Review Article

Male chronic pelvic pain: An update

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ABSTRACT

Introduction: Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) and interstitial cystitis/bladder pain syndrome collectively referred to as urologic CPPS (UCPPS) is defined by the absence of identifiable bacterial infection as a cause for the chronic pain and urinary symptoms.
Methods: A PubMed search of all recent relevant articles using the keywords/phrases: CPPS, CPPS, and male pelvic pain, was conducted.
Results: CPPS has a high worldwide prevalence and its negative impact on quality of life compares with or exceeds common chronic morbidities. Triggers include certain comestibles as well as psychosocial factors that promote catastrophizing and illness focused behavior. Several validated tools are currently available to help diagnose and direct targeted therapy. Treatment should begin with the most simple and least invasive based on the presenting clinical phenotype.
Conclusions: Although no gold-standard treatment exists, a multidisciplinary approach with multimodal therapy gives the UCPPS patient the best chance of symptom relief.

Key words: Chronic pelvic pain syndrome, male pelvic pain, prostatitis

INTRODUCTION

Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) accounts for 90% of prostatitis cases in outpatient clinics and is characterized by chronic pelvic pain symptoms lasting at least 3 months during the past 6 months, in the absence of a urinary tract bacterial infection but in the presence of urinary symptoms and sexual dysfunction.[1] CP/CPPS and interstitial cystitis/bladder pain syndrome are collectively referred to as urologic CPPS (UCPPS), defined by the absence of identifiable bacterial infection as a cause for the chronic pain and urinary symptoms. This review will focus on the latest developments in the diagnosis and treatment of this common, but often poorly understood the disorder.

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METHODS

A PubMed search of all articles from 2010 to May 2015 using the keywords/phrases: CPPS, CPPS, and male pelvic pain, was conducted. Older articles were cross-referenced when deemed applicable (i.e. size of the study or level of evidence provided).

PREVALENCE AND IMPACT ON QUALITY OF LIFE

CP/CPPS has a worldwide prevalence between 2 and 16% and is the most common urologic disease in men below 50 years old.[1] Symptoms can be present on average for 87 months before diagnosis. Its negative impact on quality of life (QOL) compares to other maladies such as myocardial infarction, angina, Crohn's disease, and diabetes mellitus.[2]

HOW TO MEASURE IT

National Institutes-chronic prostatitis symptom index

The National Institutes of Health CP symptom index (NIH-CPSI) measures the aspects of the three most important symptom domains of CP/CPPS: Pain (location, frequency, and severity; score range 0–21), voiding problems (irritating

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and obstructive symptoms; score range 0-10), and negative effects on QOL (score range 0–12) with a total score of 0–43.[3]

Urinary, psychosocial, organ specific, infection, neurologic/systemic and tenderness of skeletal muscle

The urinary, psychosocial, organ specific, infection, neurologic/systemic, and tenderness of skeletal muscle (UPOINT) system is used to classify individuals with CP/CPPS to define their unique clinical phenotype, which can be then used to guide therapy. The number of positive UPOINT domains has been shown to correlate strongly with the severity and duration of prostatitis symptoms, as measured by the NIH-CPSI.[4]

Investigators have looked at the different domains within UPOINT and found that data diverge based upon whether patients were classified as organ specific-bladder versus organ specific-prostate. They suggested that patients with more bladder centric symptoms be treated more like IC/painful bladder syndrome (PBS) patients. They found that the primary drivers of pain in CPPS cases are pelvic floor tenderness, psychological depression, and catastrophizing.[5]

Genitourinary pain index

Given the fact that CP/CPPS and IC/PBS have overlapping symptoms and treatments, investigators modified the validated and widely used NIH-CPSI into the genitourinary pain index (GUPI) to permit its use in men and women.[6] GUPI scores in men and women diagnosed with IC correlated well with ICSI and IC problem index scores. It was also responsive to a 7 point decrease in total score correlated significantly with clinical response to a trial of pelvic floor physical therapy.

TRIGGERS/INHIBITORS OF DISEASE

Food sensitivities

To evaluate for food sensitivities in men with CP/CPPS, 95 male patients who met NIH criteria for CP/CPPS were evaluated with a validated questionnaire to detect the effect of foods, beverages, and/or supplements on pelvic pain symptoms and urinary frequency/urgency.[7] Forty-seven percent reported that the consumption of certain comestibles aggravated their symptoms. The most aggravating items were spicy foods, coffee, hot peppers, alcoholic beverages, tea, and chili. Higher symptom severity was associated with increased consumption of alcohol and coffee.[7]

In contrast, 22.6% of patients reported on comestibles that alleviated their symptoms, most notably: Docusate, psyllium, water, herbal teas, and polycarbophil.[7] Thirty-five percent of patients also met the diagnostic criteria for IC/PBS. No significant differences were seen in the responses to the effects of food on symptoms. Symptom alleviation was reported from consumption of calcium glycerophosphate (Prelief), followed by baking soda and low-fat milk.

