

Studies Few But Promising at 2010 AUA Meeting

The 2010 American Urological Association's annual meeting brought fewer studies of chronic prostatitis/chronic pelvic pain (CP/CPPS) than in the past. That's because most NIH research funding for CP/CPPS is now going toward long-term studies aimed at uncovering the cause, and it will be some time before we hear about the results. Nevertheless, the 2010 meeting brought news of potential new treatment approaches and an epidemiologic surprise. In one large-scale survey, most men who had CP/CPPS symptoms did not have them five years later. The nine studies summarized here hold promise of better therapy to come for men with CP/CPPS.

EPIDEMIOLOGY

IDENTIFYING CHRONIC PROSTATITIS/ CHRONIC PELVIC PAIN SYNDROME FOR EPIDEMIOLOGIC STUDIES

J. Quentin Clemens, Ann Arbor, MI, Lara Hilton, Marika Suttorp, Sandra Berry, Santa Monica, CA

Researchers have been estimating the prevalence of CP/CPPS based on whether men report they have either perineal or ejaculatory pain and a score of at least 4 on the pain section of the NIH Chronic Prostatitis Symptom Index (CPSI). Is that enough to distinguish men who have chronic prostatitis/chronic pelvic pain (CP/CPPS) from those with benign prostatic hyperplasia (BPH) or healthy men? Yes, concluded these researchers who checked the answers to these questions against real diagnoses in the patients who participated in the development of the NIH CPSI. They calculated the proportion of diagnosed CP/CPPS cases that were correctly identified as having CP/CPPS symptoms (sensitivity), and the fraction of non-CP/CPPS cases that were correctly identified as not having CP/CPPS (specificity). The sensitivity of the question-based definition was 70%. The specificity was 91% when compared with BPH patients, and 99% when compared with controls. These criteria were used to find men with CP/CPPS symptoms the following surprising study.

DESCRIPTIVE EPIDEMIOLOGY OF UROLOGIC PAIN SYMPTOMS IN MEN AND WOMEN

Jessica Brewer, Carol Link, Watertown, MA, Paul Eggers, John Kusek, Bethesda, MD, John McKinlay, Watertown, MA

Could your CP/CPPS be gone in five years? Data from the Boston Area Community Health (BACH) survey show that only about 20% of men who had symptoms suggesting CP/CPPS in the initial survey still had the symptoms nearly five years later. That flies in the face of common wisdom that the conditions don't go away and that they get worse with age. The survey sampled adults aged 30 to 79 years old and included 1,268 men and 2,139 women (with an equal number of black, Hispanic, and white people). In the first BACH survey, 3.9% of men reported symptoms of CP/CPPS, 1.2% symptoms of interstitial cystitis, and 0.9% symptoms of both.

DIAGNOSIS/ASSESSMENT

CLINICAL PHENOTYPING OF PATIENTS WITH CHRONIC PROSTATITIS-CHRONIC PELVIC PAIN SYNDROME IN TWO SPECIALIZED EUROPEAN INSTITUTIONS

Florian Wagenlehner, Giessen, Germany, Vittorio Magri, Milan, Italy, Gianpaolo Perletti, Busto A./Varese, Italy, Sebastian Schneider, Wolfgang Weidner, Giessen, Germany

These researchers applied the UPOINT classification system to 1,219 CP/CPPS patients in Italy and Germany to characterize the population. They found that 65%, 35%, 84%, 10%, 41%, and 62% of patients had symptoms that could be related to the urinary, psychosocial, organ specific, infection, neurologic, and tenderness of skeletal muscle characteristics or “domains,” respectively. The percentages of patients with symptoms of 1, 2, 3, 4, 5, and 6 domains were 11%, 24%, 33%, 22%, 10%, and 0.3%, respectively. Clearly, the patient population is very heterogeneous. Additional phenotypes might be helpful, and how they might be used needs to be evaluated in treatment studies, said these authors. The aim of phenotype-oriented treatment is to improve the outcome by more closely matching the treatments with the underlying causes of the condition in each.

