Chronic Pelvic Pain: Peripheral, Central, and Neuropathic Origins

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Disclosure

• I have no financial interest in any of the therapies to discuss.

Objectives (CLC)

• Implement a stepwise algorithm for evaluating patients who present with chronic pelvic pain.
• Providers will distinguish patients who present with central, peripheral, and neuropathic pain syndromes.
• Diagnose and manage myofascial pain syndromes.
• CPP is an equal opportunity offender. (CLC)
ARS: Neuropathic Pain

A 根据一项 IASP 调查，患有慢性疼痛的患者需要多长时间才能获得充分的缓解？
A. 6 个月
B. 1 年
C. 3 年
D. 5 年
E. 10 年

ARS: Treating with Gabapentin:

What is the average dose to gain relief?

a. 300 mg daily
b. 900 mg daily
c. 1800 mg daily
d. 3600 mg daily

Do you treat myofascial pain in your office?

A. Yes
B. No
Do you have an algorithm for CPP?

A. Yes
B. No

A Thought to Consider

• “There are two kinds of physicians who care for women with CPP – those who don’t know the cause of pelvic pain and those who don’t know they don’t know the cause of pelvic pain.” – John Slocumb, MD
What we think we know about CP

• CP may be a disease in and of itself.
• CP is not acute pain that just lasted a really long time.
• No good correlation between the degree of peripheral inflammation and amount of pain.

Questions I Think About

• Is it time to abandon laparoscopy in the diagnosis / treatment of CPP?
• Is there a limit to the number of surgeries performed on patients with CPP?
• Should we have a diagnosis of “Failed Pelvic Surgery”? 
Case

- 32 y/o G2 P2 with 10 years history of CPP
- Diagnosed with endometriosis, adhesions.
- 8 pelvic surgeries
  - L-scope 99, 01, RSO 02, LAVH 03, L-scope 04, 05
  - LSO 06, L-scope 08 (peritoneal stripping)
- Pain is constant, daily.
- OCP, GnRH agonists, NSAIDs don’t help
- Daily oxycodone, heating pad gives some relief.

Case Continued

- She experienced relief for 3 to 6 months after each surgery.
- She heard you were a great surgeon and is sure that the 9th surgery will make a positive difference.
- She expresses that she feels endometriosis has ruined her life.

Life Line

A. Laparoscopy #9    B. Psychiatry Consult
C. GI / GU Consult    D. Education
Pain Syndromes
Characterized by widespread Hyperalgesia / Allodynia

- Tension/migraine headache
- Non cardiac Chest Pain
- Irritable bowel syndrome
- TMJD syndrome
- Idiopathic LBP, Failed back surgery syndrome
- Bladder Pain Syndrome
- Fibromyalgia, CWP
- Idiopathic LBP, Failed back surgery syndrome
- Failed pelvic surgery syndrome
Mechanistic Characterization of Pain
Combinations may be present

<table>
<thead>
<tr>
<th>Peripheral</th>
<th>Neuropathic</th>
<th>Central</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammation</td>
<td>Nerve damage/entrapment</td>
<td>Diffuse hyperalgesia</td>
</tr>
<tr>
<td>NSAID / Opioids</td>
<td>NSAID, opioids, TCA's, SNRI's, SNRI's, anticonvulsants</td>
<td>Responsive to neuroactive compounds altering levels of neurotransmitters in pain transmission</td>
</tr>
</tbody>
</table>

Procedures effective
- Osteoarthritis
- Rheumatoid arthritis
- Cancer pain
- Early endometriosis
- Diabetic neuropathy
- Post herpetic neuralgia
- Trigeminal neuralgia
- Pudendal neuralgia
- FM, IBS, IC
- Idiopathic LBP

Neural Influences on Pain and Sensory Processing

Facilitation
- Substance P
- Glutamate
- Serotonin
- Nerve Growth Factor
- Cholecystokinin

Inhibition
- D N I P
  - Norepinephrine
  - Dopamine
  - GABA
  - Cannabinoids
  - Adenosine

Adapted from D Clauw MD
Where do we want to start?

