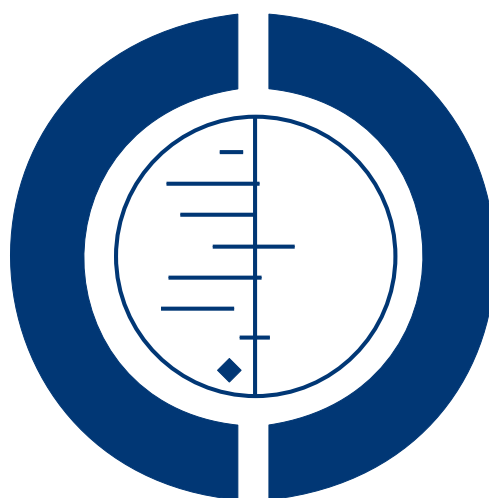


Cervico-thoracic or lumbar sympathectomy for neuropathic pain and complex regional pain syndrome (Review)

Straube S, Derry S, Moore RA, McQuay HJ



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[Intervention Review]

Cervico-thoracic or lumbar sympathectomy for neuropathic pain and complex regional pain syndrome

Sebastian Straube¹, Sheena Derry², R Andrew Moore², Henry J McQuay²

¹Department of Occupational, Social and Environmental Medicine, University Medical Center Göttingen, Göttingen, Germany. ²Pain Research and Nuffield Department of Clinical Neurosciences (Nuffield Division of Anaesthetics), University of Oxford, Oxford, UK

Contact address: Sebastian Straube, Department of Occupational, Social and Environmental Medicine, University Medical Center Göttingen, Waldweg 37 B, Göttingen, D-37073, Germany. sebastian.straube@googlemail.com.

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ABSTRACT

Background

This review is an update on 'Sympathectomy for neuropathic pain' originally published in Issue 2, 2003. The concept that many neuropathic pain syndromes (traditionally this definition would include complex regional pain syndromes (CRPS)) are "sympathetically maintained pains" has historically led to treatments that interrupt the sympathetic nervous system. Chemical sympathectomies use alcohol or phenol injections to destroy ganglia of the sympathetic chain, while surgical ablation is performed by open removal or electrocoagulation of the sympathetic chain, or minimally invasive procedures using thermal or laser interruption.

Objectives

To review the evidence from randomised, double blind, controlled trials on the efficacy and safety of chemical and surgical sympathectomy for neuropathic pain. Sympathectomy could be compared with placebo (sham) or other active treatment.

Search methods

We searched MEDLINE, EMBASE and *The Cochrane Library* to May 2010. We screened references in the retrieved articles and literature reviews, and contacted experts in the field of neuropathic pain.

Selection criteria

Randomised, double blind, placebo or active controlled studies assessing the effects of sympathectomy for neuropathic pain and CRPS.

Data collection and analysis

Two review authors independently assessed trial quality and validity, and extracted data. No pooled analysis of data was possible.

Main results

Only one study satisfied our inclusion criteria, comparing percutaneous radiofrequency thermal lumbar sympathectomy with lumbar sympathetic neurolysis using phenol in 20 participants with CRPS. There was no comparison of sympathectomy versus sham or placebo. No dichotomous pain outcomes were reported. Average baseline scores of 8-9/10 on several pain scales fell to about 4/10 initially (1 day) and remained at 3-5/10 over four months. There were no significant differences between groups, except for "unpleasant sensation",

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which was higher with radiofrequency ablation. One participant in the phenol group experienced postsympathectomy neuralgia, while two in the radiofrequency group and one in the phenol group complained of paresthesia during needle positioning. All participants had soreness at the injection site.

Authors' conclusions

The practice of surgical and chemical sympathectomy for neuropathic pain and CRPS is based on very little high quality evidence. Sympathectomy should be used cautiously in clinical practice, in carefully selected patients, and probably only after failure of other treatment options.