Psychosocial factors

Chronic pain is impacted in large part by cognitive/behavioral factors such as catastrophizing and pain-contingent rest. In particular, catastrophizing helplessness is the most important predictor of pain.[8] Catastrophizing mediation allows symptoms to become disabling by promoting negative pain ruminations. In the absence of a catastrophizing intervention or a substantial reduction in pain, CP/CPPS patients are likely to remain catastrophic in their thinking about pain for extended periods of time.[9] On the other hand, pain-contingent rest is the most important predictor of disability. This behavior is a prominent pain coping strategy in men with CP/CPPS by avoiding movement or activity due to pain. The end result is a gradual loss of mobility.

Impact of exercise

A prospective cohort study was performed among men in the Health Professionals Follow-up Study followed from 1986 to 2008 which included 20,918 men who completed CP/CPPS questions in 2008 questionnaire.[10] Leisure-time physical activity, including type and intensity of activity, was measured by questionnaire in 1986. The investigators found that higher leisure-time activity (i.e. brisk walking of at least 10 h/week) was associated with a 28% significant reduction in the risk of developing CP/CPPS compared to controls.

ECONOMIC COSTS

IC/PBS and CP/CPPS are pelvic pain conditions with unknown etiologies and no consistently effective treatment. Given the symptomatic overlap between these two conditions, investigators sought to directly compare the economic impact of each.[11] Forty-three women with IC/PBS and 62 men with CP/CPPS were evaluated using a resource use questionnaire. Eighty percent of IC/PBS and CP/CPPS reported direct medical costs in the preceding 3 months related to their pelvic pain condition. Annual direct costs were slightly higher for IC/PBS patients than CP/CPPS patients (i.e. $7043 vs. $6534, respectively, using non-Medicare rates). These costs compare with or surpass the annual direct costs associated with other chronic pain conditions such as peripheral neuropathy, low back pain, fibromyalgia, and rheumatoid arthritis. Twenty percent of IC/PBS and 25% of CP/CPPS patients reported lost wages in the previous 3 months.

TREATMENT

The UPOINT system has therapeutic value in addition to its use as a diagnostic tool. A recent study in 100 patients with CPPS measured the effect of UPOINT phenotype based therapy on patient response rate.[12] After a mean follow-up

of 50 weeks, 84% of patients responded to targeted treatment (i.e. at least 6 point drop on NIH-CPSI score). While the study was not placebo controlled, the high response rate suggests the value for this classification system both for diagnostic and for treatment applications. The various treatment options for CP/CPPS have been organized below based on the UPOINT system. It is not an exhaustive list but highlights the most common and successful approaches. In general, all treatments should begin with the least invasive focused approach.

Urinary

Addressing urinary symptoms begins with promoting dietary changes such as avoiding spicy foods, caffeine and alcohol. Additional therapies target bothersome LUTS such as frequency, urgency, hesitancy, and weak urinary flow (i.e. OAB medication and prostate medication).

Alpha adrenergic antagonist

The use of alpha blockers as monotherapy has produced mixed results in placebo-controlled trials. However, a recent multicenter, randomized study showed the beneficial effect of silodosin when compared to placebo.[13] The investigators found that a 4 mg dose of silodosin was associated with significantly greater reductions in total NIH-CPSI score and urinary symptom and QOL sub scores versus placebo. In addition, a greater percentage of CPPS patients treated with silodosin were considered as "responders" when using the global response assessment (GRA) but not when using NIH-CPSI (i.e. reduction in total score by at least (6) the investigators concluded that differences in alpha blocker, study design, or patient population (i.e. alpha blocker naïve) could explain the contradictory trial results.

5-alpha reductase inhibitor

Dutasteride reduced prostatitis symptom scores compared to placebo in men enrolled in the REDUCE study.[14] The trial was designed to evaluate whether dutasteride reduces the risk of prostate cancer diagnosis in men believed to be at high risk for prostate cancer. However, these investigators examined the effect of dutasteride versus placebo by evaluating changes in CPSI scores in men with CP/CPPS. Fifty-eight and 46% of men, respectively, were categorized as 4 points (i.e. mild) and 6 points (i.e. moderate) responders, respectively, in the dutasteride treatment group.[14] This response was significantly greater than the placebo response. The investigators theorized that dutasteride by reducing intraprostatic reflux and voiding dysfunction might ameliorate the symptoms of CP/CPPS.

