



GLOBAL INTERSTITIAL CYSTITIS
BLADDER PAIN SOCIETY

GIBS Clinical Guidelines for BPS/IC

Version 4.0 (2025)



Dedicated to our patients who have helped us understand IC/BPS more than textbooks and teachers

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Message from Patron



Dear Clinicians,

We are very happy that we got the opportunity to define the journey of Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS) on a truly global stage. It is a privilege that only a few are fortunate to experience—the chance to lead a cause that not only transforms clinical practice but also touches countless patient lives worldwide. I feel humbled that GIBS has been entrusted with this responsibility and proud that our work continues to make a meaningful difference.

It is with immense pride and a deep sense of responsibility that I present the fourth version of the GIBS Clinical Approach on IC/BPS – Guidelines, coinciding with a truly special milestone—a decade of GIBS and ten years since the release of our very first clinical guidelines in 2017.

When we launched GIBS in 2016, we envisioned a future where IC/BPS would no longer be relegated to the shadows. The release of our first guideline in 2017 was a bold and necessary step toward defining the standard of care for this under-served patient population—not only in India but globally. Today, with Version 4.0, we reaffirm our commitment to improving clinical outcomes, empowering clinicians, and advocating for patients who have long awaited recognition and relief.

A remarkable highlight in our journey has been the consensus meeting held in the USA, where our efforts gained global recognition. It is both gratifying and exciting that over time, our journey has only grown stronger—with prestigious bodies like the NIH (National Institutes of Health) and NIDDK (National Institute of Diabetes and Digestive and Kidney Diseases) joining hands with us to collaborate on setting global guidelines. For the benefit of all stakeholders, these guidelines will soon be released, marking another historic step forward for IC/BPS worldwide.

This edition is not just an update—it is an evolution. Built upon robust clinical experience, interdisciplinary inputs, and feedback from our growing global network, these guidelines continue to reflect GIBS's mission: to create accessible, evidence-based, and patient-centered care pathways for IC/BPS.

Over the past ten years, we've witnessed incredible momentum—from hosting the landmark ESSIC 2016 in Asia, to pioneering webinars, multidisciplinary summits, and patient education tools. Our upcoming achievement—progress toward US-FDA approval of generic Pentosan Polysulfate Sodium (Elmiron)—reinforces our ethos of "Innovation Made in India – For the World."

These guidelines are a culmination of that decade-long journey—carefully crafted to guide clinicians in understanding, diagnosing, and managing IC/BPS with clarity, compassion, and scientific rigor. As we look to the future, our focus is stronger than ever: to unite urologists, gynecologists, pain specialists, and researchers to drive meaningful change across the continuum of IC/BPS care.

To every clinician, researcher, and stakeholder reading this: thank you for being part of this movement. Let these guidelines be more than a reference—let them be a symbol of our collective dedication to ending the silence and suffering around IC/BPS.

Vishal Jajodia
Patron, Global Interstitial Cystitis Bladder Pain Society (GIBS)

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Introduction:

Bladder pain syndrome/Interstitial Cystitis is a chronic and severely debilitating disorder of uncertain etiology and pathophysiology which significantly diminishes quality of life. BPS/IC is common, but its definition and management are challenged by the absence of global consensus on diagnostic criteria and terminology, as well as considerable variability in symptom presentation, objective findings, and treatment outcomes. This heterogeneity is evident in the significant differences in the recommendations found in various international guidelines. The aim of the GIBS guideline for BPS/IC is to systematically collate best practices and expert opinions and offer practical recommendations concerning the definition, nomenclature, evaluation, and management relevant to the routine care of patients with BPS/IC.

Nomenclature:

There have been various revisions in the nomenclature of this condition over the past several decades. A range of terms have been used interchangeably in literature to describe the condition, including BPS, PBS, interstitial cystitis, and terms combining IC with the syndrome. The term 'Interstitial Cystitis', historically used to describe an inflammatory bladder disorder characterized by distinct cystoscopic and histologic features, has been increasingly replaced by 'Bladder Pain Syndrome'. This updated term describes a primary pain syndrome with a broader spectrum of symptomology, clinical signs and pathophysiological mechanisms, in which symptoms are generally associated with the bladder but may not be limited to it. There is now a broad international consensus on the use of the term 'Bladder Pain Syndrome (BPS)'. However, the term Interstitial Cystitis (IC) is still retained by several guidelines since omitting it may affect reimbursement and hamper the access to disability benefits in several countries. This has resulted in the recognition of the term Bladder Pain Syndrome/Interstitial Cystitis by several international societies.

GIBS Perspective on Nomenclature:

GIBS welcomes the universal shift towards use of the term Bladder Pain Syndrome as the use of the term IC alone directs attention only to inflammatory changes in the urinary bladder and excludes patients with typical symptoms but normal cystoscopic and histological findings. IC should include some form of inflammation in the deeper layers of the bladder wall which is not necessarily present in all patients. At the same time, GIBS endorses the use of the term BPS/IC due to the historical importance of the term IC, its widespread use and the financial implications for patients of relinquishing the term.

Definition:

Varying definitions have been proposed for the condition depending upon the symptomatology, duration of symptoms used as a threshold for confirming the diagnosis. All guidelines agree that BPS/IC is a diagnosis of exclusion, and all require the presence of pain, pressure or discomfort linked to the bladder, in addition to at least one urinary symptom. The duration of symptoms included in the definition of BPS/IC in different guidelines varies from six weeks to six months.