PLAIN LANGUAGE SUMMARY

Cervico-thoracic or lumbar sympathectomy for neuropathic pain

Chronic pain due to damaged nerves is called neuropathic pain and is common. Some people postulate that neuropathic pain, particularly reflex sympathetic dystrophy and causalgia, is caused by the sympathetic nervous system (a part of the autonomic nervous system that is involved in the response to stress and in the control of the functioning of many internal organs). Sympathectomy is a destructive procedure that interrupts the sympathetic nervous system. Chemical sympathectomies use alcohol or phenol injections to destroy sympathetic nervous tissue (the so-called "sympathetic chain" of nerve ganglia). Surgical ablation can be performed by open removal or electrocoagulation (destruction of tissue with high-frequency electrical current) of the sympathetic chain, or minimally invasive procedures using thermal or laser interruption. Nerve regeneration commonly occurs following both surgical or chemical ablation, but may take longer with surgical ablation.

This systematic review found only one small study (20 participants) of good methodological quality, which reported no significant difference between surgical and chemical sympathectomy for relieving neuropathic pain. Potentially serious complications of sympathectomy are well documented in the literature, and one (neuralgia) occurred in this study.

The practice of sympathectomy for treating neuropathic pain is based on very weak evidence. Furthermore, complications of the procedure may be significant.

BACKGROUND

This review is an update of a previously published review in The Cochrane Database of Systematic Reviews (Issue 2, 2003) on 'Sympathectomy for neuropathic pain' (Mailis-Gagnon 2003). We have changed the title to more accurately reflect the scope of the review.

Description of the condition

Neuropathic pain was defined rather broadly by the International Association for the Study of Pain (IASP) as pain initiated or caused by a primary lesion or dysfunction in the nervous system (Merskey 1994). This dysfunction or lesion may occur in the central nervous system (e.g. cerebrovascular accident, multiple sclerosis or spinal cord injury) or peripheral nervous system (e.g. surgery, trauma, infection). Some common examples of neuropathic pain included

in this definition are phantom limb pain, post-stroke pain, and complex regional pain syndrome (CRPS) type I (reflex sympathetic dystrophy) and type II (causalgia). Recently, a re-definition of neuropathic pain has been proposed: "pain arising as a direct consequence of a lesion or disease affecting the somatosensory system" (Treede 2008). This recent re-definition would not cover all disease entities included in the previous IASP definition and in particular it would probably exclude CRPS type I from being categorised as neuropathic pain. We wanted to be as inclusive as possible in the scope of our review and therefore considered all conditions that fulfil the old or new definition of neuropathic pain. To be unambiguous the title of this review explicitly mentions CRPS. Current treatments for neuropathic pain include:

- orally administered drugs (antidepressants, anticonvulsants, and analgesics (opioids and non opioids));
- local application of substances (capsaicin, ketamine, lidocaine, etc);

- injections of local anaesthetics, opioids and other agents on multiple sites (nerve, nerve root, epidural, intrathecal, etc);
- physical treatments (e.g. transcutaneous electrical nerve stimulation (TENS), desensitization, etc); and
- surgical interventions (decompressive, ablative and neuro-augmentative).

Psychological interventions can assist further in improving coping mechanisms when dealing with chronic pain. Neuropathic pain management is complex and usually requires a combination of different therapies and often a multidisciplinary approach to achieve the best results for the individual patient.

Description of the intervention

The concept of a dysfunctional sympathetic nervous system contributing to neuropathic pain is not new. The term 'Sympathetically Maintained Pain' (SMP), defined as pain maintained by sympathetic efferent innervation or by circulating catecholamines, was originally coined by [Roberts 1986](#). Many neuropathic pain syndromes, particularly CRPS types I and II, are thought to be SMP. Historically, this has led to attempts to interrupt the sympathetic nervous system dating back at least 80 years ([Spurling 1930](#)). Temporary and non-destructive interruption can be performed through injections of local anaesthetics or botulinum toxin, while a longer-lasting, "destructive" interruption can be achieved chemically or surgically. Chemical sympathectomies use alcohol or phenol injections to destroy ganglia of the sympathetic chain, but this effect is temporary until regeneration of the sympathetic chain occurs, usually after three to six months ([Jackson 2008](#)). Surgical ablation can be performed by open removal or electrocoagulation of the sympathetic chain, or minimally invasive procedures using stereotactic thermal or laser interruption. The effects may be longer-lasting, up to one year with radiofrequency ablation ([Jackson 2008](#)). This review will consider the evidence for chemical and surgical sympathectomy, but not short-term non-destructive interventions such as local anaesthetics and botulinum toxin.

