Management of chronic central neuropathic pain following traumatic spinal cord injury


Authors' objectives
To assess the efficacy and safety of interventions for central neuropathic pain (CNP) after traumatic spinal cord injury (TSCI).

Searching
MEDLINE, EMBASE and PsycINFO (from inception to May 2000), CINAHL, HealthSTAR and Sociological Abstracts (from inception to November 1999), and the Cochrane Library (Issue 4, 1999) were searched; the search terms were reported. In addition, the personal files of the Technical Expert Panel and the reference lists of all eligible studies were checked. No language restrictions were applied.

Study selection
Study designs of evaluations included in the review
All study designs were eligible for inclusion. Case series with less than 8 patients and case reports were tabulated and discussed separately.

Specific interventions included in the review
Studies that assessed the effects of pharmacological, surgical, psychological, pain management or self-management approaches were eligible for inclusion. The specific interventions assessed were: opioids (morphine, alfentanil), anticonvulsants (valproate, gabapentin), local anaesthetics (lidocaine), alpha-2-adrenergic agonists (clonidine), antispasticity drugs (baclofen), antidepressants (trazodone) and N-methyl-D-aspartate-receptor antagonists (ketamine); spinal cord stimulation, deep brain stimulation and transcutaneous nerve stimulation (TENS); and dorsal root entry zone lesions (DREZ) and other surgical procedures (anterior depression, spinal cord untethering, corpectomy, myelotomy and arachnoid grafting).

Participants included in the review
Studies of participants with CNP (using any definition) after TSCI, who were over 13 years of age, were included. Studies that included children with other types of CNP were included if the results for TSCI were reported separately. Studies that studied children with chronic pain, but with no further description of the pain, were excluded. The majority of the participants in the studies were male.

Outcomes assessed in the review
No inclusion criteria were specified for the outcome measures. All of the included studies reported the outcome of pain, which had been measured in various ways across the studies.

How were decisions on the relevance of primary studies made?
Six reviewers (working in pairs) independently assessed studies for inclusion. Any disagreements were resolved by discussion.

Assessment of study quality
Randomised controlled trials (RCTs) were assessed according to the criteria of the Jadad scale, while observational studies were assessed using criteria adapted from the scale of Downs and Black. Two reviewers independently assessed study quality. Any disagreements were resolved by discussion.

Data extraction
Two reviewers independently abstracted the data for all studies except case reports. For these studies, data were abstracted by one reviewer and checked by another. Any disagreements were resolved by consensus. The outcome
measures and adverse events as reported by the primary studies were abstracted.

**Methods of synthesis**

How were the studies combined?
The studies were grouped according to the intervention and combined in a narrative.

How were differences between studies investigated?
Differences between the studies in terms of the interventions, duration of treatment, outcome measures, and study design and quality were discussed in the text. Study details were also tabulated.

**Results of the review**

Thirty-five studies that assessed the effectiveness of interventions were included (n=748): 6 RCTs, 2 controlled clinical trials and 27 case series.

Pharmacological interventions.

There was limited evidence to suggest that anesthetics (2 studies), opioids (3 studies), and clonidine (2 studies) given spinaly may be effective in relieving CNP following TSCI, but further research is needed. Ketamine (1 study) resulted in a decrease in pain, whereas trazodone (1 study) and baclofen (1 study) did not. The available studies had small sample sizes and were of a poor methodological quality, so it was not possible to adequately judge the value of any individual intervention or group of interventions.

Spinal cord and deep brain stimulation techniques.

The limited evidence available suggested that spinal cord stimulation (17 studies) had a variable rate of early success and a low rate of long-term effectiveness. Deep brain stimulation (6 studies) had a low rate of early success and an even lower one of longer term effectiveness in combination with a significant number of adverse events. TENS (2 studies) may potentially reduce the sensation of ‘pain unpleasantness’ if patients have positive expectations regarding the treatment outcome.

DREZ and other surgical interventions.

All 17 studies of DREZ had very poorly defined inclusion and exclusion criteria, were uncontrolled, and did not report the severity of any adverse events experienced. All of the studies had high success rates but, given their limitations and the lack of reporting of adverse events, it is not known whether DREZ lesioning and other spinal surgeries are efficacious or associated with high risks to patients. Other surgical procedures (9 studies) produced improvements in pain in 20 to 85% of patients, but some were associated with serious side-effects.

**Authors’ conclusions**

Research on the management of CNP after TSCI in adults and adolescents is in its infancy. The authors also described the limitations of the available evidence and made recommendations for future research.

**CRD commentary**

The review question was broad, but clearly defined in terms of the interventions, participants and study designs. Several relevant sources were searched for potentially relevant studies and no language restrictions were applied. The potential for publication bias was not assessed and potentially relevant studies might have been missed. Efforts were made to minimise reviewer bias and errors during the study selection, quality assessment and data abstraction processes.

Adequate details of the included studies were tabulated. Given the differences between the included studies, the narrative synthesis of the studies was appropriate. Differences between the studies, in terms of the interventions, duration of treatment, outcome measures, and study design and quality, were discussed in the text. Overall, this was a
well-reported review. However, much of the evidence was in the form of case series and case reports, which will impact on the robustness of the authors' conclusions.

Implications of the review for practice and research
Practice: The authors stated that the lack of available evidence means that it is impossible to draw conclusions regarding the role of pharmacological interventions, and that clinicians may have to rely on the results for pharmacological interventions in other patient populations. They also stated that it is difficult to justify the use of spinal cord stimulation or deep brain stimulation, and that there is little evidence to support the use of DREZ lesioning or other spinal surgeries.

Research: The authors stated that larger studies with more rigorous designs, comprehensive reports and longer follow-up are needed to establish the effects of most of the interventions available. Efforts should be made to select a core set of validated and clinically relevant outcomes. In addition, particular emphasis should be placed upon gathering evidence on the effects of different interventions in women and adolescents. Priority should be given to interventions with established roles for the management of other types of neuropathic pain, such as tricyclic antidepressants, anticonvulsants, local anesthetics and opioids. Studies should also assess the effects of interventions given in combination, through invasive routes, or using different formulations. Further studies are also needed to assess the effects of non-pharmacological interventions, such as self-management approaches, spinal cord stimulation and DREZ lesioning. Studies are also needed to determine whether response to treatment is influenced by the level and cause of spinal cord injury, as well as the duration, distribution and characteristics of pain, and any co-morbid factors.

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