Psychosocial

Psychotherapy

Professional psychotherapy can improve the psychosocial component of CP/CPPS, in particular, by reducing catastrophizing and improving coping mechanisms. Techniques include guided imagery, progressive relaxation training, self-hypnosis, biofeedback, and cognitive behavioral therapy.[15]

Patient and spousal support

Spouses may respond to patient pain behavior in the following manner: (1) Solicitous (i.e. helps out with chores or encourages patient rest; (2) distracting (i.e. gets patient involved in activities), and (3) negative or punishing (i.e. gets angry with the patient).[16]

Investigators found that solicitous responses increase the negative impact of pain on a patient's disability while distracting responses have the opposite effect.[16] Solicitous spousal responses may act to reinforce pain behaviors while distracting spousal responses encourage patients to engage in activities which lessen the awareness or impact of pain on disability. Interestingly, the negative spousal response did not affect the association between pain and outcome in men with CPPS.

WHAT DOES THIS MEAN FOR THE UROLOGIST TREATING A PATIENT WITH CP/CPPS?

These studies suggest that urologists should encourage patients to engage in as many activities of daily living as possible.[16] That they should counsel spouses to promote and engage in group activities with the patient, including exercise programs, which will aid in patient distraction from their underlying condition.

Organ specific

Organ-specific therapies include avoiding dietary triggers listed earlier. In addition, if the majority of symptoms are localized to the bladder, then IC/PBS specific treatments may be considered (i.e. pentosanpolysulfate, hydroxyzine, intravesical therapies). Prostate specific organ-based therapies are listed below.

OnabotulinumtoxinA

The effect of onabotulinumtoxinA (onaBoNT-A) injection on CP/CPPS was evaluated in a double-blind study in 60 males.[17] Men were injected transurethrally into their lateral prostate lobes with either placebo saline or onaBoNT-A (100 or 200 units depending on prostate size). Significant improvements in symptoms scores and QOL were observed in the onaBoNT-A group compared to placebo. The most prominent changes following onaBoNT-A treatment were improvements in pain and visual analog scale score (i.e. decreasing by 79.97% and 82.1%, respectively, at 6 months follow-up).[17] Improvements in pain were observed as soon as 1 month following treatment. No improvements in pain measurements were found following saline injection.

Transurethral microwave thermotherapy

Two studies have evaluated the effectiveness of heat therapy up to 45–50°C for patients with CPPS. Nickel reported

on a randomized, double-blind, sham-controlled study that showed a 70% response rate (i.e. >50% reduction in symptoms) and a significant improvement compared to the control group.[18] A second study demonstrated a 63% response rate at 12 months follow-up.[19] In both studies, only minimal transient side effects were noted.

Extracorporeal shock wave therapy

Level 1 evidence for the beneficial effect of extracorporeal shock wave therapy (ESWT) on CP/CPPS patients was provided in a randomized, placebo-controlled study of 60 patients.[20] Low-intensity shocks were applied to the perineum on a weekly basis for 4 weeks. After a follow-up of 12 weeks, significant improvements in pain, QOL, and voiding symptoms were demonstrated in the ESWT group compared to sham-treated patients. The procedure was well-tolerated and did not require anesthesia.

Pollen extract

Phytotherapeutics are extracts of natural origin used as medicines or for health promotion. Cernilton has been used to treat CP/CPPS for over 25 years.[21] The exact mechanism is unknown but *in vitro* studies suggest a strong anti-inflammatory effect based on inhibition of cyclooxygenase and lipoxygenase pathways.

A double-blind placebo controlled evaluated the safety and efficacy of pollen extract versus placebo in men with inflammatory CP/CPPS (type IIIA).[21] The primary endpoint was a symptomatic improvement in the pain domain of the NIH-CPSI.[21] A total of 111 patients completed the study. After 12 weeks of treatment, the mean decrease in the pain domain of the NIH-CPSI scale was significantly greater in the pollen extract group compared to placebo (i.e. –4.5 vs. –2.92). Sixty-nine percent of pollen extract patients showed a 25% improvement compared to 48.5% of placebo patients ($P < 0.05$).

Infection

If a patient has never been treated with a long course of antibiotics (i.e. 30 days), that is a reasonable first option. In many cases, therapy targets infection, inflammation, and voiding problems in conjunction to include antibiotics, anti-inflammatory medications and alpha blockers, otherwise known as the "three A's" of CP/CPPS treatment. Physicians can also treat for atypical organisms based on localized semen culture results.