Shumacker reported in 1948 the dramatic cure of causalgia by either surgical sympathectomy or alcohol injection in 81% of 57 post-war cases ([Shumacker 1948](#)). However, long term follow-up of post-war cases is usually missing from this and other similarly old literature. Currently, the most common indications for chemical neurolysis of the stellate ganglion are: CRPS types I and II, post-herpetic neuralgia of the trigeminal nerve, vasospastic conditions and cancer pain of the face, neck and upper extremities ([Dobrogowski 1995](#)). The bulk of experience concerning lumbar chemical neurolysis comes from the treatment of occlusive vascular diseases, but this procedure is also performed to treat cancer pain, CRPS types I and II, post-dissectomy syndrome, phantom limb pain, herpes-zoster and the early stages of post-herpetic neuralgia ([Dobrogowski 1995](#)). The overwhelming indication for surgical

sympathectomy is primary hyperhidrosis, while other indications for much smaller populations are neuropathic pain, vascular ischaemia, and Raynaud's phenomenon ([Furlan 2000](#)).

In 1996, Nath and colleagues conducted a literature review of surgical sympathectomy for reflex sympathetic dystrophy (RSD)/CRPS ([Nath 1996](#)). They concluded that sympathectomy should be reserved for patients with severe CRPS refractory to other treatment modalities. The reported results of the intervention varied widely but seemed to show a trend that sympathectomy was somewhat effective. However, [Kingery 1997](#) reviewed the literature of controlled clinical trials for peripheral neuropathic pain and CRPS, and found no placebo-controlled trials to evaluate either local anaesthetic blocks of sympathetic ganglia or surgical sympathectomy. More recently Jackson and Gaeta ([Jackson 2008](#)) reviewed neuroablation and again found the quality of the evidence poor, concluding that no one agent was demonstrably better than any other, and that for malignant pain "short-term pain relief may outweigh risk at end of life", but for chronic benign pain it should be a treatment of last resort after careful consideration. Cetas et al. ([Cetas 2008](#)), in reviewing destructive procedures for non-malignant pain, found few studies with sufficiently rigorous methods to avoid known biases, and additional problems of small study size (risk of random chance), mixed or poorly defined diagnoses, and inadequate follow up. They concluded that "efficacy has not been well established based on contemporary standards", and that "new, prospective, standardised studies are required to advance the field".

Why it is important to do this review

Because neuropathic pain is a common disease and sympathectomy is an invasive intervention with potentially serious complications ([Furlan 2000](#)) there is a need for a systematic review of the efficacy and associated harms of sympathectomy for neuropathic pain, using strict inclusion criteria regarding study methodology and validity that minimise bias.

The previous review included one randomised trial that was not blinded, two retrospective chart reviews and one prospective observational study. In this update we chose not to include studies that were not both randomised and double blind because such studies are known to be prone to biases and have significant potential to mislead ([Moore 2006](#)). Important non-randomised or non-double blind studies are now dealt with in the Discussion.

OBJECTIVES

To review the evidence from randomised, double blind, controlled trials on the efficacy and safety of chemical and surgical sympathectomy for neuropathic pain. Sympathectomy may be compared

with placebo (sham) or other active treatment, provided both participants and outcome assessors are blind to treatment group.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled double blind trials comparing sympathectomy with placebo (sham) or other active treatment for neuropathic pain or CRPS, with at least ten participants per treatment arm. Studies could be conducted in any setting (inpatients or outpatients). Studies published only as abstracts, and uncontrolled studies (case series, case reports, uncontrolled before and after studies) and studies in which participants and outcome assessors were not blinded to treatment group were not included in this review.

Types of participants

Participants of any age, with any duration of neuropathic pain (acute, sub-acute or chronic) were included.

Participants with neuropathic pains affecting the face, and upper or lower extremities were included. Participants with pain affecting thoracic or abdominal viscera were excluded.

