Classification and treatment of prostatitis: a review of literature

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ABSTRACT

Prostatitis is one of the most common urinary tract diseases in men of all ages and is often challenging to manage. They can be classified based on the course of illness, presentation, and their etiology, and the investigation and treatment depend on how type of prostatitis. In this study we aim to look through the literature to find the various types of prostatitis and understand the respective methods of management. We did a systematic search for prostatitis using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). The terms used in the search were: prostatitis, urinary tract diseases in men, classification of prostatitis, management of prostatitis. Prostatitis is a common disease and is considered to be the third most common urological disease in men. It has been categorized into four groups: acute bacterial prostatitis, chronic bacterial prostatitis, chronic prostatitis/chronic pelvic pain syndrome, and asymptomatic inflammatory prostatitis. Treatment can be challenging, but mainly consists of use of fluoroquinolones.

Keywords: Prostatitis, Categories, Fluoroquinolones

INTRODUCTION

Prostatitis is considered to be the third most common urinary tract disease in men of all age and is known to be challenging and difficult to properly treat. Recent reports estimate that up to half of males will suffer from prostatitis at least once during their lifetime. They also estimate that up to 25% of urology consults over the world can be due to symptoms of prostatitis. Generally, prostate diseases (like benign prostatic hyperplasia and prostate cancer) affect men of older ages. However, prostatitis is different and has been reported in men of different age groups, with being common in middle-aged men. A previous study was conducted in Canada over a whole year, and found that during the study period, over 9% of study participants suffered from symptoms of prostatitis. Prevalence in other regions, including Asia, North America, and Europe were found to be similar, and can range up to 16%. Therefore, prostatitis constitutes a major health problem in men all over the world, and proper management and treatment is essential to decrease burden associated with it.

METHODS

We did a systematic search for prostatitis using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). Our search also looked for classifications, and treatment of
prostatitis. All relevant studies were retrieved and discussed. We only included full articles.

The terms used in the search were: prostatitis, urinary tract diseases in men, classification of prostatitis, management of prostatitis.

**PROSTATITIS CLASSIFICATION**

The National Institute of Health has released their new classification of prostatitis, in which they kept the old classification of chronic and acute bacterial prostatitis. However, they added a new category in this classification for called chronic nonbacterial prostatitis/chronic pelvic pain syndrome (CNP/CPPS), and another category for asymptomatic cases of prostatitis. We here enumerate the categories according to the new classification:

1. Category I (acute bacterial prostatitis):
   
   In this type of prostatitis, patients have prostatic and systemic symptoms indicating acute infection. Bacteria can be isolated in these cases.

2. Category II (chronic bacterial prostatitis):
   
   In this type of prostatitis, patient may or may not have prostate infection systems. However, most patients will have recurrent urinary tract infections caused by the same bacteria that is causing the prostatitis.

3. Category III (chronic prostatitis/chronic pelvic pain syndrome):
   
   In this type of prostatitis, patients will suffer from both prostatic pain, and symptoms related to voiding, with absence of infection symptoms.

4. Category IV (asymptomatic inflammatory prostatitis):
   
   In this type of prostatitis, patients have no symptoms of prostate or urinary tract infection, despite the presence of actual inflammation in the prostate.

**Category I (acute bacterial prostatitis)**

Acute bacterial prostatitis is characterized by voiding symptoms along with pelvic pain. It constitutes about 10% of prostatitis causes. It has two age peaks: one peak in middle age males, and another peak in elderly younger than 70 years old. Diagnosis of acute bacterial prostatitis can be made with a thorough proper history along with a good physical examination.

The underlying cause of most cases of acute bacterial prostatitis is a poly-microbial infection with *Escherichia coli* along with other organisms like *Enterococcus*, *Enterobacter*, *Proteus*, *Pseudomonas aeruginosa*, *Serratia*, *Klebsiella*, and other bacterial species.

