Zagazig Veterinary Journal, ©Faculty of Veterinary Medicine,
Zagazig University, 44511, Egypt.
Volume 53, Number 2, p:108-125 June 2025
DOI: 10.21608/zvjz.2025.335789.1270

REVIEW ARTICLE

Interstitial Cystitis Syndrome: Pathophysiology, Causes, and Management Approaches

Nada A. Elhossieny[1], Nashwa Barakat[2*], Mahmoud Abdel-maboud[1]

[1]Department of Surgery, Anesthesiology, and Radiology, Faculty of Veterinary Medicine, Zagazig University, Zagazig, 44511, Egypt
[2]Urology and Nephrology Center, Mansoura University, Mansoura,35516, Egypt.

*Correspondence: Corresponding author: Nashwa Barakat" Email: nashwab2006@yahoo.com

ARTICLE INFO

Article History:
Received:28 November 2024
Accepted: 6 January 2025
Published online: June 2025

Key words:
Interstitial cystitis,
Bladder, IC/BPS.

ABSTRACT

Interstitial cystitis (IC), also known as bladder pain syndrome (BPS), is a complex, chronic condition that predominantly alters urinary bladder, causing a range of distressing symptoms. It is characterized by irritation or inflammation of bladder lining, leading to recurring episodes of significant pelvic pain and discomfort, along with a heightened urgency and frequency of urination. In severe cases, individuals may experience debilitating pain, which can delay their daily activities and severely impact sleep, work, and personal relationships. Diagnosing and managing IC/BPS remains challenging due to an incomplete understanding of its underlying causes and its tendency to mimic symptoms of other urinary tract disorders, such as overactive bladder or urinary tract infections. Furthermore, the condition can substantially diminish a person's quality of life, as the unpredictable and persistent symptoms can be physically draining and emotionally taxing. Treatment outcomes for IC/BPS vary widely among patients, with many needing a tailored, multimodal approach involving lifestyle changes, medications, physical therapy, and, in some cases, surgical interventions. This overview examines current strategies for diagnosing and managing IC, highlighting the significance of individualized treatment in enhancing patient outcomes.

Introduction

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a complex syndrome which predominantly alters urinary bladder, causing a variety of distressing symptoms. It is marked by inflammation of bladder lining, leading to recurring episodes of significant discomfort, along with increased urgency and frequency of urination. Diagnosing and managing IC/BPS is difficult because of an unclear comprehension of its exact causes and its tendency to resemble other urinary tract disorders. u. Treatment outcomes vary widely among patients, making personalized care essential [1].

IC/BPS is typically classified into 2 subtypes: IC/BPS without Hunner's lesions and classical IC/BPS with Hunner's lesions. The classical subtype, which includes Hunner's lesions, is marked by severe symptoms, including reduced bladder capacity and more pronounced inflammatory changes in the bladder wall. These lesions are indicative of significant bladder inflammation and ulceration. On the other hand, IC/BPS without Hunner's lesions often present with fewer histological changes and no clear bladder etiology. However, patients still experience significant symptoms such as chronic pain, urgency, and frequency, along with systemic comorbidities like fibromyalgia, irritable bowel syndrome, and chronic fatigue syndrome [2].

Although diagnostic criteria are not consistent, the IC prevalence varies greatly, estimated to range from 0.01% to 2.3%. Women are five times more commonly affected than men. While the precise etiology of IC/BPS is still unclear, recent studies highlight how important a disturbed urothelial barrier function is. The detrusor muscle, muscularis propria that helps the bladder contract and relax during urination, the adventitia, which offers structural support, and the mucosa, which contains the urothelium and lamina propria, make up the bladder wall's several layers. The urothelium, which is found in the deepest mucosal layer, has multinucleated umbrella cells on its surface that create an essential barrier to stop urine from leaking into the tissues underneath [3].

IC/BPS is a chronic pelvic syndrome that lasts longer than six weeks. It manifests as discomfort, pressure, or pain localized to the urinary bladder. This syndrome is characterized by urinary tract symptoms and persistent inflammation that are unrelated to infection or other recognized causes [4,5]. IC/BPS is frequently identified through exclusion, which often leads to delayed diagnosis or misdiagnosis, particularly in men, where it can be mistaken for conditions like chronic prostatitis or overactive bladder [6]. Patients commonly report bladder or suprapubic pain alongside a strong urgency to urinate. The urgency is exacerbated when the bladder fills and only temporarily relieved by urination. This relief often results in frequent urination throughout the day and night, resistant to standard overactive bladder treatments, signaling a potential diagnosis of IC/BPS [7,8].

The overall pathophysiology and etiology of IC/BPS, regardless of subtype, are still unknown despite a plethora of theories being put forth over the years [9]. These include mast cell infiltration and neurogenic inflammation, autoimmune involvement, and damage of the epithelium of bladder [10]. The barrier function is impaired in IC/BPS patients for a number of reasons, such as the breakdown of tight junctions with dysregulated expression of some tight junction proteins (occludin, uroplakin,

and zona occludens-1, occludin, and claudins 1, 4, and 8), and the reduction of the glycocalyx layer, which is made up of proteoglycans and glycoproteins [11]. When the urothelial barrier is compromised, urine solutes like urea and potassium leak into lamina propria, activating an inflammatory response [12]. This causes a constant cycle of pain and inflammation by increasing the release of proinflammatory mediators like interleukin [IL] 1, IL6, and IL8, as well as signaling molecules like acetylcholine, adenosine triphosphate [ATP], and nitric oxide from the urothelial cells [13,14].

Classification of IC/BPS

The American Urological Association describes IC/BPS as "an unpleasant sensation [pressure, pain, discomfort] thought to be related to the urinary bladder, accompanied by lower urinary tract symptoms lasting more than six weeks, without any infection or other identifiable causes [15]. Although individuals with IC/BPS frequently have common symptoms including lower urinary tract discomfort and bladder pain, the syndrome is nevertheless a heterogeneous clinical one with many phenotypes or subtypes, each with its own distinct pathophysiological characteristics or response to treatment. Hunner lesions, which are red mucosal lesions characterized by aberrant capillary architecture connected to more severe bladder inflammation and urothelial destruction, are seen in 5% to 57% of IC/BPS patients. In contrast, patients with IC/BPS who do not have Hunner lesions typically have less severe bladder inflammation, but they also frequently report more severe symptoms and unpleasant comorbidities such as migraines, fibromyalgia, and irritable bowel syndrome, which may indicate a systemic syndrome. Evidence is mounting that suggests IC/BPS with and without Hunner lesions may have distinct pathophysiological origins, despite the fact that the etiopathophysiology of this condition is still mostly understood [2].

