Diagnosis and Treatment of Interstitial Cystitis/Bladder Pain Syndrome: AUA Guideline Amendment

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Purpose: The purpose of this amendment is to provide an updated clinical framework for the diagnosis and treatment of interstitial cystitis/bladder pain syndrome based upon data received since the publication of original guideline in 2011.

Materials and Methods: A systematic literature review using the MEDLINE® database (search dates 1/1/83-7/22/09) was conducted to identify peer-reviewed publications relevant to the diagnosis and treatment of IC/BPS. This initial review yielded an evidence base of 86 treatment articles after application of inclusion/exclusion criteria. The AUA update literature review process, in which an additional systematic review is conducted periodically to maintain guideline currency with newly published relevant literature, was conducted in July 2013. This review identified an additional 31 articles, which were added to the evidence base of this Guideline.

Results: Newly incorporated literature describing the treatment of IC/BPS was integrated into the Guideline with additional treatment information provided as Clinical Principles and Expert Opinions when insufficient evidence existed. The diagnostic portion of the Guideline remains unchanged from the original publication and is still based on Expert Opinions and Clinical Principles.

Conclusions: The management of IC/BPS continues to evolve as can be seen by an expanding literature on the topic. This document constitutes a clinical strategy and is not intended to be interpreted rigidly. The most effective approach for a particular patient is best determined by the individual clinician and patient. As the science relevant to IC/BPS evolves and improves, the strategies presented will require amendment to remain consistent with the highest standards of care.

Key Words: cystitis, interstitial; pelvic pain; urodynamics; lower urinary tract symptoms; urinary bladder diseases

Abbreviations and Acronyms

AE = adverse event
BPS = bladder pain syndrome
BTX-A = botulinum toxin A
CP = chronic prostatitis
CPPS = chronic pelvic pain syndrome
GTM = global therapeutic massage
IC = interstitial cystitis
MPT = myofascial physical therapy
QoL = quality of life
UTI = urinary tract infection

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For another article on a related topic see page 1676.

INTRODUCTION

This guideline's purpose is to provide direction to clinicians and patients regarding how to recognize interstitial cystitis/bladder pain syndrome, conduct a valid diagnostic process, and, approach treatment with the goals of maximizing symptom control and patient quality of life while minimizing adverse events and patient burden. The strategies and approaches recommended in this document were derived from evidence-based and consensus-based processes. IC/BPS nomenclature is a controversial issue; for the purpose of clarity the Panel decided to refer to the syndrome as IC/BPS and to

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consider these terms synonymous. This document provides an overview of the amendments made to the 2011 Guideline and should, therefore, be viewed in conjunction with the full Guideline available at http://www.auanet.org/education/guidelines/ic-bladder-pain-syndrome.cfm. The updated algorithm reflects these changes as well (see figure).