What is in our toolbox?
- Scalpel / Laparoscope
- Knowledge / Education
- Studies
- History / Physical
  - Rule out other pain conditions
  - Validated Instruments / Questionnaires
  - Pelvicpain.org
- Studies
- History / Physical
  - Rule out other pain conditions
  - Validated Instruments / Questionnaires
  - Pelvicpain.org

History
- HPI - (COLDERR)
- Rule out
  - Gastrointestinal disease
  - Urinary tract disease
  - Psychiatric disease (depression)
  - PHQ-2, PHQ-9, Beck Inventory, etc.
- International Pelvic Pain Society H&P form
  - Rome III questionnaire
  - PUF questionnaire
  - Drossman sexual abuse questionnaire

IBS - Rome III
- At least 3 months, with onset at least 6 months previously of recurrent abdominal pain or discomfort** associated with 2 or more of the following:
  1. Improvement with defecation; and/or
  2. Onset associated with a change in frequency of stool; and/or
  3. Onset associated with a change in form (appearance) of stool

**Discomfort means an uncomfortable sensation not described as pain.

(A term features: anemia, weight loss, family hx of colon ca, Inflammatory BD, celiac)
IC – Painful Bladder Syndrome

• Diagnosis
  ▪ Presence of pain related to the bladder usually with frequency / urgency
  ▪ Absence of diseases that could cause symptoms
• Cystoscopy with hydrodistention (no longer the GS)
• KCl Sensitivity Test
• Tools
  ▪ O’Leary – Sant Questionnaire
  ▪ PUF questionnaire

Physical Exam

• Musculoskeletal Exam
  ▪ Leg length evaluation
  ▪ SI joint evaluation
  ▪ Abdominal wall exam for trigger points
• Unimanual Exam
  ▪ Pelvic floor muscles
  ▪ Bladder, cervix, uterus

Testing for Leg Length Discrepancy
SI Joint Rotation

Physical Exam

• Musculoskeletal Exam
  • Leg length evaluation
  • SI joint evaluation
  • Abdominal wall exam for trigger points
• Unimanual Exam
  • Pelvic floor muscles
  • Bladder, cervix, uterus

Unimanual Exam
Unimanual Exam

Round up the usual suspects

Varicosities
Adhesions
Chronic my
H.F.P.

Endo
PID
Levator ani syndrome
Pudendal neuralgia
Vulvodynia

Microsoft Corporation, 1978
Differential Diagnosis

<table>
<thead>
<tr>
<th>Gynecologic Causes</th>
<th>Non-Gynecologic Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endometriosis / adenomyosis</td>
<td>Myofascial pain syndrome</td>
</tr>
<tr>
<td>Primary dysmenorrhea</td>
<td>IBS (Irritable)</td>
</tr>
<tr>
<td>Adhesions</td>
<td>IBS (Inflammatory)</td>
</tr>
<tr>
<td>PID / tubal dz</td>
<td>Carcinoma of the colon</td>
</tr>
<tr>
<td>Pelvic Varicosities</td>
<td>Diverticular disease</td>
</tr>
<tr>
<td>Pain of uterine origin</td>
<td>Chronic Appendicitis</td>
</tr>
<tr>
<td>Levator ani syndrome</td>
<td>Constipation</td>
</tr>
<tr>
<td>Vulvar vestibulitis</td>
<td>Renal / ureteral stone</td>
</tr>
<tr>
<td>Retained ovary syndrome</td>
<td>I.C. / PUS</td>
</tr>
<tr>
<td>Ovarian remnant syndrome</td>
<td>Cystitis</td>
</tr>
<tr>
<td>Neuropathic pain syndrome</td>
<td>Urethral syndrome</td>
</tr>
<tr>
<td>Chronic ovarian torsion?</td>
<td>Urethral diverticulum</td>
</tr>
<tr>
<td>Gynecologic malignancy</td>
<td>Hernia</td>
</tr>
<tr>
<td>Fibroids</td>
<td>S.I. joint malrotation</td>
</tr>
<tr>
<td>Ovulatory pain</td>
<td>Somatization disorder</td>
</tr>
<tr>
<td>Pudendal neuralgia</td>
<td>Adhesions</td>
</tr>
<tr>
<td></td>
<td>Compression of lumbar vertebrae</td>
</tr>
<tr>
<td></td>
<td>Piriformis syndrome</td>
</tr>
</tbody>
</table>

