] and glycoprotein-51 (GP-51)[39] have demonstrated potential use as clinical markers of IC. Ongoing studies are attempting to correlate urinary levels of APF and GP-51 with cystoscopic and biopsy findings as well as treatment outcomes.

Conventional Treatment

The first principle in treating IC is correcting the problem of epithelial dysfunction. Pharmaceutically, this is accomplished by instilling into the bladder a heparinoid compound, pentosan polysulfate, with a structure similar to that of bladder-surface glycosaminoglycans. Currently, this is the only pharmaceutical agent that has undergone thorough study in double-blind trials and is the only FDA-approved drug specific for IC.[40-42]

Bacillus Calmette-Guerin (BCG), a common intravesicular agent used in bladder cancer, is an attenuated strain of *Mycobacterium bovis*. Recently, BCG was tested in a double-blind, placebo-controlled study to evaluate the efficacy of six weekly BCG treatments in IC patients.[43] The treatment group initially reported a 60-percent favorable response rate with a 27-percent placebo response. Long-term follow-up revealed 89 percent of patients continued to have symptom improvement 24-33 months after initial treatment.

The mechanism of action for BCG is not clearly understood, but it is speculated it may be responsible for stimulating a T-helper 1 (Th1) response, thus leading to the destruction of inflammatory cells and a decrease in T-helper 2 (Th2) mediated allergic response. BCG also appears to increase urinary nitric oxide levels in bladder cancer patients, suggesting an additional hypothetical mechanism of action. Uncontrolled trials suggest urinary nitric oxide levels are decreased in IC patients and increased levels are often associated with symptom improvement.[44]

Concurrent etiologic factors in IC have led to recommendations of other pharmaceutical agents to address the allergic and neuroendocrine components of the disease – the antihistamine agent hydroxyzine to control the mast cell response and antidepressants such as amitriptyline to reverse neural activation in the bladder. In addition, other antidepressants are often prescribed to address the psychosocial impact of the disease.

Lifestyle Intervention

For many individuals battling IC, dietary modifications are a good first-line therapy. Between 53-63 percent of IC patients can identify acidic fluids or foods that exacerbate symptoms or cause a flare-up.[15,45] In one study, a review of three-day food diaries completed by IC patients revealed the intake of acidic substances was associated with an increase in painful bladder symptoms 2-24 hours after ingestion.[46] Acidic foods include, but are not limited to, alcoholic beverages, carbonated drinks, caffeine, spicy foods, tomatoes, and vinegar.

Foods high in arylalkylamines (tryptophan, tyrosine, tyramine, and phenylalanine) have also been implicated in triggering IC symptoms. In 1993, Gillespie evaluated 250 patients with hypersensitive bladders. He instructed patients to ingest an excess of foods high in arylalkylamines over a 24-hour period. He reported elevated 24-hour urine levels of tryptophan metabolites (kynurenine, xanthurenine, and indicans) compared to controls. Arylalkylamine-containing foods include, but are not limited to, bananas, beer, cheese, chocolate, mayonnaise, aspartame, nuts, onions, raisins, sour cream, wine, and yogurt.[46] In an earlier study by Kaufman et al, tryptophan metabolites of 3-hydroxykynurenine and hydroxyanthranilic acid were found to cause GAG disruption, providing the potential for harmful urinary metabolites to contact unprotected bladder epithelium.[47]

Due to increased urinary frequency, IC patients tend to restrict fluid intake. A decrease in urinary frequency, however, is accompanied by an increase in pain, likely due to a higher concentration of irritating agents in the urine. Furthermore, fluid restriction can lead to low levels of dehydration, which can ultimately cause myriad clinical problems. IC patients should be encouraged to drink adequate amounts of water to flush out irritating components. Anecdotally, urinary alkalinizing agents, such as potassium citrate or sodium bicarbonate (baking soda), have been useful to decrease urinary irritation.

