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Interstitial cystitis: painful bladder syndrome

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Abstract

Interstitial cystitis, or painful bladder syndrome, is a chronic inflammatory disease of a bladder of unknown etiology. It negatively affects the quality of life, causes depressive disorders, anxiety, and sexual dysfunction. Despite numerous studies, the etiology of interstitial cystitis is still unclear and it's considered as painful bladder syndrome with multifactorial origin. According to the US National Health and Nutrition Examination Survey, 470/100 000 people (60/100 000 men, 850/100 000 women) are diagnosed with interstitial cystitis. Diagnosis of the disease is difficult and is substantially based on clinical symptoms. Pelvic pain, urinary urgency, frequency and nocturia are the basic complaints in this pathology. The diagnosis requires exclusion of diseases with similar manifestations. So interstitial cystitis is frequently misdiagnosed as urinary tract infection, overactive bladder, urethral obstruction or diverticulosis, chronic prostatitis, bladder cancer, vulvodynia, endometriosis, and chronic pelvic pain. Etiopathogenesis of the disease is uncertain, which makes etiologic treatment impossible. Currently scientific discussions on the causes of disease continue as well as different treatment regimens are offered, but are often ineffective, palliative and temporary. The treatment for intersticial cystitis should focus on restoring normal bladder function, prevention of relapse of symptoms and improvement of patients' quality of life. The literature review presents current view on the terminology, epidemiology, diagnosis and treatment of interstitial cystitis.

Keywords: interstitial cystitis, bladder, pelvic pain.

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Interstitial cystitis (IC), or painful bladder syndrome (PBS), is a chronic inflammatory disease of the bladder, the etiology of which is currently unknown. This pathology is characterized by frequent urination and bladder pain, which substantially affects patients' quality of life [1]. At present, no effective radical approaches are confirmed in scientific studies for diagnosing and treating IC. Despite numerous studies in this area, the etiology of the disease is still unclear, the diagnosis is difficult, and the treatment is temporary and palliative, which makes the problem chronic.

According to the literature, IC is more common in women, with symptoms typically occurring in middle age [2–4]. It is known that, in many cases, the period from symptom onset to confirmation of diagnosis can take years [3]. A number of studies have reported reduced quality of life in IC patients, as these patients experience chronic stress, anxiety, depression, and sexual dysfunction, among other symptoms [5–8]. Comparative data are presented in the literature, which indicate that quality of life in IC patients is below that of patients with chronic renal failure [1, 9].

Terminology. As early as in 1808, Philip Syng Physick, an American physician, described bladder inflammation as an "ulcer" of the bladder and suggested that the determining symptom of this disease was inflammation of the lower urinary tract. In 1836, he expanded his concept and noted that the disease included symptoms such as frequent urinary urgency and bladder pain of unknown etiology, and he called this syndrome "painful tic of the bladder" [10]. Later, surgeons, urologists, and urogynecologists adopted the study of this pathology. In 1914, Hunner described 8 cases of ulcer in the bladder depicting the characteristic symptoms of IC [11].

In 1987, the U.S. National Institute for Diabetes and Digestive and Kidney Diseases determined the criteria for IC [12]. According to their definition, bladder pain and the presence of a typical cystoscopic pattern were the main criteria for diagnosing IC. However, considering the strict categoricity of these disease criteria, the diagnosis was not established in time for many patients with similar complaints or they were "overlooked."

Accordingly, in 2002, the International Continence Society proposed the concept of "painful bladder syndrome" and offered new definition of the disease. According to this definition, a diagnosis of IC can be established

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if the patient has suprapubic pain that increases during bladder filling and urinary urgency with a daily increase in frequency and nocturia in the absence of any identifiable pathology or confirmed urinary tract infection (UTI) [13].

Due to the complexity of diagnosing this disease in a timely fashion, in 2008, the European Society for the Study of IC/BPS (ESSIC) revised the diagnostic criteria for the disease [14, 15] and introduced a new name to describe it: "painful bladder syndrome" (PBS). ESSIC's definition enabled the inclusion of all patients with chronic pelvic pain and a feeling of pressure or discomfort associated with a full bladder. According to this definition, the presence of at least one of the following symptoms including urinary urgency and urinary frequency along with chronic pelvic pain or a feeling of pressure or discomfort associated with a full bladder is a diagnostic criterion for PBS [14, 15].