Pathophysiology of IC/BPS

Pathological findings include chronic bladder inflammation, heightened sensory nerve activity, and overactive mast cells [16]. Other abnormalities include microvascular dysfunction, disruptions in bladder cell growth, urothelial thinning, and deficiencies in protective glycosaminoglycan layer of bladder lining [17]. Bladder inflammation is also linked to decreased adhesive proteins and impaired cell growth [18]. Inflammatory markers such as TNF-α, C-reactive protein, and nerve growth factor are elevated in patients of IC/BPS, further pointing to an inflammatory etiology [19]. IC/BPS often overlaps with autoimmune conditions, with patients exhibiting higher rates of Sjogren syndrome, rheumatoid arthritis, Hashimoto's thyroiditis, and systemic lupus erythematosus. Chronic stress, present in over half of IC/BPS patients can exacerbate the condition [20]. The chronic pain linked with IC/BPS is thought to result from overactive sensory nerves and increased sensitivity within the central nervous system [21, 22].

Histopathology of IC/BPS

There are no definitive histological markers for diagnosing IC/BPS [23]. However, patients with IC/BPS display more frequent and severe bladder mucosal ulcerations, often accompanied by inflammation in the lamina propria and an accumulation of mast cells in bladder tissues. Electron microscopy has revealed urothelial defects that correspond with the severity of symptoms, suggesting a possible causal link. These histological findings, while insightful, are primarily useful for ruling out malignancies or other bladder pathologies [24].

Diagnostic Evaluation of IC/BPS

The persistent pelvic pain that can comprise pressure, suprapubic pain, or discomfort of bladder as well as pain of pelvis, is basis for diagnosing IC/BPS when no other identifiable disorders are present. A clinical diagnosis involves a thorough examination of the patient's medical history and unique situation to rule out other causes of dysfunction and bladder pain, like stroke, radiation, Parkinson's disease, cystitis caused by chemotherapy, medication, or neurological conditions like spinal cord injury, or multiple sclerosis that impair bladder function. Patients typically get an abdominal and pelvic examination as well as a urine culture and urinalysis to rule out STIs, UTIs, and malignancies of uterus, bladder, vagina, or ovaries. In order to rule out conditions like urethritis and vaginitis, patients typically have an abdominal and pelvic examination (Table 1) [1].

Table 1: Diagnostic evaluation of nterstitial cystitis/bladder pain syndrome (IC/BPS) [1].

Diagnosis	Details
Primary Symptom	Persistent pelvic pain, including suprapubic pain, bladder discomfort, and pelvic pressure, serves as the basis for diagnosing IC/BPS when other identifiable disorders are excluded.
Clinical Diagnosis	- Comprehensive medical history review to rule out other causes such as stroke, radiation, Parkinson's disease, chemotherapy-induced cystitis, or neurological conditions. - Abdominal and pelvic examinations to rule out conditions like urethritis, vaginitis, and malignancies in the uterus, bladder, vagina, or ovaries.

The physical examination usually includes a complete pelvic examination with a brief rectal exam. Often, patients with IC/BPS have tenderness in the lower abdomen, hips, and buttocks. Women often have tenderness in the vagina and around the bladder, and men may have tenderness in the scrotum and penis. For this reason, being examined can be uncomfortable. The diagnostic examination should involve laboratory tests and procedures to rule out additional diseases that cause symptoms similar to bladder pain syndrome or interstitial cystitis. These typically involve standard blood tests (metabolic panel, complete blood count, comprehensive glucose levels, and HbA1c), urine cultures, and microscopic urinalysis. Cultures of urine may be recommended even when urinalysis results are negative to detect low or borderline bacterial levels that might still have clinical significance. Interstitial cystitis can be diagnosed without a cystoscopy or urodynamic testing. The only characteristic finding for interstitial cystitis is a Hunner ulcer, more common in individuals over 50 years of age. A Hunner ulcer presents as a central scar in erythematous mucosa with radiating blood vessels and may rupture after hydrodistension, leading to bleeding. Since Hunner ulcers are uncommon in younger patients, routine cystoscopy is generally discouraged in this age group. When compared to IC/BPS patients without Hunner lesions, patients with Hunner ulcers typically had lower voided volumes, larger nocturia episodes, higher symptom scores, and a smaller bladder capacity with hydrodistension [4].

Certain urinary inflammatory biomarkers, such as prostaglandin E2, TNF-α, IL-8, and IL-6, are elevated in interstitial cystitis. No definitive biomarker for these conditions has yet been identified [25]. If foreign bodies, bladder cancer, outlet strictures, bladder stones, or obstruction are suspected, a cystoscopy may be necessary. Although findings like glomerulations [small petechial hemorrhages] are often observed, they are non-specific and not diagnostic [26].

Treatment of Hunner ulcers often involves fulguration or triamcinolone injections, with symptom relief reported in up to 97% of cases. If these treatments are ineffective, oral cyclosporine A may be considered [27]. Routine bladder biopsies are not recommended unless malignancy is suspected, as bladder cancer is rare among patients diagnosed with interstitial cystitis. However, some international guidelines suggest hydrodistension with random biopsies due to the overlap in symptoms and appearance between these conditions and bladder cancer. In a study involving 55 patients, random biopsies identified bladder cancer in 5.5% of cases [28]. Cystoscopy helps rule out malignancy, Hunner ulcers, outlet obstruction, and other conditions like strictures. Bladder lesions can resemble carcinoma-in-situ, and reactive hemorrhages—bleeding that occurs after the bladder is deflated during inspection are another possible sign of interstitial cystitis. Further treatments, including hydrodistension or intravesical injections of lidocaine or therapeutic cocktails, can be performed during cystoscopy. Patients with Hunner ulcers typically exhibit more severe inflammation and may require more intensive therapy [29].

Urodynamic studies are generally not recommended for routine diagnosis but may be useful for patients who do not react to traditional therapies or show signs of outlet obstruction, neurogenic bladder, or detrusor muscle issues. While there are no specific urodynamic findings for interstitial cystitis, reduced maximum bladder capacity (less than 300 mL) is commonly observed. Urodynamic studies typically reveal non-specific results, such as reduced bladder capacity or increased bladder pressure during filling, which do not differentiate IC/BPS from other urological conditions like overactive bladder (OAB) or urinary tract infections (UTIs). Furthermore, Biopsies are invasive and carry risks such as bleeding, infection, and bladder perforation, making them unsuitable as a routine diagnostic tool [4].

Imaging Techniques for IC/BPS Diagnosis

Planar Imaging Techniques

Cystoscopy is a widely used planar imaging method considered the standard for identifying IC/BPS patients with Hunner's lesions. It provides real-time, direct images of the bladder wall, showing characteristic features such as erythematous mucosal patches, central pale scars, and glomerulations. However, its small field of view limits its ability to detect subtle or widespread changes in the bladder wall. Ultrasound is another planar technique that uses 5–9 MHz probes to image the bladder wall. It is often employed to evaluate bladder wall thickening, renal involvement, and pelvic floor mobility. The resolution of ultrasound is limited to 1 mm, and measurements of bladder wall thickness (BWT) can vary with bladder distension [30].

