A Case-Crossover Study of Urological Chronic Pelvic Pain Syndrome Flare Triggers in the MAPP Research Network

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Purpose: Although many factors have been proposed to trigger symptom exacerbations (flares) in patients with interstitial cystitis/bladder pain syndrome and chronic prostatitis/chronic pelvic pain syndrome, few studies have investigated these factors empirically. Therefore, we embedded a case-crossover study in the Multidisciplinary Approach to the Study of Chronic Pelvic Pain longitudinal study to evaluate a range of patient reported triggers.

Materials and Methods: We assessed exposure to proposed triggers, including diet, physical activities, sedentary behaviors, stress, sexual activities, infection-like symptoms and allergies, by questionnaire a maximum of 3 times when participants reported flares and at 3 randomly selected times. We compared participant preflare to nonflare exposures by conditional logistic regression.

Results: In our full analytical sample of 292 participants only 2 factors, including recent sexual activity (OR 1.44, 95% CI 1.06–1.96) and urinary tract infection

Abbreviations and Acronyms

BFRFQ = Brief Flare Risk Factor Questionnaire

MAPP = Multidisciplinary Approach to the Study of Chronic Pelvic Pain

UCPPS = urological chronic pelvic pain syndrome

UTI = urinary tract infection

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symptoms (OR 3.39, 95% CI 2.02–5.68), which may overlap with those of flares, were associated with flare onset. On subanalyses restricted to flares with specific suspected triggers additional positive associations were observed for some factors such as certain dietary factors, abdominal muscle exercises, and vaginal infection-like symptoms and fever, but not for other factors (eg stress).

Conclusions: Except for sexual activity our findings suggest that patient reported triggers may be individual or group specific, or they may not contribute to flares. These findings suggest caution in following rigid, global flare prevention strategies and support additional research to develop evidence-based strategies.

Key Words: urinary bladder; prostatitis; cystitis, interstitial; symptom flare up; surveys and questionnaires

Interstitial cystitis/bladder pain syndrome and chronic prostatitis/chronic pelvic pain syndrome, collectively referred to as UCPPS, are chronic idiopathic conditions characterized by persistent bladder and/or pelvic pain, and urological symptoms such as urgency and frequency. The 2 conditions are common, ranging in prevalence from 1% to 7%,[1] and difficult to diagnose and treat. They are also burdensome to patients, contributing to decreased physical and mental health, sexual functioning and work participation.[2,3]

One particularly troubling aspect of UCPPS is symptom exacerbations or flares. They vary in manifestation but some can be extremely painful, long-lasting and unpredictable.[4,5] Although numerous factors have been proposed to trigger flares (eg diet and stress[5–13]), few studies have evaluated these factors empirically to determine the influence on patient symptoms.[14–17] These types of studies are important to help patients prevent flares while also minimizing the restrictions that avoiding multiple suspected triggers can impose.[5] Therefore, we embedded a case-crossover study comparing exposures before flares to exposures before times without flares in the same participant[18] in the MAPP Epidemiology and Phenotyping Study to identify factors associated with flare onset.

MATERIALS AND METHODS

Study Population and Design

The MAPP Epidemiology and Phenotyping Study was a 1-year, multisite, longitudinal study designed to characterize the usual care natural history of UCPPS, and identify subgroups with a possible different etiology and clinical course.[19,20] Participants completed an extensive battery of questionnaires at biannual clinic visits and a brief set at biweekly online assessments.[20]

As part of the case-crossover study we asked participants about the current flare status at each clinic and biweekly assessment using the question, "Are you currently experiencing a flare of your urological or pelvic pain symptoms (i.e.) symptoms that are much worse than usual?" If participants responded affirmatively, they were directed to an additional questionnaire, BFRFQ, which inquired about preflare exposures (supplementary Appendix 1, http://jurology.com/).[20] We administered this questionnaire a maximum of 3 times when participants reported a flare and at 3 randomly selected assessments without a flare (1 per 4-month period). We did not administer BFRFQ at baseline because this visit was deemed too lengthy for an additional questionnaire.

This study was approved by the institutional review board at each site. All participants provided written informed consent.

Flare Trigger Assessment

On BFRFQ participants were asked about exposures in the 3 days (diet, physical activities, sedentary behaviors and stress) or the week (sexual activities, and infection and allergy symptoms) before the flare as the flare assessment or the date of questionnaire completion as the nonflare assessment.[20] Participants were also asked about the flare onset date, symptom intensity and beliefs about current flare triggers in prespecified categories to 1) identify new flares in the last 2 weeks, 2) inform the quality of recalled preflare information, 3) categorize flares by duration and pain intensity since they might have differing etiologies and 4) explore the possibility of recall bias as participant responses might be influenced by knowledge of flare status and trigger beliefs.

Possible triggers were selected based on the published literature,[6–10,14–16,21] the ICA (Interstitial Cystitis Association) website and clinical expert opinion. Questionnaire items were based on the Harvard 131-item food frequency questionnaire,[22] IPAQ (International Physical Activity questionnaire),[23] occupational sitting questions,[24] PSS-4 (Perceived Stress Scale-4),[25] and clinical and epidemiological expertise. We selected a 3-day/1-week exposure period based on clinical expertise and chose a lengthier period for sexual activities and infections because we suspected that these factors might take longer to trigger a flare.

Statistical Analyses

Only participants with at least 1 flare and 1 nonflare assessment were included in analyses to allow for within person comparisons. We used descriptive statistics and generalized estimating equations to describe participant flare experiences and changes in symptoms during flares. We used conditional logistic regression to calculate matched ORs, 95% CIs and p values for interaction on stratified analyses. We explored each possible trigger by the presence of any exposure (any vs none), as a trend for an increasing level of exposure (ordinal) and as individual levels