Epidemiology. Depending on the methodology of the conducted studies and the diagnostic criteria used, the prevalence indices of IC and PBS are vastly different. Previous studies have reported that prevalence rates of IC were 10/100,000 of population in Finland (1975), 30/100,000 (1987), and 510/100,000 (1989) in the USA [2]. Jones and Nyberg (1997) showed that various criteria were used to identify IC in these studies; however, the U.S. National Institutes of Health (NIH) criteria were not applied [2]. In a study conducted among women in the USA, Curhan et al. (1999) revealed that the prevalence of the disease was 60/100,000 [16].

Data from a women's survey were analyzed in accordance with the NIH diagnostic criteria recommended for this kind of research, and these indicators were several times higher than those in a similar study conducted in Europe by Bade et al. (1995) (8–16/100,000) [17], which was due to various diagnostic criteria of the disease.

Subsequent studies conducted in the U.S. showed that 2.7%–6.5% of women had symptoms corresponding to the diagnostic criteria of IC/PBS [18]. Such a widespread prevalence in rates is associated with the method of the study. Researchers studied prevalence rates based on the definition of symptoms with high sensitivity (6.5%) and high specificity (2.7%) [18]. Symptoms with high sensitivity enable a diagnosis of IC/PBS in 81% of cases and those with high specificity allow the identification of cases that are not IC/PBS in 83%. These studies demonstrated that only 9.7% of women with symptoms corresponding to the diagnostic criteria of IC/PBS were diagnosed with this condition [18].

Studies conducted among men found that this disease was also diagnosed less often than it actually occurred [3, 17, 19]. A study performed in the U.S. reported that the disease prevalence among men accounted for 4.2% of highly sensitive symptoms and 1.9% of highly specific symptoms [20]. Another study, based on the number of IC/PBS patients registered in the U.S. healthcare system, calculated that the number of men with this diagnosis doubled over a 10-year period from 1992 to 2001 [21].

According to the U.S. National Health Interview Survey, the symptoms of IC/PBS occur in 500 men per 100,000 population and 865/100,000 of women. According to the same data, IC/PBS was diagnosed in 470/100,000 people (60/100,000 men and 850/100,000 women) [22]. The authors attribute the increase in disease prevalence to the increase in timely and accurate diagnosis of cases [22].

Diagnosis. Despite the fact that numerous studies have been performed on IC/PBS, diagnosing this disease remains challenging. Overall, 3–5 years typically elapse from the time the first signs of the disease appear until a diagnosis is established, which is mainly due to the association of a complex diagnosis [3, 8, 23, 24]. In turn, the complexity of the diagnosis is due to the absence of pathognomonic symptoms in the clinical presentation of the disease.

The present diagnostic criteria for IC/PBS have undergone significant changes. Typical cystoscopic and/or histological signs were required for setting the diagnosis using past criteria; however, with the new criteria, even in the absence of these symptoms, the presence of suprapubic pain, frequent urinary urgency during the day or at night, and the absence of UTI or other pathology explaining the algia manifestations began to be accepted as diagnostic criteria of the disease [25–28]. Over time, the diagnostic criteria included pain in the small pelvis, bladder pressure or discomfort, and frequent urinary urgency [25–28]. Today, this diagnosis is made on the basis of ruling out diseases with similar symptoms and clinical presentation [25–28].

According to the guidelines of the American Urological Association (AUA) (2011–2014), in the case of unpleasant sensations in the bladder (pain, pressure, discomfort) and lower urinary tract symptoms lasting for ≥6 weeks and in the absence of infection or other apparent causes of the disease, a diagnosis of IC/PBS should be made and appropriate treatment started [29, 30].