Near-Infrared Imaging

Near-infrared (NIR) imaging uses fluorochromes emitting in the NIR band,

allowing for deep tissue imaging of the bladder wall with minimal background interference. NIR spectroscopy (NIRS) is a non-invasive technique that monitors oxygenation changes in the bladder wall by analyzing oxyhemoglobin and deoxyhemoglobin concentrations. This approach shows promise in exploring ischemia-related contributions to IC/BPS symptoms [30].

Tomographic Imaging Techniques

Tomographic techniques like computed tomography (CT) and magnetic resonance imaging (MRI) provide three-dimensional imaging of the bladder wall. Computed tomography is used to detect bladder wall thickening and rule out malignancies but is limited by high radiation exposure and poor sensitivity to fibrosis. Magnetic resonance imaging, on the other hand, offers superior contrast resolution and multiplanar imaging without the need for ionizing radiation. Conventional MRI is particularly effective for soft tissue analysis but may face challenges with motion artifacts and resolution of the thin bladder wall [30].

Contrast-Enhanced MRI

Contrast-enhanced MRI (CE-MRI) improves bladder wall imaging by using gadolinium-based contrast agents (GBCAs) and superparamagnetic iron oxide (SPIO) nanoparticles. These agents enhance the visibility of different bladder wall layers. Recent advancements include novel contrast mixtures (NCM) that improve layer differentiation and reduce motion artifacts, achieving high-resolution imaging in shorter acquisition times. CE-MRI is especially useful for visualizing bladder wall pathologies in ulcerative IC/BPS patients [30].

Mechanisms Underlying IC/BPS

Bladder feelings are produced by stimulating the peripheral sensory nerves in bladder wall, which then transmit sensory information to the brain and central nervous system for processing and interpretation. It is believed that the hypersensitivity of bladder-innervating afferent neurons, which results in enhanced sensory impulses from bladder in usual, is primarily related to IC/BPS symptoms. Numerous factors, including inflammation, dysregulation in the spinal and/or cortical networks, and increased urothelial permeability, are believed to be responsible for this hypersensitivity in IC/BPS. Even though the pathophysiological mechanisms underlying afferent sensitization are not fully understood, it is widely accepted that mucosal homeostasis disruption, which is characterized by increased inflammation and urothelial permeability, is an important cause of hypersensitivity of nerves and pain associated with IC/BPS [15].

Increased Bladder Permeability

The impermeable barrier of the urothelium normally keeps the many toxic substances found in urine from reaching the sensory nerve terminals and the bladder interstitium underneath. Tight connections between hydrophobic uroplakin plaques, apical urothelial cells, and a thick layer of glycosaminoglycan mucus composed of proteoglycans and glycoproteins all contribute to the protective barrier that exists between urine and urothelial cells. Patients of IC/BPS often have a compromised urothelium, which facilitates the passage of urea and toxic irritants to the urothelial cell membranes [31].

Furthermore, according to normal people, IC/BPS patients have lower amounts of tight junction proteins such as E-cadherin and zonula occludens-1. Urinary solutes can enter the lamina propria through the urothelium due to reduced tight junction

proteins. This activates afferent nerve endings and causes the urological symptoms that are characteristic of IC/BPS. Afferent hypersensitivity can also be exacerbated by exposure to high urinary cationic components, which can enhance urothelial damage and increase urine leakage into deeper layers [32].

Inflammation

Hunner lesions typically exhibit some degree of inflammation and have greater levels of proinflammatory mediators such as chemokines, cytokines, nerve growth factor, and histamine. In comparison to normal bladders, IC/BPS bladders demonstrated to have higher levels of immune cells, such as macrophages, mast cells, eosinophils, and T and B cell markers, as well as tissue granulation, mild oedema, and overexpression of pro-inflammatory genes. Pro-inflammatory mediators have been shown in preclinical research to directly sensitize afferent nerve terminals in the bladder wall, establishing a critical connection between inflammation and heightened sensation. Increased bladder permeability due to inflammation in the bladder mucosa can create a positive feedback loop that exacerbates the inflammatory state and chronically sensitizes the peripheral afferent terminals in the bladder wall [33].

Autoimmunity

Compared to normal bladder tissue, the submucosal and urothelium layers of bladder in IC have higher concentrations of plasma cells, CD4+ and CD8+ T lymphocytes, and B lymphocytes. Immunoglobulins such as IgA, IgG, and IgM, along with γδ T cells, are also markedly elevated in IC compared to a healthy bladder wall. Furthermore, urothelial damage may be facilitated by IC patients' activation of T-helper cells and aberrant urothelial expression of HLA-DR molecules. It is unclear whether these reactions are reactive or causal because there is no consistent immune activity profile in spite of these observations [34].

Chronic Stress

The persistence, origin, and worsening of IC/BPS symptoms are believed to be largely influenced by changes in emotional states and the homeostasis of hypothalamic-pituitary-adrenal axis. These changes can have a significant impact on bladder function and sensation. Urinary urgency in response to acute stress is a common observation of stress-induced bladder function modification in healthy individuals. Nonetheless, there are robust correlations between the symptoms of IC/BPS and visceral pain diseases, like irritable bowel syndrome, and long-term stress and anxiety. Furthermore, in patients who already have IC/BPS, both chronic and acute stress can increase worsen pain and urgency [35].

IC/BPS patients had a higher prevalence of early-life stress than healthy controls, indicating that chronic stress is a substantial risk factor of IC/BPS in otherwise healthy people. Long-term psychological stress causes peripheral tissues to become more inflammatory, as seen by higher levels of proinflammatory cytokines in the bloodstream and greater bladder mast cell activity. Notably, some patients have reported that stress reduction helps to lessen the severity of their IC/BPS symptoms (Table 2) [22].

Table 2: Mechanisms of interstitial cystitis/bladder pain syndrome (IC/BPS) [22].

Mechanisms	Details
Nerve Hypersensitivity	- Hypersensitivity of bladder-innervating afferent neurons leads to increased sensory impulses. - Caused by inflammation, dysregulation in spinal/cortical networks, and increased urothelial permeability.
Increased Bladder Permeability	- Compromised urothelium allows toxic substances to reach sensory nerves. - Reduced tight junction proteins (E-cadherin, ZO-1) increase urothelial permeability. - High urinary cationic components exacerbate urothelial damage.
Inflammation	- Elevated pro-inflammatory mediators (cytokines, chemokines, nerve growth factor) and immune cells (mast cells, macrophages). - Inflammation increases bladder permeability, creating a feedback loop of sensitization and inflammation.
Autoimmunity	- Elevated levels of plasma cells, T/B lymphocytes, and immunoglobulins (IgA, IgG, IgM). - Possible abnormal expression of HLA-DR molecules and T-helper cell activation. - Exact role of immune activity (reactive or causal) remains unclear.
Chronic Stress	- Stress affects bladder function and worsens pain and urgency. - Early-life stress linked to higher IC/BPS prevalence. - Chronic stress increases inflammation and mast cell activity. - Stress reduction reported to improve symptoms.

