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CHRONIC PROSTATITIS: A CHALLENGE TO THE PHYSICIANS

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ABSTRACT

Chronic prostatitis (CP)/chronic pelvic pain syndrome (CPPS) is a common disorder seen in men under the age of 50 and has a considerable negative impact on quality of life. It is a complex and difficult condition to treat, owing to its wide symptomatology. CP/CPPS can be a challenging condition to treat, and a multimodal approach is usually required. Most of these patients have usually been on multiple courses of antibiotics without relief, leading to frustration among patients and practitioners. Diagnosis is often based on exclusion of other urologic conditions (e.g., voiding dysfunction, bladder cancer) in association with its presentation. Commonly used medications include antimicrobials, alpha blockers, and anti-inflammatory agents, but the effectiveness of these agents has not been supported in clinical trials. Small studies provide limited support for the use of nonpharmacologic modalities. Asymptomatic prostatitis is an incidental finding in a patient being evaluated for other urologic problems.

KEYWORDS: Chronic prostatitis, chronic pelvic pain syndrome.

INTRODUCTION

The name ‘prostate’ is originally derived from a Greek word ‘prohistani’ (means ‘to stand in front of’). The prostate is the largest accessory sex gland of males. It is a fibromusculo-glandular, exocrine gland that secretes alkaline fluid which constitutes about 20–30% the volume of the seminal fluid. Changes in the prostatic fluid composition and/or secretion affect sperm functions and may lead to male infertility. The gland is often associated with disorders of elderly, benign prostatic hyperplasia (BPH) and carcinoma. Prostatitis is the name given to a set of symptoms that are thought to be caused by an infection or an inflammation (swelling) of the prostate, but often physicians don’t know why it develops.

Types of prostatitis

Definition

Prostatitis describes a combination of infectious diseases (acute and chronic bacterial prostatitis), CPPS or asymptomatic prostatitis. The NIH classification of prostatitis includes:

Category I: Acute bacterial prostatitis (ABP) which is associated with severe prostatitis symptoms, systemic infection and acute bacterial UTI.

Category II: Chronic bacterial prostatitis (CBP) which is caused by chronic bacterial infection of the prostate with or without prostatitis symptoms and usually with recurrent UTIs caused by the same bacterial strain.

Category III: Chronic prostatitis/chronic pelvic pain syndrome is characterized by chronic pelvic pain symptoms and possibly voiding symptoms in the absence of laboratory confirmed UTI.

Category IV: Asymptomatic inflammatory prostatitis (AIP) which is characterized by prostate inflammation in the absence of genitourinary tract symptoms.

Acute Bacterial Prostatitis

Acute bacterial prostatitis, NIH type I, is an acute bacterial infection of the prostate; patients are typically seen in the outpatient setting or emergency department. Left untreated, it can lead to overwhelming sepsis or the development of prostatic abscess. The prevalence and incidence of acute bacterial prostatitis are not fully known.[1] By definition, an organism must be identified on culture. *Escherichia coli* is the most commonly isolated organism, but other gram-negative organisms, such as *Klebsiella*, *Proteus*, and *Pseudomonas*, and gram-positive *Enterococcus* species are often isolated as well. Other gram-positive organisms, many of which comprise normal skin flora, have also been isolated from patients with suspected bacterial prostatitis and should be treated accordingly.[2] Sexually active men younger than 35 years and older men who engage in high-risk sexual behaviors should be tested for *Neisseria gonorrhoeae* and *Chlamydia trachomatis*.

Chronic Bacterial Prostatitis

Chronic bacterial prostatitis, NIH type II, is a persistent bacterial infection of the prostate lasting more than three months. Urine cultures obtained over the course of ill-ness repeatedly grow the same bacterial strain. The NIH

Chronic Prostatitis Symptom Index from the Chronic Prostatitis Collaborative Research Network (CPCRN) is a validated questionnaire available at http://www.prostatitis.org/symptomindex.html.

