Posterior Tibial Nerve Stimulation as ambulatory neuromodulation in the treatment of chronic pelvic pain

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Introduction

Few problems more challenging than pelvic pain

Controversies in definitions, ethiologic theories, diagnostic criteria and patient care.
Pelvic Pain Syndromes

Urology: interstitial cystitis
Gynecology: endometriosis
vulvodynia
pelvic congestion syndr.
Proctology: levator syndrome
proctalgia
coccydynia
Physical Med: fibromyalgia

previously "urethral syndrome"

"where are the boundaries?"

Visceral afferents can interact at the spinal cord level and afferent nerves from more than one organ may synapse upon a single neuron in the spinal cord.
This condition is called viscero-visceral convergence. The consequence is that chronic sensory disorders of the pelvis may coexist.
The year 2003: a milestone in the history of IC & Pelvic Pain

Kyoto Meeting, March
Copenhagen Meeting, May
Washington Meeting, October

Aim:

"no exclusion criteria, but evidence based concepts"
Evidence-based data

NORDLING J. EAU Review, Vienna, March 2004
Chronic Pain Development

Pathophysiology: Peripheral and Central Sensitization

Painful acute pain occurs at the site of the injured organ. Chronic pain occurs from plastic changes in the dorsal spinal cord with release of glutamate and substance P. Central sensitization.

Dorsal horn modulation

Painful acute pain occurs at the site of the injured organ. Chronic pain occurs from plastic changes in the dorsal spinal cord with release of glutamate and substance P. Central sensitization.
Central sensitization

Peripheral organ disease shifts to CNS disease
Chronic pain: *peripheral effects*

Prolonged sensitization release Substance P and calcitonin gene relate peptide cause neurogenic inflammation

Vascular endothelium induce the release of bradykinin and produce nitric oxide that causes edema of target organs
Brain Imaging & Pain

Somatic pain

Sensory cortex (micturition control)
Visceral pain

Cyngulate gyrus circonv.call. (bladder fullness)
Brain Imaging & Pain

Pain intensity

Insula (urgency)
Afferent & efferent pathways

PAG and Rafe nuclei mesenc. (micturition cycle)
Brain Imaging & Pain

Brain reacts differently in people with chronic pain when compared with “pain-free” individuals.

Similarities with brain areas involved in control of micturition.

But

In different kinds of chronic pain, imaging can vary.

Brain imaging could tailor drug treatments.
DIAGNOSIS: Multidisciplinary Integrated Approach

Urologist (infection, cancer)
Gynecologist (uterine path., endometriosis)
Coloproctologist (cancer vs proctalgia)
Physiatrist (fibromyalgia, myofascial and musculoskeletal disorders, trigger points)
Physical Examination

Introital & Vaginal disorders
Pelvic Floor Muscles contraction
Trigger points (Q tip: a new one!)
Pelvic Floor Muscles Assessment
# Pain Assessment Scales

<table>
<thead>
<tr>
<th>Verbal Pain Intensity Scale</th>
<th>Visual Analog Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>No pain</td>
<td>No pain</td>
</tr>
<tr>
<td>Mild pain</td>
<td>Worst possible pain</td>
</tr>
<tr>
<td>Moderate pain</td>
<td>Moderate pain</td>
</tr>
<tr>
<td>Severe pain</td>
<td>Severe pain</td>
</tr>
<tr>
<td>Very severe pain</td>
<td>Very severe pain</td>
</tr>
<tr>
<td>Worst possible pain</td>
<td>Worst possible pain</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>0–10 Numeric Pain Intensity Scale</th>
<th>“Faces” Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
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<tr>
<td>1</td>
<td>1</td>
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<td>2</td>
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<td>3</td>
<td>3</td>
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Algorithm of treatment

Bladder training, fluid modification, drugs for mild pain
Bladder distention
Atarax (Idrossizina Pentosolpolisolfato) for 6-8 weeks (NIDDK Study)
Amytriptiline for strong pain
DMSO weekly for 6 weeks Maintenance: once-a-months for 6-12 months
Neuromodulation PTNS (good bladder capacity)
Ileal loop (small bladder capacity – very selected pts)

Disappointing:
Resinferatoxin
Ialuronic acid
PEA(palmitoiletanolamide)

Philip Hanno, 2005
Cannabinoids receptors

Cannabinoids block pain enhancing molecules released after an injury and cutting off a nerve pain signal before it reaches the spinal cord.