Introduction

GIBS Perspective on Definition:

GIBS believes that the definition of BPS/IC should be flexible enough to cover the entire symptomatic breadth of the condition while defining a threshold duration that allows for treatment to begin after a relatively short symptomatic period thereby avoiding unnecessary delays in treatment.

While pain is an important symptom, many patients may describe the discomfiting sensation as pressure or discomfort in the lower abdomen and/or urogenital area. They may also report the discomfort as urgency which needs to be probed into.

The ideal threshold duration for diagnosis of BPS/IC should be set at 3 months. The reason for this is as follows: The commonest condition giving rise to painful urgency is acute infective pathology of lower urinary tract in both sexes. Even after a successful eradication of microbial organism by suitable antibiotics, some symptoms may persist till the complete resolution of inflammatory process, which is generally accepted to be 6 weeks. Considering that there may be some initial delay in starting treatment, it may be accepted that by the end of three months (12 weeks), any infectious pathology giving rise to painful symptoms would have subsided. Hence, if the symptoms continue beyond 3 months, they should raise the suspicion of clinical BPS/IC. Secondly, three months as the diagnostic threshold is preferable to six weeks or six months as duration of six weeks may lead to overdiagnosis and that of six months may prolong suffering.

Phenotyping of BPS/IC:

Current evidence indicates that several established treatment modalities for BPS/IC yield suboptimal outcomes. This is because BPS/IC is a conglomeration of heterogenous clinical entities with urinary symptoms resulting from a variety of pathophysiological pathways working in bladder and non-bladder domains. The umbrella term BPS likely includes several distinct phenotypic subgroups, each with a different pathophysiological cause, unique clinical features and differing response to therapy. One such distinct bladder-specific phenotype, the so-called Hunner lesion disease, is a clearly identifiable phenotype of BPS/IC with distinct clinical, cystoscopic and histopathological features, and for which specific lesion-directed therapies are available.

Thus, classifying the patient into separate clinical phenotypes, based on their history and symptomatology which provide clinical clues to the underlying etiopathogenesis, might help create more personalized and effective treatment plans and optimize treatment outcomes. Such a classification framework would not only guide evidence-based therapy but also accommodate new data as valid biomarkers and treatment approaches become available.

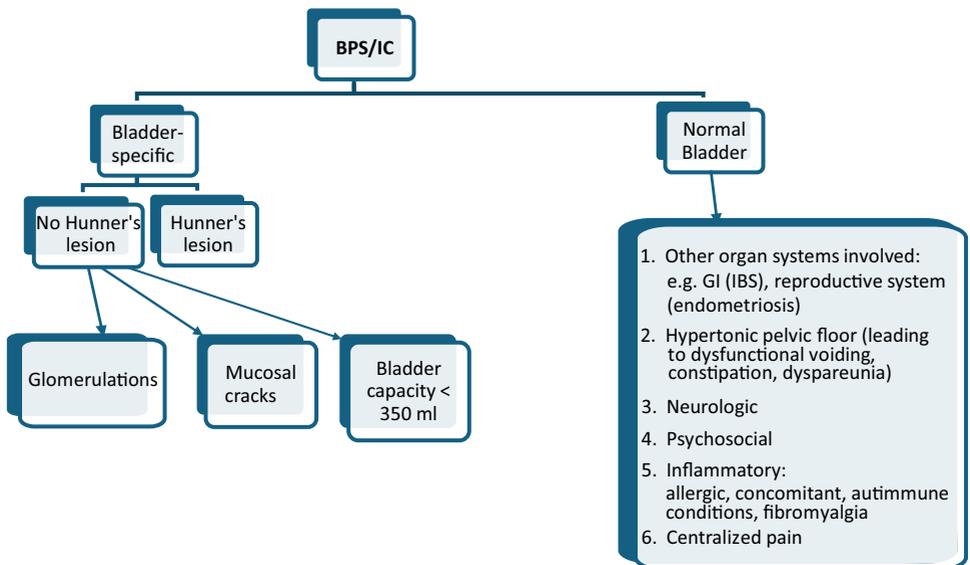
UPOINT is a 6-point clinical phenotyping classification system that classifies patients into 6 clinically identifiable domains: Urinary, Psychosocial, Organ-Specific (Hunner's and non-Hunner's), Infectious, Neurologic/systemic and Tenderness. It was an early phenotyping system that was extrapolated from the classification system developed for chronic prostatitis/chronic pelvic pain syndrome.

Taneja et. al. proposed four clinical phenotypes based on etiopathogenesis: Allergy, Dysfunctional Voiding, Neuropathic pain and Hunner's lesions. There have been phenotypes suggested based on specific biomarkers, urinary microbiome, symptomatology, urodynamic findings, cystoscopic findings, histological findings and pelvic floor hypertonicity.

Several of these proposed phenotypes remain under investigation for their potential to inform individualized treatment plans, and additional research is required to achieve reliable phenotyping. However, from clinical perspective and based on current evidence, it may be valuable to evaluate and classify patients according to phenotypes based on clinical manifestation, as it may prove beneficial in developing more tailored treatment plans.

The phenotyping system for BPS/IC based on clinical manifestation is as follows:

Algorithm of classification of BPS/IC after cysto scopy



Introduction

Patients with BPS/IC with longer symptom duration are more likely to belong to more than one clinical phenotype. Patients belonging to psychosocial and hypertonic pelvic floor phenotypes are likely to have worse symptom scores.

