BLADDER PAIN SYNDROME: A REVIEW OF LITERATURE FOR CONSRVATIVE AND MEDICAL MANAGEMENT

ABSTRACT

Nearly every other problem or disorder in this world comes with its set of consequences. People are bound to feel uncomfortable, frustrated, or debilitated due to these adverse effects or reactions that occur as a result of their problems or medical conditions. Talking in particular about the urological and nephrological diseases here, these diseases and conditions are seen to be associated with such symptoms and intensity of pain that people find themselves helpless more than often. These conditions are almost always linked to the changes in the genitourinary system. Since this system involves the confidentiality and modesty of a person, it is commonly seen that people are not that comfortable telling about their issues to others, or even doctors. This leads to an excessive delay in the diagnosis of the condition. In the long run, this leads to an unwanted rise in complications and adverse events related to the patient's condition. In this review, such a condition is being discussed - namely, the Bladder Pain Syndrome. This condition is also called interstitial cystitis, and is a chronic condition that many people have to deal with at some point or the other in their lives. In Bladder Pain Syndrome, the patient feels different levels of pain and pressure in their urinary bladder. Since it is a chronic condition, the symptoms of Bladder Pain Syndrome are seen to come and go with time. Apart from the conventional modes of treatment options that might be present for this condition, there are several other causes too that make the management of this condition easy and manageable for the people suffering from it. This review, in particular, will deal with the non-medical or lifestyle modifications that are associated with the resolution of symptoms of this condition. Although this article does not in any way promote the

use of non-medical modalities as the final treatment resort, it merely serves to highlight and make the people and medical personnel aware of what other helpful and supportive measures could be taken to help the patient deal with this condition smoothly and effectively in no time.

Keywords: bladder pain syndrome, interstitial cystitis, genitourinary problems, urinary frequency, lifestyle modifications.

INTRODUCTION

Interstitial cystitis, also known as Bladder Pain Syndrome (IC/BPD), is a chronic and inflammatory condition involving the urinary bladder. It is also known to occur due to a non-infectious cause. However, it is a very painful condition, especially for older males and females, since these populations are unable to contain their pain and their pain tolerance levels are also quite lower compared to the younger populations. (1)

In the long run, managing and treating this condition can be challenging, as the response to treatment varies greatly among individuals. Inadequately addressed symptoms of IC/BPS can significantly affect a patient's psychological and social well-being. (2)

Generally and figuratively speaking, Bladder Pain Syndrome (BPS) is a widespread condition. It affects a significant portion of the global population. The estimated prevalence rates of Bladder Pain Syndrome range from approximately 2 to 50 per 10,000 individuals worldwide. (3)

However, there is reason to believe that these numbers underestimate the true extent of the problem, as fewer than 10% of those afflicted receive an official diagnosis. A greater part of this could be attributed to the attitudes of patients who find it uncomfortable or uneasy to discuss such problems with their family members or physicians. (4)

In the past, BPS was referred to as interstitial cystitis (IC) before a change in standardized terminology. This shift in naming reflects our evolving understanding of the condition's complex

causes and the current emphasis on diagnosing it based on its symptoms. The overall impact of BPS is substantial, both physically and psychologically, which has led the World Health Organization (WHO) to recognize it as a significant public health concern.(5)

Diagnosing BPS is challenging, mirroring the difficulties encountered in its treatment. Despite the availability of numerous new treatment options, most lack a strong evidence base to support their efficacy. Although several international guidelines exist, they often provide divergent recommendations. Consequently, clinicians often find it challenging to navigate the complexities of patient care.(6)

Understanding the exact origins of Bladder Pain Syndrome (BPS) has proven to be a complex puzzle, with various pathophysiological mechanisms proposed. Among these popular theories are the possibility of chronic bacterial infections, issues with the glycosaminoglycan (GAG) layer of the bladder's urothelium, abnormal activation of mast cells beneath the bladder's surface, autoimmune-related factors, and disruptions in the autonomic nervous system. Researchers have developed treatments targeting each of these potential mechanisms, but the results have been mixed so far.(7)

Adding to the complexity, BPS appears to have connections with other systemic pain syndromes and somatic disorders like irritable bowel syndrome, chronic fatigue syndrome, and fibromyalgia. This suggests that BPS might manifest as a unique subtype within this diverse condition.(8)

The confusion surrounding the terminology used for BPS has contributed to the challenge of identifying specific subtypes that could benefit from targeted therapies, resulting in varying guideline recommendations around the world.