METHODOLOGY

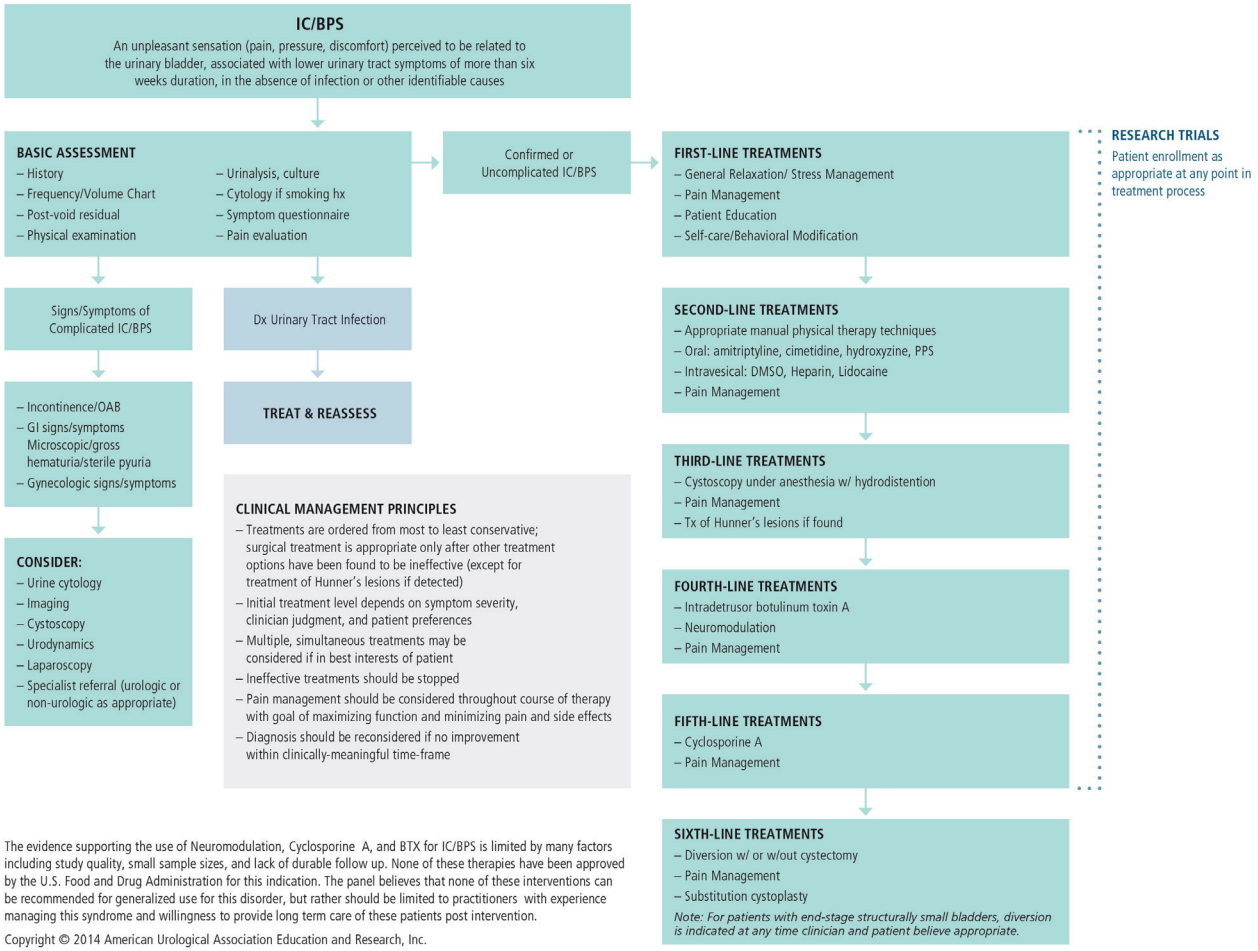
An initial systematic review was conducted to identify published articles relevant to the diagnosis and treatment of IC/BPS. Literature searches were performed on English language publications using the MEDLINE database from January 1, 1983 to July 22, 2009 using the terms "interstitial cystitis," "painful bladder syndrome," "bladder pain syndrome," and "pelvic pain" as well as key words capturing the various diagnostic procedures and treatments known to be used for these syndromes. With regard to treatment, a total of 86 articles from the original literature searches met the inclusion criteria, and an additional 31 relevant studies were retrieved as part of the update literature review process. The Panel judged that these were a sufficient evidence base from which to construct the majority of the treatment portion of the algorithm.

The initial and update reviews revealed insufficient publications to address IC/BPS diagnosis and overall management from an evidence basis and, therefore, the diagnosis and management portions of the algorithm (see figure) are provided as Clinical Principles or as Expert Opinion with consensus achieved using a modified Delphi technique if differences of opinion emerged.[1] For a complete discussion of the methodology and evidence grading, please refer to the unabridged version of this Guideline.