In the centralized pain phenotype, there is widespread pain (nonurological) involving multiple body regions outside the pelvic in addition to the pelvic pain. Additional chronic pain diagnoses such as irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, or migraine headache, may be present. There may be a 'top-down' etiology of systemic pain, involving central sensitization and decreased descending inhibition from higher brain centers to the spinal pain gate, and systemic processes (e.g. pro-inflammatory state) perpetuating pain. The bladder or pelvis may simply be a 'bystander' or pelvic manifestation of their systemic pain.

In the succeeding sections, we will discuss phenotype-specific symptomatology, diagnostic modalities and treatment plans to ensure improved treatment outcomes.

Pain or discomfort in lower abdomen and / or urogenital area

- Of more than 3 months duration
- Which may be worse on full bladder
- Along with one or more lower urinary tract irritative symptoms like urgency, frequency or nocturia
- With or without standard stigmata on cystoscopy
- Provided another discernable pathology likely to cause these symptoms have been excluded.

*While these parameters cover important aspects of the symptomology present in most BPS/IC patients, additional symptoms may be present based on the specific phenotype, for example dysfunctional voiding, constipation, dyspareunia, symptoms specific to concomitant conditions (IBS, endometriosis, autoimmune disorders etc.), neurological symptoms, centralized pain etc.

Also, BPS/IC is associated with several negative psychological, emotional, and sexual consequences, which must be considered and managed.

Clinical Approach

An optimal clinical approach needs high clinical index of suspicion and thorough clinical history, physical examination and diagnostic tests, to aid diagnosis and exclude other specific diseases that may cause pelvic pain.

Considering ground realities in India, the following evaluation is recommended:

Mandatory (Essential)	Recommended (In selected cases)	Optional
Clinical history	Urine Culture	Urodynamic study
Physical Examination	Urine cytology	
Bladder Diary	Pain mapping using a Pain Body Chart	
Urinalysis		
Ultrasonography		
Cystoscopy +/- Biopsy		
Symptom scores		
QOL scores		

Clinical History*:

A. Characteristics of pain/pressure/discomfort

1. Symptom location: suprapubic and/or urogenital area. Pain may also occur in rectum, lower back, and inner thighs.
2. Duration of symptoms: of more than 3 months duration
3. Symptom descriptors: sensation of pain, pressure or discomfort.
4. Exacerbating factors: increasing with increasing bladder content, relieved by voiding, aggravated by specific food articles or drinks
5. Relationship of the pain to different phases of the micturition cycle
6. Determining the relationship of the pain intensity to different phases of the menstrual cycle may help exclude uterine/adnexal causes of the pain.
7. If pain is relieved by passing stools or flatus, GI tract causes need to be excluded.
8. In case of dyspareunia, superficial dyspareunia may warrant ruling out vulvovaginitis or vulvodinia. Deep dyspareunia may suggest present of BPS/IC.
9. VAS score: grading the severity of pain pre-treatment and during treatment is important, using a VAS (visual analog scale) score.

*Two leading questions can be:

- If you have sudden desire to go to the restroom, what is your fear? Is it that you may leak urine which will be embarrassing or is it the fear of increasing pain while holding on? The answer may provide some clinical clues that will help distinguish OAB (overactive bladder) from BPS/IC.
- When you wake up from sleep to pass urine, is it because of the sensation of bladder fullness (desire to pass urine) or due to pain? Patients often learn to evacuate their bladder to get rid of the pain when BPS/IC is present.

B. History indicating specific phenotypes:

1. Bladder specific: Bladder specific symptoms of pain/pressure/discomfort linked to the filling phase of the bladder may be present along with one or more lower urinary tract irritative symptoms like urgency, frequency or nocturia.
2. Other organ systems: There could be symptoms specific to concomitant disorders of other organ systems like endometriosis (severe menstrual pain etc.) or bowel symptoms suggestive of IBS.
3. Hypertonic pelvic floor:
 - Dysfunctional voiding: hesitancy, interrupted flow, weak stream, straining, incomplete bladder emptying.
 - Obstructed defecation: incomplete stool evacuation, aching pain in the anal canal
 - Dyspareunia
 - Pain while sitting
 - Low back pain/tail bone pain, hip pain, groin pain
4. Neurologic:
 - Pricking/burning pain in vulva commonly, clitoris
 - Burning pain in perineum
 - Burning pain in anus, somewhat relieved on passing urine
5. Psychosocial: concomitant depression, anxiety, emotional distress, and various degrees of resultant disability, cognitive, behavioral and sexual consequences
6. Inflammatory:
 - Allergic symptoms
 - Symptoms specific to concomitant autoimmune conditions (e.g., Sjogren's syndrome, scleroderma etc.)
7. Centralized pain:
 - Widespread pain beyond the pelvis (nonurological) involving multiple body regions outside the pelvis (e.g. upper and lower extremity, head and neck) in addition to the pelvis.
 - Presence of concomitant pain diagnoses such as irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, or migraine headache.

C. History indicative of etiology apart from phenotype-specific history

1. History of recurrent urinary tract infections
2. Recent dietary changes related to intentional modification of eating habits (for example, increased consumption of health drinks, tea, green tea, coffee, or dark chocolate) or due to geographical translocation.
3. Recent drug treatment for unrelated disease

D. History of associated diseases (non-organ specific):

1. Fibromyalgia
2. Migraine
3. Mental stress

E. Past medical, surgical and gynecological history:

1. Prior pelvic surgery
2. History of urinary stone disease
3. History of pelvic inflammatory disease (vaginal discharge etc.)
4. History of pelvic irradiation
5. History of neurological diseases (indicative of neurogenic bladder)

Clinical Approach

Physical Examination:

General examination starts as soon as the patient and caretaker enter the consulting room. This includes noticing the amount of medical records they are carrying, the dismal look on the patient and her/his attendant indicative of degree of bother.

