Male Chronic pelvic pain syndrome

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What patient groups are included in this topic?

- Prostatitis?
- Patients with perineal pain?
- Patients with LUTS?
- Patients with pain upon ejaculation?
- Patients with persistent discomfort in perineal region?
- Patients with guilty feelings?
How common is the condition?

- 8% of all visits to urologists and 1% of all primary care physicians annually in USA
- Population based prevalence of prostatitis symptoms 8.2% (2.2-9.7%)
  - If validated National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) used:
    - Nigeria: 12.2%
    - Malaysia: 8.0%
    - Canada: 6.6%
    - Singapore: 2.7%
National Institutes of Health classification (1999)

I. Acute bacterial prostatitis

II. Chronic bacterial prostatitis (≈5-15%)

III. Chronic pelvic pain syndrome (CPPS)
   A. Inflammatory CPPS
   B. Non-inflammatory CPPS

IV. Asymptomatic inflammatory prostatitis
Stamey’s four glass test

Figure 1. The Meares–Stamey 4-Glass Urine Test.
In the Meares–Stamey 4-glass test, the initial 10 ml of the urinary stream, depicted as voided bladder 1 (VB1), represents the urethral specimen. A midstream specimen obtained from the bladder is depicted as voided bladder 2 (VB2). Prostatic massage is performed with gentle digital pressure moving from the lateral margin of the superior portion of a selected lobe of the prostate toward the apex, for approximately 1 minute (longer massage may inhibit the fluid outflow). Several drops of expressed prostatic secretion (EPS) should emerge from the urethra within 2 to 3 minutes after the massage is completed. The EPS and the first 10 ml of urine after prostatic massage, depicted as voided bladder 1 (VB1), represent the microbiologic environment of the prostate. In the 2-glass test, only steps VB2 and VB3 are used, but the test still offers a reasonably accurate method of screening for prostatitis. Information used in this figure is from Nickel.42
Diagnosis

• No “gold standard” diagnostic test
• Pain – perceived in perineum, suprapubic area, penis testes, groin or even lower back
• Absence of other lower urinary tract pathology
  – Urinary tract infection
  – Urogenital cancer
  – Urethral stricture
  – Neurogenic bladder
• Minimum of 3 out of the past 6 months
Other associations

• Lower urinary tract symptoms
• Sexual function
  – Pain upon ejaculation
  – Erectile dysfunction
• Psychological
• Social factors
Investigation

- Urethral swab, urine culture and Stamey’s 4-glass test
- Uroflowmetry
- PSA in selected patients with LUTS
- NIH-CPSI

✗ Semen Culture
✗ Prostate imaging
✗ Cystoscopy without hematuria
Etiology

• No single aetiological explanation

• Infection
  – E Coli, Enterococcus
  – Altered prostatic host defense

• Pelvic floor muscle abnormalities

• Genetic, anatomical, neuromuscular, endocrine

• Psychological mechanisms
Symptom assessment

• NIH Chronic prostatitis collaborative research network

• Three important domains
  – Pain
  – Urinary function
  – Quality of Life or impact
### NIH-Chronic Prostatitis Symptom Index (NIH-CPSI)

**Pain or Discomfort**

1. In the last week, have you experienced any pain or discomfort in the following areas?
   - a. Area between rectum and testicles (perineum)  
   - b. Testicles  
   - c. Tip of the penis (not related to urination)  
   - d. Below your waist, in your pubic or bladder area

   Yes No

   1 0 0

2. In the last week, have you experienced:
   - a. Pain or burning during urination?  
   - b. Pain or discomfort during or after sexual climax (ejaculation)?

   Yes No

   1 0 0

3. How often have you had pain or discomfort in any of these areas over the last week?
   - 0 Never  
   - 1 Rarely  
   - 2 Sometimes  
   - 3 Often  
   - 4 Usually  
   - 5 Always

4. Which number best describes your AVERAGE pain or discomfort on the days that you had it, over the last week?
   - 0 1 2 3 4 5 6 7 8 9 10
   - NO PAIN AS BAD AS YOU CAN IMAGINE

5. How often have you had a sensation of not emptying your bladder completely after you finished urinating, over the last week?
   - 0 Not at all  
   - 1 Less than 1 time in 5  
   - 2 Less than half the time  
   - 3 About half the time  
   - 4 More than half the time  
   - 5 Almost always