Pain origin: Participants with central or peripheral neuropathic pain syndromes were included in this review. However, participants with cancer pain were excluded: studies of cancer pain will include participants with both nociceptive and neuropathic pain, as the discrimination between the two pain mechanisms is rarely attempted or reported.

Types of interventions

Only studies of destructive surgical or chemical sympathectomy were included. Studies of temporary sympathetic blockade were not considered in this review because it is a non-destructive technique and its effect is of shorter duration.

Surgical sympathectomy in this review is defined as the surgical ablation or coagulation of the cervico-thoracic or lumbar sympathetic chain by means of open, endoscopic, laser or radiofrequency procedures. Trials of surgical ablation of the celiac plexus were excluded.

Chemical sympathectomy is defined as the percutaneous ablation of the cervico-thoracic or lumbar sympathetic chain by the injection of phenol or alcohol solution. This procedure promotes a prolonged but not permanent sympathetic denervation. Studies of celiac and trigeminal blocks were excluded.

Types of outcome measures

Information was sought on participant characteristics: age, sex, condition treated, and duration of condition.

Primary outcomes

The primary outcome sought was participant-reported pain relief lasting for a minimum of 4 weeks. We chose dichotomous outcomes corresponding with definitions of moderate or substantial benefit as defined by the IMMPACT group (Dworkin 2008):

- Participants with $\geq 30\%$ pain relief, or at least “much improved” in Patient Global Impression of Change (PGIC)
- Participants with $\geq 50\%$ pain relief, or “very much improved” in PGIC.

Secondary outcomes

Secondary outcomes sought included:

- Participants with $< 30\%$ or “mild” pain relief, or undefined improvement.
- Pain relief lasting < 4 weeks.
- Adverse events and complications.
- Occurrence of persistent serious new or expanded pain (e.g. long-lasting post-sympathectomy neuralgia or other neuralgias).

Search methods for identification of studies

Electronic searches

The following databases were searched:

- MEDLINE (via Ovid) to May 2010.
- EMBASE (via Ovid) to May 2010.
- Cochrane CENTRAL, Issue 5, 2010.
- Oxford Pain Relief Database (Jadad 1996)

See [Appendix 1](#) for the search strategy for MEDLINE (via OVID), [Appendix 2](#) for the search strategy for EMBASE, and [Appendix 3](#) for the search strategy for CENTRAL.

There were no language restrictions.

Searching other resources

Reference lists of review articles and included studies were searched.

We had personal communication with experts in the field of neuropathic pain, including the editorial board of the Cochrane Pain, Palliative and Supportive Care review group.

Data collection and analysis

Review authors were not blinded to the authors' names and institutions, journal of publication, or study results at any stage of the review. Two review authors independently selected the studies for inclusion, assessed methodological quality, and extracted data. Disagreements were resolved through discussion.

Selection of studies

Titles and abstracts of studies identified by the searches were reviewed on screen to eliminate those that clearly did not satisfy inclusion criteria. Full reports of the remaining studies were obtained to determine inclusion in the review.

Data extraction and management

Two review authors independently extracted data from included studies using a standard data extraction form. Disagreements were settled by discussion with a third review author. Data would be entered into RevMan 5.0 by one author if appropriate. The following data were sought from all studies:

- demographics: age and sex of participants;
- pain type;
- duration of symptoms;
- previous and present treatments;
- number of sympathetic blocks before sympathectomy;
- if the sympathetic blocks were considered successful enough to warrant sympathectomy;
- type and approach of sympathetic block;
- levels of denervation;
- primary and secondary outcomes.
- duration of follow up;
- incidence of immediate and late complications;
- type of complication.

For continuous variables, means and standard deviations of changes would be extracted if appropriate.

Assessment of risk of bias in included studies

Studies were assessed for methodological quality using a five-point scale (Jadad 1996) that considers randomisation, blinding, and study withdrawals and dropouts, and for trial validity using a 16-point scale (Smith 2000). Risk of bias tables were completed for randomisation, allocation concealment, and blinding.