A. General Examination

1. Gait of the patient
2. Mental state of the patient
3. Somatic signs of anxiety like pallor, sweating etc.

B. Abdominal examination

1. Scars of previous surgeries
2. Any abdominal masses
3. Tenderness in abdomen, mainly suprapubic. Any other area of tenderness may be noted.

C. Pelvic examination

The pelvic examination needs to be done carefully, especially in patients with hypertonic pelvic floor phenotype. The key points are outlined below:

- Pelvic examination begins with a visual inspection of the perineum at rest and when patients are asked to contract their pelvic floor musculature, assessing symmetry, coordination, and movement.
- Palpation of the pelvic floor muscles should be done with a single digit, especially in patients of hypertonic pelvic floor phenotype, applying consistent, gentle but firm pressure, to determine resting tone and identify trigger points, myofascial bands and pain along the levator ani, piriformis, and obturator internus muscles.
- With a single digit still in the vagina, the patient should be instructed to perform a pelvic floor muscle contraction (Kegel) to evaluate strength and coordination.
- For patients with severe anxiety or pain concerns, delay the pelvic exam to a future visit. Use the initial appointment to build trust, set goals, and discuss treatment options instead of increasing anxiety with an internal exam.
- Palpate the anterior vaginal wall for bladder tenderness, especially in full bladder.
- Digital rectal examination should also be done and resting anal tone, anal squeeze pressure, and tenderness needs to be assessed.

D. Focused neurological examination needs to be done, when indicated.

A. Bladder diary: Bladder diary (of at least one day duration, ideally three days) is an essential preliminary investigation which involves the measurement of voided urine volume and fluid intake with respect to time, along with notation of any urinary leakage, pain, etc. It is an economic and non-invasive investigation that provides critical insight into bladder function. A bladder diary of 24 hours, which involves measuring the urine output from the second void of the day to the first day of the next day, is often sufficient and practical.

B. Ultrasonography: USG is a mandatory test as it aids in avoiding overdiagnosis of BPS/IC and diagnosing concomitant pelvic pathologies that require immediate attention: e.g. high post-void residual. USG is a useful and cost-effective test in limited resource peripheral settings that helps in preventing inappropriate treatments.

C. Cystoscopy with or without biopsy: Although not required by some guidelines (AUA), GIBS considers cystoscopy essential for diagnosing BPS/IC because objective findings are necessary for diagnosis, prognostication and ruling out other treatable conditions. Cystoscopy helps to exclude clinically confusing conditions and diagnose serious diseases, e.g. transitional cell carcinoma, proliferative cystitis and uretero-vesical junction calculi. It helps confirm the diagnosis of intravesical foreign bodies, urethral diverticula, bladder cancer and vesical stones etc., suspected based on symptomatology and non-invasive tests like urine microscopy and radiology. Also, diagnosis and treatment (fulguration) of Hunner's phenotype of bladder-specific BPS/IC can only be done on cystoscopy.

Hydrodistension during cystoscopy is not mandatory for diagnosis, as glomerulations can be seen on overdistension of a bladder with small capacity, Therefore, its role is only for therapeutic purposes after establishing the diagnosis.

Biopsy is not required for diagnosing BPS/IC but should be reserved only to exclude important differential diagnoses by histopathological examination like carcinoma-in-situ, tuberculous cystitis, when there is clinician suspicion or when there is a lesion of uncertain nature.

It must be remembered that absence of any cystoscopic stigmata does not exclude BPS/IC as BPS is a conglomeration of heterogenous disorders, some of which may not be associated with bladder-specific inflammatory changes.

D. Urinalysis and Urine Culture: GIBS believes that Urinalysis is an essential test. However, Urine culture is recommended only in the presence of high suspicion based on Urinalysis: e.g. positive nitrites, leukocyte Esterase and/ or significant pus cells due to high specificity (nitrites) and sensitivity (pus cells and leucocyte esterase) of these values for diagnosing Urinary Tract Infection (UTI). However, it must be noted that AUA (American Urological Association) dictates that Urine culture may be indicated even in patients with a negative urinalysis to detect lower levels of bacteria that are clinically significant but not readily identifiable with a dipstick or on microscopic exam.

Investigations

- E. Symptom scores and QOL scores:** These are recommended as standardized tools to obtain baseline symptoms, including severity of bother and impact on quality of life, tracking of the impact of symptomatology, evaluating treatment effectiveness and tailoring interventions to address specific needs of the patients. GIBS recommends the Apollo Clinical Scoring System (Appendix 1) which is a peer-reviewed validated questionnaire that can be universally used. The other commonly used standardized questionnaires are the O'Leary-Sant Interstitial Cystitis Symptom Index (ICSI) and Problem Index (ICPI) and the King's Health Questionnaire (KHQ).
- F. Urine cytology:** Urine cytology is recommended when there is history of chronic smoking and/ or unevaluated microhematuria and in case of persistent irritative lower urinary tract symptoms with no response to initial treatment (provided all essential tests were negative).
- G. Pain mapping using a Pain Body Chart** is recommended in patients with centralized pain.
- H. Urodynamics:** There is consensus between various guidelines that Urodynamics should only be performed in patients with a complex history in whom alternative diagnoses may be present (e.g., voiding dysfunction, overactive bladder, and stress urinary incontinence).

