



**INSTITUTE OF
HEALTH ECONOMICS**
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NERVE BLOCKS FOR NEUROPATHIC PAIN

ADDENDUM TO SUMMARY OF THE LITERATURE

**Canadian Pain Society Special Interest Group on
Neuropathic Pain**

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SCOPE OF THE ADDENDUM

This addendum was prepared in response to a request from the Canadian Pain Society Special Interest Group on Neuropathic Pain (NeP SIG) to broaden the inclusion criteria for clinical practice guidelines, with the aim of making the evidence-base more clinically relevant.

This addendum was conducted according to a predefined methodology that was formulated in consultation with NeP SIG representatives. It does not represent a systematic review of the literature on nerve blocks for the treatment of neuropathic pain; thus, no firm conclusions are offered on the safety or effectiveness of this intervention. In addition, the evidence was only summarized and no attempt was made to assess the veracity of the information contained within the included guidelines.

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METHODS

Modification to the inclusion criteria

Participants

In the original document, data were collected on adult patients (18 years of age or older) with a peripheral or central neuropathic pain condition of any duration. However, given the dearth of clinically useful guidelines on the use of nerve blocks for neuropathic pain, this inclusion criterion was broadened to include patients of any age with a peripheral or central neuropathic pain condition of any duration.

SUMMARY OF ADDITIONAL GUIDELINES

Two additional clinical practice guidelines (CPGs) were included as a result of removing the age limit on patients included in CPGs (Table 1). Study profiles of the included CPGs are summarized in Table 2. The relevant recommendations from each of the included CPGs are provided in Table 3.

Table 1: Summary of additional included guidelines

Study	Year	Quality Rating	Pain Condition
Netherlands Society of Rehabilitation Specialists and the Netherlands Society of Anaesthesiologists ¹	2006	Good (25.5/28)	Complex regional pain syndrome type I
New Zealand Accident Compensation Corporation ²	2005	Good (23.5/28)	Persistent non-cancer pain

STUDY PROFILES – CLINICAL PRACTICE GUIDELINES

Table 2: Study profiles for *clinical practice guidelines* on nerve blocks for neuropathic pain

Guideline	Target Population	Selection Criteria/Outcomes	Methods
<p>Netherlands Society of Rehabilitation Specialists and the Netherlands Society of Anaesthesiologists (2006)¹</p> <p>Objective: To achieve uniformity in the diagnosis and treatment in the various centres and to define the contexts in which multidisciplinary care should be provided to patients with complex regional pain syndrome type I (CRPS-I).</p> <p>Target users: All medical practitioners involved in treating patients with CRPS-I, such as general practitioners, rehabilitation specialists, rheumatologists, anaesthesiologists, neurologists, paediatricians, surgeons, neurosurgeons, plastic surgeons, orthopaedic surgeons, company doctors, insurance doctors, psychologists, physiotherapists, and occupational therapists.</p> <p>Financial support: Order of Medical Specialists in the context of the Evidence-Based Guidelines Development programme.</p> <p>Conflict of interest: None. Files available on request.</p>	<p>Age: Children and adults.</p> <p>Included conditions: CRPS-I.</p> <p>Excluded conditions: Not stated.</p>	<p>Interventions: Medical, interventional, and surgical treatment.</p> <p>Study inclusion/exclusion criteria: Meta-analyses, systematic reviews, randomised controlled trials and controlled trials. When these were not available, comparative cohort, comparative patient control, or non-comparative trials were included. Studies were included if they had adequate size, adequate follow-up, adequate exclusion of selection bias, and the results could be translated to the local context in the Netherlands.</p>	<p>Literature search: Time period: 1980 to June 2004. Limits: English, German, French, Italian, or Dutch language publications. Databases: MEDLINE, EMBASE, the <i>Cochrane Library</i>, CINAHL, and PsycINFO. Other sources: Additional reports were identified from manual searches, recent guidelines on CRPS-I, and the reference lists of retrieved studies.</p> <p>Appraisal of study quality: Members of the project group assessed the quality of the included studies on the basis of Evidence-Based Guidelines Development assessment forms. Articles of moderate or poor quality were excluded. The remaining included studies were then graded according to their evidential strength.</p> <p>Formulation of recommendations: A number of subgroups with representatives of relevant disciplines were set up. A group of core editors was responsible for coordination and consultation between the subgroups. The project group produced texts, either individually or in subgroups, that were discussed at plenary meetings and approved after comments had been taken into account. The plenary project group met ten times to discuss the results of the subgroups. The subgroups' texts were integrated into a single draft guideline by the core editors. These guidelines were presented for comment at a national guidelines meeting. Once the comments had been taken into account, the guidelines were adopted by the full project group and sent to the relevant professional bodies for approval.</p> <p>External review: Peer review by relevant professional bodies.</p> <p>Evidence linked to recommendations: Yes.</p>