Claire Fowler, 2004
First, Mc Guire (83) described the percutaneous tibial nerve stimulation in 22 incontinent patients, placing a transcutaneous electrode on posterior nerve and a plane electrode on the controlateral one.

Stoller modified this technique placing plane electrode on the same side of the transcutaneous one.
PTNS works as neuromodulation through percutaneous electrical stimulation
PTNS: background

Known traditional acupuncture point (Sp-6)
Bladder
PTNS: rationale

Electrostimulation of posterior tibial nerve
- no genital area
  _ afferent stimulation of S3 metamer
PTNS : rationale

Posterior tibial nerve
S3 Fibers
Plantar flexion of big toe (S3)
Indications:

Overactive bladder
Non obstructive urinary retention

Chronic pelvic pain
Pediatric indication
Neurogenic bladder
PTNS: procedure

Sp-6 acupuncture
- 34 G needle
needle is inserted approximately 2 inches cephalad to the medial malleolus Needle connection to the stimulator
Fixed parameters of stimulation puls 200 μs freq 20 Hz except to:
- amplitude

Until to obtain sensitive/ motor answer
PTNS: procedure

Ambulatory treatment
Once a week
stimulation bilateral
30 minutes
Evaluation period: 6-8 weeks
Level of stimulation increases gradually.

Model:

<table>
<thead>
<tr>
<th>Date n°seat</th>
<th>Level Reached</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>20/XI/03</td>
<td>6 (dx)</td>
<td>dim. Urg or stop urg. Inc etc.</td>
</tr>
</tbody>
</table>
PTNS literature prints no side effects or complication up to now
WE WILL FOCUS ON:

Placebo effect

Stimulation parameters

Mechanism of action
Placebo effects

Need of controlled studies

28-43% pharmacologic studies vs. 60-70% PTNS
*Burgio, 1998; Madersbacher, 1998, Thuroff, 1999

63% success in PTNS group vs. 0% in placebo group
Vohra AK, ICS 2002

Effect of periodicity of stimulation
Mechanism of action

Restoring balance:
- sacral level
- pontine level?
- suprapontine level?

Demonstrated effects with PET studies and electrophysiologic during SNS

Blok B. Neurourol Urodyn 2002
Braun PM. Eur Urol. 2002
According to Gate Control Theory (Melzack e Wall), stimulation of great nervous trunks gets lower A-delta and C sensitive fibers function.

- As in TENS and Acupuncture (GPA), PTNS could be responsible of endorphines liberation in medulla.

- Chang et al: Nociceptive neurotransmitter decreasing after PTNS (c-fos gene).
Mechanism of action

c-fos protein served as a metabolic marker for sacral neurons in a rat model. c-fos is upregulated after noxious stimuli to the bladder (acetic acid). Electro-acupuncture of the hind leg before instillation of acetic acid significantly reduces c-fos expression.

Conclusion: electro-acupuncture reduces spinal neuronal cell activity.

Chang, Stoller, Lue et al, J. Urol. 1998
TENS AND VAGINAL STIMULATION IN THE TREATMENT OF CHRONIC PELVIC PAIN AND INTERSTITIAL CYSTITIS


Vestibulodinia: Sinergia tra Palmitoiletanolamide + trans-Polidatina e TENS (Transcutaneous Electrical Nerve Stimulation)

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†Outpatient Department of Vulvar Disease, V. Buzzi Hospital; and‡ Centre of Gynecology, San Raffaele Resnati Hospital, Milan; and§ Private Gynecological Outpatients’ Department, Parma, Italy

