Endometriosis and Cancer: New Perspectives in Management of Chronic Pelvic Pain

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Disclosure

- Speaker- Covidien, Cephalon
- Speaker/Instructor- Kimberly Clark
Epidemiology

- Prevalence of 3.8% in women aged 15-73 resulting in about 10% of all referrals to gynecologists

- Approximately 15-20% of women aged 18-50 years have chronic pelvic pain of greater than 1 year’s duration

- Signs and symptoms of CPP may be evident in at least 50% of patients with pre-existing sexual or physical abuse
Chronic Pelvic Pain Impact

- 50% of pts have mood disturbances or depression
- 26% spend more than ½ day in bed with pain
- 58% report restricting usual activities

Gallup survey:
- 75% seek no med care
- 20% see GYN
- 10% see other physician
- 1% seek mental health care provider visits

Mathias SD; Kuppermann M; Liberman RF; Lipschutz RC; Steege JFOb
JFObstet Mar;321-7 stet Gynecol 1996 Mar;87(3):321
COMPLEX INNERVATION:

-SOMATIC:
- Ilioinguinal & Ilioilhypogastric nerves (L1)
- Genitofemoral nerves (L1, L2)
- Pudendal Nerves: S2, S3, S4
- Superior Hypogastric Plexus: Sympathetic fibers T12, L1 and L2 plus visceral nociceptive afferents from same levels

-VISCERAL
- Hypogastric Nerves and Inferior Hypogastric Plexus: sympathetics, parasympathetics and visceral nociceptive afferents S2, S3, S4
- Ganglion Impar: caudal end of sympathetic chain
ILIOHYPOGASTRIC, ILIOINGUINAL AND GENITOFEMORAL NERVES

- Iliohypogastric nerve: L1
- Abdominal wall skin over the pubis

- Ilioinguinal nerve: L1
- Skin over the root of the penis, anterior & upper scrotum, lateral labia majora, superior inner thigh

- Genitofemoral nerve: L1, L2
- Scrotum, labia majora, skin below the inguinal ligament
Hypogastric Plexus

- Formed from pelvic visceral afferent and efferent sympathetic nerves
- Receive parasympathetic fibers from S2-S4
- Contain no somatic nerves
- HPB is useful in the treatment of cancer pelvic pain, cervical, endometrial, prostatic, testicular and colorectal cancers
Hypogastric Plexus Block - Approaches
### Efficacy

Table III - Characteristics of Evaluated Outcomes of Major Studies on Superior Hypogastric Plexus Block to Treat Chronic Pelvic Pain

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Pain Evaluation</th>
<th>Quality of Life</th>
<th>Functional Status</th>
<th>MEDD#</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plancarte et al. 1990</td>
<td>VAS * and VPS$^5$</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>de Leon Casasola et al. 1993</td>
<td>VAS and opioids</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Wechsler et al. 1995</td>
<td>VAS</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Chan et al. 1997</td>
<td>VAS</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Plancarte et al. 1997</td>
<td>VAS and opioids</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Rosenberg et al. 1998</td>
<td>Without objective tools</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>de Oliveira et al. 2004</td>
<td>VAS and opioids</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

# MEDD: morphine equivalent daily dose
* VAS: visual analog pain scale
$^5$ VPS: verbal pain scale
Efficacy-

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Indication</th>
<th>Patients (n)</th>
<th>Follow up</th>
<th>Efficacy</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plancarte et al. 1990</td>
<td>Oncologic pelvic pain</td>
<td>28</td>
<td>To death</td>
<td>Mean 70% pain decrease</td>
<td>None</td>
</tr>
<tr>
<td>de Leon-Casasola et al. 1993</td>
<td>Oncologic pelvic pain</td>
<td>26</td>
<td>6 months</td>
<td>Mean 69% pain decrease</td>
<td>None</td>
</tr>
<tr>
<td>Plancarte et al. 1997</td>
<td>Oncologic pelvic pain</td>
<td>227</td>
<td>6 months</td>
<td>Mean 72% pain decrease#</td>
<td>None</td>
</tr>
<tr>
<td>Mercadante et al. 2002</td>
<td>Oncologic pelvic pain</td>
<td>22</td>
<td>To death</td>
<td>Worse pain relief as compared to celiac plexus block</td>
<td>None</td>
</tr>
<tr>
<td>de Oliveira et al. 2004</td>
<td>Oncologic pelvic pain</td>
<td>60</td>
<td>8 weeks</td>
<td>↓ pain, ↑ quality of life, ↓ opioid consumption</td>
<td>Hypotension and diarrhea</td>
</tr>
</tbody>
</table>

