Identification, Pharmacologic Considerations, and Management of Prostatitis

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ABSTRACT

Background: Prostatitis is a collection of signs and symptoms that occur as a result of inflammation or swelling of the prostate gland. There are many different causes for prostatitis, including infection; occasionally no clear etiology for the inflammation is found. Effective treatment often depends on identification of the cause, but a microbiologic organism is not always detectable, especially in cases of chronic prostatitis.

Objective: The aim of this article was to review identification and treatment options for prostatitis, including pharmacologic and nonpharmacologic interventions.

Methods: Relevant information was identified through a search of MEDLINE (1966–June 2010), International Pharmaceutical Abstracts (1970–June 2010), and EMBASE (1947–June 2010). Randomized, controlled trials that examined prostate cancer, benign prostatic hypertrophy, or procedures related to the prostate (ie, biopsies) were excluded.

Results: A working classification system for prostatitis was developed in 1999, but there are few randomized controlled trials that distinguish between the various treatment options. Bacterial prostatitis can be acute or chronic but always requires some degree of antimicrobial therapy. Pharmacologic features of fluoroquinolones make them the preferred agents for most patients. These antibiotics can become trapped in a chronically inflamed prostate due to pH differences between prostatic tissue and serum. Many fluoroquinolones have penetration ratios (prostate level:serum level) of up to 4:1. A study in European men (N = 117) who received levofloxacin 500 mg/d with a diagnosis of chronic bacterial prostatitis demonstrated clinical success rates of 92% (95% CI 84.8%–96.5%), 77.4% (95% CI, 68.2–84.9%), 66.0% (95% CI, 56.2%–75.0%), and 61.9% (95% CI, 51.9%–71.2%) at 5–12 days, 1 month, 3 months, and 6 months after treatment. Additionally, there have been numerous randomized, placebo-controlled trials in patients with chronic prostatitis that have studied α-blockers, steroid inhibitors, anti-inflammatory agents, and bioflavonoids. Treatment responses to α-blockers appear to be greater with longer durations of therapy in α-blocker–naïve patients (National Institutes of Health-Chronic Prostatitis Symptom Index [NIH-CPSI] score reduction of at least 3.6 points after 6 weeks of tamsulosin therapy [$P = 0.04$] and up to 14.3 and 9.9 point NIH-CPSI score reductions with 14 weeks of terazosin and 24 weeks of alfuzosin therapy, respectively [$P = 0.01$ for both]). Combination therapy with an α-blocker, an anti-inflammatory, and a muscle relaxant does not appear to offer significant advantages over monotherapy (12.7 vs 12.4 point reduction in NIH-CPSI scores) and a stepwise approach to therapy involving antibiotics followed by bioflavonoids and then α-blockers appears to effectively reduce symptoms for up to 1 year in patients with chronic prostatitis (mean NIH-CPSI point reduction of 9.5 points compared with baseline, $P < 0.0001$). Patients who have had multiple unsuccessful treatment regimens may benefit from direct stimulation of the pelvic muscles through electromagnetic or electroacupuncture therapy.

Conclusions: Prostatitis can resemble various other medical conditions but proper classification and an understanding of the pharmacologic features and expectations of the medications used to treat it can help identify effective treatment strategies. Fluoroquinolones are the preferred agents for treating bacterial causes of prostatitis and have demonstrated efficacy in some cases of chronic prostatitis when an organism has not been identified. However, the use of agents with anti-inflammatory or antiadrenergic properties may be necessary in combination with or after trying antimicrobial agents. (*Am J Geriatr Pharmacother.* 2011;9:37–48)

Key words: Bacterial prostatitis, chronic prostatitis, NIH-CPSI, prostatitis.