Treatment of IC/BPS

Before starting treatment, the American Urological Association recommends educating patients about the disease and the importance of multimodal therapy, emphasizing that patient education is a crucial part of the treatment plan. There is no single treatment capable of completely curing the condition or fully eliminating symptoms for most patients. Patients should be informed that optimal symptom management often requires combining several treatment options and that the condition can be chronic, with periods of exacerbation and remission. Since the underlying etiology is mostly unclear,

treatment focuses on symptom management. If basic pain management approaches are insufficient, other therapies could be explored, and a pain management consultation may be considered as part of a multidisciplinary approach. Failure of multiple treatments may indicate a need to reassess the diagnosis [36]. Angiogenesis and inflammation play vital roles in IC/BPS pathophysiology, according to mounting scientific data. The suppression of several cytokines, growth factors, chemokines, and mast cells are examples of possible treatment approaches. Other approaches for targeted or immune-modulating therapeutics include controlling neurogenic inflammation and directly targeting angiogenic pathways [37].

Treatment Options

Non-Pharmacological Treatments

All IC/BPS patients are initially advised to use non-pharmacological therapies, such as dietary and behavioral changes, to assist lessen the severity of their symptoms. It is thought that acidic urine exacerbates irritation of bladder, which might be particularly risky for IC/BPS patients with impaired urothelium since it increases inflammation. Urine pH can be lowered to reduce bladder irritation by dietary changes that restrict or exclude specific items, like coffee, citrus, and alcohol [38].

Behavioral changes include a variety of approaches, including stress reduction, bladder training, and fluid intake control. By progressively lengthening the intervals between voids over a period of one to three months, bladder training is used to manage urgency. Patients with mild to moderate symptoms of IC/BPS may benefit most from this treatment, which is frequently used for other urological diseases such overactive bladder syndrome. Additionally, patients are recommended to use stress-reduction strategies, such as consistent exercise, breathing exercises, and psychotherapy as necessary [39].

Conservative Treatments

These include pelvic floor relaxation exercises, dietary modifications, myofascial release, and stress reduction techniques [40].

Oral Medications

Cimetidine (400 mg divided twice daily), amitriptyline (25-75 mg), and hydroxyzine (10–50 mg) are the main oral drugs. Pentosan polysulfate (100 mg divided twice or three times daily) could be useful for certain patients, however there is a chance that it can cause irreversible retinal damage. Gabapentin (300–2100 mg divided three times daily) may be helpful for pain relief; Cyclosporine A2-3 mg/kg divided twice daily, is advised for individuals with Hunner ulcers that did not react to fulguration or triamcinolone injections; and Overactive bladder drugs can aid with urine symptoms but are often insufficient when administered alone [37].

The only Food and Drug Administration (FDA)-approved oral treatment for IC/BPS is pentosan polysulfate (PPS). PPS, a substance that resembles heparin, is intended to restore the urothelium's impermeability by mimicking bladder glycosaminoglycans (GAGs). According to clinical research, PPS helps some people with mild bladder urgency, pain, and frequency of urine without causing adverse effects. Long-term PPS usage, however, carries dangers, including the potential for retinal impairment, vision problems, gastrointestinal diseases, and hair loss. Even though there aren't many recently licensed medications for IC/BPS, new clinical research indicates that patients who don't respond to approved

oral and intravesical treatments may benefit from repurposing immunosuppressive medications like Cyclosporine A (CyA) and certolizumab pegol [41].

The American Urological Association recommends CyA as a fifth-line treatment for people who are not responding to other medications because it has demonstrated more efficacy for patients with Hunner lesions. To assess certolizumab pegol's potential in IC/BPS treatment, larger, longer-term trials are still needed. There haven't been many novel oral medicines for IC/BPS, despite the fact that many early-stage medications never make it to clinical use. As a result, current drugs have been tested and are commonly used to treat symptoms. Tricyclic antidepressants, such as amitriptyline, and histamine receptor blockers, such as hydroxyzine and cimetidine, have been shown to be somewhat beneficial [4].

Intravesical Instillations

In patients who do not respond to oral or non-pharmacological therapy, intravesical instillations might be suggested. Non-surgical treatments that work well are intravenous medication instillations. Dimethyl sulfoxide, bupivacaine or lidocaine with sodium bicarbonate, heparin, and other intravesical medications such as hyaluronic acid (40 mg/50 mL vial, weekly instillations for 4–12 treatments, then monthly until symptoms resolve), chondroitin sulfate (20 mL vial of 2.0%, retained 30 minutes weekly for 6 weeks, then monthly until symptoms resolve), triamcinolone (1 mL vial of triamcinolone (40 mg/mL) diluted in 9 mL (total 10 mL), to be injected in aliquots of 1 mL), and misoprostol are suggested pharmacological combinations [40].

The FDA has approved dimethylsulfoxide (DMSO), 50 mL solution of 50% DMSO for 30–60 minutes, once weekly for 6 weeks, for IC/BPS when it is given via a temporary urethral catheter. The ideal length of induction therapy, maintenance therapy, and duration for DMSO are still unknown, though. For IC/BPS patients, particularly those with Hunner lesions, DMSO relieves pain and urine frequency by lowering inflammation, relaxing smooth muscles, and inhibiting sensory nerve activity. However, within two months of treatment, many patients return in their symptoms [42].

Voltage-gated sodium channels of sensory nerves that innervate the bladder are blocked by lidocaine, a local anesthetic. The therapeutic effects of lidocaine are increased when it is alkalinized with sodium bicarbonate, which improves its absorption through the urothelium and into the cytoplasm of neurons. By aiding in the restoration of urothelial impermeability, heparin, glycosaminoglycan, is believed to offer further advantages for IC/BPS treatment. Patients with IC/BPS have shown symptom alleviation from clinical trials employing the intravesical instillation of lidocaine/heparin. However, the best way to combine heparin and lidocaine is still up for debate, and the requirement for urethral catheterization restricts the treatment's widespread application [43].

Procedures

Patients might be evaluated for treatments, such as neuromodulation or bladder hydrodistension, if behavioral modifications, oral medicines, and intravesical instillations are unable to control symptoms (Table 3). About 30% to 55% of individuals may see a reduction in their urine symptoms after undergoing bladder hydrodistension, which includes putting high pressure (60–80 cm H_2O) to

the bladder for a short time (less than 10 minutes) but after a few months, the improvement frequently wanes and requires more treatments [38]. By electrically stimulating the nerves involved in bladder filling, neuromodulation aids in the regulation of urinary symptoms [44]. Pudendal and sacral nerves stimulation are the two main neuromodulation methods being investigated for IC/BPS at this time [4].