Don’t get burned

Myofascial Pain: Look for it
Myofascial Pain Syndrome

"a focus of hyperirritability in a muscle or its fascia that is symptomatic with respect to pain....."

Myofascial Pain Syndrome: Is it real?

- > 1800 articles listed on PubMed
- Slocumb, AJOG 1984
  - Found in 131 of 177 patients (74%)
  - 89% success rate within 5 visits

Myofascial Pain: Diagnosis

- Palpation is the Key
- Exquisite Spot Tenderness
- Palpable Muscle Band
- Local Twitch
- Jump Sign
- Patient Recognition
Icing / Stretching

Myofascial Pain
Trigger Point Injections

0.5% bupivacaine
0.5 to 1 mL / site

Possibilities to Consider

• Wrong diagnosis
  • A defined pain state exists but has been improperly diagnosed and treated.
  • Example – Treating for recurrent UTIs when the patient actually has IC (PBS).

• True, true, unrelated
  • A defined pain state exists, has been correctly identified, but happens to be present in an incidental form.
  • Example – Treating for endometriosis when the pain is really central in nature.
If only

3. Find x.

Here it is \(-1\)

Technically speaking...

Life Line

A. Laparoscopy #9  B. Psychiatry Consult

C. GI / GU Consult  D. Education
Education (CPP Case)

- Does her case sound like endometriosis?
  - Constant, daily pain, refractory to all therapy.
- Endometriosis-related pain is understudied.
  - Only 2 studies in the Cochrane database for endometriosis-related pain.
  - 6% - 42% of asymptomatic women undergoing laparoscopic tubal sterilization have endometriosis.
- Endometriosis is often asymptomatic.

A Symptomatic Endometriosis

- [Bar chart]

A Hesiolysis: Does it make sense?

- [Image of a fitness center]
Adhesions:
Do They Cause Pain?

- Maybe, likely NOT as much as we have thought.
- Rapkin – more adhesions in infertile controls
  - (AJOG 1986:68:13-5.)
- Peters – Surgical RCT – no difference at 12 months
  - (BJOG 1992;99:59-62)
  - (Ned Tijdschr Geneeskd, 2004 – Multicenter RCT)
- Swank – Surgical RCT – no difference at 12 months
  - (Lancet 2003;361:1247-51.)

Viscero-Somatic Convergence
or Convergence-Projection
5 Pathways Pain Exits the Pelvis

1. Inferior hypogastric plexus to presacral plexus
2. Pelvic parasympathetic nerves through dorsal roots of S2-4
3. Sacral sympathetic nerves to sacral paravertebral nerves
4. Superior rectal afferent nerves to inferior mesenteric plexus
5. Ovarian plexus in the IP ligament (spinal levels T10 and T11)

Is This Central Pain?

- Overload of nociceptive stimuli to DH resulting in metabolic, biochemical, and electrophysiologic changes.
- Activation of NMDA receptors within DH
- Loss of inhibition at DH / ↓ nociceptive threshold (alldynia)
- Duration + severity may result in permanent biochemical changes = centralization
- Exaggerated reflex output with end organ dysfunction / spontaneous firing of DH neurons
### Non-Opioid Adjuvants: Ion Blockers