BACKGROUND

Definition

The bladder disease complex includes a large group of patients with bladder and/or urethral and/or pelvic pain, lower urinary tract symptoms and sterile urine cultures, many with specific identifiable causes. IC/BPS comprises a part of this complex. The Panel used the IC/BPS definition agreed upon by the Society of Urodynamics, Female Pelvic



Interstitial cystitis/bladder pain syndrome algorithm

Medicine & Urogenital Reconstruction: "An unpleasant sensation (pain, pressure, discomfort) perceived to be related to the urinary bladder, associated with lower urinary tract symptoms of more than six weeks duration, in the absence of infection or other identifiable causes."[2] This definition was selected because it allows treatment to begin after a relatively short symptomatic period, preventing treatment withholding that could occur with definitions that require longer symptom durations (i.e. six months). Definitions used in research or clinical trials should be avoided in clinical practice, as many patients may be misdiagnosed or diagnosis and treatment may be delayed if these criteria are used.[3]

IC/BPS Symptoms

Since the original publication of this Guideline, three papers reported data from the RICE (RAND Interstitial Cystitis Epidemiology) study.[4–6] One of the RICE study objectives was to develop an IC/BPS case definition for use in epidemiological studies that had known sensitivity and specificity. Berry et al reported findings from a literature review, a structured expert panel process and a telephone interview validation study to derive an IC/BPS definition.[4] They note that none of the existing epidemiological definitions had high sensitivity or high specificity. As a result of this process, two definitions emerged, one with high sensitivity that correctly identified IC/BPS cases 81% of the time (with 54% specificity) and one with high specificity that correctly excluded nonIC/BPS cases 83% of the time (with 48% sensitivity). The definitions are captured in an 11-item questionnaire. See the Appendix for definitions, which the Panel notes that these are epidemiological case definitions and are not appropriate for use as diagnostic criteria.

Berry et al used the questionnaire to determine prevalence of IC/BPS among adult females in the U.S.[5] This study yielded prevalence estimates from 2.7% to 6.53% (approximately 3.3 to 7.9 million U.S. women age 18 or older). Only 9.7% of women who met the definitions reported having been given an IC/BPS diagnosis. Suskind et al modified the case definition for use in men and used an additional case definition derived from the NIH-Chronic Prostatitis Symptom Index to assess the prevalence and overlap between IC/BPS and chronic prostatitis/chronic pelvic pain syndrome in men.[6] This study yielded a prevalence estimate of 2.9% to 4.2% for IC/BPS and a prevalence of 1.8% for CP/CPPS. The overlap between the two syndromes was approximately 17%. The authors note that these findings suggest that the prevalence of IC/BPS in men approaches its prevalence in women and, therefore, it may be greatly under diagnosed in the male population."

Typical Course and Comorbidities

IC/BPS is most commonly diagnosed in the fourth decade or after, although the diagnosis may be delayed depending upon the index of suspicion for the disease and the criteria used to diagnose it.[7] A history of a recent culture proven UTI can be identified on presentation in 18% to 36% of women, although subsequent cultures are negative.[8,9] Initially it is not uncommon for patients to report a single symptom such as dysuria, frequency or pain, with subsequent progression to multiple symptoms.[10,11] Symptom flares, during which symptoms suddenly intensify for several hours, days or weeks, are not uncommon. There is a high rate of prior pelvic surgery (especially hysterectomy) and levator ani pain in women with IC/BPS, suggesting that trauma or other local factors may contribute to symptoms.[12]

It is important to note, however, that the high incidence of other procedures, such as hysterectomy or laparoscopy, may be the result of a missed diagnosis and does not necessarily indicate that the surgical procedure itself is a contributing factor to symptoms. It is also common for IC/BPS to coexist with other unexplained medical conditions, such as fibromyalgia, irritable bowel syndrome, chronic fatigue syndrome, Sjogren's syndrome, chronic headaches and vulvodynia.[13,14] These associations suggest that there may be a systemic dysregulation in some patients. Finally, patients with IC/BPS frequently exhibit mental health disorders, such as depression and anxiety. While these symptoms may be reactive in some IC/BPS patients, there is also some evidence that there may be a common biological mechanism involved.