Chlamydia and Neisseria gonorrhoeae have a higher prevalence and should be considered in sexually active patients with acute bacterial prostatitis. Immunocompromised males (HIV patients for example) can develop acute bacterial prostatitis due to an infection with *Candida*, *Salmonella*, and *Cryptococcus.* In cases where there is a history of transurethral manipulation, acute bacterial prostatitis can be due to Pseudomonas species. These cases are usually resistant to normal anti-pseudomonal agents. The use of antibiotics peri-operatively has led to a significant decrease in the incidence of postoperative acute bacterial prostatitis. However, this practice has, on the hand, led to a significant increase in acute bacterial prostatitis caused by fluoroquinolone- resistant *Escherichia coli.*

Diagnosis of acute bacterial prostatitis can be made clinically. This requires a complete proper history along with a thorough physical examination. Examination for acute bacterial prostatitis cases should include the perineum, external genitalia, prostate, and the abdomen. However, doing a prostate massage is not recommended when acute bacterial prostatitis is suspected. Patients should also be examined for the presence of incomplete bladder emptying, and this should be recorded. A urinalysis with urine culture should be done, even if clinical diagnosis is confirmed. Culture is done using a midstream urine sample. The presence of more than ten white blood cells in the high-power field will further help confirm the diagnosis.

Imaging studies can be helpful in acute bacterial prostatitis but are not required. Transrectal ultrasound of the prostate can be helpful to visualize the presence of an abscess, and before initiation of treatment. A bladder scan is required in acute bacterial prostatitis patients who have associated voiding problems or urinary retention, where bladder imaging is also recommended. Levels of prostate-specific antigen (PSA) are often elevated in cases of acute bacterial prostatitis. However, it is not recommended to measure its levels due to low sensitivity and specificity. Moreover, its elevation may lead to further unnecessary investigations for prostate cancer.

Treatment of acute bacterial prostatitis depends mainly on antibiotics therapy. Empiric treatment depends on the patient and the most common causes in this population. When dealing with patients with severe disease, intravenous penicillin with a beta-lactamase inhibitor are recommended. Other options include aminoglycosides, third-generation cephalosporins, fluoroquinolones. In patients who are younger than 35 years and/or sexually active, coverage for chlamydia and Neisseria gonorrhoeae is recommended. Mild cases are treated with an oral fluoroquinolone. In areas where resistant *Escherichia coli* is prevalent, it is not recommended to use trimethoprim-sulfamethoxazole as an empirical therapy. Treatment should be continued for a month.

In cases of acute bacterial prostatitis associated with severe urinary retention of obstruction, catheterization is
recommended. Patients who are contraindicated to receive a urethral catheter can receive a suprapubic tube placement. When there is dehydration, vomiting, high fever, increased heart rate, decreased blood pressure, increased respiratory rates, signs of shock, or any manifestation associated with sepsis, hospitalization is mandatory. Moreover, high risk patients like diabetics, immunosuppressed, and older patients, are recommended to be hospitalized. When there is an associated refractory abscess, incision and drainage are required. The best way to perform this is through the transurethral route.

Nonsteroidal anti-inflammatory drugs are recommended in acute bacterial prostatitis to relieve associated inflammation symptoms like fever. Alpha-blockers are recommended in cases of the presence of obstruction or voiding problems.

**Category II (chronic bacterial prostatitis)**

Similar to acute bacterial prostatitis, chronic bacterial prostatitis is also caused by a bacterial infection. However, rather than presenting with acute symptoms, chronic bacterial prostatitis can last for three months or even more progressing slowly before diagnosis. Chronic bacterial prostatitis constitutes less than 5% of prostatitis cases, making it relatively rare, and usually missed by clinicians. Due to its slow progression nature, with nonspecific symptoms, diagnosis of chronic bacterial prostatitis can be difficult. Moreover, bacterial count is usually low making it impossible to culture bacteria in most cases. Chronic bacterial prostatitis is generally associated with urinary tract infections. Most cases occur due to poly-microbial infection with both gram-negative and gram-positive organisms. Organisms involved in chronic bacterial prostatitis include Neisseria gonorrhoea, chlamydia, escherichia coli, along with any bacteria that is associated with urinary tract infections and/or sexually transmitted diseases.