Measures of treatment effect

Relative risk (or 'risk ratio', RR) would be used to establish statistical difference. Numbers needed to treat to benefit (NNT), numbers needed to treat to harm (NNH) and pooled percentages would be used as absolute measures of benefit or harm.

Unit of analysis issues

We accepted randomisation to individual participant only.

Assessment of heterogeneity

It was planned to assess heterogeneity visually (L'Abbe 1987).

Data synthesis

It was planned that data would be combined for analysis where there were at least two studies and 200 participants (Moore 1998). Relative risk of benefit or harm would be calculated with 95% confidence intervals (CIs) using a fixed-effect model (Morris 1995). NNT and NNH with 95% CIs would be calculated using the pooled number of events by the method of Cook and Sackett (Cook 1995). A statistically significant difference from control would be assumed when the 95% CI of the relative risk of benefit or harm did not include the number one.

Subgroup analysis and investigation of heterogeneity

Issues for potential subgroup analysis were clinical diagnosis, method of ablation (surgical or chemical), and anatomical location of the lesions.

Sensitivity analysis

No sensitivity analyses were planned, since it was thought highly unlikely that there would be sufficient data.

RESULTS

Description of studies

See: [Characteristics of included studies](#); [Characteristics of excluded studies](#).

Included studies

We identified only one randomised double blind trial that qualified for inclusion in this review and this trial did not compare sympathectomy versus sham or placebo. Manjunath 2008 randomised 20 participants with lower limb CRPS type I to receive either percutaneous radiofrequency thermal lumbar sympathectomy or lumbar sympathetic neurolysis with phenol. Ten participants were randomised to each group. Participants were required to satisfy the diagnostic criteria for CRPS (Bruehl 1999), have symptoms lasting more than six months despite management in a multidisciplinary setting, have been unresponsive to medications for more than six months (visual analogue scale (VAS) score of > 6/10), and

have responded to a diagnostic block with 1% lidocaine on three occasions.

Radiofrequency treatment was performed with a radiofrequency cannula introduced 5 cm lateral to the spinous processes of L2, L3, and L4. The cannula position was assessed radiographically in anteroposterior and lateral views. A volume of 0.5-1 ml of ionic radio contrast medium (urografin 75%) was injected. Radiofrequency lesioning was performed for 90 s at a temperature of 80°C; a second lesion was made 5 mm anterior to the first. In the phenol group 3 ml of 7% phenol was injected at each level.

Pain was assessed with a number of pain scores (VAS score, intensity of pain, sharp pain, hot pain, dull pain, sensitive sensation, deep pain, and surface pain) each measured on a 0 to 10 scale at baseline and at 1 day, 7 days, 2 months and 4 months after the procedure.

Details are in the 'Characteristics of included studies' table.

Excluded studies

The four studies included in the earlier review did not meet our inclusion criteria for randomised, double-blind studies ([AbuRahma 1994](#); [Greipp 1990](#); [Haynsworth 1991](#); [Mailis 1994](#)). Details are in the 'Characteristics of excluded studies' table. Other articles identified in the searches could be eliminated on the basis of their titles and abstracts, without reading the full report.

Risk of bias in included studies

The one included study achieved the maximum score of five on the Oxford Quality Scale and 13/16 on the Oxford Pain Validity Scale, where points were lost because of the small group sizes.

The Risk of Bias assessment showed that the study did not report on the method of allocation concealment, but was not at high risk of bias.

Details are in the 'Characteristics of included studies' table.

Effects of interventions

Efficacy

In both treatment groups there were statistically significant reductions from baseline in all the utilised pain scores. In both groups initial average pain scores of 8 to 9/10 fell to about 4/10 initially (after 1 day) and remained at 3 to 5 over four months. There were no significant between-group differences in mean pain scores, except for the "unpleasant sensation" score that was higher in the radiofrequency group. No dichotomous efficacy outcomes were reported.

Adverse events

All participants complained of soreness at the site of injections lasting 5 to 7 days. One participant in the phenol group experienced postsympathectomy neuralgia. Two participants in the radiofrequency group and one in the phenol group complained of paresthesia during needle positioning. The number of participants with serious adverse events was not reported.