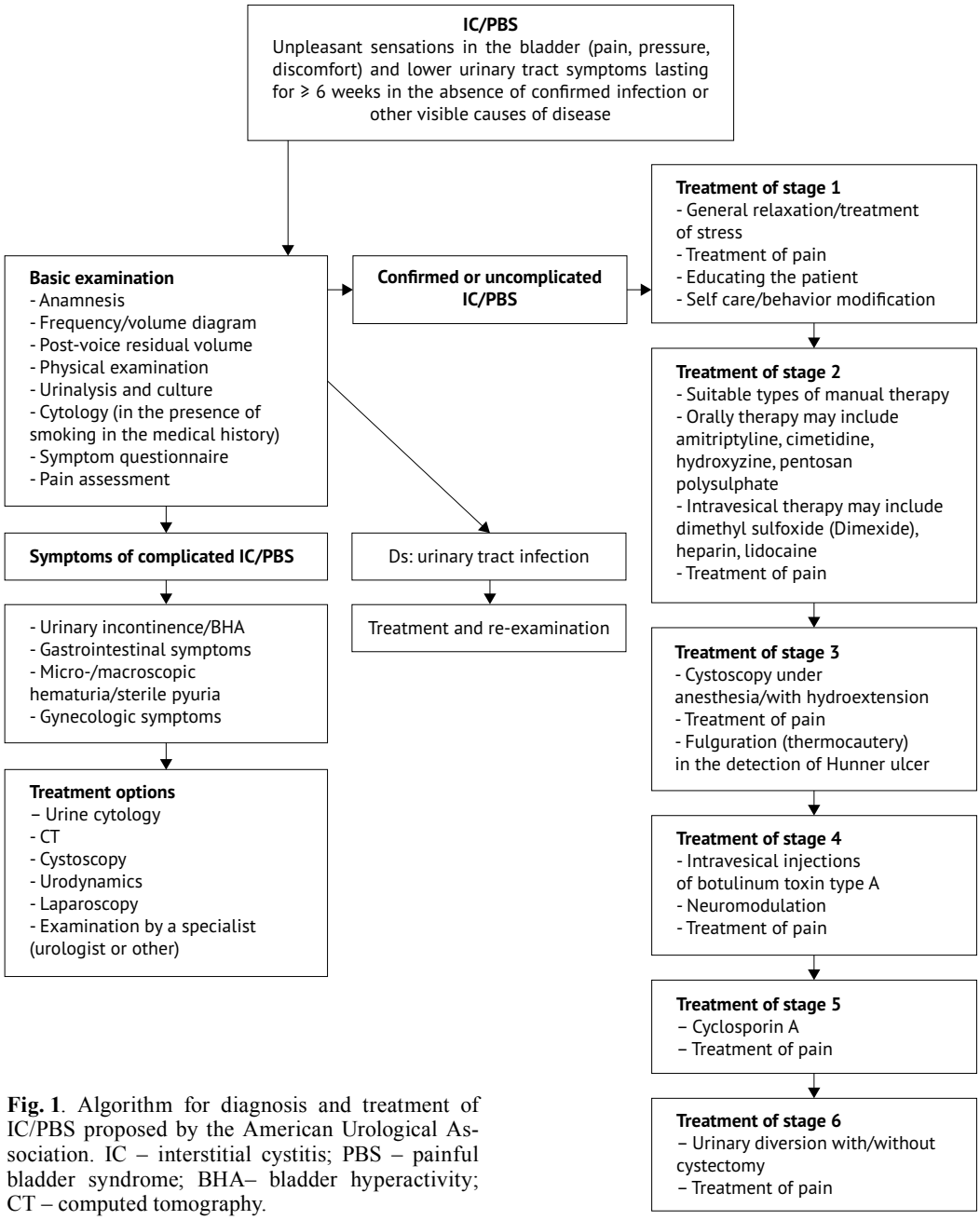

Fig. 1. Algorithm for diagnosis and treatment of IC/PBS proposed by the American Urological Association. IC – interstitial cystitis; PBS – painful bladder syndrome; BHA– bladder hyperactivity; CT – computed tomography.

Diagnostic studies and treatment of IC/PBS are currently performed according to the clinical diagnostic algorithm proposed by the AUA [29, 30] (Figure 1).

According to the literature, the main symptoms of this pathology include pain in the small pelvis, urinary urgency, frequent urination, and nocturia [31]. According to Driscoll et al., 89% of patients at the initial stage of the disease have only one of these symptoms, and pain in the small pelvis appears a few years later in 44% [23]. Ito et al. evaluated 238 IC/PBS patients and noted that frequent urination was the most common symptom (90.7%), followed by urinary urgency (61.6%) and bladder pain (46%) [3].