6. How often have you had to urinate again less than two hours after you finished urinating, over the last week?
   - 0 Not at all  
   - 1 Less than 1 time in 5  
   - 2 Less than half the time  
   - 3 About half the time  
   - 4 More than half the time  
   - 5 Almost always

**Impact of Symptoms**

7. How much have your symptoms kept you from doing the kinds of things you would usually do, over the last week?
   - 0 None  
   - 1 Only a little  
   - 2 Some  
   - 3 A lot

8. How much did you think about your symptoms, over the last week?
   - 0 None  
   - 1 Only a little  
   - 2 Some  
   - 3 A lot

**Quality of Life**

9. If you were to spend the rest of your life with your symptoms just the way they have been during the last week, how would you feel about that?
   - 0 Delighted  
   - 1 Pleased  
   - 2 Mostly satisfied  
   - 3 Mixed (about equally satisfied and dissatisfied)  
   - 4 Mostly dissatisfied  
   - 5 Unhappy  
   - 6 Terrible

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**Scoring the NIH-Chronic Prostatitis Symptom Index Domains**

- **Pain:** Total of items 1a, 1b, 1c, 1d, 2a, 2b, 3, and 4 =
- **Urinary Symptoms:** Total of items 5 and 6 =
- **Quality of Life Impact:** Total of items 7, 8, and 9 =
Treatment

• Expectation of treatment outcome

• Review of previous treatment history

• Multi-modality treatment

• A long journey
Treatment options

- Antibiotics
- Alpha-blockers
- NSAIDs
1. Antibiotics

- Fluoroquinolones / co-trimoxazole
- 4-6 weeks for chronic bacterial prostatitis

Role for CPPS
- ?placebo effect
- ?Eradication or suppression of noncultured microorganisms
- ?Independent anti-inflammatory effects in some antibiotics
• Systemic review and network meta-analysis (Anothaisintawee, JAMA 2011)

  – Total symptom scores (-9.8; 95% CI, -15.1 to -4.6)
  – Pain scores (-4.4; 95% CI, -7.0 to -1.9) (total: 21)
  – Voiding scores (-2.8; 95% CI, -4.1 to -1.6) (total: 10)
  – QOL scores (-1.9; 95% CI, -3.6 to -0.2) (total: 12)
• Antibiotics may be considered for antibiotics naïve patients with recent diagnosis of CP / CPPS, regardless of culture results
• Avoid for previously treatment with CPPS of long duration
• Leukocytes and culture results do not predict treatment outcome
2. Alpha blockers

- Associated with lower urinary tract symptoms
- May be related to poor relaxation of bladder neck
- May diminish intraprostatic ductal reflux
Efficacy

• Improvement only in men with recent onset disease and on therapy more than 6 weeks

• Class effect

• Beneficial effect may wean off next 6 months after discontinuation
  – Total symptom scores (-1.7; 95% CI, -2.3 to -0.5)
  – Pain scores (-1.1; 95% CI, -1.8 to -0.3) (total: 21)
  – Voiding scores (-1.4; 95% CI, -2.3 to -0.5) (total: 10)
  – QOL scores (-1.0; 95% CI, -1.8 to -0.2) (total: 12)
Combination with alpha-blockers and antibiotics

- Total symptom scores (-13.8; 95% CI, -17.5 to -10.2)
- Pain scores (-5.7; 95% CI, -7.8 to -3.6) (total: 21)
- Voiding scores (-3.7; 95% CI, -5.2 to -2.1) (total: 10)
- QOL scores (-2.8; 95% CI, -4.7 to -0.9) (total: 12)
3. NSAID

- Decrease prostatic inflammation
  - Leukocytes in prostatic secretion / semen
  - Elevated cytokine in semen
- Early studies showed improvement in dysuria, strangury and painful ejaculation (Canale, 1993)
• Only two RCTs: Rofecoxib (out of market) and celecoxib (Zhao Braz J Med Bio Res)
  – Total score: -3.4
  – **Pain and QOL improvement**; not urinary subscore
  – Loss of benefit after stopping the drugs for 2 weks

• Meta-analysis pooled the results of these two RCTS
  – Anti-inflammatory drugs were 80% more likely to have a favourable response than placebo
Recommendation of other agents in EAU guideline

• Opioids
  – Modest pain relief in some refractory condition
  – Risk of addiction, side effects, reduced QOL

• 5-alpha reductase inhibitors
  – No studies powered to show the benefit

• Allopurinol
  – No benefit noted in RCT / Cochrane library review

• Muscle relaxants
  – Studies poorly documented the response
  – Use in combination with alpha blockers / antibiotics
If these agents do not work...