E. coli is the most commonly isolated organism, but other gram-negative organisms such as *Klebsiella*, *Proteus*, and *Pseudomonas* are also common. After *E. coli*, gram-positive *Enterococcus* is the next most commonly isolated pathogen. Research suggests that the *E. coli* strains often seen in chronic bacterial prostatitis have a higher virulence factor and greater degree of biofilm formation than the strains seen in uncomplicated urinary tract infections, which could explain why bacterial prostatitis is so difficult to treat.[3]

Asymptomatic Prostatitis

Asymptomatic prostatitis, NIH type IV, is diagnosed when inflammatory cells are identified on prostate biopsy or leukocytes are noted on semen analysis during urologic evaluation for other reasons. The clinical significance of this type of prostatitis is uncertain, and treatment is based on the primary reason for the urologic evaluation. When the indication for biopsy is an elevated PSA level, it is important to remember that normalization of the PSA value after antibiotic or 5-alpha reductase inhibitor therapy does not rule out the diagnosis of prostate cancer, and continued urologic evaluation is warranted.

Chronic Prostatitis/Chronic Pelvic Pain Syndrome

Chronic prostatitis/chronic pelvic pain syndrome is subdivided into two categories: NIH type IIIA (inflammatory) and IIIB (non-inflammatory). Differentiation between these groups has been made based on the presence of leukocytes in expressed and post-massage prostatic secretions, urine, or semen. One of the greatest challenges with the treatment of chronic prostatitis/chronic pelvic pain syndrome is that there is no clear understanding of the etiology; however, suggested explanations include infection, autoimmunity, and neuromuscular spasm. In 2006, the CPCRN published a prospective analysis of NIH type III prostatitis symptoms over two years.[4] This group concluded that symptoms vary widely among patients, there is no evidence that the disease worsens, and approximately one third of patients will improve with or without treatment. Chronic prostatitis is more frequent than is commonly thought. As Roberts et al[5] point out, one report of autopsy studies[6] found a prevalence of 6.3% histologic inflammation of the prostate, whereas in another series[7] this figure was as high as 44%. It should be noted, however, that although prostatitis means literally an inflammation of the prostate gland, conditions falling within the definition of ‘‘prostatitis syndrome’’ on merely clinical grounds may not be associated with inflammation.

Bacteria recognized as aetiologic agents for chronic bacterial prostatitis.

_ Gram-negative Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa
_ Gram-positive Streptococcus faecalis (Enterococcus)
Corynebacteria.

Staphylococcus saprophyticus, S. epidermidis, S. aureus
Chlamydia trachomatis
Mycoplasma genitalium
Ureaplasma urealyticum
_ Anaerobes
_ Viruses

The pathogenesis of bacterial prostatitis is unknown. According to Schaeffer[8], ascending urethral infection after vaginal or rectal inoculation of the urinary meatus during sexual intercourse is likely to play an important role, sometimes as a complication of urethritis. Haematogenous or lymphatic spread may also occur. Pathogenesis is even more obscure for category III prostatitis. Chronic bacterial prostatitis can follow acute prostatitis, be due to indwelling catheters, or appear ex novo. The formation of biofilms may play an important role in maintaining chronic infection in prostatitis secondary to catheters or stones. Prostatic calculi or microcalcifications can also be observed but their clinical significance is obscure, because they can be found in normal, asymptomatic subjects. It cannot be ruled out that prostatic calculi may help to maintain local inflammation and produce moderate pain, acting as foreign bodies.[8] Larger calculi are more frequently associated with symptoms. It was noteworthy that these abnormalities detected by TRUS were observed with nearly equal frequencies in all CPS categories, including prostatodynia, suggesting a possible organic pathology also for the latter category of patients.[9]

Treatment

Empiric therapy should be started at the time of evaluation; coverage can be tailored to the isolated organisms once urine culture results are available. Mild to moderately ill patients may be treated in the outpatient setting; severely ill patients or those with possible urosepsis require hospitalization and parenteral antibiotics. Once patients have become afebrile, they may be transitioned to oral antibiotics based on the culture results. Minimal duration of treatment is four weeks; however, the optimal period has been shown to be six weeks, because of the possible persistence of bacteria, with repeat evaluation recommended at that time.[10]