# 159 patients (79%) with positive response to diagnostic blockade were selected for superior hypogastric neurolitic block

Ganglion Impar Block

- Ganglion is the caudal end of the Sympathetic Chain and only midline structure anterior to the sacrococcygeal ligament

- Perineal pain with sympathetic component

- Vulvodynia

- Proctitis, Prostatitis, Coccydynia, Ca prostate, Ca rectum
Ganglion Impar Block
Differential Nerve Block

- Information for pain conditions that elude specific diagnoses
- Controversial, although more objective assessment of pain
- Identifying psychosocial, cognitive, visceral and somatic contributions in patient’s pain
- Rationale: selective blockade of specific neurological pathways
- Help to determine if psychological component contributing whether pain is mediated via sympathetic or somatic fibers
- Prognosticate a patient’s likelihood for success from interventions

Differential Nerve Block

- LA through an epidural catheter to achieve surgical anesthesia in the dermatomal distribution that overlaps the patient’s site of pain
- Visceral or non-visceral
- Significance of abolishment of visceral pain that outlasts the duration of LA block is important in establishing the diagnosis of chronic abdominal pains of unclear origin
Pharmacologic Management: Non Malignant Pain

- No well designed DBRCT—largely empirical
- **Antidepressants:**
  - Noradrenalin/serotonin reuptake inhibitors $\gg$ SSRI
    - Amitriptyline, Doxepin
    - Venlafaxine, Nefazodone
- **Antiepileptics:**
  - Gabapentin/Pregabalin...
- **Other agents:**
  - NSAIDs
  - Opioids
  - NMDA antagonists: Ketamine, dextromethorphan
Visceral Pain Characteristics

• Characteristics:
  • Referral/transferral to cutaneous structures
  • Diffuse and difficult to localize
  • Enhanced autonomic and/or motor reflexes
  • Cutaneous and deep tissue hyperalgesia

• Stimuli:
  • Hollow organ distention
  • Ischemia
  • Inflammation
  • Muscle spasm
  • Traction
Spinal Cord Stimulation
ORIGINAL ARTICLE

Neuromodulation of Pelvic Visceral Pain: Review of the Literature and Case Series of Potential Novel Targets for Treatment

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SCS for visceral pelvic pain
Kapural et al, Pain Medicine 2006

- 6 female patients severe visceral pelvic pain
- Treated for an average of 14.8 years (from 4 to 38)
- Series of hypogastric blocks (in average 5.3)
- All received SCS systems with two leads implanted
- Pain Disability Index (PDI) questionnaires before the implant and recently following implant
- Opioid use calculated as MSO4 milligram equivalents
<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Years of pain</th>
<th>Diagnosis</th>
<th>Symptoms</th>
<th>Previous invasive Treatments</th>
<th>Differential block</th>
<th>Trial (days)</th>
<th>Stim (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No1</td>
<td>32</td>
<td>12</td>
<td>Vulvar vestibulitis</td>
<td>Pelvic pain, dyspareunia</td>
<td>Surgeries, Hypogastic LA+neurolytic (PHE)</td>
<td>Visceral</td>
<td>14</td>
<td>55</td>
</tr>
<tr>
<td>No2</td>
<td>58</td>
<td>38</td>
<td>Endometriosis, pelvic adhesion</td>
<td>Pelvic pain</td>
<td>Surgeries, Hypogastic LA+neurolytic (PHE)</td>
<td>Visceral</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>No3</td>
<td>45</td>
<td>14</td>
<td>Utero-vag prolapse, pelvic adhesions</td>
<td>Pelvic pain, rectal pain</td>
<td>Surgeries, Hypogastic LA</td>
<td>none</td>
<td>7</td>
<td>19</td>
</tr>
<tr>
<td>No4</td>
<td>31</td>
<td>10</td>
<td>Vulvodynia, endometriosis, pelvic adhesion</td>
<td>Pelvic pain, dyspareunia</td>
<td>Surgeries, TAH, Hypogastic LA</td>
<td>none</td>
<td>7</td>
<td>70</td>
</tr>
<tr>
<td>No5</td>
<td>35</td>
<td>11</td>
<td>Endometriosis, pelvic adhesion</td>
<td>Pelvic pain</td>
<td>Surgeries, Hypogastic LA</td>
<td>Visceral</td>
<td>8</td>
<td>18</td>
</tr>
<tr>
<td>No6</td>
<td>48</td>
<td>4</td>
<td>Urinary retention, pelvic adhesion</td>
<td>Pelvic pain, urinary urgency</td>
<td>Surgeries, Hypogastic LA+neurolytic (PHE)</td>
<td>Visceral and SS</td>
<td>14</td>
<td>10</td>
</tr>
</tbody>
</table>
Pain and Disability