TREATMENT

DUTASTERIDE REDUCES PROSTATITIS SYMPTOMS COMPARED TO PLACEBO IN MEN ENROLLED IN THE REDUCE (REDUCTION BY DUTASTERIDE OF PROSTATE CANCER EVENTS) STUDY

J. Curtis Nickel, Kingston, Canada, Teuvo L.J. Tammela, Tampere, Finland, Claudio Teloken, Porto Alegre, Brazil, Timothy H. Wilson, Ivy L. Fowler, Roger S. Rittmaster, Research Triangle Park, NC

Five-alpha reductase inhibitors (5ARIs) are used to treat benign prostate enlargement (BPH) and reduce prostate cancer risk, but they may also ease CP/CPPS symptoms. Some doctors have used 5ARIs this way “off label,” but now, an analysis of data from the Reduction by Dutasteride of Prostate Cancer Events (REDUCE) trial lends some evidence to that approach. Among the 679 men in the trial with prostatitis-like pain, CPSI scores dropped significantly more for the men taking the 5ARI dutasteride than for those taking placebo, a mean of 5.2 points compared with 2.7. The difference was also significant for the 649 men with prostatitis-like syndrome: those who took dutasteride had their scores improve by 4.2 points compared with 2.8 for those taking placebo. Pain, urinary, and quality of life subscores also showed significant differences. Also, there were significantly more men who had at least 4- and 6-point reductions in their CPSI scores in the dutasteride group than the placebo group. Among the men with prostatitis-like pain who took dutasteride, 63% had a 4-point reduction and 49% had a 6-point reduction, compared with 59% and 37% for men taking placebo. Among the men with prostatitis-like syndrome who took dutasteride, 58% had a 4-point reduction and 46% a 6-point reduction, compared with 47% and

35% of those taking placebo. The study doesn't support 5ARIs as therapy for all men with CP/CPPS, but when men have other reasons to take a 5ARI, the drug may help ease CP/CPPS symptoms.

PHENOTYPICALLY DIRECTED MULTIMODAL THERAPY FOR CHRONIC PROSTATITIS/CHRONIC PELVIC PAIN SYNDROME: A PROSPECTIVE STUDY USING UPOINT

Daniel Shoskes, Cleveland, OH, Robert Dolinga, Cleveland, OH, Curtis Nickel, Kingston, Canada

Researchers who developed a “phenotyping” or classification system for CP/CPPS have now applied it to treatment. Overall, the results were good when men were treated with therapies thought to be appropriate to their phenotype. It wasn't feasible, however, for these researchers to do a placebo-controlled study. Nevertheless, this study was a start at proving the concept. One hundred patients who had had symptoms for an average of two years were offered multimodal therapy based on their positive “domains.” For example, men with urinary symptoms received alpha blockers or antimuscarinics; those with organ-specific (prostate) symptoms got quercetin; those with neurologic symptoms got pregabalin (Lyrica); and those with muscle tenderness got physical therapy. The most common domains were organ specific (70%), tenderness (64%), and urinary (59%). Eighty-four percent of the men had at least a 6-point improvement in their NIH-CPSI scores. That didn't depend on how many domains were positive for the patient or how high the initial NIH-CPSI score was.

CHRONIC PELVIC PAIN IS ASSOCIATED WITH MAST CELL ACTIVATION AND IS AMENABLE TO MAST CELL DIRECTED THERAPIES.

Praveen Thumbikat, Charles Rudick, David Klumpp, Anthony Schaeffer, Chicago, IL

Mast cells, which play roles in allergy, inflammation, and pain, have long been connected with interstitial cystitis (IC). But they may also play a role in CP/CPPS. And if they do, antihistamines might help. Antihistamines are actually a staple of IC therapy, but their effectiveness has been limited. The therapy might be more effective for CP/CPPS and IC if antihistamines were given in the right combinations. That's an avenue researchers from Northwestern University in Chicago are pursuing, based on their experiments in mice with a kind of induced CP/CPPS involving mast cells. These mice show hypersensitivity to touch and pain referred to the abdomen, similar to many CP/CPPS patients. The team also found evidence that a similar process may be at work in men with CP/CPPS, since they have products of mast cell degranulation in their prostatic fluid. The mice with induced prostatitis showed increased numbers and activation of mast cells in the prostate along with more dense nerves and expression of nerve growth factor, thought to play a role in pain. Mice genetically lacking in mast cells did not show any evidence of pelvic pain. A combination of two types of antihistamines plus a mast cell stabilizer reduced pain in mice with the induced prostatitis much more than any of those drugs alone. The combination included the histamine-1 blocker cetirizine (the allergy medicine Zyrtec), the histamine-2 blocker ranitidine (the stomach acid reducer Zantac), and cromolyn sodium (used in Nasalcrom). Each of those reduced pain only about 20 to 30 percent alone, but the combination reduced pain 64 percent, so

the investigators think that, together, these drugs may have a synergistic effect. More research should tell us if some combination of medicines could help men with CP/CPPS.