Not all IC patients are sensitive to the same foods. An elimination/challenge diet is the gold standard in such cases, paying particular attention to foods high in acids and arylalkylamines. After avoidance of these foods for a six-week period, individuals should reintroduce the eliminated foods one at a time and be aware of aggravating symptoms that can appear as quickly as a few hours after reintroduction.

The quality of life for many IC patients has been shown to be worse than that of patients undergoing dialysis for end-stage renal disease.[48] In severe cases, pain is unremitting and an individual may have urinary frequency up to 60 times a day. Nocturia can be as often as every 20 minutes, resulting in subsequent sleep deprivation. Due to such strains on an individual's life, an IC patient is often unable to work, perform daily life activities, and in severe cases, unable to leave the house. The economic impact of the disease in 1987 was estimated at $1.7 billion annually,[48] a figure that has undoubtedly risen in 16 years.

Mental and emotional stressors appear to be precipitating factors for IC relapse. In a study by Koziol et al, 60 percent of patients with IC reported stress as a causative factor for disease recurrence.[45] Norepinephrine levels appear to be uniformly elevated in patients with IC, suggesting neuroendocrine involvement and neurogenic inflammation.[49]

One study compared 45 IC patients with age-matched controls.[50] A significant relationship between stress and urgency was observed in the IC patients. Furthermore, it was noted that in individuals with moderate-to-severe disease, pain was associated with increased levels of stress. Greater stress was noted among individuals with increased nocturnal frequency. Stress-symptom relationships were not observed among controls. It is important to recognize that in the case of IC, stress can be both a consequence of IC symptoms

and a source of symptom exacerbation. Either way, it is essential, in the treatment of this syndrome, to address the mental/emotional implications for each individual.

Nutritional Supplementation

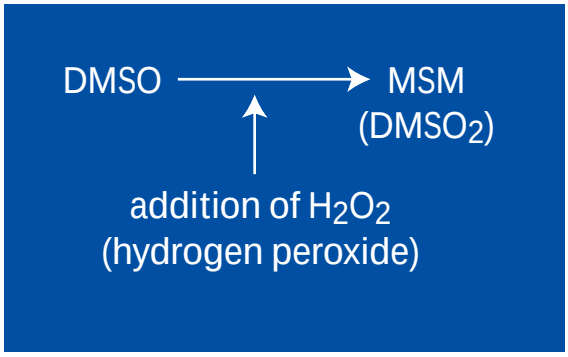
Sulfur Donors

Dimethylsulfoxide (DMSO) has been used in the treatment of IC since the 1960s. The effect of DMSO may be due to its ability to initially release and deplete substance P from the bladder wall and stimulate mast cell degranulation.[44] Perez-Marrero et al reported the first placebo-controlled trial of DMSO for IC in the *Journal of Urology* in 1988.[51] In this trial, 33 patients were randomly assigned to receive either 50 cc of 50-percent DMSO or a 50-cc placebo (saline) instilled in the bladder at two-week intervals for two sessions of four treatments each. Fifty-three percent of the DMSO group reported marked improvement of symptoms, compared with 18 percent in the placebo group. In the DMSO group, 93 percent exhibited objective signs of improvement in cystometric urge and pain at maximum cystometric capacity, compared to 35 percent in the placebo group. Due to DMSO's distinct smell, blinding is difficult, resulting in 70 percent of patients identifying their treatment.