Table 2: Study profiles for *clinical practice guidelines* on nerve blocks for neuropathic pain (cont'd)

Guideline	Target Population	Selection Criteria/Outcomes	Methods
<p>New Zealand Accident Compensation Corporation (2005)²</p> <p>Objective: To assist health practitioners and consumers make informed decisions in the management of persistent non-cancer pain.</p> <p>Target users: Health practitioners and consumers.</p> <p>Financial support: Not reported.</p> <p>Conflict of interest: Some members of the advisory group who are in clinical practice receive payments from the New Zealand Accident Compensation Corporation for the use of interventional pain management procedures. Some members of the advisory group received fees for providing services to various pharmaceutical companies.</p>	<p>Age: People over the age of 12 years.</p> <p>Included conditions: Persistent non-cancer pain.</p> <p>Excluded conditions: Pain due to malignancy; acute resolving pain such as postoperative pain; childbirth; dysmenorrhoea; dental pain; infection such as postherpetic neuralgia; systemic inflammatory conditions; migraine; angina; other visceral pain; peripheral vascular disease; haematological disorders.</p>	<p>Interventions: Infusions, injections, intradiscal electrothermal therapy, nerve blocking procedures, neuroablation, neuromodulation.</p> <p>Study inclusion criteria: Systematic reviews; guidelines; randomized controlled trials; quasi-randomized controlled trials; concurrent control and case-control studies with at least 10 participants; case series and cohort studies with at least 50 participants. Case series and cohort studies with fewer than 50 participants were included if they reported on adverse events or safety concerns associated with the intervention in question.</p> <p>Study exclusion criteria: Studies that: reported on healthy volunteers or involved experimentally induced pain; did not report pain control or pain relief as a primary outcome; were graded as low quality.</p>	<p>Literature search: <u>Time period:</u> See databases. <u>Limits:</u> English language publications. <u>Databases:</u> MEDLINE (1966 to April 2004), EMBASE (1988 to April 2004), PsycINFO (1974 to April 2004), the <i>Cochrane Database of Systematic Reviews</i>, the American College of Physicians Journal Club, the Database of Abstracts of Reviews of Effects, the Cochrane Central Register of Controlled Trials, and the TRIP database. <u>Other sources:</u> Additional reports were identified from manual searches of five journals (January 2003 to April 2004): <i>Spine</i>, <i>The Spine Journal</i>, <i>Clinical Journal of Pain</i>, <i>Regional Anaesthesia and Pain Medicine</i>, and <i>Pain Research and Management</i>. The <i>Journal of Negative Results in Biomedicine</i> and the proceedings of the International Association for the Study of Pain 9th and 10th world conferences were searched for relevant material, as were the reference lists of retrieved studies.</p> <p>Appraisal of study quality: Researchers from the New Zealand Health Technology Assessment unit appraised all eligible experimental studies, guidelines, systematic reviews, and health technology assessments using the Generic Appraisal Tool for Epidemiology (GATE) checklists.³ Observational studies were assessed with an alternative rating system.⁴</p> <p>Formulation of recommendations: The whole body of evidence for each intervention was considered by the advisory group and clinical practice recommendations were made using a considered judgement form.</p> <p>External review: Not reported.</p> <p>Evidence linked to recommendations: Yes, for most recommendations.</p>