- Phytotherapy
- Pentosan polysulphate
- Extracorporeal shock wave therapy
- Posterior tibial nerve stimulation
- Psychological treatment
Phytotherapy

• **Pollen Extracts**
  – Prostat/Poltit (Elist, 2006)
  – Cernilton (Wagenlehner, 2009)
  – Reduction in inflammatory markers in rats

• **Quercetin** (Bioflavonoid) (Shoskes, 1999)
  – Antioxidant
  – tyrosine kinase inhibitor
  – anti-inflammatory
• Pain score improvement: 2-3
• Voiding score improvement: 0.8-1.5

• Minimal side effects
  – Headache
  – Tingling of the extremities
  – Reversible
Pentosan polysulphate

• A drug used in interstitial cystitis in female

• Usual dose in interstitial cystitis: 300mg daily

• Acted as a protective barrier in the urinary tract
• RCT with 16 week 900mg PPS vs placebo (Nickel, J Urol 2005)

• Improvement in
  – clinical global improvement ~19%
  – NIH-CPSI ~10% (but p =0.068)

• Diarrhoea / nausea /headache
• One patient (1 out of 50) has impaired liver function
Extracorporeal shock wave therapy

• Low intensity shockwave using a perineal approach without anesthesia
  – Duolith SD1, Storz Medical
  – Weekly treatment
  – 3000 pulses, maximum total energy flow density: 0.25mJ/mm², for 4 weeks
  – Electromagnetic shock wave
  – Penetration: 35-65mm
• Proposed mechanisms
  – Interrupting the flow of nerve impulses by hyperstimulation of nociceptors
  – Healing of tissue by revascularization processes
  – Reduction of muscle tone and spasticity

(Vahdatpour, IRSN Urology, 2013)
RCT from Zimmermann (Eur Uro 2009)

- **Pain**
  - VAS: 33% in 1 week and 50% after 4-12 week
- **NIH-CPSI**: - 17% in 12 week
- **Erectile Dysfunction**
  - IIEF: 5.3% in 1 week and 10.5% in 12 week
- **Voiding condition**
  - IPSS: 15% in 1 week and 25% in 12 week

- No side effects (perineal pain / voiding problem)
- Short term data available
Percutaneous tibial nerve stimulation

- Neuromodulation

- 26G stainless steel needles inserted 5cm cephalad and from the medial malleolus and posterior to the edge of the tibia

- Pulse rate 20Hz

- 12 weeks, 30 min each
Fig. 2. Comparison of the groups for NIH-CPSI.

Fig. 3. Comparison of the groups for VAS for pain.

Kabay, Urol Int 2009
• Effective in short term
• Improved urgency
• Avoid implanting electrode
• Minimal side effects
• ?Maintenance therapy

Fig. 4. Comparison of the groups for VAS for urgency.

Kabay, Urol Int 2009
Psychological treatment

- Psychological status is also targeted as
- As many as 78% of patients reporting depression and 60% having met criteria for a major depressive disorder
- Greater depression and not having a partner for support were associated with poorer CPPS outcome
• A feasibility study for 8 session self-management program
  – Provider workbook: patient tasks and agenda topic
  – Urology nurse/ equivalent health care worker: leading the one-hour weekly session
  – Manage patient burden or confusion
  – Starting the value of the cognitive and behavioural approach used in the program
  – Practice positive communication
  – Revise risk factors modifications
• Improvement in NIH-CPSI score 7.25
  – Pain domain 3.38 points
  – QOL impacy domain
  – NOT in urinary domain

• Risk factor reduction esp. reduction in catastrophizing were most associated with score improvement
Take home messages

- CPPS in male is a common problem and has multi-factorial causes
- NIH-CPSI as a useful tool to measure the pain, urinary and QOL / impact domains
- Antibiotics and alpha blockers are effective treatments but mainly for patients with short duration of disease and are treatment naïve
- Phytotherapy, pentosan polysulphate, extracorporeal shock wave therapy, posterior tibial nerve stimulation and psychological treatment can be helpful in CPPS management in different domains