This technique requires placing a tiny electrode close to the sacral nerve and implanting a generator beneath skin of upper buttock region. A neurotransmitter then sends electrical signals to the sacral nerve, which helps control voiding function at the level of the lower spine. Pudendal and sacral nerves are stimulated. With this method, the electrode is positioned close to the pudendal nerve, but the generator is still in the upper buttock. During bladder filling, impulses help regulate the pelvic floor muscles by stimulating the pudendal nerve [45].

Cystoscopy and Hydrodistension

Patients with persistent symptoms may benefit from cystoscopy with short-duration, low-pressure hydrodistension. Hunner ulcers, if present, can be treated during the procedure [4].

Advanced Treatments for Resistant Cases

If patients do not respond to previous therapies, they could be candidates for advanced treatments such as Botulinum toxin A injections into the bladder, Neuromodulation, Misoprostol (intravesical or oral), Cyclosporine A, and Tibial nerve stimulation [15].

Surgical Intervention

Surgery is only performed on patients whose symptoms are still severe and cannot be controlled by any of the previously mentioned treatments [4]. Table 3 summarized IC/BPS treatments.

Table 3: The interstitial cystitis/bladder pain syndrome (IC/BPS) treatments [15].

Type of Treatment	Treatment Name	Target
Non-Pharmacological	**Diet Modification**	Helps manage voiding frequency by avoiding dietary triggers that aggravate symptoms.
	Bladder Training	Reduces bladder pain by adopting behavioral techniques to extend intervals between urinations.
Oral Medications	**Pentosan Polysulphate [PPS]**	Decreases bladder wall permeability to alleviate irritation, and reduces pain, urgency, and frequency of urination.
Intravesical Instillations	**Dimethylsulfoxide [DMSO]**	Relaxes bladder muscles, blocks nerve signals, reduces inflammation, and alleviates bladder pain and frequency.
	Lidocaine	Numbs sensory nerves in the bladder to ease pain, urgency, and nighttime urination issues [nocturia].
	Heparin	Restores bladder lining function and reduces nerve sensitivity, relieving pain, urgency, and nocturia.

Procedures	**Hydrodistension**	Expands bladder capacity to reduce urinary urgency and frequency, and provides temporary pain relief.
	Neuromodulation	Adjusts neural pathways regulating bladder activity, easing symptoms of urgency and frequency.

Novel Management Trials in Animal Studies of IC/BPS

IC/BPS animal models are crucial to develop an animal model that faithfully mimics the human condition in order to find novel treatment targets for a disease. This makes it possible for researchers to test novel therapies targeted at symptom relief and to comprehend the underlying mechanisms causing symptoms. Because there are so many different potential pathophysiological explanations for hypersensitivity and bladder dysfunction in IC/BPS, it has been very challenging to develop realistic animal models and efficient treatments. Several animal models created to illustrate IC/BPS complex pathophysiology. Though, bulk of animal models have concentrated on recreating the core symptoms of bladder pain and hypersensitivity using a variety of ways because IC/BPS full pathophysiology is still unclear and encompasses multiple subclassifications [15].

To understand the underlying causes of chronic cystitis and to create effective treatments, animal models of the disease are used. Various factors contribute to the heightened bladder sensitivity observed in interstitial cystitis, including increased permeability of the urothelium, chronic inflammation, and psychological or chronic stress. During normal bladder function, sensory signals remain regulated, but in interstitial cystitis, these signals become exaggerated, causing hypersensitivity of the bladder's sensory nerves. This hypersensitivity has a vital role in the development of painful symptoms. Many animal models developed to mimic intricate pathophysiology of interstitial cystitis. However, because the condition's underlying mechanisms remain incompletely understood and encompass several subtypes, these models primarily aim to replicate key symptoms, such as bladder hypersensitivity and pain, through diverse experimental approaches [46].

Models focused on bladder-related mechanisms use methods such as increasing bladder permeability or inducing chemical cystitis. These ducing substances like acetic acid, protamine sulfate, hydrogen peroxide, hydrochloric acid, lipopolysaccharide, or zymosan into the bladder via a catheter. Cyclophosphamide, though injected intraperitoneally, is metabolized to acrolein in liver and eliminated through urine, causing bladder inflammation and damage. Autoimmune cystitis models are created by injecting bladder tissue homogenate or urothelial antigens subcutaneously, triggering autoimmune responses through interactions with MHC Class II molecules on cell membranes. In transgenic autoimmune models, urothelium-ovalbumin (URO-OVA) mice express an OVA antigen on urothelial cell membranes. Injecting OVA-primed lymphocytes or OT-I splenocytes into these mice activates an autoimmune

response upon interaction with the OVA antigen [37].

Psychological stress models induce bladder hypersensitivity by disrupting the hypothalamic-pituitary-adrenal axis through chronic stress. Examples include water avoidance stress and neonatal maternal separation, which impair the animal's ability to manage stress over time, influencing bladder activity. Cross-organ sensitization models involve introducing ethanol or TNBS into the colon, causing colonic inflammation that heightens bladder sensitivity. This occurs through viscero-visceral communication between overlapping sensory networks shared by the colon and bladder, leading to increased afferent sensitivity in both organs [15].

Urothelial Permeability Models

Relatively few animal models exclusively concentrate on role of increased urothelial permeability in pathogenesis of IC/BPS, despite a wealth of clinical evidence to support this idea. The most popular technique for precisely inducing urothelial permeability is the in vivo bladder instillation of protamine sulfate [47].

By deactivating the sulfated polysaccharides in the GAG layer, proton sulfate improves urothelial permeability. This raises the urothelium's transcellular permeability and permits increased absorption of urine solutes. Protamine sulfate only mildly damages the urothelial tissue at low doses (1–10 mg/ml), causing sloughing and increased permeability that goes away in 7 days [48]. However, it can cause neutrophil infiltration into the mucosa and urothelial ulceration at higher dosages (50 mg/ml). Studies looking at bladder sensory responses have shown inconsistent results, and its impact on bladder function is unknown. One day following infusion, for example, a single low dosage of protamine sulfate (1 mg/ml) caused bladder afferent hypersensitivity ex vivo [35]. On the other hand, mice given protamine sulfate (10 mg/ml) showed decreased visceromotor responses to painful bladder distension, suggesting that the bladder was sending less sensory information to the spinal cord. But by day 7, elevated pelvic sensitivity and voiding parameters had reverted to normal, which is in line with the urothelial barrier's recovery in bladders treated with modest doses [15].