Conceptualizing IC/BPS

It is not known whether IC/BPS is a primary bladder disorder or whether the bladder symptoms of IC/BPS are secondary phenomena resulting from another cause. Converging data from several sources suggest, however, that IC/BPS can be conceptualized as a bladder pain disorder that is often associated with voiding symptomatology and other systemic chronic pain disorders. Specifically, IC/BPS may be a bladder disorder that is part of a more generalized systemic disorder, at least in a subset of patients. It has been suggested that IC/BPS is a member of a family of hypersensitivity disorders that affects the bladder and other somatic/visceral organs and has many overlapping symptoms and pathophysiology.[15,16] An additional hypothesis is that IC/BPS might be just a part of the continuum of painful vs nonpainful overactive bladder syndrome.[17,18]

Impact on Psychosocial Functioning and Quality of Life

The effects of IC/BPS on psychosocial functioning and QoL are pervasive and insidious, damaging work life, psychological well-being, personal relationships and general health.[19] QoL is poorer in IC/BPS patients than in controls.[19,20] Rates of depression are also higher.[20,21] In addition, IC/BPS patients have significantly more pain, sleep dysfunction, catastrophizing, depression, anxiety, stress, social functioning difficulties and sexual dysfunction than do nonIC/BPS age-matched women.[22] Health-related QoL in women with IC/BPS is worse than that of women with endometriosis, vulvodynia or overactive bladder.[23] Given that IC/BPS causes considerable morbidity over the course of a patient's life and loss of work during the most productive years of work and family life, significant negative psychological and QoL impacts are not surprising.[19]

Sexual dysfunction has an especially important impact on the QoL of IC/BPS patients. In IC/BPS patients sexual dysfunction is moderate to severe,[24] and occurs at high rates compared to controls.[25,26] In women with treatment refractory IC/BPS poor sexual function is a primary predictor of poor mental QoL.[27] Pain appears to mediate sexual dysfunction and its associated effects on QoL. Women with IC/BPS report rates of intercourse, desire and orgasm frequency in their adolescence that are similar to those reported by controls, but rates diverge in adulthood when IC/BPS patients report significantly more pain, fear of pain with intercourse and more sexual distress.[25] The strong link between IC/BPS symptoms and psychosocial functioning and QoL makes clear the critical importance of optimizing treatment of IC/BPS symptoms. Successful treatment of the medical condition clearly brings improvement in functioning and QoL. In addition, response to therapy is associated with improved sexual function and sleep, with concomitant improvements in QoL.[22,24]

Symptoms

Pain (including sensations of pressure and discomfort) is the hallmark symptom of IC/BPS. Typical IC/BPS patients report not only suprapubic pain (or pressure, discomfort) related to bladder filling, but pain throughout the pelvis, including in the urethra, vulva, vagina and rectum, and in extra genital locations such as the lower abdomen and back.[9,26,28] Warren et al found that by using "pelvic pain" as the key descriptor 100% of his population fit the case definition.[29] It is important that the term "pain" encompass a broad array of descriptors. Many patients use other words to describe symptoms, especially "pressure" and may actually deny pain.[28] Finally, pain that worsened with specific foods or drinks and/or worsened with bladder filling and/or improved with urination contributed to a sensitive case definition of IC/BPS.[9]

The prototypical IC/BPS patient also may present with marked urinary urgency and frequency but because these symptoms may indicate other disorders, they do not exclusively indicate the presence of IC/BPS. Voiding frequency is almost universal (92% of one population)[26] but does not distinguish the IC/ BPS patient from other lower urinary tract disorders. Change in urinary frequency is valuable to evaluate response to therapy but is of little help in diagnosis. Urinary urgency is also extremely common (84% of the same population)[26] but urgency is considered to be the characteristic symptom of overactive bladder and, thus, it can actually confound the diagnosis. There may, however, be qualitative differences in the urgency experienced by IC/BPS patients compared to overactive bladder patients. IC/BPS patients may experience a more constant urge to void as opposed to the classic ICS definition of a "compelling need to urinate which is difficult to postpone."[30,31] Typically IC/BPS patients void to avoid or to relieve pain, whereas overactive bladder patients void to avoid incontinence. Symptoms of urinary urgency and frequency may precede symptoms of pain.[11] Median time to the development of a full symptom complex of frequency, urgency and pain was reported to be two years in one study.[11]