<table>
<thead>
<tr>
<th>VAS pain score</th>
<th>before</th>
<th>after</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PDI score</th>
<th>before</th>
<th>after</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>80</td>
<td>40</td>
</tr>
</tbody>
</table>
Results

• Follow-up was 30.6 months

• Median VAS pain score decreased from 8 to 3

• All patients > 50% of the pain relief

• PDI changed from 58 to 19.7

• Opioid use decreased from 22.5 to 6.6 mg of MSO4 equivalent per day

• Two revisions (lead migration) but if calculated per years of SCS- one revision per 2.6 years of stimulation.
Spinal Interventions:

• Intrathecal Drug delivery systems

• Intrathecal/Epidural block and neurolysis
  – Intractable pelvic cancer pain with somatic involvement may be alleviated by destruction of appropriate somatic sensory nerve fibers.
  – Intrathecal neurolysis is preferred for unilateral pain and carries a reduced risk of motor fiber destruction
  – There is a real risk of incontinence or lower extremity paresis
Chronic pain  Vs  Cancer pain

Chronic pain
• Function
• Pain Control
• Adjuvants
• Psychological factors
• Monitoring

Cancer Pain
• Opioids, Opioids, Opioids
• Pain Control
• Empathy
• Symptom Control
WHO Three-Step Analgesic Ladder

1. Pain persisting or increasing
   - Non-opioid ± Adjuvant

2. Pain persisting or increasing
   - Opioid for mild to moderate pain
     - + Non-opioid ± Adjuvant

3. Freedom from cancer pain
   - Opioid for moderate to severe pain
     - ± Non-opioid ± Adjuvant

(Adapted from WHO diagram)
The Fourth Step?

Limitations of the WHO ladder
Ahmedzai et al; current opinion in supp and pall care; 2007;1;3-7

• 3 step approach – non-evidence based

• Mechanism based approaches important

• Freedom from cancer pain at top of ladder – an unrealistic goal
WHO ladder and Cancer pain

• Still relevant?

• ‘Step 4’ i.e last resort options often offer fewer se’s and better pain control

• Focus on Opioid sparing techniques with Cancer pain also

• Are Opioids the adjuvant?
Question the ‘WHO’ dogma

Use of adjuvants, opioid sparing techniques, to avoid morbidity and opioid tolerance

Treat pain early

Adopt chronic pain treatment strategies

MONITORING- Georgia Board Guidelines, REMS program, PDMP
Revised Pain Medicine Paradigm

- Neurodestruction
- Electrical
- Chemical
- Neuromodulation
- Balanced Analgesic Approach
- Opioid Trial
- Opioids
- Pharmacotherapeutic Management
- Ablative Procedures (if mechanical pain generator amenable to isolation)
- Non-Invasive / Invasive Diagnostics
- Physical / Manual / Occupational Modalities for ROM

Cognitive/Behavioral Therapy
- Spiritual Therapy
- Complementary Medicine

8/06 AB

Courtesy of Daniel Bennett, MD
Cancer Pain Treatment Strategy

Multidisciplinary Care
- Primary Care
- Oncologist
- Pain Specialist
- Physical therapist
- Surgeon
- Psychologist
- Palliative Care

Multimodal Care
- Adjuvant Medications
- Procedures/Injections
- Opioids
- Topicals

Holistic Approaches
- Massage
- Yoga
- Meditation
- Acupuncture
Concluding Remarks

1. Realistic Expectations
   - Severe Pain → → Moderate Pain
   - Moderate Pain → → Mild Pain

2. Early intervention → → Better Results