Another study of 736 patients found that frequent urination (92%) was the most common complaint, followed by nocturia (87%),

urinary urgency (84%), and bladder pain (63%) [8]. A number of studies have also indicated the importance of determining the nature of the pain: increased pain with increased volume of urine in the bladder, decreased pain after urination, frequent urination to relieve pain, increased pain after intercourse, and pain associated with seasonal allergy [28, 32]. According to the AUA, pain (including pressure or discomfort) is the main symptom of IC/PBS [33].

The literature states that to diagnose and evaluate treatment results, the frequency and volume of urination must be evaluated during the day [3, 25, 28]. According to these data, urinating ≥8–10 times during the day and having a urine volume <120 ml are criteria corresponding to the presence of IC/PBS [3, 25, 28].

Currently, various surveys and questionnaires are used to screen and evaluate the efficiency of IC/PBS treatment [34]. The most common are screening questionnaires for the Pelvic Pain and Urinary Urgency/Frequency symptom scale and the O'Leary-Sant Interstitial Cystitis Symptom and Problem Index (OLS) [28, 35]. Both questionnaires include questions related to the symptoms of pain, frequent urinary urgency, and nocturia in addition to the effect of these symptoms on quality of life.

The literature shows the importance and need for a thorough physical, clinical, and laboratory examination of IC/PBS patients to rule out diseases with similar symptoms including UTI, overactive bladder, urethral obstruction or diverticulum, chronic prostatitis, bladder cancer, vulvodynia, endometriosis, and chronic pelvic pain [28, 31, 36]. Moreover, performing laboratory tests, computed tomography, and measuring the post-void residual volume of urine play an important role in the differential diagnosis of the disease [26, 37, 38].

According to some authors, cystoscopy is the most important diagnostic approach for IC [25]. Other authors believe that this method is not so informative and is indicated only in patients with hematuria or significant microhematuria, especially those with a history of smoking [38, 39]. These authors do not believe that, from a diagnostic standpoint, cystoscopy has an advantage in relation to anamnesis, physical examination, or urinalysis but it is necessary for ruling out bladder cancer in IC/PBS patients [38]. Cystoscopy with hydrodistention can reveal glomerulations and/or Hunner ulcers, which are absolute criteria for a diagnosis of IC/PBS. If pathology is not detected, this is not a basis for ruling out the diagnosis [40].

Another diagnostic method of IC/PBS is urodynamics, which studies the functions of filling and emptying the bladder, bladder volume, and sensations due to the variation in urethral pressure. In IC/PBS patients, a decrease in all urodynamic parameters and bladder volume is noted [41, 42]. Bladder volume <350 ml and the feeling of urinary urgency when it is filled to 150 ml is characteristic of IC/PBS [25].

Treatment. According to the clinical algorithm developed by the AUA [29, 30], the treatment of IC/PBS covers 6 stages—from conservative therapy to invasive interventions (see Figure 1).

Stage 1 includes informing and educating the patient about the disease, general principles of relaxation, stress management, treatment of pain, self-care rules, and changing habits [29, 30].

In stage 2, patients receive manual therapy, massage, and acupuncture aimed toward pain relief. In addition, a combination of oral and intravesical pharmacologic agents including amitriptyline, cimetidine, hydroxyzine, pentosan sulfate, dimethyl sulfoxide, heparin, and lidocaine, are indicated [29, 30].

Stage 3 of treatment is hydro-bougienage of the bladder during cystoscopy under general anesthesia. Laser therapy, coagulation, or triamcinolone injection is recommended in case Hunner ulcer is detected [29, 30].

If previous methods of therapy have not provided adequate control over the disease and patient quality of life, the patient moves on to the next stages. At stage 4, an injection of botulinum toxin type A into the bladder wall is given, and neuromodulation is performed [29, 30].

Treatment at stage 5 involves the use of cyclosporin A [29, 30]. And finally, at stage 6, surgical intervention (cystoplasty, urinary diversion with or without cystectomy) is performed [29, 30].

In conclusion, IC/PBS is a complex disease that needs more study. According to the AUA [29, 30], most of the proposed treatment methods are not defined, so it is always necessary to proceed from a "risk-benefit" standpoint when choosing a particular treatment course.

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