DISCUSSION

The practice of sympathectomy (both surgical and chemical) for neuropathic pain is based on poor quality evidence. We found only one double blind RCT assessing the efficacy of this intervention that qualified for inclusion in this review. Based on very limited evidence from a pilot study radiofrequency lumbar sympathectomy and lumbar sympathectomy with phenol seem about equally efficacious.

Lower quality evidence on the effectiveness of sympathectomy is largely positive. A meta-analysis on causalgia ([Hassantash 2003](#)) included 110 articles (case series and case reports) and 1528 participants. Seven hundred and ninety one participants were treated with sympathectomy of the diseased extremity. In 721 participants (91%) the condition responded. In 21 cases where the first sympathectomy was unsuccessful a second sympathectomy was performed and was always successful. According to [Hassantash 2003](#), therefore, a total of 94% of participants were "cured" by sympathectomy. A systematic review on the effectiveness and complications of chemical sympathectomy for neuropathic pain of the extremities including controlled and non-controlled studies described meaningful pain relief (there defined based on degree and duration (> 2 weeks) of pain relief) in 28/63 (44%) participants, non-meaningful pain relief in 12/63 participant (19%); in 23/63 participants (37%) the pain relief could not be classified ([Furlan 2001](#)).

In comparison to other treatments, lower quality evidence suggests that sympathectomy is at least not inferior. A retrospective review of patient charts of 27 CRPS patients ([Greipp 1990](#)) found that the four treatment methods physiotherapy, physiotherapy plus TENS, nerve blocks, and sympathectomy provided participants with at best temporary pain relief. Outcomes were similar with the different treatment methods.

Similarly, current evidence does not support large differences in efficacy between different types of sympathectomy. A randomised but not double blind trial with 17 participants with reflex sympathetic dystrophy of the lower extremities (CRPS type I) ([Haynsworth 1991](#)) found that radiofrequency sympathectomy produced sympatholysis similar to that produced by phenol, although with a lower incidence of post-sympathectomy neuralgia. A non-randomised and non-blinded prospective observational

study with 14 participants with upper or lower extremity CRPS (Mailis 1994) found that surgical and phenol sympathectomy produced similar rates of pain relief in the short term. In the long term there was a non-significant trend for better outcomes in the phenol group.

Regarding adverse events, the study included in this review found that all participants complained of soreness at the site of injections lasting 5 to 7 days and that one participant in the phenol group experienced postsympathectomy neuralgia. A systematic review investigating the late complications of surgical sympathectomies for a range of indications (Furlan 2000) found that neuropathic complications (after cervico-dorsal and lumbar surgical sympathectomy) occurred in 11.9% of all participants, however, they were more common if the indication was neuropathic pain rather than palmar hyperhidrosis (25.2% versus 9.8%). The same review found that, with cervico-dorsal sympathectomy, compensatory hyperhidrosis occurred in 52.3%, gustatory sweating in 32.3%, phantom sweating in 38.6%, and Horner's syndrome in 2.4% of participants.

AUTHORS' CONCLUSIONS

Implications for practice

This review is an update of a previous Cochrane review (Mailis-Gagnon 2003), using refined inclusion criteria. It demonstrates that the practice of sympathectomy for neuropathic pain is based on little high quality evidence. Only one pilot study, with 20 participants and in CRPS type I (which cannot serve as a model for other neuropathic pain conditions), satisfied our inclusion criteria. There was no comparison of sympathectomy versus sham or placebo. Lower quality evidence seems to suggest that sympathectomy for neuropathic pain can work, at least in some cases. The risk-benefit assessment is complicated by the fact that serious complications of sympathectomy are common. Because there is no good evidence for the effectiveness of sympathectomy - particularly with regard to long term effectiveness outcomes - its should

be used with great caution if at all outside a research context, in carefully selected patients after thorough assessment and probably only after failure of other treatment options. This stands in contrast to the use of pharmacotherapy in neuropathic pain, where there is a wealth of high quality evidence.

