Diagnosis and treatment of chronic prostatitis/chronic pelvic pain syndrome

JONATHAN REES AND ANDREW DOBLE

Chronic prostatitis is a poorly understood and difficult-to-treat condition. The authors discuss a guideline produced by the Prostatitis Expert Reference Group (PERG), which provides a framework for initial assessment and effective management in the community. Roger Kirby and Culley Carson comment from a secondary-care perspective on page 17.

Chronic prostatitis (CP) is a common condition with a huge impact on the quality of life of many men. Based on a population of more than 10,600 participants, a systematic review found a population-based prevalence of prostatitis symptoms of 8.2% (range 2.2–9.7%). However, the condition is poorly understood, underdiagnosed and difficult to treat. As a result, there is a lack of good evidence and guidance, for primary care in particular, on how to recognise the condition and carry out effective management in the community.

GUIDELINE DEVELOPMENT
The Prostatitis Expert Reference Group (PERG) was convened in 2013 by the charity Prostate Cancer UK, to undertake a review of the literature and produce a guideline suitable particularly for non-specialist use. Members of PERG were selected from a network of clinical experts in the urology field across a broad range of disciplines, including primary care, urology (medical and specialist nursing), pain, physiotherapy and psychology, from across England. In addition, PERG included a technical team of representatives from Prostate Cancer UK and Hayward Medical Communications, who had a background in communication, policy development and evidence research.

The guideline covers only symptomatic, chronic forms of prostatitis; thus, the patient populations under the National Institutes of Health (NIH) classification categories I (acute bacterial prostatitis) and IV (asymptomatic inflammatory prostatitis) were not considered during guideline development. Due to the limited number of published randomised controlled trials (RCTs) in CP/chronic pelvic pain syndrome (CPPS), the PERG concluded that the guidelines would benefit from a supporting web-based Delphi consensus panel. This is an anonymous group technique, delivered via the online Survey Monkey platform, designed to gather individual opinions from experts in areas where high quality, published evidence is currently lacking, and transform these into a group consensus.

Most men with CP do not have an ongoing infection, and only a small minority can be categorised as having chronic bacterial

Box 1. Symptom-scoring questionnaires for the clinical assessment of chronic bacterial prostatitis and chronic prostatitis/chronic pelvic pain syndrome

- NIH-Chronic Prostatitis Symptom Index (CPSI) – a nine-item questionnaire with a total score of 0–43, measuring:
  - pain (four questions evaluating pain location, frequency and severity, 0–21)
  - voiding (two questions evaluating voiding and storage symptoms, 0–10)
  - impact on quality of life (three questions, 0–12)
- International Prostate Symptom Score (IPSS) – an eight-item questionnaire, measuring urinary symptoms and impact on quality of life
- International Index of Erectile Function (IIEF-5) or Sexual Health Inventory for Men (SHIM) – a five-item questionnaire for the screening and diagnosis of erectile dysfunction
- Patient Health Questionnaire-9 (PHQ-9) and Generalised Anxiety Disorder-7 (GAD-7) – questionnaires to assess the frequency of depressed mood and anxiety

VIDEO AND BLOG
This article on chronic prostatitis is complemented by both a short video and a blog on the Trends website. Do you agree with the guideline? Have your say at: www.trendsmenshealth.com

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prostatitis (CBP), based on positive midstream urine or sexually transmitted infection screen. The majority can be classified as NIH classification III, i.e CP/CPPS. While some of the symptoms experienced by men with CP/CPPS do originate from the prostate, it is increasingly understood that many do not, and are generated by other structures within the pelvis, or by neuropathic mechanisms within the sensory nervous system. It is for this reason that the term CPPS is used, to emphasise that the prostate may not be to blame and that a more holistic approach to managing patients with these symptoms is required.

PRESENTATION
CP/CPPS typically presents with a range of symptoms, which can be broadly grouped into four categories:
- **Urogenital pain:** typically pain is felt in the perineum, but can also be in the lower abdomen, groins, low back, testes, tip of the penis, etc. Pain is often neuropathic in nature – it is suggested that pain may start with an original episode of infection or inflammation, but continues after resolution of this initial insult due to pain sensitisation.
- **Urinary symptoms:** CP/CPPS is often associated with lower urinary tract symptoms – voiding (e.g. hesitancy and weak stream), storage (e.g. urgency and frequency), and sometimes dysuria or urethral burning independent of micturition.
- **Sexual dysfunction:** erectile dysfunction (ED), ejaculatory dysfunction (particularly ejaculatory pain or discomfort) and loss of libido are common.
- **Psychosocial symptoms:** anxiety and depression frequently affect these men, with cognitive and behavioural consequences severely impacting on quality of life.

ASSESSMENT
To aid with the clinical assessment of CBP and CP/CPPS, both in terms of initial evaluation and during therapeutic monitoring, a validated symptom-scoring instrument may be used (Box 1).

