Spinal cord stimulation is effective in management of complex regional pain syndrome (CRPS) I: Fact or Fiction

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Introduction

• CRPS I is a debilitating neuropathic pain disorder characterized by burning pain and allodynia that affects the lives of millions and has an enormous social and economic impact
• Present evidence shows that CRPS I can be managed by neurostimulation in carefully-selected patients, for the short to medium term
• Its long-term effectiveness remains unclear and controversial
Objective
To demonstrate the efficacy of spinal cord stimulation (SCS):
• in restoring pain control
• improving quality of life
• enhancing functional status

Over the long-term
IASP Diagnostic Criteria:
Clinical Diagnosis, No Confirmatory Lab Tests Exist

1. The presence of an initiating noxious event

2. Continuing pain, allodynia or hyperalgesia – pain is disproportionate to inciting event

3. Evidence of edema, changes in skin blood flow, or abnormal sudomotor activity in the region of the pain

4. Diagnosis by exclusion of other conditions that would otherwise account for the degree of pain and dysfunction

Criteria 2–4 must be satisfied

When Should SCS be Used?

• Increasing evidence to suggest that SCS is no longer ‘last resort’ in the treatment of refractory neuropathic pain
• Early intervention with SCS may result in greater efficacy\(^1\)
• SCS is a central component of an effective rehabilitation strategy\(^2\)

Clinical Evidence for SCS in CRPS

• Clinically effective (supported by grade A evidence)\(^1\):
  – Provides good quality pain relief
  – Debate on degree of functional improvement generated

• Timely treatment provides the best results\(^2\):
  – Patients who do not respond to conventional treatment by 12–16 weeks should be given a trial of more interventional therapies such as SCS
  – Evidence suggests that early treatment reduces the risk of worsening pain and can significantly curb or even eliminate it

• Cost effective\(^1\):
  – Lifetime cost saving of €58,470 compared with physical therapy alone
  – Results in a cost-effective QALY of €22,580

2. Stanton-Hicks MD et al. Pain Practice 2002; 2(1): 1-16
The efficacy of SCS in the management of CRPS I is being challenged.....

• Kemler et. al (2008) reported that SCS+PT was more effective than PT alone in improving pain at 6 months and 2 years but not at 5 years.

• Currently there is no long-term data on the role of SCS in CRPS I management
Kemler (08): Mean VAS Scores Over Time

- Demonstrated regression of effectiveness of SCS after 3 years in both main and subgroup analyses.

Possible reasons for Reduced Effectiveness

1) True pain increase in the group treated with SCS
2) Normal decay over time
3) Exaggerated pain relief during trial stimulation
4) Spontaneous remission in PT group (2 patients had total remission of pain)
5) Probability that some of the cases in the SCS arm may be higher stage of CRPS I
Possible reasons for Reduced Effectiveness

6) ITT was not employed
   - Kemler excludes one SCS+PT randomized patient due to a special implant and excludes four PT only randomized patients due to SCS implant
   - cannot be sure that the two treatment groups are directly comparable at 5 years or if selection bias existed
Our Study
• Based on these findings, we were motivated to review our database- long-term follow-up (mean 87.9 months)

Our Objective
• To quantify the degree of regression occurring over time and its affect on the various parameters
• To identify if a subgroup exists- in which patients experience reduced pain, improved functional status, and quality of life over the long-term
Study Design

- Retrospective
- Database of 196 patients with SCS
  - 31 patients who met the IASP criteria for CRPS I with disease duration of at least six months
  - 3 refused to participate
  - 3 lost to follow-up
- Cohort of 25 patients
Demographics

• Mean follow-up period of 87.9 months
  - range: 18.1-234.6 months
  - median: 62.96 months

• Longest reported follow-up to the best of our knowledge

• 13 males and 12 females

• Mean age of 51.2 years (32-92 yrs)

• 10 patients had upper extremity pain

• 15 presented with lower extremity pain
Staging of CRPS I

- **Stage I (Acute):** pain, hyperalgesia, allodynia, vasomotor dysfunction, edema and sudomotor disturbance
- **Stage II (dystrophic):** ↑ pain, sensory dysfunction, continued vasomotor dysfunction, motor and trophic changes
- **Stage III (atrophic):** ↓ pain, ↑ sensory, vasomotor disturbance, ↑ trophic dysfunction.