IC/BPS Inflammatory Models

Most IC/BPS animal models are made to have an inflammatory phenotype. The bladder urothelium has been irritated by chemotherapeutics, bacterial products, chemicals, fungal ligands, and by encouraging autoimmunity against the urothelium. Because they promote inflammation of bladder, which leads to hypersensitivity, frequent urination, and pelvic discomfort, these inflammatory models are useful in simulating the primary symptoms of IC/BPS. However, aside from certain instances of cystitis, they might not precisely represent the underlying pathophysiology of IC/BPS in humans [15].

Cyclophosphamide

The most popular drug for causing rodents to develop cystitis is cyclophosphamide (CYP). For certain solid tumors and B-cell cancers, it is a chemotherapeutic medication. Similar to the most severe IC/BPS phenotypes, chronic bladder inflammation and hemorrhagic cystitis are common and serious adverse effects of CYP medication in people. Acrolein, a highly reactive aldehyde, is produced in the liver by CYP metabolism and then eliminated by the bladder. An inflammatory reaction is triggered when acrolein builds up in

bladder and interacts with luminal urothelial umbrella cells. To cause cystitis in rodents, both chronic and acute CYP dosage regimens have been used. This causes increased urothelial permeability and a hypersensitive condition that manifests as altered voiding habits and pelvic hypersensitivity [49]. The characteristics of IC/BPS animal models are summarized in Table (4).

Table 4: The characteristics of interstitial cystitis/bladder pain syndrome (IC/BPS) animal models [15].

Animal Model	Key Characteristics	Relevance to IC/BPS
Chemical-Induced Models	Irritation caused by chemical agents [e.g., cyclophosphamide, hydrochloric acid].	Mimics bladder inflammation and pain observed in IC/BPS.
Autoimmune Models	Induced immune response leads to chronic inflammation and bladder dysfunction.	Resembles immune-mediated mechanisms in IC/BPS patients.
Neuropathic Models	Nerve injury or sensitization causes altered sensory signaling.	Represents chronic pain and hypersensitivity in IC/BPS.
Genetic Models	Animals with specific genetic modifications leading to bladder abnormalities.	Explores genetic contributions to IC/BPS susceptibility.
Infection-Based Models	Bladder irritation caused by bacterial or viral infections.	Studies the role of infections in triggering IC/BPS symptoms.
Psychological Stress Models	Chronic stress exposure leads to heightened bladder sensitivity and inflammation.	Highlights the connection between psychological stress and IC/BPS symptom exacerbation.
Combination Models	Utilizes multiple factors [e.g., chemical irritation and stress] to replicate complex disease mechanisms.	Provides a holistic approach to understanding multifactorial causes of IC/BPS.

Future Directions for IC/BPS Research

Biomarker Discovery

Advancing the identification and validation of biomarkers is crucial for enhancing diagnostic precision and personalizing treatments for IC/BPS. Techniques such as proteomics, transcriptomics, and bioinformatics offer insights into disease-specific pathways, paving the way for molecularly targeted interventions.

Artificial Intelligence and Bioinformatics

The integration of AI and bioinformatics is transforming the analysis of complex datasets. These technologies can identify patterns, predict biomarkers, and classify patients into molecular subtypes, enabling more precise and effective treatment approaches.

Innovative Imaging Techniques:

Emerging imaging modalities, including high-resolution MRI, near-infrared imaging, and advanced contrast-enhanced methods, are improving the detection of bladder wall changes and the monitoring of treatment responses. These innovations aim to provide non-invasive and accurate diagnostic tools.

Targeted Therapies

Research is increasingly focused on developing treatments that address specific molecular mechanisms such as neurogenic inflammation, immune dysregulation, and angiogenesis. These targeted therapies aim to reduce symptoms and improve patient outcomes.

Personalized Medicine

Stratifying patients based on clinical phenotypes, pain patterns, and molecular profiles allows for tailored treatment plans. Combining pharmacological, physical, and psychological interventions offers a multidimensional approach to managing IC/BPS.

Advanced Animal Models

Improved animal models that closely mimic human IC/BPS symptoms are essential for translational research. These models can help refine therapeutic strategies and enhance the relevance of preclinical studies to human applications.

Multidisciplinary Collaboration

Collaboration between researchers, clinicians, and institutions is key to addressing IC/BPS challenges. Standardized methodologies and shared datasets will accelerate discoveries and improve clinical applications.

Early Detection and Prevention:

Advancements in biomarkers and imaging are expected to facilitate early detection of IC/BPS, enabling timely interventions that may prevent disease progression [50].

Conclusion

Interstitial cystitis (IC) management emphasizes personalized, multimodal treatment, combining lifestyle changes, medications, and advanced options like neuromodulation or botulinum toxin for severe cases, with surgery as a last resort. Animal models provide critical insights into IC mechanisms, triggers, and therapies, replicating aspects like inflammation, immune response, and nerve sensitization. Combination models offer a comprehensive understanding, advancing research and treatment development to improve patient outcomes.

Conflict of interest

None of the authors have any conflict of interest to declare

Funding

There was no funding of any kind awarded to the present project.

References

[1] Siedlak A, Kułakowska A, Lepczyński B, Kłakowicz P, Lechowski S. Diagnosis and treatment of interstitial cystitis - literature review. J Educ Heal Sport. 2023;15(1):63–6.

[2] Akiyama Y, Yao J-R, Kreder KJ, O'Donnell MA, Lutgendorf SK, Lyu D, et al. Autoimmunity to urothelial antigen causes bladder inflammation, pelvic pain, and voiding dysfunction: a novel animal model for Hunner-type interstitial cystitis. Am J Physiol Physiol [Internet]. 2020 Dec 14;320(2):F174–82. Available from: https://doi.org/10.1152/ajprenal.00290.2020

[3] Homma Y, Akiyama Y, Tomoe H, Furuta A, Ueda T, Maeda D, et al. Clinical guidelines for interstitial cystitis/bladder pain syndrome. Int J Urol [Internet]. 2020 Jul 1;27(7):578–89. Available from: https://doi.org/10.1111/iju.14234

[4] Clemens JQ, Erickson DR, Varela NP, Lai HH. Diagnosis and Treatment of Interstitial Cystitis/Bladder Pain Syndrome. J Urol. 2022 Jul;208(1):34–42.

[5] Hanno P, Dmochowski R. Status of international consensus on interstitial

cystitis/bladder pain syndrome/painful bladder syndrome: 2008 snapshot. Neurourol Urodyn. 2009;28(4):274–86.

[6] Bogart LM, Berry SH, Clemens JQ. Symptoms of interstitial cystitis, painful bladder syndrome and similar diseases in women: a systematic review. J Urol. 2007 Feb;177(2):450–6.

[7] Clemens JQ, Clauw DJ, Kreder K, Krieger JN, Kusek JW, Lai HH, et al. Comparison of baseline urological symptoms in men and women in the MAPP research cohort. J Urol. 2015 May;193(5):1554–8.

[8] Arora HC, Shoskes DA. The enigma of men with interstitial cystitis/bladder pain syndrome. Transl Androl Urol. 2015 Dec;4(6):668–76.

