Efficacy and outcome of sacral nerve stimulation in slow transit constipation: A randomised, double-blind, placebo-controlled, two phase crossover study.

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Australian and New Zealand Clinical Trial Registry: 12611001192976
Background

Sacral nerve stimulation for constipation

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Background: For over 10 years sacral nerve stimulation (SNS) has been used for patients with constipation resistant to conservative treatment. A review of the literature is presented.

Methods: PubMed, MEDLINE and Embase databases were searched for studies demonstrating the use of SNS for the treatment of constipation.

Results: Thirteen studies have been published describing the results of SNS for chronic constipation. Of these, three were in children and ten in adults. Test stimulation was successful in 42–100 per cent of patients. In those who proceeded to permanent SNS, up to 87 per cent showed an improvement in symptoms at a median follow-up of 28 months. The success of stimulation varied depending on the outcome measure being used. Symptom improvement correlated with improvement in quality of life and patient satisfaction scores.

Conclusion: SNS appears to be an effective treatment for constipation, but this needs to be confirmed in larger prospective studies with longer follow-up. Improved outcome measures need to be adopted given the multiple symptoms that constipation may be associated with. Comparison with other established surgical therapies also needs consideration.

Paper accepted 17 August 2012
Published online in Wiley Online Library (www.bjs.co.uk). DOI: 10.1002/bjs.8944
# Randomised control trials

**(Treatment Efficacy of sacral nerve stimulation in constipation)**

<table>
<thead>
<tr>
<th>Author</th>
<th>Lower bowel disorder</th>
<th>Study Design</th>
<th>Outcome measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kenefick, 2002</td>
<td>Constipation</td>
<td>RCT</td>
<td>Stool Frequency</td>
</tr>
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</table>

- suggests that SNS can “reduce symptoms in some people with constipation”


- 14 constipated women with evacuatory dysfunction and rectal hyposensitivity; treatment with temporary sacral nerve stimulation (SNS)
  - in comparison to sham, SNS improve rectal sensitivity and percentage of successful defecating episodes.

Primary Aim: To assess, in patients with slow transit constipation, the clinical outcome in response to supra-sensory compared to sham stimulation.

Secondary Aim: To assess, in patients with slow transit constipation, the clinical outcome in response to sub-sensory compared to sham stimulation.
Primary Outcome Measure:
Proportion of patients, who on more than 2 days per week for at least 2 of 3 weeks, report a bowel movement associated with a feeling of complete evacuation during supra-sensory stimulation.

Secondary Outcome Measure:
Proportion of patients, who on more than 2 days per week for at least 2 of 3 weeks, report a bowel movement associated with a feeling of complete evacuation during sub-sensory stimulation.

Tertiary outcome measures:
For both supra and sub sensory stimulation determine the effects of sacral nerve stimulation upon: Abdominal pain score, abdominal bloating score, laxative-free days, quality of life scores.
Patient Eligibility

- Experience a feeling of incomplete evacuation on less than 3 days per week, for at least 2 of 3 weeks of the baseline/surveillance phase.
- Aged 18 – 75yrs
- Confirmed colonic slow transit
- Normal anorectal manometry
- Unsatisfactory symptomatic response to standard therapies including laxatives, dietary modification, biofeedback
Patient Ineligibility

- Metabolic, neurogenic or endocrine disorder(s) known to cause constipation.

- Drugs which list constipation as a potential side effect deemed to be clinically relevant by the referring physician

- Prior abdominal radiotherapy

- Prior abdominal surgery (except cholecystectomy, appendicectomy, inguinal hernia repair, splenectomy, fundoplication; oophorectomy or hysterectomy)

- Current or planned pregnancy

- Co-morbidity considered by the clinician or the investigators to put the patient at risk from surgical electrode implantation

- Current or prior history of malignancy.
Stratification and randomisation

Patients were stratified on the basis of the following potential correlates to outcome:

a) symptomatic response to PNE (defined as achieving \( > 2 \) days per week on which a complete bowel motion is experienced for 2 of 3 weeks);

a) duration of constipation (\( \leq \) 10yrs)

a) prior hysterectomy

b) study site (St.George Hospital or Concord Hospital; Sydney NSW).