The clinical evaluation should lead to the exclusion of all pathologies that can mimic the symptoms of BPS/IC:

- Bladder diseases: Overactive bladder, neurogenic bladder, benign or malignant bladder tumor, bladder calculus. Radiation cystitis, chemotherapy induced cystitis (Cyclophosphamide ketamine, tiaprofenic acid etc.)
- Genitourinary infections: Bacterial cystitis, tubercular cystitis, urethritis, prostatitis (within 3 months period). chronic pelvic inflammatory diseases. active genital herpes, vaginal candidiasis
- Gynecological diseases: Endometriosis, uterine myoma vaginitis, climacteric disturbance, uterine/ cervical/vaginal cancer
- Other conditions: Polyuria, pelvic floor muscle spasm due to other reasons, vulvodynia, vestibulodynia, pelvic congestion syndrome.

Multiple treatment options, varying from conservative treatments to invasive options, have been proposed over the last several decades; unfortunately, most of them lack high level evidence. The most optimal treatment would depend upon the severity and possible etiopathogenesis of the disease along with clinical judgement and patient preference. Treatment decisions should be made after shared decision-making, with the patient informed categorically about the risks and benefits of various treatment options and the alternatives.

However, the best approach for most optimal outcomes is to individualize the treatment plan and tailor the treatment to the specific phenotype. Multimodal treatment plans that incorporate behavioral, physical, and psychological treatments, while focusing on specific phenotypes, are beneficial. This approach abandons the traditional stepwise treatment plan, instead recognizing the condition's heterogeneity. It may also need the involvement of multidisciplinary teams including urogynecologists, urologists, gynecologists, gastroenterologists, pain specialists, psychiatrists, psychologists, physiotherapists, etc.

The treatment plan for a specific patient may include concurrent, multimodal therapies. Except for patients with Hunner's lesions, initial treatment should typically be nonsurgical. The management plan for patients without Hunner's lesions is best categorized into behavioral/non-pharmacologic, oral medications, intravesical instillations, procedures, and major surgery.

A. Behavioral/ non-pharmacological treatment: It includes the following components:

- 1. Patient Education:** A comprehensive treatment plan needs to begin with patient education regarding bladder function, description of the condition and its chronicity, and the available treatment options along with their risks and benefits. Counseling the patient regarding the natural history of the diseases including its waxing and waning nature, setting realistic expectations of the treatment outcomes and that there is no single curative treatment option, is essential. The patient needs to be made aware of the fact that multiple treatment options may need to be tried (including combination therapy) before symptomatic relief is obtained.
- 2. Self-Care and Behavioral Modifications:** The patients must be counselled to alter or avoid specific behaviors which have been reliably proven to worsen symptoms. Behavioral modification could include:
 - Altering the concentration and/or volume of urine, either by fluid restriction or additional hydration
 - Dietary modification: Avoiding known dietary bladder irritants, e.g. caffeine containing products such as coffee and tea, acidic foods such as citrus products, spicy food, sodas, alcohol, artificial sweeteners, etc. An elimination diet can be used to determine which foods or fluids are contributing to symptoms.
 - Application of heat or cold to areas of hypersensitivity and trigger points.
 - Strategies to manage BPS/IC flare-ups, e.g. meditation, imagery etc.
 - Treating constipation: having a fiber-rich diet may be beneficial.
 - Avoiding wearing tight-fitting clothing
 - Avoiding exercises that may worsen symptoms, e.g. Kegel exercises (especially in hyperfunctioning pelvic floor phenotype)
 - Bladder retraining with urge suppression.

Treatment Guidelines

3. **Stress Management:** Stress management is needed, especially in those with psychosocial phenotype, to improve coping techniques and manage stress-induced symptom flares. Patients need to learn to cope with stresses linked to family, work and past traumatic experiences. Stress management techniques could include meditation techniques, pranayama practice, yoga etc. Involvement of a psychiatrist and a psychologist may be necessary.
4. **Manual physical therapy techniques and pelvic floor relaxation biofeedback therapy:** Involvement of a physical therapist may be needed, especially in patients with hypertonic pelvic floor phenotype. The beneficial techniques may include maneuvers that resolve pelvic, abdominal and/or hip muscular trigger points, lengthen muscle contractures, and release painful scars and other connective tissue restrictions. Pelvic floor strengthening exercise (e.g. Kegel exercises) should be avoided. Biofeedback therapy with/without electrical stimulation for relaxation may be beneficial.

B. Oral medications:

Based on the phenotype, various oral medications may prove beneficial:

Medication	Dose	Phenotype in which useful	Adverse effects
Amitriptyline	10 – 75 mg/day	Bladder -specific, centralized pain, neurologic	Constipation, palpitation, dry mouth, weight gain etc.
Hydroxyzine	25 - 75 mg/day	Inflammatory, bladder-specific	Drowsiness, confusion in elderly people etc.
Gabapentin	Gabapentin (100 to 300mg HS)	Neurological	Dizziness, drowsiness, diarrhea, blurred vision, headaches, memory problems, mood changes, dry mouth etc.
Pregabalin	75 mg OD in women > 55 kgs in weight	Neurological	Dizziness, blurred vision, xerostomia, nausea, weight gain, headache, polyphagia, constipation, mood changes, memory problems etc.

Treatment Guidelines

Medication	Dose	Phenotype in which useful	Adverse effects
Pentosan polysulfate (takes three to six months for optimal response): helps to replenish the GAG layer of the bladder	100 mg thrice a day on empty stomach	Bladder -specific	Nausea, diarrhea, hair loss, headache, rectal bleeding etc. Retinal examination should be done at baseline and after a year of medication. Patients should be counseled about the potential risk of eye damage and vision -related injuries (pigmentary maculopathy particularly) .
Skeletal muscle relaxants: Cyclobenzaprine, diazepam suppositories, clonazepam, baclofen	Dosage varies based on the skeletal muscle relaxant used	Hyperfunctioning pelvic floor disorder	Adverse effects vary based upon the relaxant used.