The Urinary, Psychosocial, Organ-specific, Infection, Neurological/systemic and

<table>
<thead>
<tr>
<th>Examinations and investigations</th>
<th>Setting</th>
<th>Specialist</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-specialist</td>
<td>Specialist</td>
<td>Core</td>
</tr>
<tr>
<td><strong>Physical examinations</strong></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Digital rectal examination</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>- including assessment of external genitalia and pelvic floor muscle dysfunction</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Abdomen</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>- to exclude other causes of abdominal pain</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Urine dipstick and/or MSU for culture/microscopy</strong></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Four-glass or two-glass test</strong></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Voided bladder 1</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>- represents the urethra</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Voided bladder 2</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>- represents the bladder</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Expressed prostatic secretions</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>- represents the prostate</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Voided bladder 3</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>- represents the prostate</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Tests to rule out differential diagnoses</strong></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>PSA testing to exclude prostate cancer</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>STI screen (e.g. via NAATs)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Uroflowmetry, retrograde urethrogram or cystoscopy (to exclude BOO, urethral stricture or bladder neck stenosis)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Prostate biopsy (only if prostate cancer is suspected on basis of PSA and/or DRE results)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Transrectal ultrasound (only in refractory patients in whom a prostatic abscess or other pathology is suspected)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Diagnostic cystoscopy if bladder cancer is suspected</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Urethral swab and culture if urethritis is suspected</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>MRI if prostatic abscess is suspected</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

MSU, midstream urine; STI, sexually transmitted infection; NAATs, nucleic acid amplification tests; BOO, bladder outlet obstruction; DRE, digital rectal examination; MRI, magnetic resonance imaging.

Table 1. Summary of physical examinations and investigations to consider during the clinical assessment of chronic bacterial prostatitis and chronic prostatitis/chronic pelvic pain syndrome.
LUTS, lower urinary tract symptoms; NSAIDs, non-steroidal anti-inflammatory drugs; PHQ-9, Patient Health Questionnaire-9; GAD-7, Generalised Anxiety Disorder-7; MDT, multidisciplinary team; BSSM, British Society for Sexual Medicine.

Figure 1. Treatment algorithm for patients with chronic bacterial prostatitis and chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS)²
Tenderness (UPOINT) scale, a more recently devised tool, aims to stratify patients into specific symptom-led phenotypes; the clinical domains assessed are urinary symptoms, psychosocial dysfunction, organ-specific findings, infection, neurological/systemic routes, and tenderness of muscles. The UPOINT scale may be used particularly by clinicians with an interest in CP/CPPS or in a research setting. Its value is to provide a symptom-directed focus to treatment and it has demonstrated the value of multimodal therapy.

The investigations and physical examinations that should be considered during clinical assessment, including whether they are considered as a core or optional part of the assessment and in which setting they are typically completed (eg non-specialist versus specialist), are summarised in Table 1 (page 13).

**DIAGNOSIS**
To establish a diagnosis of CBP or CP/CPPS, the patient should, by definition, have a history of persistent or recurrent symptoms, and the absence of other urogenital pathology (eg active urethritis, urogenital cancer, urinary tract disease), for a minimum of 3 out of the past 6 months. However, some men have fluctuating symptoms and, in practice, the diagnosis is often suspected after a shorter duration of symptoms.

A definitive diagnosis of CBP relies on the presence of (typically recurrent) urinary tract infection and isolation of an aetiologically recognised organism from prostatic fluid or urine. However, in many cases, patients respond to antibiotic intervention in the absence of a confirmed infection – in such cases, a CBP diagnosis can be suspected but is not certain, since the response may be due to the anti-inflammatory or antineuropathic effect of the antimicrobial agent. There is no gold standard for a definitive diagnosis of CP/CPPS; instead, it is typically based on a patient history, symptoms and the exclusion of other causes (eg non-demonstrable infection and other urogenital pathology).

**TREATMENT STRATEGIES**
PERG undertook a review of the literature for all treatments for CBP and CP/CPPS. There are many areas where the evidence base is weak, and the Delphi consensus process was used to try to ascertain expert opinion. The guideline recommends an initial course of an antibiotic for all patients, with simple analgesia/anti-inflammatories, but at an early stage recommends a symptom-based approach to treatment (Figure 1). Where neuropathic pain is suspected, early use of antineuropathic agents such as tricyclic antidepressants or gabapentin should be considered (Table 2).

**REFERRAL**
Early referral to specialist services is suggested for men with severe symptoms or where there is diagnostic uncertainty. This may be to a urologist with an interest in CP/CPPS, a pain physician or sexual health clinic, depending on local expertise in this condition.