All randomisation was conducted by the NH&MRC clinical trial centre
Study Outline

Phase I: Subsensory v Sham
- Sham
- Wash Out
- 3 weeks
- Sham
- Wash Out
- 2 weeks
- Sham
- Wash Out
- 2 weeks
- Sham
- Wash Out
- 3 weeks

Phase II: Suprasensory v Sham
- Sham
- Wash Out
- 3 weeks
- Sham
- Wash Out
- 2 weeks
- Sham
- Wash Out
- 3 weeks
- Sham
- Wash Out
- 3 weeks
- Sham
- Wash Out
- 2 years

Permanent implantation

PNE

Stratification & Randomisation

Randomisation

Long-term follow up

18 weeks
CONSORT flow diagram

- Determining Eligibility (n = 238; 2007-11)
- Signed Consent (n = 59)
- PNE (n = 59)
- RCT (n = 55)
- Long term follow up (n = 53)
Patient Demographics
(RCT; n = 55)

• Age; 44 ± 15 yrs (4 males)

• Duration of symptoms:
  • 1-2 yrs = 9%
  • 2-5 yrs = 7%
  • 5-10 yrs = 13%
  • >10 yrs = 71%

• Laxative use:
  • 1-3 d/w = 47%
  • 4-7 d/w = 53%

• Response to peripheral nerve evaluation
  • n = 16 (29%)
Primary outcome: supra-sensory phase (n = 53)

<table>
<thead>
<tr>
<th>Treatment arm for supra-sensory</th>
<th>No. of patients</th>
<th>No. of patients with a successful response</th>
<th>Success rate (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sham</td>
<td>53</td>
<td>11</td>
<td>20.8</td>
<td>12.0-33.5</td>
</tr>
<tr>
<td>Stimulation</td>
<td>54</td>
<td>16</td>
<td>29.6</td>
<td>19.1-42.8</td>
</tr>
</tbody>
</table>

The response rate was with 20.8% with sham and 29.6% with stimulation. (p = 0.23)
Secondary outcome: sub-sensory phase (n = 55)

<table>
<thead>
<tr>
<th>Treatment arm for sub-sensory</th>
<th>No. of patients</th>
<th>No. of patients with a successful response</th>
<th>Success rate (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sham</td>
<td>55</td>
<td>14</td>
<td>25.4</td>
<td>15.8-38.3</td>
</tr>
<tr>
<td>Stimulation</td>
<td>55</td>
<td>14</td>
<td>25.4</td>
<td>15.8-38.3</td>
</tr>
</tbody>
</table>

The response rate was with 25.4% with both sham and stimulation. (p = 0.95)
Additional Measures

**Stool frequency**

**Straining**

**Laxative Use**

**Bowel Movements (per week)**

- BL
- Sham 1
- Sham 2
- Suprasensory

**Day per week**

- BL
- Sham 1
- Sham 2
- Suprasensory
Additional Measures

Abdominal Pain

Severity

0 1 2 3

BL Sham 1 Subsensory Sham 2 Suprasensory

Satisfaction

Severity

0 1 2 3

BL Sham 1 Subsensory Sham 2 Suprasensory

Abdominal Bloating

Severity

0 1 2 3

BL Sham 1 Subsensory Sham 2 Suprasensory

Bothersome

Severity

0 1 2 3

BL Sham 1 Subsensory Sham 2 Suprasensory
Quality of Life

(SF36)

PF = physical Function
RP = role physical
BP = body pain
GH = general health
Vit = vitality
SF = social functioning
RE = role emotional
MH = mental health
Fifty three patients that entered the long-term follow-up.

- Sixteen patients (30%) had had the sacral nerve stimulator explanted and had dropped out of the study.

- Fourteen patients (26%) still had the stimulating device implanted but the stimulation was turned off.

- Seven patients (13%) were still receiving stimulation but reported that they were not satisfied with the treatment.

- Seventeen (31%) reported some level of satisfaction and requested that the stimulation remain on.

- Only nine patients (17%) met our primary endpoint.
Colonic scintigraphy
(Baseline vs 1 year)
Conclusion

• In patients with slow transit constipation, in comparison to sham stimulation, sacral nerve stimulation had no significant effects upon
  - Frequency of complete bowel movements
  - Stool frequency
  - Straining
  - Quality of life

• These data suggest that sacral nerve stimulation is not an effective treatment for most patients with slow transit constipation
Acknowledgements

**Surgical placement**
A/Prof David Lubowski  
A/Prof Peter Stewart

**Statistical analysis**
Prof Val Gebski  
Prof Mike Jones

**Patient Selection & Study Design**
Prof Ian Cook  
Prof Val Gebski

**Trial maintenance**
Ms Linda Hunt  
Ms Vicki Patton

**Supported by**
- NHMRC
- Medtronic

[Logos of associated institutions]
Is PNE a predictor of treatment outcome?

- PNE n = 16
- Subsensory n = 14
- Suprasensory n = 16

Venn Diagram:
- PNE
- Subsensory
- Suprasensory

Counts:
- PNE: 6, 2, 2, 4
- Subsensory: 2, 4, 4
- Suprasensory: 6, 2, 2