THE ROLE OF MEPARTRICIN IN CATEGORY III CHRONIC NONBACTERIAL PROSTATITIS/ CHRONIC PELVIC PAIN SYNDROME (CPPS): A RANDOMIZED PROSPECTIVE PLACEBOCONTROLLED TRIAL.

Aldo Franco De Rose, Paolo Traverso, Tommaso Montanaro, Giorgio Carmignani, Genoa, Italy

Mepartricin, an antimicrobial that reduces levels of sex hormones, produced significant improvements in NIH-CPSI, pain, quality-of-life scores in men with CP/CPPS. This drug has been tested in the condition before, but this new study uses a higher dose (80 mg/day) than a previous study (40 mg/day), and showed better responses. This small, placebo-controlled trial included 30 patients, with 15 receiving active treatment and 15 receiving placebo for 60 days. NIH-CPSI scores dropped from an average of 24 to 6 in the active treatment group, compared with 25 to 19 in the placebo group—a 70% improvement compared with an 18% improvement. Pain scores dropped from 12 to 3 in the mepartricin group compared with only 10 to 9 in the placebo group. Quality-of-life scores improved from 10 to 4 in the treatment group, compared with 10 to 9 in the placebo group. Urinary dysfunction, however, was not different. Levels of the hormones LH, FSH, and testosterone were not affected, whereas levels of 17 beta estradiol were significantly lower in the mepartricin group than in the placebo group at the end of the study. This change in estradiol levels may play a role in the improvement, said the authors.

THE EFFICACY OF ANTICHOLINERGICS FOR CHRONIC PROSTATITIS/CHRONIC PELVIC PAIN SYNDROME IN YOUNG AND MIDDLE AGED PATIENTS -SINGLE-BLINDED, PROSPECTIVE, MULTI-CENTER STUDY

Hyung-Jee Kim, Cheonan, Korea, Republic of, Yoon-Su Kyung, Cheonan, Korea, Republic of, Seung Hyo Woo, Daejeon, Korea, Republic of, Doo sang Kim, Cheonan, Korea, Republic of, Young Seop Jang, Daejeon, Republic of Korea

The overactive bladder (“gotta go”) drug solifenacin (Veicare) seems to ease CP/CPPS symptoms, especially urinary symptoms. In this Korean study, 96 young and middle-aged men with CP/CPPS received the antibiotic ciprofloxacin (Cipro) (49 men) or ciprofloxacin and solifenacin (47 men) for two months. The patients filled out symptom questionnaires at the beginning and after one and two months. Those that took both drugs had significant reductions in the NIH-CPSI scores and all its subscores, the total International Prostate Symptom Score, and its urine storage subscore. Scores related to erectile function improved, but not significantly. The researchers said they tried to eliminate confusion of BPH and CPPS by limiting the study to young and middle-aged men. Many middle-aged men, however, have BPH.

SOCIAL ISSUES

CATASTROPHIZING AND SPOUSAL RESPONSES IN MEN SUFFERING FROM CP/CPPS

Dean A. Tripp, Jessica Ginting, J. Curtis Nickel, Kingston, Canada, Kathleen J. Propert, Philadelphia, PA, John Kusek, Chronic Prostatitis Collaborative Research Network, Bethesda, MD

This study found that the association between pain and poor quality of life in 188 men with CP/CPPS was stronger when the men showed higher levels of “catastrophizing,” that is, seeing a negative situation as worse than it is. The study also found that pain and disability were most strongly related when spouses were more solicitous and supportive, such as doing more tasks and work for their partners. But, the authors said, it isn’t clear whether this relationship indicates a reaction to the pain and disability or whether the solicitous support helps create or maintain disability. A questioner from the audience at the meeting pointed out that lack of support from spouses, friends, or family can lead to negative consequences.