Terms such as interstitial cystitis (IC), hypersensitive bladder, chronic pelvic pain, and painful bladder syndrome have all been employed to describe this condition. The International Continence Society (ICS) has taken steps to standardize the nomenclature, distinguishing hypersensitive bladder, IC/BPS, and IC with Hunner's lesions as separate phenotypes. It is important to note that while IC and BPS have often been used interchangeably, it is now recognized that IC with Hunner's lesions likely represents a distinct disease process and should be treated accordingly.(9)

MANAGEMENT AND TREATMENT PROTOCOLS FOR BLADDER PAIN SYNDROME

Despite Bladder Pain Syndrome posing significant challenges in getting diagnosed, there are several treatment modalities that have been proposed. These treatment and management protocols are helpful in reducing the risk of complications that might arise in the context of Bladder pain Syndrome. At the same time, they are also used when a person has become refractory to treatment with any conservative management or lifestyle changes.

An overview of the various treatment modalities that are popularly employed for Bladder Pain Syndrome is enlisted here as follows:

Oral Pharmacological Agents:

The first line of treatment for Bladder Pain Syndrome is the use of oral drugs. These drugs help restore the normal functioning of the bladder, while at the same time, also ensure the control of symptoms in an individual.

Some of the most commonly used oral drugs are:

- **PentosanPolysulfate (PPS):**

Pentosanpolysulfate (PPS) is a semi-synthetic medication that has been employed both orally and through bladder instillation as a treatment for Bladder Pain Syndrome (BPS). Despite being licensed for the treatment of BPS/Interstitial Cystitis (IC), the available evidence presents a conflicting picture, and recent reports of potential eye-related side effects associated with prolonged use have raised concerns about its safety and utility.(10)

A meta-analysis, encompassing data from four randomized placebo-controlled trials involving 448 patients, revealed encouraging findings regarding the use of oral PPS. It indicated significant improvements in various BPS symptoms, including pain, urgency, and frequency. Success in these trials was defined as a greater than 50% reduction in symptoms. However, it is worth noting that this analysis did not find a significant reduction in nocturia. On the other hand, more recent randomized trials have produced mixed results, further complicating the assessment of PPS's effectiveness in treating BPS.(11)

- **Amitriptyline:**

Amitriptyline, classified as a tricyclic antidepressant, exerts its effects by inhibiting the reuptake of neurotransmitters like serotonin and noradrenaline. Although not officially approved for use in Bladder Pain Syndrome (BPS), it has found common application in managing neuropathic pain and has demonstrated its effectiveness in this specific patient group through the results of two randomized trials.(12)

In a multi-center, randomized controlled trial, researchers examined patients who had not previously received treatment and were able to tolerate a minimum dose of 50 mg of amitriptyline. The findings revealed that these patients reported significantly greater

improvements in their symptoms compared to those who received a placebo. Specifically, 66% of the patients in the amitriptyline group experienced a moderate to marked improvement in their symptoms from baseline, while only 47% in the placebo group reported similar improvements. It is important to note that when all doses were collectively analyzed, the improvement was not statistically significant.(13)

- **Cyclosporine A:**

  Oral Cyclosporine, commonly referred to as CyA, is a medication primarily known for its immunosuppressive properties, often prescribed to organ transplant recipients and individuals with Crohn's disease to control immune responses. (14)

  Recently, it has emerged as a potential treatment option showing positive effects in specific Bladder Pain Syndrome (BPS) patients. However, it comes with its own set of risks, and patients may experience severe side effects. As a result, it is typically reserved for individuals with refractory BPS, those who haven't experienced improvements with other oral or intravesical agents. The administration of Cyclosporin A should be undertaken by healthcare professionals familiar with its use, and close monitoring of blood pressure is essential.(15)

  In a randomized trial that compared Cyclosporin A to PentosanPolysulfate (PPS), it was found that CyA demonstrated greater effectiveness in improving various BPS-related parameters, including frequency, the O'Leary Sant symptom score, and VAS pain scores.

