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Review Article

Bladder Pain Syndrome: Clinical Diagnosis and Management Strategies

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Abstract

Background: Bladder Pain Syndrome (BPS) is a difficult entity to manage, without specified diagnostic criteria, often referring to a combination of symptoms without identifiable pathology. Treatments are inconsistent in reliability, leading to significant impacts on patient quality of life.

Objectives: This review article provides an overview of the clinical assessment and evidence-based management strategies for Painful Bladder Syndrome (PBS). Emphasis is placed on a practical set of recommendations relevant to general practice.

Discussion: BPS requires a targeted history and examination of the urogenital system, with exclusion of sinister causes. Multidisciplinary input is suggested. Initial treatment is primarily conservative with stress reduction techniques, dietary changes, exercise regimens, smoking cessation, and physical therapy. Pharmacological agents are variable in efficacy. Pentosan polysulfate is often the agent of choice. Urology input is suggested if conservative and pharmacological intervention fail. Treatments may involve minor procedures or neuromodulation, with radical options reserved for very specific cases.

Introduction

Bladder Pain Syndrome (BPS) is an entity which Painful Bladder Syndrome (PBS) or Interstitial Cystitis (IC) fall under, and is a form of chronic pelvic pain [1]. It has been defined by the International Society of Bladder Pain Syndrome (ESSIC) as suprapubic pain accompanied by other symptoms including urinary urgency, frequency, nocturia, in the absence of any Urinary Tract Infection (UTI) or obvious pathology [2]. IC is defined similarly to PBS, though requires cystoscopic and/or histological features typical of the disease (glomerulations and Hunner's ulcers) [3]. Its diagnostic criteria remain elusive and is often used to describe a constellation of symptoms, resulting in few consistently reliable treatment options. It is a debilitating condition leading to high rates of depression, anxiety, sleep disturbances and social life interference, impacting both physical and mental quality of life [4]. This article provides an overview of the current understanding of and management strategies for PBS. A Medline literature search was performed, and relevant clinical guidelines summarized. We make a practical set of recommendations applicable to the general practice setting.

Clinical Assessment

Diagnosis is complex and partly based on the exclusion of other diseases. Pertinent differentials must be considered and excluded prior to a diagnosis of PBS. Prostatic/gynaecological/urethral/bladder disease, genitourinary infections, and pelvic floor disease are all considerations. Urothelial carcinoma is of particular concern, as it can often present with irritative voiding symptoms

and dysfunction, with or without macroscopic haematuria. Patients with macroscopic haematuria should be referred promptly for exclusion of urothelial carcinoma [5,6].

Clinical History

A comprehensive history and examination of the urogenital system remains integral the work-up of BPS. Burden of disease on patient quality-of-life, pain history (if present) and past medical history are important. Clinical features include pelvic pain – often described as "pressure" – related to bladder filling, with common sites being suprapubic, urethral, vulval, vaginal and rectal. A history of recurrent culture-negative UTIs is often described by the patient. Irritative voiding symptoms such as urgency, frequency, urge/stress incontinence and nocturia may be associated (defined in Table 1) [7,8].

Term	Definition
Urinary urgency	Inability to defer voiding
Urge incontinence	Urgency causing non-voluntary urinary incontinence
Stress incontinence	Non-voluntary urinary incontinence related to increased intra-abdominal pressure
Urinary frequency	Eight or more voids per 24 hours
Nocturia	Awakening to void ≥1 instance per night

Table 1: Definition of symptoms.

Potential risk factors and triggers that may exacerbate symptoms should be explored. Validated questionnaires can aid in establishing baseline characteristics and assessment of treatment efficacy (Table 2) [7,9-12].

Risk factors	Behavioural triggers	Food triggers	Validated questionnaires
• Pelvic surgery	• Stress	• Citrus fruits	• Bladder Pain/Interstitial Cystitis Symptom Score (BPIC-SS)
• UTI	• Constrictive clothing	• Caffeinated beverage	• Interstitial Cystitis Symptom Index (ICSI)
• Urological disease	• Sexual intercourse	• Alcoholic beverages	
• Pelvic radiation		• Spicey food	
• Autoimmune conditions			

Table 2: Relevant history taking.

Physical Examination

Examination should be of the lower abdomen, followed by assessment of bladder fullness and suprapubic tenderness. A vaginal exam is recommended in females, with documentation of vulval, vaginal and surrounding organ pain. Digital rectal exam is recommended for males, with appropriate documentation of scrotal-anal region pain [7].