Presentation of Male IC Patients

Historically, IC/BPS in men has been considered relatively unusual with a female-to-male ratio of 10:1.[32,33] However, uncontrolled clinical series over the past two decades have suggested that the incidence of male IC/BPS may be higher than previously observed.[34] Early clinical symptoms may begin with mild dysuria or urinary urgency. Mild symptoms may progress to severe voiding frequency, nocturia and suprapubic pain. The presence or absence of glomerulations on endoscopy is too nonspecific to make the diagnosis of the disease in anyone who does not fit the symptom complex as defined.

Clinical findings mirror those of the female IC/BPS patient. On examination, suprapubic tenderness is common along with external (perineal) tenderness and internal (levator muscle) tenderness/spasticity. Cystoscopy with hydraulic distention of the bladder in men with IC/BPS commonly demonstrates diffuse glomerulations.[34] Some data suggest that Hunner lesions are more common in male IC/BPS patients.[35]

Male IC/BPS vs Chronic Prostatitis

CP/CPPS, or NIH (National Institutes of Health) type III prostatitis,[36] is characterized by pain in

the perineum, suprapubic region, testicles or tip of the penis.[37] The pain is often exacerbated by urination or ejaculation. Voiding symptoms such as sense of incomplete bladder emptying and urinary frequency are also commonly reported, but pain is the primary defining characteristic of CP/CPPS. It is clear that the clinical characteristics that define CP/CPPS are very similar to those previously described for IC/BPS. In general, the Panel believes that the diagnosis of IC/BPS should be strongly considered in men whose pain is perceived to be related to the bladder. However, it is also quite clear that certain men have symptoms that meet criteria for both conditions (IC/BPS and CP/CPPS). In such cases the treatment approach can include established IC/BPS therapies as well as other therapies that are more specific to CP/ CPPS.

GUIDELINE AMENDMENTS

Diagnosis

The diagnosis of IC/BPS can be challenging. Patients present with a wide spectrum of symptoms, physical exam findings and clinical test responses. This complexity causes significant misdiagnosis, under diagnosis and delayed diagnosis. Insufficient literature was identified to constitute an evidence base for diagnosis of IC/BPS in clinical practice. The lack of evidence is not surprising given the many definitions of the disorder used and the focus of most trials on NIDDK (National Institute of Diabetes and Digestive and Kidney Diseases) diagnostic criteria (note that the NIDDK diagnostic criteria are not appropriate for use outside of clinical trials).[38,39] For this reason, this section is based on Clinical Principles or Expert Opinions with consensus achieved using a modified Delphi technique when differences of opinion emerged. This section is intended to provide clinicians and patients with a framework for determining whether a diagnosis of IC/BPS is appropriate. It is not intended to replace the judgment and experience of the individual clinician faced with a particular patient. The update literature review did not reveal any additional publications to change any of the statements related to diagnosis.

Treatment

The Panel assessed the available data for each treatment to determine whether a specific intervention demonstrated sufficient efficacy to be included as a treatment alternative. The types of studies available (randomized trials, observational studies); quality of individual studies; consistency of outcome across studies; and generalizability of samples, settings and interventions were examined and overall evidence strength was determined. Treatment alternatives were then categorized as clinical principles, expert opinion or evidence-based statements and divided into first-, second-, third-, fourth-, fifth- and sixth- line groups. This hierarchy was derived by balancing the potential benefits to the patient with the invasiveness of the treatment, the duration and severity of potential AEs, and the reversibility of potential AEs. Note that the hierarchy was not established based on evidence strength.