Additionally, urinary alkalinizers can be used.

- **Pharmacological Pain Management:** Effective pain management is a fundamental component of the overall treatment strategy. The principles underlying the same should be like those for management of other chronic pain conditions. The aim of pharmacotherapy for BPS/IC is to identify the most effective medication or combination of medications while minimizing adverse effects.

Detailed guidelines on pain management are included in Appendix 2.

C. Intravesical instillations:

Intravesical instillations of anti-inflammatory medication, analgesics, or agents that replenish the GAG layer of the bladder have proved to be effective. While the instillation of lidocaine/sodium bicarbonate and pentosan polysulfate have been given grade A recommendation, there are several regimens of bladder instillations, and they are detailed in Appendix 3.

Bladder instillations help to achieve high intravesical drug concentrations with minimal systemic side-effects. Disadvantages include the need for intermittent catheterization, which can be painful in BPS/IC patients, cost, and risk of infection.

Treatment Guidelines

D. Procedures:

1. Cystoscopy with hydrodistension with fulguration of Huner's lesions (under anesthesia): Cystoscopy with low-pressure (60 to 80 cm H₂O), and short duration (approximately 3 minutes) hydrodistension is a common treatment for BPS/IC.

The procedure helps in three ways:

- First the bladder is inspected for other pathologies which could be responsible for the symptoms (e.g., vesical stones and tumors) and for Hunner's lesion. Fulguration of Hunner's lesion through electrocautery is a curative treatment. Injection of triamcinolone can also be done cystoscopically, but this is not widely done in India.
 - If there are no other bladder pathologies or Hunner's lesions, then the distension can be continued as a treatment. Hunner's lesions may be easily identified on distension when cracking and mucosal bleeding ensue.
 - Disease 'staging' can be done, and anatomic bladder capacity can be determined, thereby identifying the patients who have reduced capacity due to fibrosis.
2. Intradetrusor onabotulinum toxin A injection may be administered if other treatments have not provided adequate improvement in symptoms and quality of life. However, patients with Hunner's lesions have not been found to benefit from Botox injection.
 3. Sacral neuromodulation: Sacral neuromodulation has been shown to improve quality of life in the patients in whom other treatments have not been effective. But it must be noted that neuromodulation is not yet FDA-approved for BPS/IC treatment.

E. Major surgeries:

Augmentation cystoplasty, and urinary diversion with/without cystectomy may be considered in carefully selected patients with bladder-centric symptoms, or when there is an end-stage small fibrotic bladder, for whom all other treatments have failed to provide symptomatic relief or improvement in quality of life.

Appendix 1

Apollo clinical Scoring System for Interstitial Cystitis / Bladder Pain syndrome

1. Urgency (0-5)

How often have you felt the strong need to urinate with little or no warning?

0. Not at all
1. Less than 1 in 5 times
2. Less than half the time
3. About half the time
4. More than half the time
5. Almost always

2. Frequency (0-5)

How often have you had to urinate less than 2 hours after you finished urinating?

0. Not at all
1. Less than 1 time in 5
2. Less than half the time
3. About half the time
4. More than half the time
5. Almost always

3. Nocturia (0-10)

How often did you most typically get up at night to urinate?

0. Never
2. Once
4. 2 times
6. 3 times
8. 4 times
10. 5 times or more

4. Pain (0-20)

Have you felt Burning, pain, discomfort, or pressure in your bladder?

0. Not at all
4. Once a day
8. A few times a day
12. Fairly often
16. Almost always
20. Persistent pain that is not reduced after emptying bladder

5. Sexual dysfunction (0-5)

A) Female

0. No problem in sexual activity
1. Can engage in sexual activity with minimal discomfort.
2. Non penetrative genital contact can be tolerated.
3. No genital contact can be tolerated.
4. Vulvodynia
5. Aversion to sexual thoughts

B) Male

0. No problem in sexual activity
1. Post ejaculatory discomfort.
2. Moderate to severe pain post ejaculation
3. Pain at the time of erection
4. Complete loss of erection
5. Loss of libido with ED

6. Psychological impact (0-5)

How much have the symptoms bothered you mentally (score 0-5):

- 0.No problem
- 1.Very small problem
2. Small problem
3. Medium problem
4. Big problem
- 5.Suicidal tendency

Total Score..... / 50

Pain Management Protocol in BPS/IC

Appendix 2

Step I Assesment, Assurance, Education

- History and Physical examination, dietary history, stress history, map area of pain look for myofascial bands
- Reassurance and patient education

Step II Reassurance Education

- Start NSAIDs or Paracetamol or weak opiods like tramadol/tapentadol/buprenorphine according to pain score
- Add Gabapantine / Pregablin and Amitryptiline
- Physical Therapy
- Cognitive Behavioural Therapy

Step III Reassessment Reassurance Education

- Strong Opiods like morphine/fentanyl
- Myofascial Block
- Gbapantine/pregablin + Amitryptiline
- Physical Therapy
- Congnitive Behavioural Therapy

Step IV Reassessment Reassurance Education

- Pudental Nerve Block
- Increase dose of Weak or strong opiods
- Increase doses of gabapantine / pregablin + Amitryptiline
- Physical Therapy
- Congnitive Behavioural Therapy