In a study using DMSO in the treatment of inflammatory genitourinary disorders including IC, 100 cases of "classic" IC were treated, with 54 percent reporting good or excellent results and 35 percent reporting fair or poor results. Over half experienced long-term satisfaction.[52] One limitation to using DMSO is a garlic-like breath odor and taste in the mouth due to pulmonary excretion of a small percentage of the DMSO as dimethyl sulfide.[53] In addition, some patients report a burning sensation and pelvic pain after intravesicular DMSO treatment, likely due to DMSO-induced release of histamine from mast cells or transient chemical cystitis.[54]

Due to the side effects of DMSO, Dr. Stanley Jacob at the Oregon Health and Science University has pioneered treatment with methylsulfonylmethane (MSM), also known as dimethyl sulfone (DMSO2) (Figure 2). To date, he has treated approximately 200 patients with IC. Treatment appears to be better tolerated, as MSM does not have the same odor as DMSO.[55] Intravesicular treatment with MSM is often combined with oral, topical, and IV administration. An oral dose of MSM should start at 1 g daily, gradually increasing the dose to 18 g under physician supervision. While the benefit from DMSO is obtained faster, patients do not tolerate it as well. It is estimated that approximately 80 percent of patients show improvement with MSM treatment, although it has not yet been subjected to controlled clinical trials.

Figure 2. Conversion of DMSO to MSM



Chondroitin Sulfate

One longstanding etiologic theory is that symptoms of interstitial cystitis can arise from deficits or damage to the GAG layer in the bladder lumen. A study compared chondroitin sulfate proteoglycans on the luminal surface of bladders of IC patients with those of controls.[56] Bladder biopsy specimens revealed a significant difference in IC versus controls in the prevalence of chondroitin layers. Further studies have revealed chondroitin sulfate is a potent mast-cell inhibitor.[57]

Heparin, a pharmaceutical with a similar structure to chondroitin sulfate, has also shown *in vivo* inhibition of histamine release.[58] In addition,

many IC sufferers respond clinically to treatment with intravesicular GAGs, such as heparin[59] and Elmiron® (pentosan polysulfate).[40] Although no research has been performed to date, oral chondroitin sulfate at doses of 1200 mg daily has been used clinically, with moderate success and no side effects.

L-Arginine

Nitric oxide deficiency may have a fundamental role in the inflammatory and urodynamic abnormalities present in IC. Since trials suggest urinary nitric oxide levels are decreased in IC patients and increased levels are often associated with symptom improvement,[44] L-arginine, the natural precursor of nitric oxide, has been studied in a series of trials, albeit with mixed results.

Two randomized, placebo-controlled trials have been conducted as well as three uncontrolled trials. Sample sizes were relatively small in all studies, ranging from eight to 53 patients. Dosages of L-arginine ranged from 1.5-2.4 g daily for 1-6 months. While only one study showed no change in symptoms or nitric oxide levels,[60] other studies revealed a relative, but statistically insignificant reduction in IC symptoms following L-arginine supplementation.[61-64] It is likely these studies did not reveal statistical significance due to small sample size; therefore, L-arginine may be considered in the treatment of IC, as side effects have not been observed with supplementation.

Plant Sterols

As mentioned, the suspected mechanism of action of BCG is believed to be immunomodulation – stimulation of a Th1 response, resulting in destruction of inflammatory cells and a dampening of the Th2 response. Sterols and sterolins, also known as phytosterols, are fats present in all plants, including fruits and vegetables. Although chemically similar to the animal fat cholesterol, they have been shown to exhibit unique biochemical effects, such as immune modulation. *In vitro* studies have revealed that plant sterols, in a ratio of 200:1 (beta-sitosterol:beta-sitosterolin) can selectively enhance activity of Th1 cells, while leaving unchanged or dampening the effect of Th2 cells. In addition to decreasing the inflammatory cytokines associated with IC, plant sterols can also result in maintenance of cortisol and elevation of DHEA levels, thereby decreasing cortisol:DHEA ratios and buffering a negative stress response.[65]