Implications for research

High quality evidence from double blind RCTs with placebo (sham) comparators is needed to determine whether sympathectomy can relieve neuropathic pain. Studies need to be conducted in different neuropathic pain syndromes to determine when - if at all - sympathectomy would be effective. Studies also need to assess different types of sympathectomy to determine which is best. Comparison is furthermore needed with less invasive techniques (neuropathic pain medications, local anaesthetic blocks, and botulinum toxin). Blinding will be a considerable challenge in direct comparisons between sympathectomy and less invasive techniques and will involve sham procedures in some participants. Despite this challenge, it is important to remember that blinding, even in circumstances where it may be difficult to achieve effectively, is necessary if bias is to be limited in pain trials.

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Treede RD, Jensen TS, Campbell JN, Cruccu G, Dostrovsky JO, Griffin JW, Hansson P, Hughes R, Nurmikko T, Serra J. Neuropathic pain: redefinition and a grading system for clinical and research purposes. *Neurology* 2008;**70**(18): 1630–5.

References to other published versions of this review**Mailis-Gagnon 2003**

Mailis-Gagnon A, Furlan AD. Sympathectomy for neuropathic pain. *Cochrane Database of Systematic Reviews* 2003, Issue 2. [DOI: 10.1002/14651858.CD002918]

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Manjunath 2008

Methods	Randomised, double blind, active control Radiofrequency lesioning carried out at 80°C for 90 s at each site; phenol ablation carried out with 7% phenol. For both procedures, radiofrequency cannula was positioned, with stimulation at 50 and 2 Hz to identify proximity to sensory and motor nerves, and maintain blinding. Participants remained in prone position for 30 minutes Participants monitored on ward for 24 hours. Follow up at 1 and 7 days, and 2 and 4 months
Participants	Complex regional pain syndrome. History of failure to respond (pain intensity > 6/10) to treatment with oral pregabalin, amitriptyline, carbamazepine over >6 months, and response (pain intensity < 4/10) after diagnostic sympathetic block with lidocaine on three occasions N = 20 M/F not reported Mean age 52 years in radiofrequency group, 39 years in phenol group
Interventions	Radiofrequency lumbar sympathectomy, n = 10 Phenol lumbar sympathectomy, n = 10
Outcomes	Nine pain outcomes, each assessed on a 0-10 scale Adverse events Withdrawals
Notes	Oxford Quality Score: R = 2, DB = 2, W = 1; Total = 5/5 Oxford Pain Validity Score: 13/16

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Low risk	"computer-generated" random numbers
Allocation concealment?	Unclear risk	Not reported
Blinding? All outcomes	Low risk	Patients blinded by creating similar scene for both procedures. Investigator collecting data not involved in procedures and unaware of the group to which patients were assigned

DB - double blinding; N - number of participants in study; n - number of participants in treatment group; R - randomisation; W - withdrawals

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
AbuRahma 1994	Not RCT (included in 2002 review)
Greipp 1990	Not RCT (included in 2002 review)
Haynsworth 1991	Not double blind (included in 2002 review)
Mailis 1994	Not RCT (included in 2002 review)

DATA AND ANALYSES

This review has no analyses.

APPENDICES

Appendix 1. Search strategy for MEDLINE (via OVID)

1. Exp Sympathectomy/
2. (sympathectomy OR sympatholysis OR sympathicotomy).mp
3. 1 OR 2
4. Exp Neuralgia/
5. (complex regional pain syndrome OR reflex sympathetic dystrophy OR causalgia OR phantom limb pain OR allodynia OR diabetic neuropath* OR trigeminal neuralgia OR post-herpetic neuralgia OR neuropathic adj2 pain).mp
6. 4 OR 5
7. randomized controlled trial.pt.
8. controlled clinical trial.pt.
9. randomized.ab.
10. placebo.ab.
11. randomly.ab.
12. trial.ab.
13. groups.ab.
14. OR/7-13
15. 3 AND 6 AND 14

Appendix 2. Search strategy for EMBASE (via OVID)