<table>
<thead>
<tr>
<th>Active Drug</th>
<th>+ trials/total</th>
<th>mean daily dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gabapentin</td>
<td>4/4</td>
<td>1800 mg</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>&gt;10</td>
<td>600 mg</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>3/4</td>
<td>567 mg</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>1/2</td>
<td>300 mg</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>1/1</td>
<td>400 mg</td>
</tr>
<tr>
<td>Mexiletine</td>
<td>2/5</td>
<td>340 mg</td>
</tr>
</tbody>
</table>

### Antidepressants and Neuropathic Pain RCTs

<table>
<thead>
<tr>
<th>Active Drug</th>
<th>+ trials/total</th>
<th>mean daily dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline</td>
<td>5/5</td>
<td>80 mg</td>
</tr>
<tr>
<td>Imipramine</td>
<td>3/3</td>
<td>150 mg</td>
</tr>
<tr>
<td>Desipramine</td>
<td>2/2</td>
<td>184 mg</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>1/1</td>
<td>40 mg</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>0/1</td>
<td>--</td>
</tr>
<tr>
<td>Citalopram</td>
<td>1/2</td>
<td>25 mg</td>
</tr>
</tbody>
</table>

### TCA Properties

<table>
<thead>
<tr>
<th>Drug</th>
<th>Anticholinergy</th>
<th>Hypotension</th>
<th>Sedation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Imipramine</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Clomipramine</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Desipramine</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

(Consider cyclobenzaprine 5 mg q hs - up to 20 mg daily)
How do TCAs work?

Reuptake Inhibitors

<table>
<thead>
<tr>
<th>SSRI</th>
<th>SNRI</th>
<th>NSRI</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>fluoxetine</em>&lt;sup&gt;4&lt;/sup&gt;</td>
<td><em>venlafaxine</em>&lt;sup&gt;2&lt;/sup&gt;</td>
<td><em>milnacipran</em>&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td><em>sertraline</em>&lt;sup&gt;4&lt;/sup&gt;</td>
<td><em>duloxetine</em>&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td><em>paroxetine</em>&lt;sup&gt;4&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>escitalopram</em>&lt;sup&gt;4&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>citalopram</em>&lt;sup&gt;4&lt;/sup&gt;</td>
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</table>

<sup>n</sup>*Fluoxetine becomes a dual reuptake inhibitor at >45 mg

NNT

(Number of patients that need to be treated to achieve therapeutic response)

<table>
<thead>
<tr>
<th>Category</th>
<th>NNT (NPP)</th>
<th>NNT (CP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCA&lt;sup&gt;1&lt;/sup&gt;</td>
<td>3.1</td>
<td></td>
</tr>
<tr>
<td>SSRI&lt;sup&gt;1&lt;/sup&gt;</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Pregabalin&lt;sup&gt;2&lt;/sup&gt;</td>
<td>3.9 - 5.0</td>
<td>5.6 - 11</td>
</tr>
<tr>
<td>Gabapentin&lt;sup&gt;1&lt;/sup&gt;</td>
<td>4.3</td>
<td></td>
</tr>
</tbody>
</table>

<sup>1</sup>Saarto CDSR 2005, <sup>2</sup>Moore CDSR 2009, <sup>3</sup>Wiffen CDSR 2005
Tramadol

- Mode of action is not completely understood
- 2 complimentary mechanisms applicable
  - Binding of parent and M1 metabolite to opioid receptors
  - Weak inhibition of reuptake of norepinephrine and serotonin
- Cases of abuse and dependence have been reported
- Manufacturer recommends against use in patients with known drug abuse history.

Beyond Medications

- Proper Sleep
  - Bed is for sleep, not counting sheep
- Exercise
  - Gold level evidence that aerobic exercise is beneficial
- Diet – Nutrition
- Patients must agree to play an active role
  - Don’t let them be enablers
- Manage Stress
  - Pain psychologist

Conclusions

- Distinguish between cyclic, acute, and chronic causes of pain
- Patient education is often more powerful than surgery in the treatment of chronic pain.
- Understand Musculoskeletal causes for CPP.
- Treat peripheral pain with peripherally targeted therapies
- Treat central pain with centrally targeted therapies.