SUMMARY OF RELEVANT DATA – CLINICAL PRACTICE GUIDELINES

Table 3: Summary of relevant data extracted from *clinical practice guidelines* on nerve blocks for neuropathic pain

Guideline/ Quality Rating	Synopsis of Recommendations	Supporting Evidence*						
		SR/MA	NR	RCT	NRCS	CS	G	Other
Netherlands Society of Rehabilitation Specialists and the Netherlands Society of Anaesthesiologists (2006) ¹ (The Netherlands) Quality rating: Good (25.5/28)	The evidence available is insufficient to allow any conclusions to be drawn on the efficacy of local anaesthetics in the sympathetic ganglia when treating patients with complex regional pain syndrome type I (CRPS-I).			1 5		1 6		
	Intravenous sympathetic blockade has no place in the treatment of patients with CRPS-I.	3 7-9						
	Intravenous administration of 10-20 mg of ketanserin can be considered for the treatment of patients with CRPS-I. Routine administration of reserpine, droperidol, and atropine is not recommended for patients with CRPS-I.	1 8		2 10,11				
	Patients with cold CRPS-I who do not respond adequately to vasodilating medication can be considered for percutaneous sympathetic blockade using local anaesthetics. If a trial blockade has proved successful, definitive sympathetic blockade using radiofrequent lesions, phenol, or alcohol can be considered in the context of a trial.	1 12		1 13		6 14-19		

Table 3: Summary of relevant data extracted from *clinical practice guidelines* on nerve blocks for neuropathic pain (cont'd)

Guideline/ Quality Rating	Synopsis of Recommendations	Supporting Evidence*						
		SR/MA	NR	RCT	NRCS	CS	G	Other
New Zealand Accident Compensation Corporation (2005) ² (New Zealand) Quality rating: Good (23.5/28)	<p><i>Common peroneal nerve block</i></p> <ul style="list-style-type: none"> There is medium quality evidence that common peroneal nerve block is effective in the very short term for the treatment of adults with sciatic radicular pain. Pain relief was only measured for 15 minutes after the procedure. The RCT did not report on safety, however, it is known that this technique may carry an increased risk of nerve injury (peripheral neuritis), compared to other nerve blocks. <p>Common peroneal nerve block is not recommended for the treatment of adults with sciatic radicular pain. This procedure is unlikely to be used in isolation for sciatic radicular pain.</p>			1 20				
	<p><i>Intravenous (IV) regional sympathetic block</i></p> <ul style="list-style-type: none"> There is consistent evidence that IV regional sympathetic block with guanethidine is not effective in the treatment of adults with complex regional pain syndrome. There is some evidence from two very small trials that IV regional sympathetic block with bretylium or ketanserin may be effective. There is evidence from one medium quality RCT that IV regional sympathetic block with magnesium and lidocaine is effective in the short-term, compared to IV sympathetic regional block with lidocaine alone, for the treatment of adults with chronic limb pain. Significant adverse effects, which include hypotension, hypertension and tachycardia, have been reported with guanethidine and bretylium. Magnesium Bier's block is a painful procedure with post-treatment aching in muscles or bones. <p>IV regional sympathetic blocks are not recommended for the treatment of complex regional pain syndrome.</p> <p>No recommendation was made for chronic limb pain because there was insufficient evidence to support or refute the effectiveness of magnesium/lidocaine IV regional sympathetic blocks for the treatment of adults with chronic limb pain.</p> <p>The use of magnesium in IV regional sympathetic blocks should be restricted to the research setting. Currently the clinical relevance of IV regional sympathetic block is in the multimodal setting, for which we have no evidence on which to comment. There is potential severe risk from IV injection of guanethidine and bretylium. (cont'd next page)</p>	5 7-9,21,22		2 23,24	1 25			

Table 3: Summary of relevant data extracted from *clinical practice guidelines* on nerve blocks for neuropathic pain (cont'd)