When suspecting chronic bacterial prostatitis, the first step is to obtain a thorough medical history and perform a physical examination of the prostate, perineum, pelvic floor, external genitalia, and abdomen. The gold standard for detecting prostate infection is Pre- and Post-Massage Test. Pre- and Post-Massage Test has two main types: 4-glass, and 2-glass. The 2-glass Pre- and Post-Massage Test is considered to be a simple, easy, and accurate method to detect bacteria. Physician will perform a systematic message of the prostate (lobe by lobe) to get prostatic secretions. The presence of bacteria in these secretions will confirm the diagnosis of chronic bacterial prostatitis. Semen analysis is not generally required in cases of chronic bacterial prostatitis. Budía et al, performed a study on 895 patients with chronic bacterial prostatitis and concluded that semen analysis can have higher sensitivity that analyzing prostatic secretions for the diagnosis of chronic bacterial prostatitis. Therefore, although not required, semen analysis may be beneficial to help establish a diagnosis. Ultrasound of the prostate can detect the presence of pathology and prostatitis but cannot differentiate the type of prostatitis. Therefore, its use is not generally required. Urodynamics can be used to rule our urethral and bladder dysfunctions in selected cases.

Management and treatment of chronic bacterial prostatitis can be rather challenging. The reason behind this is that most antibiotics have low penetration into the prostatic cells, making it difficult to achieve total eradication of the organism. Penetration of antimicrobial agents into the prostatic cells is facilitated by being a drug with low binding to proteins, high solubility in lipids, and low ionization. Fluoroquinolones are considered the best agents to manage and treat chronic bacterial prostatitis. Their pharmacokinetic characteristics make them able to penetrate infected prostatic cells. Treatment of chronic bacterial prostatitis with Fluoroquinolones has been associated with improvement in up to 90%. However, long-term treatment is required to be able to achieve this. Generally, Fluoroquinolones can achieve complete eradication in chronic bacterial prostatitis caused by escherichia coli, Enterobacteriaceae, along with other agents. However, cases caused by pseudomonas or Enterococci are associated with less rates of treatment success due to drug resistance. In such cases, the use of trimethoprim-sulfamethoxazole for about 3 months is recommended. Other drugs that have been used in the treatment of chronic bacterial prostatitis include aztreonam, cephalosporins, piperacillin, aminoglycosides, erythromycin and imipenem. Other than antibiotics therapy, the use of alpha blockers have been recommended. It has been associated with less recurrence rates and better symptoms relief.

**Category III (chronic prostatitis/ chronic pelvic pain syndrome (CP/CPPS))**

This type of prostatitis is usually found in males who present with vague genital discomfort, with sexual problems and voiding symptoms. The pathophysiology underlying the disease is not well understood until now. It constitutes up to 95% of non-bacterial prostatitis cases and is estimated to occur in up to 14% of males. Chronic pelvic pain syndrome is associated with significant decrease in quality of life of patients and will negatively affect daily activities of patients.

The exact etiology underlying chronic prostatitis is controversial and not well understood. Urine cultures are almost always negative. Several studies on a molecular basis have been conducted in attempts to detect the etiology of chronic pelvic pain syndrome, with no concrete answer yet. Possible suggested etiologies of the disease include the presence of an occult infection, raised levels of uric acid, inflammatory processes, autoimmune disease, and neuromuscular mechanisms. Psychological factors have been addressed in several studies to be important predisposing factors to chronic pelvic pain syndrome. Patients who are generally
predisposed, can have the symptoms after they are exposed to a trigger like trauma, psychological distress, inflammation, or any other stressor.\textsuperscript{19}

Due to its unclear etiology, the diagnosis of chronic pelvic pain syndrome is considered very difficult and challenging, with the absence of a gold standard test.\textsuperscript{20} Generally, the diagnosis is made after exclusion of other causes in a male who has had pelvic pain for longer than here months, with the absence of symptoms related to infections, and the absence of other possible diagnoses. Evaluation of patients depends mainly on thorough and detailed medical history that extends to other systems (especially the nervous system). Careful physical examination is essential.

The national institute of health has developed a questionnaire to be used in the assessment of chronic pelvic pain syndrome. This questionnaire, known as the National Institute of Health Chronic Prostatitis Symptom Index, contains 9 sections that cover three main areas: quality of life, voiding symptoms, and pain.\textsuperscript{21} Despite the presence of several limitations associated with this questionnaire, it is considered to be an essential tool for the assessment of chronic pelvic pain syndrome. Psychological consultation and behavioral therapy should be provided to all patients with suspected chronic pelvic pain syndrome. Physicians should also investigate the presence of obstruction or urinary retention, with documenting this issue. Underlying urinary retention may sometimes be the triggering factor of the disease. Sometimes, further investigations may lead to the discovery of an occult epithelial malignancy. Prostatic secretions collection and analysis could sometimes be performed in suspected chronic pelvic pain syndrome cases, to help differentiate it from bacterial prostatitis.\textsuperscript{22}