Investigators recently used culture-independent molecular techniques to characterize the microbiota of male UCPPS patients and compared it to controls.[22] They were not able to show a clear difference in the microbiome between the two patient populations. One specific organism, *Burkholderiacenocepacia*, was more prevalent in VB1 in UCPPS patients and has been described by some as pathogenic.[22] However, the investigators concluded their data were not strong enough to recommend empiric antimicrobial treatment of this particular organism.

Neurologic/systemic

Neurologic treatments include the use of neuropathic pain drugs such as pregabalin, gabapentin, and amitriptyline. These approaches also include pain management referral for consideration of nerve blocks.

Pregabalin

A randomized double-blind placebo controlled study in 324 CP/CPPS patients evaluated pregabalin versus placebo.[23] The primary endpoint was a 6 point decrease in the NIH-CPSI score. Forty-seven percent of pregabalin-treated patients demonstrated a 6 point decrease in NIH-CPSI scores versus 36% of placebo-treated patients, but the difference was not significant (i.e. $P = 0.07$). However, the GRA response rate was significantly higher in the pregabalin versus the placebo group (i.e. 31% *vs.* 19%). Most patients had long-standing symptoms and were treated for only 6 weeks. Investigators hypothesized that longer treatment in men with a shorter duration of symptoms or more neurologically based symptoms might have led to significant changes in NIH-CPSI scores.[23]

Neuromodulation

Scarce data exists on the application of neuromodulation for men with CPPS. A three-arm randomized trial in 36 men with CP/CPPS compared electroacupuncture (EA) with advice and exercise (A and E; sitz baths and 30 min of fast paced walking), sham acupuncture (needle only) and A and E, and A and E alone.[24] The primary endpoint was a change in NIH-CPSI score at 6 weeks. The patients received 20 min treatments twice weekly for 6 weeks.

Thirty-two men completed the study. At 6 weeks, the NIH-CPSI total score and pain component score decreased in the EA group compared to the two other groups.[24] In addition, postmassage urine prostaglandin E2 levels decreased significantly only in the EA group. Six acupuncture points were used, targeting the S2 and S3 foramen and also localizing the myofascial trigger point of the piriformis muscle.

Tenderness of skeletal muscle

These treatments target spasms and trigger points in the abdomen and/or pelvis.

Physical therapy

Patients with UCPPS often have myofascial trigger points that reproduce the character and location of their pain when palpated. It is unknown whether these musculoskeletal abnormalities are the consequence of a lower urinary tract disorder or are a primary abnormality that results in lower urinary tract symptoms. In either case, physical therapy is increasingly being incorporated in the care plan of CP/CPPS patients.

A large randomized trial compared myofascial physical therapy (i.e. MPT) to global therapeutic massage (GTM) in 47 patients with UCPPS, including 21 men with CPPS.[25] Overall, a significantly greater percentage of IC/PBS and CP/CPPS patients responded to MPT than to GTM (i.e. 57% *vs.* 21%). Interestingly, men with CP/CPPS responded much more significantly to GTM than predominantly women patients with IC/PBS (i.e. 40% *vs.* 7%).(25) These results suggest that patients with CP/CPPS respond differently to GTM or, alternatively, that men with CP/CPPS may respond in a more positive fashion to GTM provided by female physical therapists.

OnabotulinumtoxinA

Investigators targeted the bulbospongiosus muscle as a trigger point for onaBoNT-A injections in men with CPPS. A total of 29 men were randomized to receive either onaBoNT-A (100U) or normal saline injections into the bulbospongiosus muscle and perineal body.[26] At 1 month follow-up, a significantly greater response in GRA scores were noted in the onaBoNT-A group compared to placebo (30% *vs.* 13%). Although no significant difference in change in total CPSI score was noted between groups, the onaBoNT-A treated group had a greater decrease in CPSI pain subdomain scores compared to placebo ($P = 0.05$). The treatment was well-tolerated.

Sono-electro-magnetic therapy

A single-center, randomized, placebo-controlled, and double-blind study was conducted in 60 men with refractory CPPS evaluating noninvasive sono-electro-magnetic therapy.[27] Patients applied the portable device to their perineum for 10 min twice daily. At 12 weeks, 70% in the active group were considered treatment responders compared to only 30% in the placebo group. However, the investigators used a decrease in NIH-CPSI score of 4 points as a significant change compared to many other studies that used a 6 point decrease as a positive treatment response. They also found that the therapy was more beneficial to patients with shorter symptom duration (i.e. 12 months or less).

CONCLUSION

UCPPS is a common urologic condition afflicting males. Several tools are currently available to help diagnose and direct targeted therapy. Although no gold-standard treatment exists, a multidisciplinary approach with multimodal therapy appears to give patients the best chance of symptom relief.

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Conflicts of interest

There are no conflicts of interest.

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