[9] Doiron RC, Tolls V, Irvine-Bird K, Kelly K-L, Nickel JC. Clinical Phenotyping Does Not Differentiate Hunner Lesion Subtype of Interstitial Cystitis/Bladder Pain Syndrome: A Relook at the Role of Cystoscopy. J Urol. 2016 Oct;196(4):1136–40.

[10] Lin Z, Hu H, Liu B, Chen Y, Tao Y, Zhou X, et al. Biomaterial-assisted drug delivery for interstitial cystitis/bladder pain syndrome treatment. J Mater Chem B. 2021 Jan;9(1):23–34.

[11] Kuret T, Peskar D, Erman A, Veranič P. A systematic review of therapeutic approaches used in experimental models of interstitial cystitis/bladder pain syndrome. Biomedicines. 2021;9(8).

[12] Winder M, Tobin G, Zupančič D, Romih R. Signalling molecules in the urothelium. Biomed Res Int. 2014;2014:297295.

[13] Jiang Y-H, Jhang J-F, Hsu Y-H, Ho H-C, Wu Y-H, Kuo H-C. Urine biomarkers in ESSIC type 2 interstitial cystitis/bladder pain syndrome and overactive bladder with developing a novel diagnostic algorithm. Sci Rep. 2021 Jan;11(1):914.

[14] Jiang Y-H, Jhang J-F, Hsu Y-H, Ho H-C, Wu Y-H, Kuo H-C. Urine cytokines as biomarkers for diagnosing interstitial cystitis/bladder pain syndrome and mapping its clinical characteristics. Am J Physiol Renal Physiol. 2020 Jun;318(6):F1391–9.

[15] Tay C, Grundy L. Animal models of interstitial cystitis/bladder pain syndrome. Front Physiol. 2023;14:1232017.

[16] Jhang J-F, Jiang Y-H, Kuo H-C. Current Understanding of the Pathophysiology and Novel Treatments of Interstitial Cystitis/Bladder Pain Syndrome. Biomedicines. 2022 Sep;10(10).

[17] Shie J-H, Kuo H-C. Higher levels of cell apoptosis and abnormal E-cadherin expression in the urothelium are associated with inflammation in patients with interstitial cystitis/painful bladder syndrome. BJU Int. 2011 Jul;108(2 Pt 2):E136-41.

[18] Lopez SR, Mangır N. Current standard of care in treatment of bladder pain syndrome/interstitial cystitis. Ther Adv Urol. 2021;13:17562872211022478.

[19] Jiang Y-H, Jhang J-F, Kuo H-C. The clinical application of intravesical botulinum toxin A injection in patients with overactive bladder and interstitial cystitis. Tzu chi Med J. 2023;35(1):31–7.

[20] Jiang Y-H, Jhang J-F, Hsu Y-H, Kuo H-C. Usefulness of Urinary Biomarkers for Assessing Bladder Condition and Histopathology in Patients with Interstitial Cystitis/Bladder Pain Syndrome. Int J Mol Sci. 2022 Oct;23(19).

[21] Yueh H-Z, Yang M-H, Huang J-Y, Wei JC-C. Risk of Autoimmune Diseases in Patients With Interstitial Cystitis/Bladder Pain Syndrome: A Nationwide Population-Based Study in Taiwan. Front Med. 2021;8:747098.

[22] Birder LA. Pathophysiology of interstitial cystitis. Int J Urol Off J Japanese Urol Assoc. 2019 Jun;26 Suppl 1:12–5.

[23] Jhang J-F, Hsu Y-H, Jiang Y-H, Ho H-C, Kuo H-C. Clinical Relevance of Bladder Histopathological Findings and Their Impact on Treatment Outcomes among Patients with Interstitial Cystitis/Bladder Pain Syndrome: An Investigation of the European Society for the Study of Interstitial Cystitis Histopatholog. J Urol. 2021 Jan;205(1):226–35.

[24] Natale F, Campagna G, Marturano M, Caramazza D, Panico G, Vacca L, et al. Is There a Role for Bladder Biopsy in the Diagnosis of Non-Hunner Lesions Interstitial Cystitis? Urol Int. 2023;107(3):257–62.

[25] Argade S, Chermansky C, Tyagi P. Biomarkers for interstitial cystitis/painful bladder syndrome. Womens Health (Lond Engl). 2016 Jan;12(1):87–90.

[26] Wennevik GE, Meijlink JM, Hanno P, Nordling J. The Role of Glomerulations in Bladder Pain Syndrome: A Review. J Urol. 2016 Jan;195(1):19–25.

[27] Ronstrom C, Lai HH. Presenting an atlas of Hunner lesions in interstitial cystitis which can be identified with office cystoscopy. Neurourol Urodyn. 2020 Nov;39(8):2394–400.

[28] Chen Y, Ying Z, Xiao Y, Liu Y, Wu S. The diagnostic and therapeutic efficacy of cystoscopy with hydrodistension and random biopsies in clinically suspected interstitial cystitis/bladder pain syndrome. Eur J Obstet Gynecol Reprod Biol. 2021 Oct;265:156–61.

[29] Sholan R. Clinical manifestations and results of cystoscopy in women with interstitial cystitis/bladder pain syndrome. North Clin Istanbul. 2020;7(5):417–24.

[30] Tyagi P, Moon C-H, Janicki J, Kaufman J, Chancellor M, Yoshimura N, et al. Recent advances in imaging and understanding interstitial cystitis. F1000Research. 2018;7.

[31] Mancini M, Janssen D, Morlacco A, Ammirati E, Giammo A. Chapter 19 - Expertise Area 2.5: Bladder pain syndrome/Interstitial cystitis (BPS/IC). In: Feitz WFJ, Tidman JBT-R and CU, editors. Academic Press; 2024. p. 229–43. Available from: https://www.sciencedirect.com/science/article/pii/B9780323999342000073

[32] Jafari N V., Rohn JL. The urothelium: a multi-faceted barrier against a harsh environment. Mucosal Immunol. 2022;15(6):1127–42.

[33] Grundy L, Caldwell A, Garcia-Caraballo S, Grundy D, Spencer NJ, Dong X, et al. Activation of MrgprA3 and MrgprC11 on Bladder-Innervating Afferents Induces Peripheral and Central Hypersensitivity to Bladder Distension. J Neurosci Off J Soc Neurosci. 2021 Apr;41(17):3900–16.

[34] de Magalhaes TF, Haddad J. Chapter 47 - Biomarkers in bladder pain syndrome: A new narrative. In: Rajendram R, Patel VB, Preedy VR, Martin Anaesthesia, and Analgesia CRBT-F and A of P, editors. Academic Press; 2022. p. 527–38. Available from: https://www.sciencedirect.com/science/article/pii/B9780128189887000145

[35] Grundy L, Caldwell A, Garcia Caraballo S, Erickson A, Schober G, Castro J, et al. Histamine induces peripheral and central hypersensitivity to bladder distension via the histamine H(1) receptor and TRPV1. Am J Physiol Renal Physiol. 2020 Feb;318(2):F298–314.