Urethral swab could be obtained in cases where there is penis pain, urethral pain, history of sexually transmitted diseases, history of high sexual behavior, and dysuria. When there is significant voiding dysfunction, it is also recommended to perform urodynamic studies. The detection of any underlying cause will help determine treatment plan and will significantly improve prognosis.\textsuperscript{21} A study was conducted in 1994 on 34 patients with refractory chronic pelvic pain syndrome, and found that out of 34 patients, 31 did in fact have an evidence suggesting obstruction of the bladder outlet. However, relief of this obstruction led only the improvement of symptoms in one patient.\textsuperscript{23} Chronic pelvic syndrome patients who also have hematuria or irritative symptoms should undergo cystoscopy.\textsuperscript{21}

Due to the unclear nature of the disease and the absence of a clear underlying mechanism, treatment of chronic pelvic pain syndrome is considered to be rather difficult and challenging. Treatment with fluoroquinolones have been found to improve more than half cases of chronic pelvic pain syndrome. In fact, randomized trials have been conducted and proved fluoroquinolones efficacy in the disease.\textsuperscript{24} The use of alpha-blockers in chronic pelvic pain syndrome has also been found to be beneficial and leads to significant improvement in symptoms.\textsuperscript{25} The combination of a fluoroquinolone with an alpha-blocker was proven to improve symptoms significantly more than a fluoroquinolone alone.\textsuperscript{26}

The use of nonsteroidal anti-inflammatory drugs has been shown to decrease the inflammatory process in the prostate leading to improvement of symptoms. Therefore, their use is recommended in all cases to decrease the pain and improve quality of life.\textsuperscript{27} Hormonal treatment with Finasteride was also suggested to be beneficial in cases of chronic pelvic pain syndrome. However, the use of it solely has not been proven to achieve efficacy.\textsuperscript{28} Further larger studies are needed to assess the efficacy of the use of Finasteride along with other hormonal therapy in the treatment of chronic pelvic pain syndrome.

Other pharmacological therapies that have been used to improve symptoms of chronic pelvic pain syndrome include benzodiazepines, antidepressants, neuro-modulators (like pregabalin), and anti-anxiolytics. However, no solid evidence is currently available to confirm the efficacy of their use.\textsuperscript{29} Some studies suggested the use of opioids to relieve symptoms associated with chronic pelvic pain syndrome. However, this is a largely controversial area, and disadvantages associated with opioids are considered to be a great limitation.\textsuperscript{30}

**Category IV (asymptomatic inflammatory prostatitis)**

Asymptomatic inflammatory prostatitis is characterized by the presence of white blood cells in prostatic secretion, and the presence of inflammation in the prostate gland, with the absence of any signs or symptoms on the patient. It is considered to be a rather uncommon type. Asymptomatic inflammatory prostatitis is associated with two main characteristic signs: the presence of white blood cells and pus cells in prostatic fluids, and the significant elevation in PSA levels. Asymptomatic inflammatory prostatitis is significantly associated with benign prostatic hyperplasia.\textsuperscript{31}

Diagnosis of asymptomatic inflammatory prostatitis is usually made incidentally while the patient is undergoing tests for another issue. PSA levels are usually elevated in patients which aids the diagnosis. Semen analysis, prostatic biopsy, and prostatic secretions analysis can all be used to confirm the diagnosis.\textsuperscript{32}

Due to the absence of symptoms in asymptomatic inflammatory prostatitis, treatment is usually unnecessary. Some physicians prescribe antibiotics as a treatment. However, no solid evidence is present to support this practice.\textsuperscript{31}
CONCLUSION

Prostatitis is a common disease and is considered to be the third most common urological disease in men. It has been categorized into four groups: acute bacterial prostatitis, chronic bacterial prostatitis, chronic prostatitis/chronic pelvic pain syndrome, and asymptomatic inflammatory prostatitis. Chronic prostatitis/chronic pelvic pain syndrome is considered to be the most challenging type of prostatitis due to unknown etiologies and nature. It is also associated with significant impairments in quality of life and daily activities. Treatment of chronic prostatitis/chronic pelvic pain syndrome can be challenging for clinicians. However, fluoroquinolones have been proven to improve quality of life in about half of patients. Further larger studies are required to improve guidelines of prostatitis treatment.

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