There is no preferred first-line treatment for patients with chronic pelvic pain syndrome. It is reasonable to try antimicrobials, alpha blockers, or anti-inflammatory medications first; however, if a patient does not respond to treatment, repeated trials are not warranted. In addition, it is important to consider multimodal therapy with a combination of medications or possible adjunctive therapy with nonpharmacologic modalities. Men with

chronic pelvic pain syndrome represent a highly complex group of patients, and urology referral is often necessary.

a. Antimicrobials

Antimicrobials cannot be recommended for men with longstanding, previously treated CP/CPPS. However, uncontrolled clinical studies suggest that some clinical benefit can be obtained with antimicrobial therapy in antimicrobial naïve early onset prostatitis patients.

b. Alpha-blockers

Alpha-blockers cannot be recommended as a first line monotherapy. However, there is some evidence that alpha-blocker naïve men with moderately severe symptoms who have relatively recent onset of symptoms may experience benefit. Alpha-blocker therapy appears to provide benefit in a multimodal therapeutic algorithm for men with voiding symptoms. Alpha-blockers must be continued for over 6 weeks (likely over 12 weeks).[11]

c. Anti-inflammatory

Anti-inflammatory therapy is helpful for some patients, but is not recommended as a primary treatment; however, it may be useful in an adjunctive role in a multimodal therapeutic regimen.

d. Phytotherapies

Phytotherapies (specifically quercetin and the pollen extract, cernilton) are optional recommendations for first line and combination multimodal therapy.

e. Other medical therapies

Other medical therapies, such as 5-alpha-reductase inhibitor therapy, pentosanpolysulfate and pregabalin, while not recommended as primary monotherapy, may provide benefit in selected patients (older men with LUTS for 5-ARI therapy, men with associated pain perceived bladder pain and irritative voiding symptoms for pentosanpolysulfate and neuropathic type pain for pregabalin).

f. Other potential medical therapies

Muscle relaxants, saw palmetto, corticosteroids, and tricyclic antidepressants have all been suggested and used, but recommendations will have to wait for results from properly designed randomized placebo controlled trials.

g. Physiotherapies

A number of physical therapies have been recommended[12] but they also suffer from a lack of prospective controlled data obtained from properly designed controlled studies. Prostatic massage, perineal or pelvic floor massage and myofascial trigger point release has also been suggested as a beneficial treatment modality for patients, however focused pelvic physiotherapy has yet to be shown to provide more benefit compared to SHAM physiotherapy. Biofeedback, acupuncture and electromagnetic therapy also show promise, but like all the other physical therapeutic modalities, require sham controlled trials before recommendations can be made.

h. Psychotherapies

Psychological support and therapy has been advocated based on new psycho-social modelling of this syndrome.[13] This treatment ideally would include a cognitive behavioral therapy program. A referral to a psychologist or psychiatrist should be considered mandatory in patients with severe depression and/or suicidal tendencies.

i. Surgery

The evidence for surgical therapies has been reviewed.[14] A number of minimally invasive therapies such as balloon dilation, neodymium: Yag laser, transurethral needle ablation, microwave thermotherapy have been suggested. Further assessment of heat therapy employing sham controls, standardized inclusion- exclusion criteria and validated symptom outcome measures are recommended. Pudendal nerve blocks or neurolysis surgery have been suggested for CPP that can be shown to be secondary to pudendal nerve entrapment. Other surgery, such as radical transurethral resection of the prostate and total prostatectomy, should not be encouraged and is not recommended at this time for CP/CPPS since no definitive clinical series or long-term follow-up has ever been presented.[15]

CONCLUSIONS

CP remains a controversial condition with little agreement regarding the best treatment option. No formal evaluation standard exists, and clinicians should tailor diagnostic studies to a patient's specific symptoms and complaints while maintaining awareness that CP/ CPPS remains a diagnosis of exclusion. The difficulty in finding efficacious treatment for any given patient likely lies in the heterogeneous nature of both the manifestation of causative conditions and the patient responses. It is important for the patient that he be informed as soon as possible about his condition, including the necessary diagnostic steps and possible therapies, and that a specific plan for his diagnosis and treatment be established. This is the best way to develop trust between doctor and patient. This trust is critical to get an acceptable result after several unsuccessful attempts are made at treatment.

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