[36] Santos TG Dos, Miranda IAS de, Nygaard CC, Schreiner L, Castro R de A, Haddad JM. Systematic Review of Oral Therapy for the Treatment of Symptoms of Bladder Pain Syndrome: The Brazilian Guidelines. Rev Bras Ginecol e Obstet Rev da Fed Bras das Soc Ginecol e Obstet. 2018 Feb;40(2):96–102.

[37] Hu J-C, Tzeng H-T, Lee W-C, Li J-R, Chuang Y-C. Promising Experimental

Treatment in Animal Models and Human Studies of Interstitial Cystitis/Bladder Pain Syndrome. Vol. 25, International Journal of Molecular Sciences. 2024.

[38] Garzon S, Laganà AS, Casarin J, Raffaelli R, Cromi A, Sturla D, et al. An update on treatment options for interstitial cystitis. Prz menopauzalny = Menopause Rev. 2020 Mar;19(1):35–43.

[39] 39. Ueda T, Hanno PM, Saito R, Meijlink JM, Yoshimura N. Current Understanding and Future Perspectives of Interstitial Cystitis/Bladder Pain Syndrome. Int Neurourol J [Internet]. 2021 Jun 30;25(2):99–110. Available from: https://doi.org/10.5213/inj.2142084.042

[40] Vollstedt A, Tennyson L, Turner K, Hasenau D, Saon M, McCartney T, et al. Evidence for Early Cyclosporine Treatment for Hunner Lesion Interstitial Cystitis. Female Pelvic Med Reconstr Surg. 2022 Jan;28(1):e1–5.

[41] Grigoryan B, Kasyan G, Pivazyan L, Pushkar D. Pentosan polysulfate in patients with bladder pain syndrome/interstitial cystitis with Hunner's lesions or glomerulations: systematic review and meta-analysis. Ther Adv Urol. 2022;14:17562872221102808.

[42] Yoshimura N, Homma Y, Tomoe H, Otsuka A, Kitta T, Masumori N, et al. Efficacy and safety of intravesical instillation of KRP-116D (50% dimethyl sulfoxide solution) for interstitial cystitis/bladder pain syndrome in Japanese patients: A multicenter, randomized, double-blind, placebo-controlled, clinical study. Int J Urol Off J Japanese Urol Assoc. 2021 May;28(5):545–53.

[43] 43. Digesu GA, Tailor V, Bhide AA, Khullar V. The role of bladder instillation in the treatment of bladder pain syndrome: Is intravesical treatment an effective option for patients with bladder pain as well as LUTS? Int Urogynecol J. 2020 Jul;31(7):1387–92.

[44] Padilla-Fernández B, Hernández-Hernández D, Castro-Díaz DM. Current role of neuromodulation in bladder pain syndrome/interstitial cystitis. Ther Adv Urol. 2022;14:17562872221135940.

[45] Hernández-Hernández D, Padilla-Fernández B, Castro Romera M, Hess Medler S, Castro-Díaz D. Long-term Outcomes of Sacral Nerve Stimulation in Pelvic Floor Dysfunctions. Int Neurourol J. 2021 Dec;25(4):319–26.

[46] Karamali M, Shafabakhsh R, Ghanbari Z, Eftekhar T, Asemi Z. Molecular pathogenesis of interstitial cystitis/bladder pain syndrome based on gene expression. J Cell Physiol. 2019 Aug;234(8):12301–8.

[47] Hurst RE, Greenwood-Van Meerveld B, Wisniewski AB, VanGordon S, Lin H, Kropp BP, et al. Increased bladder permeability in interstitial cystitis/painful bladder syndrome. Transl Androl Urol. 2015 Oct;4(5):563–71.

[48] Greenwood-Van Meerveld B, Mohammadi E, Tyler K, Van Gordon S, Parker A, Towner R, et al. Mechanisms of Visceral Organ Crosstalk: Importance of Alterations in Permeability in Rodent Models. J Urol. 2015 Sep;194(3):804–11.

[49] Yang Y, Zhang H, Lu Q, Liu X, Fan Y, Zhu J, et al. Suppression of adenosine A(2a) receptors alleviates bladder overactivity and hyperalgesia in cyclophosphamide-induced cystitis by inhibiting TRPV1. Biochem Pharmacol. 2021 Jan;183:114340.

الملخص العربى

متلازمة التهاب المثانة الخلالي: الفيزيولوجيا المرضية، الأسباب، وطرق العلاج

ندى الحُسيني[1]، نشوى بركات[2]، محمود عبد المعبود[1]*

[1]قسم الجراحة والتخدير والأشعة، كلية الطب البيطري، جامعة الزقازيق، الزقازيق، 44519، مصر

[2]مركز أمراض المسالك البولية والكلى، جامعة المنصورة، المنصورة، مصر

التهاب المثانة الخلالي، المعروف أيضًا باسم متلازمة ألم المثانة، هو حالة معقدة ومزمنة تؤثر بشكل رئيسي على المثانة البولية، مسببة مجموعة من الأعراض المزعجة. يتميز المرض بالتهاب أو تهيج في بطانة المثانة، مما يؤدي إلى نوبات متكررة من الألم الشديد في منطقة الحوض والانزعاج، بالإضافة إلى زيادة ملحوظة في التبول من حيث الإلحاح والتكرار. في الحالات الشديدة، قد يعاني الأفراد من آلام منهكة تؤثر على الأنشطة اليومية وتؤثر بشدة على النوم والعمل والعلاقات الشخصية. تشخيص وإدارة التهاب المثانة الخلالي/متلازمة ألم المثانة يظل تحديًا نظرًا لعدم الفهم الكامل للأسباب الكامنة وراءه وميوله لتقليد أعراض اضطرابات أخرى في الجهاز البولي، مثل التهابات المسالك البولية أو فرط نشاط المثانة. بالإضافة إلى ذلك، يمكن أن تقلل الحالة بشكل كبير من جودة حياة المريض، حيث أن الأعراض غير المتوقعة والمستمرة قد تكون مرهقة جسديًا ونفسيًا. تختلف نتائج علاج التهاب المثانة الخلالي/متلازمة ألم المثانة بشكل كبير بين المرضى، حيث يحتاج العديد منهم إلى نهج علاجي متعدد الأبعاد يشمل تغييرات في نمط الحياة، الأدوية، العلاج الطبيعي، وفي بعض الحالات التدخلات الجراحية. يستعرض هذا البحث الاستراتيجيات الحالية لتشخيص وإدارة التهاب المثانة الخلالي، مسلطًا الضوء على أهمية الرعاية الشخصية في تحسين نتائج المرضى.