Laboratory Testing

Initial investigations consist of urinalysis and urine culture to exclude infective causes, with consideration of urine cytology if haematuria is present, or if there is a history of smoking. "Sterile pyuria" should be cultured for exclusion of tuberculosis and fastidious organisms [13]. Antiproliferative factor may be used as a biomarker for the diagnosis of PBS, though its specificity is low and is often confounded by other factors [14]. A bladder diary may prove useful in providing objective information regarding fluid volume intake, triggers (alcohol, caffeine), incontinence episodes and determination of nocturnal polyuria. Ultrasonography of the urinary tract including pre-void and post-void residuals can be considered.

Management Strategies

Management strategies are listed in Table 3. BPS management should be based on a bio-psychosocial model and should be performed in a holistic patient-centred approach, with active patient involvement. Treatment can be approached in a stepwise fashion, from conservative behavioral and lifestyle modification, to medical, to minimally invasive surgical, and finally radical surgical treatments. Expectation management in chronicity of disease and the lack of efficacy of any single treatment regimen is important on initial diagnosis [15-17]. Current guidelines and literature

indicate multi-modal, tailored approaches are key in ongoing control [15-21]. Treatments should be periodically reassessed, and ineffective treatments stopped [15]. Multidisciplinary team input with urologists, gynaecologists, pain specialists and mental health practitioners may also be considered.

• Modifying lifestyle behaviours
• psychotherapy
• Physical therapy
• Pharmacotherapy (refer to Table 4)
• Intravesical instillations (refer to Table 5)
• Surgery

Table 3: Key points on management strategies.

Conservative Management

Conservative measures are a cost-effective and risk-free strategy on initial diagnosis, forming sustainable and accessible options for long-term management. Physical therapy has shown symptom improvement in over 50% of patients [19]. These strategies include [15-20]:

- Stress reduction techniques including psychotherapy, hypnotherapy
- Dietary changes to avoid food triggers (e.g. reducing caffeine, spicy foods, alcohol, citrus fruits) including elimination diets and weight loss
- Exercise regimens
- Smoking cessation
- Urinary concentration/volume alteration by fluid restriction/ hydration
- Social support: early involvement and education of family members, support group education
- Physical therapy – hot/cold packs, pelvic floor muscle relaxation, trigger point myotherapy, connective tissue release, muscle coordination training, Thiele massage, acupuncture, reflexology, bladder training

Simple analgesics like nonsteroidal anti-inflammatories can ease the burden of symptoms.

Pharmacotherapy

Pharmacotherapy agents have variable success rates, and are associated with significant non-compliance or discontinuation rates due to minimal long-term efficacy [21]. However, they form the mainstay of ongoing management if conservative measures fail. Current guidelines indicate several agents with varying recommendations across multiple guidelines (Table 4) [15-20].

Medication class	Agent	Route, dose	PBS listing	Adverse effects
Tricyclic antidepressant	Amitriptyline	Oral, starting at 10mg and titrating to 75-100mg daily	Yes	Sedation, dry mouth, blurred vision, constipation, orthostatic hypotension, long QT syndrome
Antihistamine	Cetirizine	Oral, 10mg daily	No; available over the counter	Drowsiness, fatigue, headache, nausea, dry mouth
Pentosan Polysulfate	Pentosan polysulfate sodium	Oral, 100mg three times a day	No	Thrombocytopenia, macular damage
Calcineurin inhibitor	Ciclosporin A	Oral, 1.5 – 3mg/kg	No	Hypertension, nephrotoxicity, immunosuppression
PBS: Pharmaceutical Benefits Scheme				

Table 4: Agents available in Australia with varying supporting recommendations across multiple guidelines.

Pentosan polysulfate is a mainstay oral therapeutic, being the most-studied oral medication for PBS. Effectiveness is variable. Some trials report no differences in symptom improvement, but others show improvement compared to placebo [15]. Its mechanism of action is thought to reduce urothelial permeability by reinforcing the Glycosaminoglycan (GAG) layer in urothelium, allowing restoration of the urothelial layer and reducing noxious stimulation of the sub-mucosal nerves [15-20]. Antihistamines are thought to reduce bladder symptoms by inhibiting mast cell histamine release [22]. Tricyclics may act in a similar way, however there is limited robust evidence [20]. There is emerging evidence for low-dose Cyclosporin A as a treatment option, with studies showing a greater efficacy than pentosan polysulfate in patients with Hunner's ulcers or active bladder inflammation [15-19]. However, there are significant adverse effects associated, leaving it as a relatively last-line treatment option often requiring urological input.