Intravesical Treatment:

Intravesical agents offer a distinct advantage by being administered directly into the bladder, which helps minimize the systemic side effects commonly associated with oral therapies.

Among these intravesical treatments, glycosaminoglycan (GAG) layer therapies have garnered significant attention and have been the subject of numerous randomized trials. Researchers have explored their mechanisms of action, which encompass repairing the defective GAG layer and reducing neurogenic inflammation and hypersensitivity within the bladder.(16)

These investigations have revealed variable clinical improvements associated with different intravesical agents.

Some of the notable options include dimethyl sulfoxide (DMSO), hyaluronic acid (HA), chondroitin sulfate (CS), heparin, PentosanPolysulfate (PPS), and lidocaine. (17)

Each of these agents brings its unique set of characteristics to the table in the quest to alleviate the symptoms of bladder pain syndrome.

CONSERVATIVE AND LIFESTYLE MANAGEMENT OPTIONS FOR PEOPLE WITH BLADDER PAIN SYNDROME

However, a brighter and much more convenient option of treatment exists for people who are not ready to take any medical or surgical treatment.

For such patients, it is usually recommended that a trial of such modalities should be given before embarking on a full-fledged treatment program with these conservative management tips. Some of the commonly employed lifestyle modifications and conservative management tops are given as follows:

Use of Cannabinoids:

Otherwise considered to be a controversial topic and an illegal substance of abuse in some parts of the world, the uses and benefits of Cannabinoids are not hidden from anyone. Due to extensive research being done on the topic, there have been several new benefits that have been discovered just recently. (18)

Researchers have extensively explored their use in managing various chronic pain conditions. Notably, the activation of the Cannabinoid 2 receptor has demonstrated the ability to mitigate the severity of established cystitis in mouse models, as indicated by scientific studies.

However, when it comes to clinical studies involving human subjects, the research has been somewhat constrained, primarily consisting of case reports. While these initial reports have shown promising results, it is clear that further investigation and more extensive clinical trials are needed to better understand the potential therapeutic benefits of cannabinoids in managing cystitis and related conditions. The full scope of their effectiveness and safety profile in human populations remain subjects requiring more in-depth exploration.

Hot & Cold Packs:

It was found that taking warm baths can help relax the pelvic muscles and reduce discomfort. Epsom salts can further add to the relief being experienced.

Moreover, applying a heating pad or warm compress to the lower abdomen or pelvic area can provide relief from pain and muscle tension. (19)

Sitz baths involve sitting in a shallow basin of warm water. This can help soothe the irritated bladder lining and provide relief.

Similarly, Applying a cold pack or ice wrapped in a thin cloth to the lower abdomen or pelvic region can help reduce inflammation and numb the area, potentially providing relief from pain and urgency.

Dietary Modifications:

While the dietary triggers for IC can vary from person to person, there are some general guidelines that may help reduce symptoms and improve overall comfort.

Some foods and beverages are known to exacerbate IC symptoms in many individuals. Common triggers include citrus fruits (e.g., oranges, lemons, and limes), tomatoes, spicy foods, coffee and caffeine-containing beverages, alcohol, carbonated drinks, artificial sweeteners, and high-acid foods and beverages. Such foods must be avoided at all costs. (20)

Limiting or avoiding foods like cranberries, vinegar, and products with high citric acid content can also be helpful in some cases.

Bladder And Behavioral Modifications:

An important modification that needs to be done on urgent grounds is the training of the bladder and the general behavior of the person. Bladder training involves scheduled voiding to help stretch the bladder and increase its capacity. It can be useful for managing urgency and frequency. It is advised to gradually increase the time between bathroom visits to train the bladder to hold more urine.(21)

Moreover, stress can exacerbate IC symptoms. Practicing stress-reduction techniques such as meditation, deep breathing exercises, yoga, or mindfulness can help reduce stress and improve bladder health.

CONCLUSION

Although the Bladder Pain Syndrome is a chronic, inflammatory condition, there is a lot that could be done to manage and live with the patient peacefully. Once a person gets diagnosed with this condition, it is already known that they will be suffering from it for a long time to come. However, if a person learns to navigate their way through small but doable conservative management strategies, then they could very easily get through life effectively and smoothly. All that is required from one is to remain consistent with their routine and the rest will simply follow suit.

