Management of (some) nociceptive pains

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Nociceptive pain

“Nociceptive pain - pain commensurate with tissue damage associated with an identifiable somatic or visceral lesion”

Cherry 2015 Oxford Textbook Palliative Medicine

<table>
<thead>
<tr>
<th>Nociceptive Pain</th>
<th>Somatic Pain</th>
<th>Visceral Pain</th>
<th>Neuropathic Pain</th>
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</thead>
<tbody>
<tr>
<td><strong>Somatic Pain</strong></td>
<td>Arises from the musculoskeletal system</td>
<td>Arises from the visceral organs such as the gastrointestinal tract and pancreas</td>
<td>Injury to the central or peripheral nervous system</td>
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<td></td>
<td>Achy, dull, throbbing, sore</td>
<td>Gnawing, squeezing, cramping</td>
<td>Shooting, burning, electriclike sensation, tingling, stabbing</td>
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<td></td>
<td>Localized</td>
<td>Can be diffuse and poorly localized; often referred pain to distant sites</td>
<td>Can follow a nerve path or be poorly diffuse</td>
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<td></td>
<td>Example: fracture, postoperative, infection</td>
<td>Example: pancreatitis</td>
<td>Example: phantom limb pain, complex regional pain syndrome</td>
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</tbody>
</table>

Nociceptive pains

• Tenesmus
• Bladder Spasm
• Oesophageal Spasm
Tenesmus

“the painful sensation of incomplete evacuation of the bowel, resulting in the sensation of needing to defaecate many times daily”

Prevalence – up to 14% in rectal cancer  Rao Cancer 1978

Very distressing symptom
Severely affects QOL

Esnaola  J Clin Oncol 2002
Tenesmus

- Most common cause is rectal cancer
- Any pelvic malignancy
- IBD
- Pelvic radiotherapy
- Faecal impaction
- Anal fissure
Pain and Tenesmus

- Neuropathic pain from tumour invasion of lumbosacral plexus
- Inflammation causing pain through somatic afferents
- Smooth muscle contraction causing pain though autonomic afferents
Management of Tenesmus

Treat underlying disease
- Constipation
- Haemorrhoids
- Anal fissure
- IBD
- Anticancer therapies
  - But RT can cause tenesmus

Beard 1997 J Clin Onc
Treatment of tenesmus - Symptomatic treatments

Calcium Channel blockers
• Diltiazem 30mg qds (2 patients)  
  Stowers 2014
• Nifedipine 10-20mg bd (3/4 patients)  
  McLoughlin 1997

Nitrates
• GTN ointment 0.2-0.4% bd in anal fissure  
  Nelson 2012 Cochrane
Systematic review of treatments for tenesmus - Pharmacological treatments

Neuropathic agents

• Methadone 2.5 mg tds (4 patients)  Sanchez Posada 2004
• Mexiletine hydrochloride 50mg tds (5 patients)  Yoshino 2012

Local Anaesthetics

• Bupivacaine intrathecally (1 patient) and rectally (1 patient)  Zaporowska-Stachowiak 2014
Treatments for tenesmus

No evidence found for;

• Opioids (except methadone)  
  Hanks 1991 Br Med Bull

or

• Benzodiazepines  
  Hunt 1991 Pall Med

• Phenothiazines
• Baclofen
Systematic review of treatments for tenesmus – interventional treatments

• Lumbar sympathectomy (10 out of 12 patients)  
  Bristow 1988

• Superior hypogastric plexus block (3 patients)  
  Turker 2005

• Endoscopic laser therapy using ND-YAG laser (ELT)  
  (21 out of 26)  
  Gevers 2000  
  (4 out of 8)  
  Bown 1986
Management of tenesmus - Conclusion

• Treat/exclude underlying disease
• Strongest evidence for endoscopic laser therapy using YAG
• Weak evidence for;
  • Ca channel blockers
  • Neuropathic agents – methadone/mexilitine
• Lumbar sympathectomy
Aetiology of bladder spasms

• Inappropriate detrusor contractility
  • UTI
  • Pelvic malignancy
  • Urinary catheter
  • Radiation
  • Stones
  • Caffeine

• Obstructed bladder outflow

• Neurological problems
Efferent pathways

Spinal Cord

Inferior mesenteric ganglion

Hypogastric nerve
(sympathetic)

Pelvic ganglion
(parasympathetic)

Pelvic nerve

Pudendal nerve
(somatic)