Each set of treatments is presented below. One source of uncertainty was the Panel's observation that most treatments may benefit a subset of patients that is not readily identifiable before treatment and that no treatment reliably benefits most or all patients. Therefore, on average and for a particular patient, uncertainty exists for most treatments regarding the balance between benefits and risks/burdens.

First-line treatments. The Panel believes that all patients should be offered these treatments. The first-line treatment approaches presented in the full-length Guideline are based on Clinical Principles; insufficient literature was available to guide an evidence-based version. As such, these statements remain unchanged from the original guideline.

Second-line treatments. **Guideline Statement 13:** "Appropriate manual physical therapy techniques (e.g. maneuvers that resolve pelvic, abdominal and/or hip muscular trigger points, lengthen muscle contractures, and release painful scars and other connective tissue restrictions), if appropriately trained clinicians are available, should be offered to patients who present with pelvic floor tenderness. Pelvic floor strengthening exercises (e.g. Kegel exercises) should be avoided." ***(Standard; Evidence Strength: Grade A)***

Many patients with IC/BPS exhibit tenderness and/or banding of the pelvic floor musculature, along with other soft tissue abnormalities.[12,40] It is not known whether those muscular abnormalities are usually primary pain generators (giving rise to associated secondary bladder pain) or are themselves secondary phenomena elicited by the primary bladder pain of IC/BPS. Whatever their etiology, when such soft tissue abnormalities are present, clinical experience and a limited but high quality literature suggest that manual physical therapy can provide symptom relief. Specifically, Fitzgerald et al reported findings from a randomized controlled trial that tested ten 60-minute sessions over 12 weeks of myofascial physical therapy compared to global therapeutic massage in IC/BPS patients.[41] At 3 months 59% of the MPT group reported moderate or marked improvement compared to 26% in the GTM group, a statistically significant difference.

Improvements in pain, urgency, frequency and scores on the IC symptom index, IC problem index and female sexual function index also were greater in the MPT group than in the GTM group, although the differences were not statistically significant. Very importantly, there is no evidence that physical therapy aimed at pelvic floor strengthening (such as Kegel exercises) can improve symptoms and, in fact, this type of pelvic floor therapy may worsen the condition.

No well-designed studies have evaluated the possible therapeutic role of other forms of massage or other forms of bodywork, although interventions aimed at general relaxation have proven helpful in most other forms of chronic pain and can be recommended to IC/BPS patients.

Third-line treatments. While additional information was found through the update literature search related to third-line treatments, these statements remain unchanged from the original guideline.

Fourth-line treatments. **Guideline Statement 19:** "Intradetrusor botulinum toxin A (BTX-A) may be administered if other treatments have not provided adequate symptom control and quality of life or if the clinician and patient agree that symptoms require this approach. The patient must be willing to accept the possibility that intermittent self-catheterization may be necessary post-treatment." ***(Option; Evidence Strength: Grade C)***

The update literature review retrieved ten new studies, including one randomized controlled trial and nine prospective observational studies reporting on a total of 378 patients. It should be noted that several studies appear to include overlapping patient groups. As a group, these studies represent a major shift in how BTX-A is administered to treat IC/BPS in several ways, including the combination of BTX-A with hydrodistension, the use of primarily the 100 U dose, the use of repeat treatments with symptom return and following patients for years rather than months. Following evaluation of the new literature, the use of BTX-A was designated as a fourth-line treatment (as opposed to fifth-line in the original guideline).

Combining BTX-A with hydrodistension. The randomized control trial compared group 1) BTX-A 200 U in the posterior and lateral bladder walls with hydrodistension two weeks later, group 2) BTX-A 100 U in the same sites with hydrodistension and group 3) hydrodistension with a second hydrodistension two weeks later.[42] Patients were followed for two years. Patients designated as successes based on a GRA were 80% at 3 months to 47% at 24 months in group 1, 72% at 3 months to 21% at 24 months in group 2 and 48% at 3 months to 17% at 24 months in group 3. Only the BTX-A groups demonstrated significant improvements in pain VAS scores and maximum bladder capacity. Importantly, the 200 U dose did not exert a greater effect than the 100 U dose. Rates of AEs were much higher and more serious in the 200 U group with almost half of the group experiencing dysuria and a third of the group exhibiting a large post-void residual. These AEs were of sufficient concern that the remaining patients who had been randomized to receive 200 U instead were treated with 100 U, accounting for the imbalance in group size.