Surgical

Minimally Invasive: Instillations

Multiple instillation agents can be used with varying efficacy for varying time periods, ultimately attempting to restore the architecture of the GAG layer and thus natural protection provided. They are often used in combination with each other [15-20] Table 5.

Agent	Proposed mechanism
Dimethyl Sulfoxide	Thought to provide a combination of an anti-inflammatory response, collagen dissolution and detrusor relaxation
Hyaluronic acid and Chondroitin Sulfate	Thought to repair defects in the GAG layer
Pentosan Polysulfate	Similar mechanism to oral administration - reduce urothelial permeability by reinforcing the glycosaminoglycan (GAG) layer
Heparin	Postulated to promote urothelial regrowth
Lidocaine	Local anaesthetic with anti-inflammatory properties

Table 5: Intravesical instillation agents.

Minimally Invasive: Procedural

Hydrodistension

Hydrodistension has an unknown mechanism of action, but has been shown to damage the sub-mucosal nerve plexus in animal models [20]. It also provides the proceduralist an opportunity to inspect for other possible causes (stones, tumours) [15]. Treatment effect diminishes over the course of months, and efficacy varies due to differing practices of hydrodistension. It can however, be repeated, and therapeutic in up to 56% for two to three months [19,20]. Risks include the need for general anaesthetic, bladder rupture rarely, and an exacerbation of symptoms immediately following procedure [15,19,20].

Treatment of Hunner's Ulcers

Local treatment of Hunner's ulcers can provide significant symptomatic relief in patients with PBS, as high as 97% [22]. Treatment options include cauterization, injection with corticosteroids and transurethral resection, and studies have demonstrated continued symptom relief greater than 3 years post-treatment [22,23].

Intravesical Botulinum Toxin A (Botox)

Botox intravesical injections are administered via cystoscopy into the wall of the bladder to provide an anti-nociceptive effect on bladder afferent pathways, inhibiting neurotransmitter release of the bladder's sub-urothelial layer and inducing flaccid paralysis of the bladder [17,19,20]. The treatment is effective for months, with recent data showing an average length of effect of 5.4 months [19]. It can be used in conjunction with hydrodistension and/or repeated, but carries the risk of general anaesthetic and urinary retention, requiring temporary or self-catheterization [15-20].

Sacral Neuromodulation

Sacral neuromodulation is accomplished by implanting an electrode in the region of the S3 vertebra, inhibiting detrusor action by stimulating spinal inhibitory systems[25]. There is a lack of long-term evidence regarding efficacy, with some studies reporting 72% success at 5 years, and others reporting 80% within an undefined time period [16], [19-20]. Adverse events ranged between 0-50%, with similar explantation rates [17,20]. Current evidence indicates significant improvement in urgency related symptoms, with a recent meta-analysis demonstrating significant improvement in nocturia, frequency and voided volumes [26,27]. Less invasive neuromodulation modalities like transcutaneous electrical nerve stimulation, percutaneous tibial nerve stimulation and pudendal nerve stimulation may help [16,17,19].

Radical

In patients where treatment options have been expended, bladder augmentation cystoplasty, subtotal cystectomy and urinary diversion with or without cystectomy may be considered. The decision for surgery requires careful patient selection, and counselling regarding morbidity and associated risks of major abdominal surgery. Surgery may not rid the patient of their pain, and they must understand they may be swapping one set of problems for another. There is weak evidence to suggest benefit with these procedures [17]. Augmentation cystoplasty involves bladder enlargement by adding a piece of bowel to the bladder. Urinary diversion involves conduit creation from bowel for the ureters to drain into.

Conclusion

BPS is debilitating physically, psychologically, and socially. There are multiple treatment options available in the general practice setting, and management can be approached in a stepwise fashion. If conservative and pharmacological treatments fail, or sinister causes require exclusion, urology specialist referral is recommended.

Keypoints

- BPS is a difficult entity to manage, requiring MDT input.
- History and examination focuses on exclusion of other sinister causes.
- Conservative measures can improve symptoms in over 50% of patients.
- Pentosan Polysulfate is a common first-line pharmacotherapeutic.
- Urology referral should be considered early for further treatment options if failing initial management.

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