When a patient’s pain is severe and refractory to initial treatment, or when the pain is significantly impairing the patient’s lifestyle and ability to participate in daily activities, it is worth referring him to a specialist pain service. Specialist treatments provided may include:

<table>
<thead>
<tr>
<th>Analgesic class</th>
<th>Drug name</th>
<th>Starting dose</th>
<th>Maintenance dose</th>
<th>Common adverse effects</th>
<th>PERG practical points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gabapentinoids</td>
<td>Gabapentin</td>
<td>100–300mg at night</td>
<td>600mg three times daily</td>
<td>Dizziness, sedation, dyspepsia, dry mouth, ataxia, peripheral oedema, weight gain</td>
<td>Few drug interactions. Safe in overdose. Gut transport mechanism can become saturated, limiting absorption from gastrointestinal tract</td>
</tr>
<tr>
<td>Perisaline</td>
<td>Pregabalin</td>
<td>50–75mg at night</td>
<td>300mg twice daily</td>
<td>Dizziness, sedation, dyspepsia, dry mouth, ataxia, peripheral oedema, weight gain</td>
<td>Linear pharmacokinetics</td>
</tr>
<tr>
<td>Tricyclic antidepressants/serotonin-norepinephrine reuptake inhibitors</td>
<td>Amitriptyline</td>
<td>10mg in evening</td>
<td>50–75mg in evening</td>
<td>Sedation, dry mouth, blurred vision, urinary retention, constipation, postural hypotension, weight gain</td>
<td>Many patients obtain pain relief at lower dose</td>
</tr>
<tr>
<td></td>
<td>Duloxetine</td>
<td>30mg in evening (or in morning, if insomnia)</td>
<td>60–120mg once daily</td>
<td>Nausea, sedation, insomnia, headache, dizziness, dry mouth, constipation</td>
<td>Less sedating. May cause insomnia in some patients</td>
</tr>
</tbody>
</table>

*Table 2. Antineuropathic treatment options (based on information from the British National Formulary and PERG expert consensus)*
Patients with chronic bacterial prostatitis (CBP) or chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) should be managed according to their individual symptom pattern – no single management pathway is suitable for all patients with these conditions.

Most patients with CP/CPPS do not have an infection, and repeated use of antibiotics such as quinolones should be avoided where no obvious benefit from infection control is evident or cultures do not support an infective aetiology.

Early use of antineuropathic pain medication should be considered for all CBP and CP/CPPS patients refractory to initial treatments. If neuropathic pain is suspected, ensure a quick referral to the multidisciplinary team (MDT), which includes pain specialists.

Early referral to specialist services should be considered when patients fail to respond to initial measures. Referral should ideally be to a clinician with an interest in the management of CBP and/or CP/CPPS, but not necessarily a urologist.

An MDT approach should be implemented and made available to CBP and CP/CPPS patients. The MDT should include urologists, pain specialists, nurse specialists, specialist physiotherapists, GPs, cognitive behavioural therapists/psychologists and sexual health specialists.

Patients should be fully informed about the possible underlying causes and treatment options of CBP and CP/CPPS. The MDT responsible for the management of these patient groups should be able to explain the chronic pain cycle and other relevant information to improve patient understanding of the conditions.

CONCLUSION

Treatment of CP is difficult, but not impossible. When the condition is suspected, it is vital that time is spent discussing the diagnosis with the patient and understanding his individual symptom patterns and concerns, as this will be important in targeting appropriate therapies. The PERG guideline provides a framework for initial assessment and management in a non-specialist setting. Box 2 illustrates the priorities identified by the group for implementation in clinical practice.

Declaration of interests: none declared.

REFERENCES


Editors’ comment

ROGER KIRBY AND CULLEY C. CARSON

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John Rees and Andrew Doble are to be congratulated on producing an excellent report. Prostatitis is a very common affliction of younger and middle-aged men. In the USA, prostatitis is diagnosed in 8% of all visits to a urologist and 1% of all primary care physician visits. The term prostatitis refers, in its strictest sense, to histological inflammation of the tissue of the prostate gland. Like all forms of inflammation, it can be associated with an appropriate response of the body to an infection, but it very frequently occurs in the absence of infection.

The cause of this sometimes very bothersome disorder is still mysterious. Many years ago Roger Kirby performed a small study when a junior doctor at St Thomas’s Hospital. We proved by using instillations of Indian ink into the bladder that voided urine was capable of refluxing backwards into the prostatic ducts. We postulated at that stage that this phenomenon might initiate a chronic inflammatory process within the prostate.

Much more recently we reported a case of a family practitioner whose chronic prostatitis responded dramatically to treatment with a phosphodiesterase type 5 (PDE5) inhibitor. The longer acting PDE5 inhibitor tadalafil has been proven in randomised controlled trials to be effective in the treatment of erectile dysfunction. In addition, it has been shown to have a beneficial impact on LUTS in men with BPH, who also often suffer from concomitant difficulties with erections. Recently a meta-analysis of 17 trials has confirmed that tadalafil also significantly improves ejaculatory function.

In addition to the symptom of pelvic pain, men with chronic abacterial prostatitis/prostatodynia also frequently complain of associated LUTS and ejaculatory discomfort. Consequently treatment with tadalafil at a dose of 5mg/day for a period of time seems logical. It could be surmised that many of its beneficial effects might stem from an improvement of blood flow to pelvic organs as a consequence of its anti-inflammatory and vasodilatory activity, as well as a relaxant effect on smooth muscle, as has been previously suggested in the case of LUTS by Andersson et al.

Clearly a randomised controlled trial will be required to test this hypothesis, but in the absence of a proven infection, a trial of PDE5 inhibitor treatment would seem considerably more logical than prolonged antibiotic treatment, which is only likely to increase the risks of antibiotic resistance.

REFERENCES