Bioflavonoids

Mast cell inhibition is considered a reasonable goal in the treatment of IC. The drug hydroxyzine, a commonly used antihistamine and anxiolytic, has shown promise in open-label trials of IC and is currently being evaluated in a randomized study as a part of the NIH's Interstitial Cystitis Clinical Trials Group (ICCTG). Quercetin, a naturally occurring bioflavonoid found in high concentration in red wine, onions, and green tea, has also been shown to experimentally reduce the release of mast cell histamine.[66-68] Quercetin has recently demonstrated effectiveness in the treatment of category III chronic prostatitis, a condition with many parallels to IC.[69] Thirty men with prostatitis were randomized to receive either placebo or quercetin 500 mg twice daily for one month. After one month, 20 percent of the placebo group and 67 percent of the quercetin group reported at least 25-percent improvement in symptoms. Therapy was well tolerated. Chronic prostatitis, like IC, is a chronic, pelvic pain syndrome that has had limited success with other therapies. Because this trial revealed significant symptom relief with minimal side effects, research on quercetin's impact on IC is indicated.

Melatonin

Melatonin, the chief secretory product of the pineal gland, is a direct free radical scavenger and an indirect antioxidant that acts to stabilize cell membranes, making them less susceptible to oxidative insult, ultimately decreasing inflammation.[70,71] As a free radical-generating system, lipid peroxidation has been linked to inflammation-induced tissue damage with malondialdehyde levels being a good indicator of peroxidation rates.

In a recent study, melatonin showed promising results in exerting urothelial protection by

preserving the urothelial GAG layer in rats exposed to protamine sulfate, a known bladder irritant.[72] In this study, melatonin, dosed at 20 mg/kg, was given to rats following intravesicular injection of protamine sulfate. This group was compared to a control group and a protamine sulfate group not treated with melatonin. The melatonin group demonstrated increased epithelial integrity and decreased mast cells and lipid peroxidation. Protamine sulfate caused a significant increase in malondialdehyde levels. In the melatonin-treated group, there was an inhibition of malondialdehyde levels, indicating a reduction in lipid peroxidation and cellular injury. Although further studies are necessary to prove efficacy and safety, melatonin appears to be a promising agent in the treatment of IC.

Other Treatment Options

Individuals with IC often exhibit high-tone pelvic floor dysfunction, which manifests as variable pelvic pain. Treatment to restore normal tone and function to the pelvic floor musculature should not be overlooked. Also known as coccygodynia, tension myalgia of the pelvic floor, levator ani spasm syndrome, and levator syndrome, this dysfunction has been reported to appear in response to anal infection, bladder inflammation, chronic trauma, and sacroiliac misalignment.[73-75] Literature supports the use of transrectal Thiele massage, biofeedback, and electrogalvanic stimulation as treatment modalities to relieve high-tone muscle spasm.[76-80] Thiele massage can be performed transrectally or transvaginally by applying pressure to the pelvic floor muscular fibers longitudinally from origin to insertion. Ten to fifteen sweeps of maximally tolerated pressure is performed on each side, followed by myofascial massage. Physical therapy and home exercises to re-align the pelvic floor have proven to be beneficial in the short term with long-term results yet to be determined.[81] Most importantly, therapies applied for high-tone pelvic floor dysfunction present little risk for the patient and have highly therapeutic stress reduction benefits as well.

Discussion

Many forms of therapy are available to IC patients, although not all therapies will be effective in every individual. Often, combining several different approaches is necessary before a patient has significant symptom relief and tissue repair. The initial goal of therapy should be symptom reduction, with an emphasis on improvement in quality of life. Complete remission, which is attainable for some, should not be anticipated immediately. Further treatment of IC should be focused on four principles: restore epithelial function of the bladder wall by establishing new growth at the GAG layer, control food allergies, decrease mast cell response, and decrease the body's stress response by regulating the neuroendocrine system.

Currently, few randomized, placebo-controlled trials have been performed in IC populations; however, many forms of treatment have been shown to be effective in similar painful inflammatory conditions. As many of these trials address similar pathological states as those featured in IC, crossover in treatment regimens has become widely accepted by many physicians. Lastly, it is imperative that physicians consider IC in their differential diagnosis so fewer cases go undiagnosed and untreated.

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