J Lower Gen Tract Dis, 2012
**Figura 1.**
Riduzione della minima soglia percettiva dello stimolo sensitivo (CPT) delle fibre C valutata al Neurometer in pazienti affetti da dolore associato a vestibulodinia trattate con Pelvilen® Forte 400mg + 40mg in associazione alla Stimolazione Elettrica Transcutanea (TENS).
T0 = Basale; T1 = Fine trattamento con Pelvilen® Forte 400mg + 40mg.
PTNS Chronic pelvic pain

n=33
Subjective cure rate 42 % (14)

Objective cure rate 21 % (7)

Michael R. van Balken, Vera Vandoninck
European Urology 2003
### Patient characteristics

<table>
<thead>
<tr>
<th>N</th>
<th>Age</th>
<th>Main localization pain</th>
<th>Surgical procedures</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>31</td>
<td>Soprapubic</td>
<td>Medications-SNS</td>
</tr>
<tr>
<td>2</td>
<td>28</td>
<td>Bladder Region</td>
<td>Medications, hydrodistention</td>
</tr>
<tr>
<td>3</td>
<td>45</td>
<td>Bladder Region</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>42</td>
<td>Soprapubic\Bladder Region</td>
<td>Urethrotomy</td>
</tr>
<tr>
<td>5</td>
<td>53</td>
<td>Soprapubic</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>38</td>
<td>Soprapubic</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>40</td>
<td>Perineal</td>
<td>-</td>
</tr>
<tr>
<td>8</td>
<td>30</td>
<td>Soprapubic\Bladder Region</td>
<td>-</td>
</tr>
<tr>
<td>9</td>
<td>54</td>
<td>Soprapubic\Bladder Region</td>
<td>TUMT</td>
</tr>
<tr>
<td>10</td>
<td>39</td>
<td>Bladder Region</td>
<td>-</td>
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<td>11</td>
<td>37</td>
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<tr>
<td>16</td>
<td>29</td>
<td>Perineal</td>
<td>-</td>
</tr>
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</table>

SNS = Sacral Nerve Stimulation  
TUMT = Transurethral microwave thermotherapy
Exclusion criteria

- Age under 18
- Symptoms existing for less than 6 months
- Pregnancy or the intention to become pregnant during the course of the study
- Active urinary tract infection or recurrent urinary tract infections (recurrent infections: ≥5 during the last 12 months)
- Bladder of kidney stone
- Sexually transmitted disease
- Carcinoma in situ, bladder malignancy, interstitial cystitis
- Uncontrolled diabetes or diabetes with peripheral nerve involvement
- Severe cardiopulmonary disease
- Neurological disease like MS, M. Parkinson, CVA, biped spine or spinal cord lesion
- Concomitant use of Elmiron or bladder installations like DMSO, BCG, Chloropectin or Heparin
- Change in analgesics within 2 weeks prior to or during the study
- Physiotherapy at the same time as the study
- Electrotherapy (for example TENS) at the same time as the study
Decrease of mean Visual Analogue Scale for pain (1 week) after twelve weeks of treatment

<table>
<thead>
<tr>
<th>Objective cure N=3 (18.7%)</th>
<th>Subjective responders N=7 (45%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients N=16</td>
<td></td>
</tr>
<tr>
<td>≥50%</td>
<td>5 (71.4%)</td>
</tr>
<tr>
<td>≥ 25%, &lt;50%</td>
<td>9 (56.3%)</td>
</tr>
<tr>
<td>No improvement</td>
<td>4 (25%)</td>
</tr>
</tbody>
</table>

Subjective responders:
- 5 (71.4%)
- 9 (56.3%)
- 4 (25%)
PTNS Chronic Pelvic Pain

N = 16

Subjective cure rate 45%

Objective cure rate 18.7%

IUGA 2006 Adile - Gugliotta
Conclusion

Posterior tibial nerve stimulation is an effective and minimally invasive option for the treatment of patients with chronic pelvic pain. Furthermore, research is needed on the mode of action, long-term effects and selection criteria, to increase the benefit.
Maybe our future will be quite... happy!!!