Bladder

NE(-) β₂-AR, β₃-AR

Ach(+) M₃, M₂

ATP P₂X₁

NE(+) α₁-AR

NO(-) ↑cGMP

EUS

Ach(+) Nicotinic
Management of Bladder Spasms

• Encourage fluids
• Treat constipation
• Review drugs and caffeine intake
• Exclude UTI
• Exclude urinary retention
Management of Bladder Spasms - Indwelling urinary catheters

• Ensure tip of catheter is not against bladder wall
• Ensure drainage is free with no blockage or airlocks
• Consider upsizing catheter to improve drainage
• Secure catheter well to prevent pulling
Pharmacological management of bladder spasm – antimuscarinic drugs

• Oxybutinin, Tolterodine, Solifenacin, Darifenacin
  Athanasopoulos 2011 Adv Urol

• Similar efficacy, vary in tolerability

• Solifenacin reduced frequency but not severity of bladder spasms
  Peng 2017 Am J Mens Health

• Dry mouth, eyes, constipation, sedation, delirium
Pharmacological management of bladder spasm – antimuscarinic drugs

• TCAs eg amitriptyline 10mg nocte
• Hyoscine butylbromide 20mg SC/CSCI
• Hyoscine hydrobromide
Pharmacological management - Beta 3 adrenoceptor agonist

Mirabegron 25-50mg daily
- Superior to control in 3 RCTs
  
- Primary endpoints were incontinence episodes but lower severity of urgency and bother scores
- Systematic review showed similar efficacy to antimuscarinics
  
  Maman 2014 Europ Urol
- But – better tolerated than antimuscarinics
  
  Yeowell 2018 BMJ
- NICE recommend second line after antimuscarinics
Pharmacological management of bladder spasm

- **Opioids**
  - Epidural morphine
  - Intravesical opioids

  Chiang 2005 J Paed Child Health
  Olswang et al 1984 Pain
  Duckett et al 1997 Urol; McCoubrie et al 2003 JPSM

- **Intravesical Bupivacaine, Baclofen and Oxycodone**

  Wallace et al 2013 J Pall Care
Pharmacological management - Botox

• Botulinum toxin A
• More effective than placebo in 4 RCTs
• Similar in efficacy to anticholinergics
• Effect takes 3-4 days and wears off after 6-9 months
• Increased risk of urinary retention and UTIs but risk reduced by reduced dose of Botox

Olivera et al 2016 AJOG
Other treatments

• Percutaneous posterior tibial nerve stimulation
  • NICE – recommended after MDT review in women with OAB 2019
• TENS
• Acupuncture
• Sacral nerve stimulation
Conclusion – management of bladder spasm

• Sort out reversible causes
• Weak evidence in bladder spasm
• M/R Oxybutinin
• Consider newer antimuscarinic
• Intravesical opioids
• Role for mirabegron and Botox
Oesophageal spasm
Chest pain and/or dysphagia

Diffuse oesophageal spasm

Hypertensive peristalsis
(Nutcracker oesophagus)
Oesophageal spasm

• (Exclude cardiac pain)
• Gastric reflux
• Primary nerve/motor disorder
• Cancer – extrinsic and intrinsic
Oesophageal Spasm – pharmacological management

Exclude/treat GORD

• High dose PPI
  Crozier 1991 Am J Gastroenterol
  Martinek 2016 Annal NY Acad Sci

First line therapy;

• Nitrates
  McDonnell 1999 Pall Med; Swamy 1997 Gastroenterol

• Calcium channel blockers
  • Diltiazem 60-90mg qds
    Cattau 1991 Am J Gastroent
  • Nifedipine
    Cargill 1982 NEJM
Oesophageal Spasm– pharmacological management

• SSRIs
  Handa 1999 J Clin Gastroenterol

• Peppermint oil
  Pimentel 2001 J Clin Gastroenterol

• Imipramine
  Peghini 1998 Gut; Cannon 1994 NEJM

• Hyoscine hydrobromide
  Murray-Brown 2016 BMJ Support and Pall Care
Oesophageal Spasm— pharmacological management

• Botulinum toxin A  
  Storr 2001 Gastrointest Endosc

• Balloon dilatation  
  Irving 1992 Gastrointest Radiol

• Myotomy  
  Filicori 2019 Surg Endosc
Conclusion

• Exclude/treat GORD
• Really weak evidence
• Nitrates
• Calcium channel blockers
• SSRIs (treat depression)
• Botox if available
Reading list

• Tenesmus


• Oesophageal spasm

Tutuian R and Castell D. 2006 Review article: oesophageal spasm – diagnosis and management. Alimentary pharmacology and therapeutics. 23(10): 1393-1402

• Bladder Spasm


Thank you!