Re-treatment with BTX-A. Giannantoni et al treated patients with 200 U in the lateral bladder walls and trigone with re-treatment when benefits began to decline (mean re-treatment interval 5.25 months).[43] Patients were followed for two years. Most measured outcomes exhibited significant improvement that was maintained over time with repeat injections.

Pinto et al injected 100 U into the trigonal wall with re-treatment upon symptom return and followed patients for up to three years.[44,45] Duration of improvements in pain VAS, frequency, voided volume and QoL were 9 to 10 months after each treatment. Nearly a third of patients had UTIs after treatment 2 (but not after the other treatments). No urinary retention was reported and no clean intermittent self-catheterization was required.[44]

Shie et al injected 100 U in the posterior and lateral bladder walls with re-treatment every six months regardless of symptom status for a total of four treatments.[46] After treatment one but not treatments two through four, hydrodistension was performed. Patients were followed for two years with improvements in pain VAS, O'Leary-Sant scores and frequency restored with each treatment. These authors did not address AEs.

Re-treatment with BTX-A and hydrodistension. Kuo,[47,48] and Lee and Kuo[49] injected 100 U into the posterior and lateral bladder walls followed by hydrodistension. The BTX-A plus hydrodistension treatment was repeated every six months unless improvements were maintained. Patients were followed for two years. Generally, after each treatment improvements were noted in pain VAS scores, IC symptom index and IC problem index scores, frequency, nocturia and bladder capacity. GRA based success rates were high, ranging from 50% to 77% at various time points. Importantly, two of the three reports note that patients with Hunner lesions did not improve with this regimen and were treated successfully with electrocautery or electrofulguration. AEs consisted of UTIs in approximately 10% of patients (after one of up to four treatments), dysuria in approximately 42% with rates diminishing as number of

treatments increased, acute urinary retention in 1 (after treatment 2), hematuria in 1 and necessity for clean intermittent self-catheterization in 1 (after treatment 3).

Based on the substantial new evidence retrieved in this update literature review, with consistent reports of substantially reduced morbidity with use of the 100 U dose, the Panel judged that use of BTX-A at the 100 U dose is appropriate as a fourth-line treatment. The Panel notes that BTX-A should be administered by experienced practitioners and that patients must be willing to accept the possibility that intermittent self-catheterization may be necessary after treatment. This option is not appropriate for patients who cannot tolerate catheterization, and is relatively contraindicated for patients with any evidence of impaired bladder emptying.

Fifth-line treatments. While additional information was found through the update literature search related to fifth-line treatments, these statements remain unchanged from the original guideline.

Sixth-line treatments. While additional information was found through the update literature search related to sixth-line treatments, these statements remain unchanged from the original guideline with the exception of a statement related to the use of resiniferatoxin, which is not approved for use in the United States.

FUTURE RESEARCH

Patients with IC/BPS constitute a previously under recognized and underserved population in need of adequate medical management. Over the last 20 years there have been significant efforts directed at understanding the etiology and the therapeutic challenges of this disease. These efforts were spearheaded by U.S. patient support groups that have urged the National Institutes of Health to fund research studies to better understand IC/BPS pathophysiology and to fund clinical studies to identify valid treatment approaches.

Treating IC/BPS patients presents a significant challenge in clinical practice. Treatment approaches may be local (directed to the bladder) or systemic, range from behavioral to pharmacological, and may include many types of adjunctive therapy approaches intended to optimize quality of life. Although there are evidenced-based data supporting certain treatment approaches for patients in clinical studies, the unsolved question in clinical practice remains: Who is the ideal patient for a given treatment approach? Thus, until phenotyping improves and specific phenotype driven therapies can be recommended, treatment of IC/BPS often requires a trial and error algorithm based approach.