1. Exp Sympathectomy/
2. (sympathectomy OR sympatholysis OR sympathicotomy).mp
3. 1 OR 2
4. Exp Neuralgia/
5. (complex regional pain syndrome OR reflex sympathetic dystrophy OR causalgia OR phantom limb pain OR allodynia OR diabetic neuropath* OR trigeminal neuralgia OR post-herpetic neuralgia OR neuropathic adj2 pain).mp
6. 4 OR 5
7. clinical trials.sh.
8. controlled clinical trials.sh.
9. randomized controlled trial.sh.
10. double-blind procedure.sh.
11. (clin* adj25 trial*).ab.
12. ((doubl* or trebl* or tripl*) adj25 (blind* or mask*)).ab.
13. placebo*.ab.
14. random*.ab.
15. OR/7-14
16. 3 AND 6 AND 15

Appendix 3. Search strategy for CENTRAL

1. Exp MESH descriptor Sympathectomy
2. (sympathectomy OR sympatholysis OR sympathicotomy):ti,ab,kw
3. 1 OR 2
4. Exp MESH descriptor Neuralgia
5. ("complex regional pain syndrome" OR "reflex sympathetic dystrophy" OR causalgia OR "phantom limb pain" OR allodynia OR "diabetic neuropath*" OR "trigeminal neuralgia" OR "post-herpetic neuralgia" OR "neuropathic adj2 pain"):ti,ab,kw
6. 4 OR 5
7. Randomized controlled trial:pt
8. MESH descriptor Double-blind Method
9. random*:ti,ab,kw.
10. OR/7-9
11. 3 AND 6 AND 10
12. Limit 11 to Clinical Trials (CENTRAL)

WHAT'S NEW

Last assessed as up-to-date: 18 May 2010.

Date	Event	Description
27 June 2012	Amended	Contact details updated.

HISTORY

Protocol first published: Issue 1, 2001

Review first published: Issue 2, 2003

Date	Event	Description
15 January 2010	New citation required and conclusions have changed	One study (Manjunath 2008), with 20 participants, satisfied the inclusion criteria. It did not show a difference between radiofrequency lumbar sympathectomy and lumbar sympathectomy with phenol over 4 months following the intervention. The practice of sympathectomy for neuropathic pain is based on little high quality evidence and carries a risk of serious complications. The four studies included in the earlier review were excluded because they were not randomised, double blind, controlled trials
15 January 2010	New search has been performed	This review was updated with a new search in December 2009. The review title was changed to reflect the scope of the review more accurately. Study inclusion criteria and primary outcomes were revised: review now in-

(Continued)

		cludes only studies of the highest methodological quality (randomised and double blind), and uses more rigorous outcomes as defined by the IMMPACT group. Further searching to May 2010 found no additional studies
13 May 2009	Amended	Contact details updated.
14 October 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

SS and SD carried out searches, identified studies for inclusion and extracted data. All authors were involved in discussions about updating the Methods section (Inclusion criteria and Outcomes), and in writing the final review. All authors read and approved the final manuscript. SS will be responsible for the update.

DECLARATIONS OF INTEREST

SS, RAM, HJM, SD have received grants and research support from charities, government, academic, and industry sources at various times. RAM and HJM have consulted for various pharmaceutical companies and have received lecture fees from pharmaceutical companies related to analgesics and other healthcare interventions, including companies that manufacture drugs used to treat neuropathic pain. No pharmaceutical company had any involvement in funding or carrying out this review.

SOURCES OF SUPPORT

Internal sources

- Pain Research Funds, UK.

External sources

- NHS Cochrane Collaboration Programme Grant Scheme, UK.
- NIHR Biomedical Research Centre Programme, UK.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

This updated review differs from the earlier review primarily in the methodological quality of included studies and the choice of efficacy outcomes. It now includes only studies of the highest methodological quality (randomised and double blind) because these are known to be less prone to bias (Moore 2006), which is of utmost importance in pain studies where outcomes are subjective, and uses more rigorous outcomes as defined by the IMMPACT group (Dworkin 2008).

INDEX TERMS

Medical Subject Headings (MeSH)

Catheter Ablation [methods]; Complex Regional Pain Syndromes [*therapy]; Leg [innervation]; Neck; Neuralgia [*therapy]; Phenol; Randomized Controlled Trials as Topic; Sympathectomy [*methods]; Sympathectomy, Chemical [methods]; Sympatholytics; Thorax

MeSH check words

Humans