Step V Reassessment Reassurance Education

- Superior Hypogastric Plexus Block
- Increase dose of Weak or strong opiods
- Increase doses of gabapantine / pregablin + Amitryptiline
- Physical Therapy
- Congnitive Behavioural Theraph

Appendix 3

Intravesical drugs are administered due to achieve high drug concentrations at the target site while reducing the systemic side-effects. We present a comprehensive summary of these drugs/cocktail mixtures used for intravesical instillations:

1. Heparin: Intravesical dose ranges from 10,000 IU to 40,000 IU.
Given as daily instillations for 3-4 months (Patients are taught self-instillations)
2. Lidocaine: 2% usually 20–30 mL
Alkalinization increases urothelial penetration of lidocaine and therefore is expected to improve efficacy but it also can increase systemic absorption and potential toxicity. No published studies have directly compared lidocaine with and without alkalinization. No studies have directly compared different lidocaine concentrations.
3. Sodium Hyaluronate solution:
 - a. Hyacyst: available in two doses: 40 mg and 120 mg
Weekly administration for 4 weeks
 - b. Cystistat: 40 mg in 50 ml
Weekly administration for 4 to 8 weeks.
4. Chondroitin sulfate: 0.2%
Induction: 20 mL of 2% CS once weekly for 6-8 weeks, dwell 30–60 min.
Maintenance: monthly instillations for 3–6 months.
Can also be used in combination with Hyaluronic acid rather than as monotherapy.
5. Pentosan polysulfate intravesical preparation:
 - Prepare the following: 5 ml Sodabcarb solution in 5 ml syringe.
20 ml 2% xylocaine solution in 20 ml syringe.
30 ml Pentosan polysulfate intravesical preparation
 - Clean, drape and instil xylocaine jelly to anaesthetise the urethra and trigone.

Intravesical Treatment

6. Cocktail Therapies

a. Anaesthetic cocktail – Robert Moldwin

- 1:1 mixture of 0.5% Bupivacaine and 2% Lidocaine jelly – about 40 ml total.
- Heparin sulphate: 10,000- 20,000 IU
- Triamcinolone 40-80 mg
- Gentamycin 80 mg

b. Hydrocortisone and Heparin cocktail –Rajesh Taneja

- Hydrocortisone 200 mg
- Heparin 25,000 IU
- In physiological saline to 40 ml volume

c. Heparin Cocktail: Kristene Whitmore

- Heparin 10,000 units/ml: 2 ml
- Solu-Cortef (hydrocortisone sodium succinate): 125 mg
- Gentamicin 80 mg/2ml: 2 ml
- Sodium Bicarbonate 8.4%: 50 ml
- Marcaine 0.5%: 50 ml

d. Pentosan polysulfate cocktail - Jurjen J. Bade

- Pentosan polysulfate sodium 300mg (=3 ampules each 100mg)
- Lidocaine 2%: 10cc
- Sodium bicarbonate 4.2% (but can also be 4.8%): 10cc

e. Heparin cocktail with alkalinized lidocaine – C. Lowell Parsons

- Heparin sulphate 40,000 IU (4ml)
- Lidocaine 2%: 8 mL
- Sodium bicarbonate 8.4%: 3 mL

f. Marcaine with steroid cocktail – Nagendra Mishra

- 0.5% Bupivacaine: 40 ml
- Heparin sulphate 10,000 IU
- Dexamethasone 2 cc
- Sodium bicarbonate 20 ml

g. Anaesthetic cocktail: Kristene Whitmore

- 0.5% Bupivacaine: 20 mL
- Heparin 10,000 IU: 10 mL
- Hydrocortisone: 100 mg in 5 mL of normal saline
- Sodium bicarbonate 48 mmol: 40 mL
- Triamcinolone 40-80 mg

h. DMSO cocktail: Philip Hanno

- DMSO 50%: 50 cc
- Sodium bicarbonate 44 meq (one ampule)
- Triamcinolone 40 mg
- Heparin sulphate 20,000 IU
- ± Gentamicin 80 mg

i. Payne Cocktail: Christopher Payne

- DMSO 50%: 50 cc
- Sodium bicarbonate: 5 ml
- Hydrocortisone: 100 mg
- Bupivacaine 0.5%: 10 ml
- ± Heparin sulphate 20,000 IU

Appendix 4

1. Diagnostic and therapeutic cystoscopy in bladder pain syndrome/interstitial cystitis: systematic review of literature and consensus on methodology

Abstract

Introduction and hypothesis: Cystoscopy has been routinely performed in patients suspected to be suffering from bladder pain syndrome/interstitial cystitis (BPS/IC) across the globe. The methodology reported by various guidelines appears to have differences in the techniques and hence there is a need for a review of all those techniques in order to arrive at a consensus. The aim was to review the literature describing the prevalent techniques of cystoscopy for patients of BPS/IC and try to evolve a consensus.

Methods: The group the Global Interstitial Cystitis, Bladder Pain Society (GIBS) has worked collectively to systematically review the literature using the key words, “Cystoscopy in Hunner’s lesions, bladder pain syndrome, painful bladder syndrome and interstitial cystitis” in the PubMed, COCHRANE, and SCOPUS databases. A total of 3,857 abstracts were studied and 96 articles referring to some part of technique of cystoscopy were short-listed for review as full-length articles. Finally, six articles with a description of a technique of cystoscopy were included for final tabulation and comparison. The group went on to arrive at a consensus for a stepwise technique of diagnostic and therapeutic cystoscopy in cases of BPS/IC. This technique has been compared with the previously described techniques and may serve to be a useful practical guide for treating physicians.