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Disclaimer

The original version of this Interstitial Cystitis/Bladder Pain Syndrome Guideline was created in 2011 by a multi-disciplinary Panel assembled by the Practice Guidelines Committee (PGC) of the American Urological Association Education and Research, Inc. (AUA). This amended Interstitial Cystitis/Bladder Pain Syndrome Guideline was drafted in 2014 by a Guideline Amendment Panel. This amendment updates the original guideline document to reflect literature released following the original publication.

The mission of the original and amendment Panels was to develop clinical guideline recommendations based on an in-depth evidence report of the peer-reviewed literature. The recommendations are based on evidence strength, or where evidence is not available, on Delphi-modification consensus statements. The purpose of each guideline is to provide physicians and non-physician providers (primary care and specialists) with a consensus of principles and treatment plans for the management of Interstitial Cystitis/Bladder Pain Syndrome Guideline. While these guidelines do not necessarily establish the standard of care, AUA seeks to recommend and to encourage compliance by practitioners with current best practices related to the condition being treated.

Funding of the original and amendment Panels was provided by the AUA. Panel members receive no remuneration for their work. Panel members' potential conflicts of interest are subject to rigorous and on-going review during the development of the original Guideline and amendment Panel members are screened for conflicts throughout the amendment process.

As medical knowledge expands and technology advances, AUA guidelines are subject to change. Evidence-based guidelines statements are not absolute mandates but thoroughly considered strategies for best practice under the specific conditions

described in each document. For all these reasons, the guidelines do not pre-empt physician judgment in individual cases. Treating physicians must take into account variations in resources, and patient tolerances, needs, and preferences. Similarly, conformance with any clinical guideline cannot assure a successful outcome. These guidelines and best practice statements are not intended to provide legal advice.

The guideline text may include information or recommendations about certain drug or device use ('off label') that are not approved by the Food and Drug Administration (FDA), or about medications or substances not subject to the FDA approval process. AUA urges strict compliance with all government regulations and protocols for prescription and use of these substances. The physician is encouraged to understand and carefully follow all available prescribing information about indications, contraindications, precautions and warnings.

Although guidelines are intended to encourage best practices and to reflect available technologies with sufficient data as of the date of close of the literature review, guidelines are necessarily time-limited. Guidelines cannot include evaluation of all data on emerging technologies, pharmaceuticals or management practices, including both those that are FDA-approved, or those which may immediately come to represent accepted clinical practices. For this reason, the AUA does not regard emerging technologies or management techniques not addressed by this guideline as manifestly experimental or investigational. These emerging technologies or techniques may simply be too new to be included or fully incorporated in the Panel's evidence-based evaluation at the time the guideline is developed.

APPENDIX

RICE BPS/IC Case Definitions[5]

High Sensitivity Definition	High Specificity Definition
Sensitivity 81%, specificity 54% for BPS/IC vs endometriosis, vulvodynia and overactive bladder Pain, pressure or discomfort in the pelvic area and daytime urinary frequency 10+ or urgency due to pain, pressure or discomfort, no fear of wetting	Sensitivity 48%, specificity 83% for BPS/IC vs endometriosis, vulvodynia and overactive bladder Pain, pressure or discomfort in the pelvic area and daytime urinary frequency 10+ or urgency due to pain, pressure or discomfort, no fear of wetting; and symptoms did not resolve after treatment with antibiotics; and no treatment with hormone injection therapy for endometriosis

Exclusion criteria: bladder cancer, urethral diverticulum, spinal cord injury, stroke, Parkinson disease, multiple sclerosis, spina bifida, cyclophosphamide treatment, radiation treatment to pelvic area, tuberculosis affecting the bladder, uterine cancer, ovarian cancer, vaginal cancer, genital herpes, pregnancy

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