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INTRODUCTION

Prostatitis is a collection of signs and symptoms that occur as a result of various causes of inflammation or swelling of the prostate gland. It occurs more commonly in older men, with 1 study showing an 8% increase in risk with every 5-year increase in age ($P = 0.01$), but it can be diagnosed in any adult male.[1] Expenditures for Medicare enrollees ≥65 years were $27 million, compared with $3 million (no reported statistics) for those <65 years, in 2001 and have remained level since 1992. Physician office visits accounted for more than half of these expenditures.[2] The variability in presenting symptoms, especially among older men, and age-related changes in pharmacokinetic parameters can make it difficult to properly identify and treat prostatitis. Therapies for older adults have been based on general studies that included men of various ages. Treatment selections were standardized in clinical trials but attention to renal dosing and side effect identification may be more important for older adults. This article reviews general concepts associated with prostatitis with a focus on identifying the different categories and evidence-based approaches to treatment.

METHODS

Relevant information was identified through a search of MEDLINE (1966–June 2010), International Pharmaceutical Abstracts (1970–June 2010), and EMBASE (1947–June 2010). Articles related to epidemiology, diagnosis, and pharmacologic concerns were identified using the terms *prostatitis diagnosis, epidemiology, symptoms,* and *distribution/pharmacokinetics*. Articles about treatment were identified using the term *prostatitis* and limited to randomized controlled trials. Trials that examined prostate cancer, benign prostatic hypertrophy, or procedures related to the prostate (ie, biopsies) as well as non-English articles were excluded. References were also identified through screening of citations in articles gathered.

ANATOMY AND PATHOPHYSIOLOGY

The prostate is an encapsulated, multilobar, walnut-sized glandular organ that sits in front of the rectum but behind and below the bladder. It is wrapped around the urethra as the urethra passes out of the bladder to the penis. The portion of the urethra that passes through the prostate is called the prostatic urethra. A large portion of the base of the prostate is continuous with the bladder wall while the apex of the prostate is in contact with the urogenital diaphragm. The prostate consists of a central lobe with lateral lobes on either side and is composed of 70% glandular elements and 30% fibromuscular stroma. The prostatic glands drain into the urethra; however, glands in the periphery have a poor drainage system. This may be the reason that this peripheral zone is the most common area involved in chronic prostatitis (CP). As the prostate enlarges with age, causing decreased urinary flow through the organ, urine refluxes into the prostatic ducts and may lead to chronic inflammatory changes in the glands.[3]

The prostate also has a nonglandular fibromuscular anterior lobe. The entire organ is surrounded by the prostatic capsule and receives its blood supply from the prostatic branch of the inferior vesical artery, which is a branch of the internal iliac artery. The prostate gland produces an alkaline fluid that carries semen out through the urethra.[3] The normal forward flow of urine and ejaculate through the urethra help protect the prostate from infection.

Prostatitis is swelling of the prostate gland due to bacterial or nonbacterial causes. Based on the anatomy of the gland, swelling can obstruct the flow of urine and lead to lower urinary tract symptoms as well as sexual dysfunction.[4,5] Bacterial causes of prostatitis are often a consequence of a urinary tract infection or sexual transmission of an organism, but can also occur after manipulation of the gland during procedures such as biopsies and resections. Although antibiotic prophylaxis can usually prevent the latter, a retrospective analysis of 1339 patients who received ciprofloxacin 500 mg before undergoing a transrectal ultrasound-guided biopsy still identified an incidence of acute prostatitis to be 2.1%.[6]

The majority of bacterial prostatitis is caused by gram negative bacteria, of which *Escherichia coli* is the most commonly identified organism. Although usually susceptible to many antibiotics, fluoroquinolone-resistant or extended-spectrum β-lactamase (ESBL) producing species are becoming a problem and a cause for treatment or prophylaxis-failures.[6,7] Sexually transmitted organisms, such as *Neisseria gonorrhoeae* and *Chlamydia trachomatis,* can also infect the prostate, and in 1 study, prostatitis was identified in 37% of men who received treatment for gonococcal urethritis.[8] Nonbacterial causes of prostatitis can be difficult to identify but have included nanobacteria, elevated prostatic pressures, voiding dysfunction and bladder neck dyssynergia, male interstitial cystitis, pelvic floor myalgia, functional somatic syndrome, and emotional disorders.[5] Regardless of the cause of prostatitis, molecular analysis of the inflammatory process has demonstrated an upregulation of DNA transcription regulator nuclear factor-κB. This nuclear factor increases the cellular production of pro-