Some patients may not progress to later stages while others may do so at a variable rate

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1 Bonica JJ. *The Management of Pain* Philadelphia: Lea and Febiger; 1953
Demographics: Staging

Stage of CRPS

- Stage I: 9
- Stage II: 5
- Stage III: 2

N = 25
Outcomes: Pain Intensity

VAS

baseline 3 months 1 year last follow-up

Mean 87.9 mths

p-value=0.001
Outcomes: Functional Status

Oswestry Disability Index

p-value = 0.003

Mean 87.9 mths
Outcomes: Employment

- Prior to implantation, 3 patients in the Stage I group were employed
- The number increased to 5 at last follow up (3 males; 2 females)

Only Stage I patients were gainfully employed
Outcomes: Depression

Beck Depression Inventory

- Baseline
- 3 months
- 1 year
- Last follow-up

Mean 87.9 mths

p-value = 0.001
Outcomes: Quality of Life

EQ-5D

Baseline, 3 months, 1 year, last follow-up

Mean 87.9 mths

p-value = 0.003
Outcomes: Quality of Life

**SF-36**

- **Mental Health**
- **Role Emotional**
- **Social Functioning**
- **Vitality**
- **General Health**
- **Body Pain**
- **Role-Physical**
- **Physical Function**

* denotes statistical significance on specific component of SF-36 (p<0.05)

Aggregate p-value=0.001
Outcome Predictors

- Multiple Regression Analysis reveals that treatment delay (>12 months) correlates with:
  - ↑ pain intensity (VAS; r=0.726, p<0.02)
  - ↑ depression (BDI; r=0.615, p<0.05)
  - ↓ functional status (ODI; r=0.841, p<0.01)
  - ↓ health status (SF-36; r=-0.723, p<0.04).
Outcome Predictors

Greatest improvement in SF-36 and VAS scores occurred in younger patients (≤40) in stage I who received the intervention within a year of diagnosis

\( r=0.667, \ p<0.03 \)
### Outcomes: Medication Usage

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Baseline (# of patients)</th>
<th>Last follow up (same dose)</th>
<th>Change/Improvement (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-depressant</td>
<td>17</td>
<td>12</td>
<td>5 (29%) ↓</td>
</tr>
<tr>
<td>Anti-convulsant</td>
<td>14</td>
<td>8</td>
<td>4 (42%) ↓↓</td>
</tr>
<tr>
<td>NSAID</td>
<td>9</td>
<td>6</td>
<td>3 (33%) ↓↓</td>
</tr>
<tr>
<td>Narcotic</td>
<td>10</td>
<td>9</td>
<td>1 (10%) ↓</td>
</tr>
</tbody>
</table>
CRPS I Spread

• Contiguous spread: All patients in this series experienced a gradual enlargement in the area affected over time.

• Independent spread: In 3 cases there was spread of the disease from upper to lower limb, or vice versa. Independent spread occurred within 1 year of implantation.

• Mirror Spread: In 1 patient there was spread of pathology to the contra lateral lower limb.

Stimulation does not appear to retard disease spread.

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Upper Vs. Lower Limb CRPS I

• SCS therapy appeared equally efficacious in patients with upper or lower limb pathology

• There was no statistically significant difference in outcome
Patient Satisfaction

- Patients were asked:
  - “Are you satisfied with the pain relief provided by your treatment?”
  - “Based on your experience so far would you have agreed to this treatment?”

- 88% of patients replied yes to both questions
Conclusions

• SCS delivers durable pain relief, enhances functional status, and patient quality of life. These benefits persist over long-term follow-up

• Treatment delay exceeding 1 year limits the effectiveness of intervention

• SCS should be considered earlier in the treatment continuum in order to maximize patient outcomes and the opportunity for successful rehabilitation
Our Findings Support Recent IASP recommendations

The IASP Expert Group recommends SCS be instituted within 12-16 weeks following symptom onset should conventional treatment fail.
Thank-you
References


Signs and Symptoms of CRPS

Courtesy of Robert J. Schwartzman, MD, MCP Hahnemann School of Medicine
Signs and Symptoms of CRPS

Stanton-Hicks M. JPSM 2006; in publication
What is Spinal Cord Stimulation?

alleviates pain by sending electrical impulses via implanted leads to the spinal cord

– The impulses activate pain-inhibiting neuronal circuits in the dorsal horn and induce a tingling sensation (paresthesia) that masks the sensations of pain
Mechanism of Action of SCS

• No clear answer; Area of active research
• Likely has:
  – Spinal effects:
    • Gate-control theory of pain
    • Blockade of neural transmission
  – Supraspinal effects:
    • Blockade of neural transmission
    • Inhibition of the sympathetic nervous system
    • Release of neuromodulators and neurotransmitters (GABA\textsubscript{B} receptors, 5-HT, Gly, Adenosine)

1. Melzack R, Wall PD. Science 1965;150: 971-9
2. Linderoth B, Meyerson BA. In: Surgical Management of Pain. 2002; 505–26