Conclusion: It is important to have a uniform standardized technique for performing a diagnostic and therapeutic cystoscopy in patients with BPS/IC. Consensus on one such a technique has been arrived at and described in the present article.

Taneja R, Pandey S, Priyadarshi S, Goel A, Jain A, Sharma R, Purohit N, Bandukwalla V, Tanvir, Ragavan M, Agrawal A, Shah A, Girm Z, Ajwani V, Mete U. Diagnostic and therapeutic cystoscopy in bladder pain syndrome/interstitial cystitis: systematic review of literature and consensus on methodology. Int Urogynecol J. 2023 Jun;34(6):1165-1173. doi: 10.1007/s00192-023-05449-w. Epub 2023 Jan 28. PMID: 36708406.

Abstracts of Relevant Publications

2. Evaluation of outcomes of clinical phenotyping-based treatment for bladder pain syndrome/ interstitial cystitis

Abstract

Introduction: Bladder pain syndrome/Interstitial cystitis (BPS/IC) is clinically of diverse types because different causes contribute to the development of their symptoms. It is important to classify patients into various groups based on the possible etiopathogenesis of their condition. Treatment may be tailored to each specific group according to the possible cause.

Methodology: Twenty-five patients diagnosed with BPS/IC were categorized into four different clinical phenotypes (CP) based on their history of symptoms, allergy, dysfunctional voiding, neuropathic pain, and the presence of Hunner's ulcer. Some patients could be classified into multiple groups. The patients were given oral pentosan polysulfate, and treatment specific to their CP. Patients in CP1, CP2, and CP3 groups received, respectively hydroxyzine, clonazepam, and amitriptyline. Patients with Hunner's lesions (HL) (CP4) underwent hydro distension and ablation of the lesion, followed by intravesical instillation of heparin and hydrocortisone. The patients were evaluated using the Apollo clinical scoring (ACS) system and their clinical scores were recorded at 1, 3, and 6 month(s).

Results: Among the 25 patients, 5, 7, 4, and 9 patients were classified into CP 1 – CP4 groups respectively, and were all subjected to ACS assessment. In CP1 group (allergy group), 80% (4/5) of patients responded well to the treatment and 20% (1/5) had unsatisfactory responses. In CP2 group (dysfunctional voiding group), 71.42% (5/7) patients had good, and 28.57% (2/7) had excellent responses. In CP3 group (neuropathic pain group), 28.57% (3/4) patients had excellent, and 75% (1/4) patients had good responses. In CP4 group (HL group), 33.33% (3/9) patients had unsatisfactory, 44.44% (4/9) achieved good, and 22.22% (2/9) had excellent responses. Overall, 16% (4/25) patients had unsatisfactory, 56% (14/25) attained good, and 28% (7/25) had an excellent response at the completion of the study.

Conclusion: Using clinical phenotyping-based features indicative of etiology could potentially improve treatment outcomes by targeting the specific pathological processes contributing to the patients' symptoms.

Sharma A, Taneja R, Raheja A, Mehta K, Taneja N, Singh A. Evaluation of outcomes of clinical phenotyping-based treatment for bladder pain syndrome/interstitial cystitis. Bladder. 2024;11(1):e21200004. DOI: 10.14440/bladder.2024.0010.

Abstracts of Relevant Publications

3. Validation study of new clinical scoring - "Apollo Clinical Scoring system" for bladder pain syndrome/interstitial cystitis and comparison of outcome with standard "O'Leary-Sant score"

Abstract

Aim: Validation of the recently published newer clinical scoring system for bladder pain syndrome/interstitial cystitis and comparison of the results with the pre-existing standard O'Leary-Sant score.

Introduction: The symptoms are our primary guide to disease severity analysis, treatment, and response monitoring. The combined ICSI/ICPI (O'Leary-Sant Interstitial Cystitis Symptom and Problem Index) consist of a four-item symptom and problem index focusing on urgency, frequency, nocturia, and pain. A new scale, assigning more weight to pain and nocturia and adding the domains of sexual dysfunction and psychological impact, has been published by one of the authors (El Khoudary et al. J Women's Health 2002. 18:1361-1368; 7).

Material and methods: This is a prospective study conducted to validate a newer clinical scoring system, named the 'Apollo Clinical Scoring' (ACS) system for patients with bladder pain syndrome/ interstitial cystitis (BPS/IC), and to compare its outcome with the simultaneously applied standard O'Leary-Sant (OLS) score. Thirty-five patients of BPS/IC diagnosed using the ESSIC definition were enrolled in the study and followed for 6 months. Intraclass correlation coefficient (ICC) for test-retest reliability, and Cronbach's α for measure of internal consistency, were applied to both scoring systems.

Results: Intraclass correlation coefficient for ACS was 0.715 and for OLS was 0.689. Cronbach's α for ACS was 0.736 and for OLS was 0.698.

Conclusion: The present study suggests that the recently devised Apollo Clinical Scoring (ACS) system for patients of BPS/IC is internally consistent and a reliable scoring system. When compared with OLS in parallel setting, the newer ACS appeared to be marginally better.

Taneja R, Singh AK, Sharma A, Taneja N, Raheja A. Validation study of new clinical scoring - "Apollo Clinical Scoring system" for bladder pain syndrome/interstitial cystitis and comparison of outcome with standard "O'Leary-Sant score". Int Urogynecol J. 2024 Jun;35(6):1137-1144. doi: 10.1007/s00192-023-05641-y. Epub 2023 Aug 29. PMID: 37642668.

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