REFERENCES

1. Huffman MM, Slack A, Hoke M. Bladder Pain Syndrome. Prim Care. 2019 Jun;46(2):213–21.

2. Interstitial Cystitis - StatPearls - NCBI Bookshelf [Internet]. [cited 2023 Sep 25]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK570588/

3. Berry SH, Elliott MN, Suttorp M, Bogart LM, Stoto MA, Eggers P, et al. Prevalence of symptoms of bladder pain syndrome/interstitial cystitis among adult females in the United States. J Urol. 2011 Aug;186(2):540–4.

4. Suskind AM, Berry SH, Ewing BA, Elliott MN, Suttorp MJ, Clemens JQ. The prevalence and overlap of interstitial cystitis/bladder pain syndrome and chronic prostatitis/chronic pelvic pain syndrome in men: results of the RAND Interstitial Cystitis Epidemiology male study. J Urol. 2013 Jan;189(1):141–5.

5. Cho YS. Interstitial Cystitis/Bladder Pain Syndrome: A Urologic Mystery. Int Neurourol J. 2016 Mar;20(1):3–4.

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

7. Lim Y, Leslie SW, O'Rourke S. Interstitial Cystitis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [cited 2023 Sep 26]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK570588/

8. Yang MH, Huang JY, Chen SL, Wei JCC. Association of Interstitial Cystitis/Bladder Pain Syndrome with Stress-Related Diseases: A Nationwide Population-Based Study. J Clin Med. 2021 Nov 30;10(23):5669.

9. D'Ancona C, Haylen B, Oelke M, Abranches-Monteiro L, Arnold E, Goldman H, et al. The International Continence Society (ICS) report on the terminology for adult male lower urinary tract and pelvic floor symptoms and dysfunction. Neurourol Urodyn. 2019 Feb;38(2):433–77.

10. Margines JB, Hobbs SD. Pentosan Polysulfate Maculopathy. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [cited 2023 Sep 26]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK589706/

11. Sairanen J, Tammela TLJ, Leppilahti M, Multanen M, Paananen I, Lehtoranta K, et al. Cyclosporine A and pentosan polysulfate sodium for the treatment of interstitial cystitis: a randomized comparative study. J Urol. 2005 Dec;174(6):2235–8.

12. Thour A, Marwaha R. Amitriptyline. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [cited 2023 Sep 26]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK537225/

13. Foster HE, Hanno PM, Nickel JC, Payne CK, Mayer RD, Burks DA, et al. Effect of amitriptyline on symptoms in treatment naïve patients with interstitial cystitis/painful bladder syndrome. J Urol. 2010 May;183(5):1853–8.

14. Tapia C, Nessel TA, Zito PM. Cyclosporine. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [cited 2023 Sep 26]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK482450/

15. Tedesco D, Haragsim L. Cyclosporine: A Review. J Transplant. 2012;2012:230386.

16. Tyagi P, Kashyap M, Hensley H, Yoshimura N. Advances in intravesical therapy for urinary tract disorders. Expert Opin Drug Deliv. 2016 Jan;13(1):71–84.

17. Ward K, Kitchen MO, Mathias SJ, Khanim FL, Bryan RT. Novel intravesical therapeutics in the treatment of non-muscle invasive bladder cancer: Horizon scanning. Front Surg. 2022 Jul 26;9:912438.

18. National Academies of Sciences E, Division H and M, Practice B on PH and PH, Agenda C on the HE of MAER and R. Therapeutic Effects of Cannabis and Cannabinoids. In: The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research [Internet]. National Academies Press (US); 2017 [cited 2023 Sep 26]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK425767/

19. Bosch PC, Bosch DC. Treating Interstitial Cystitis/Bladder Pain Syndrome as a Chronic Disease. Rev Urol. 2014;16(2):83–7.

20. Li J, Yi X, Ai J. Broaden Horizons: The Advancement of Interstitial Cystitis/Bladder Pain Syndrome. Int J Mol Sci. 2022 Nov 23;23(23):14594.

21. Lin KBS, Wu MP, Lin YK, Yen YC, Chuang YC, Chin HY. Lifestyle and behavioral modifications made by patients with interstitial cystitis. Sci Rep. 2021 Feb 4;11(1):3055.