Guideline/ Quality Rating	Synopsis of Recommendations	Supporting Evidence*						
		SR/MA	NR	RCT	NRCS	CS	G	Other
New Zealand Accident Compensation Corporation (2005) ² (cont'd)	<p><i>Spinal nerve block</i></p> <ul style="list-style-type: none"> One medium quality case series provided information on the effectiveness of lumbar spinal nerve block in the treatment of patients with acute and chronic osteoporotic vertebral fractures and radicular pain unresponsive to conservative treatment. <p>There is insufficient evidence to support or refute the use of spinal nerve block in the management of persistent non-cancer pain.</p>					1 26		
	<p><i>Sympathetic ganglion block</i></p> <ul style="list-style-type: none"> One high quality systematic review of mostly low quality non-randomized studies concluded that there was a low rate of pain relief, which was consistent with a placebo response in patients treated with sympathetic nerve block with anaesthetic for complex regional pain syndrome. Two medium quality systematic reviews concluded that the low quality of the evidence precluded definite conclusions relating to the effectiveness of this intervention for complex regional pain syndrome. One small medium quality RCT reported significant short-term pain relief. A total of 19 RCTs were assessed. One guideline recommended that nerve block procedures should be limited to those patients in which functional capacity can be improved. There have been reports of rare, severe complications from this procedure. <p>The general use of lumbar sympathetic ganglion block is not recommended for the treatment of adults with complex regional pain syndrome. However, it may be considered in the research setting.</p>	3 7,8,12		2 27,28			1 29	

Table 3: Summary of relevant data extracted from *clinical practice guidelines* on nerve blocks for neuropathic pain (cont'd)

Guideline/ Quality Rating	Synopsis of Recommendations	Supporting Evidence*						
		SR/MA	NR	RCT	NRCS	CS	G	Other
New Zealand Accident Compensation Corporation (2005) ² (cont'd)	<p><i>Trigeminal nerve block</i></p> <ul style="list-style-type: none"> • There is evidence from a medium to high quality RCT of 17 patients of short-term effectiveness (1 week, number needed to treat = 2) for five weekly trigeminal nerve block injections of streptomycin and anaesthetic. In the longer term (>6 months), trigeminal nerve block injections including streptomycin were no more effective than injections of anaesthetic alone (number needed to treat = 12). A second medium quality RCT of 20 patients reported no significant difference between blocks using anaesthetic and streptomycin and anaesthetic alone. • There were no direct comparisons of trigeminal nerve block and other interventions (such as medical management) for idiopathic trigeminal neuralgia. • Trigeminal nerve block with streptomycin has been reported to cause marked swelling of the face and hyperaesthesia in and around the site of the block for up to 7 days. Complications of bupivacaine/methylprednisolone trigeminal nerve blocks include systemic toxicity to local anaesthetic, vasovagal syncope, and ecchymoses at injection site. <p>Trigeminal nerve block is not recommended for the treatment of adults with trigeminal neuralgia.</p>			2 30,31		2 Refer- ences for these studies were not pro- vided.		

*The integers listed in the Supporting Evidence columns represent the total number of discrete studies. Thus, when there are multiple publications for a single study, the integers are less than the number of references listed below them.

QUALITY ASSESSMENT RESULTS – CLINICAL PRACTICE GUIDELINES

Table 4: AGREE tool quality assessment results for included clinical practice guidelines (two appraisers)

Guideline Characteristic		Netherlands Society of Rehabilitation Specialists & the Netherlands Society of Anaesthesiologists (2006) ¹		NZ Accident Compensation Corporation (2005) ²	
Scope/ purpose	1.Objectives	4	4	3	3
	2. Clinical question	3	4	4	4
	3. Target population	4	3	4	3
Stakeholder involvement	4. Relevant professional groups represented	4	4	2	4
	5. Patients' perspectives included	2	2	2	2
	6. Target users defined	4	4	3	2
	7. Piloted among target users	2	4	2	2
Rigour of development	8. Systematic search conducted	4	4	4	4
	9. Selection criteria described	3	4	4	4
	10. Methods used to formulate recommendations described	2	4	2	4
	11. Benefits, side effects, risks considered	4	4	4	4
	12. Link between recommendations and evidence	4	4	4	4
	13. External review by experts	2	4	1	2
	14. Updating procedure described	4	4	3	3
Clarity/ presentation	15. Specific, unambiguous recommendations	4	4	4	4
	16. Different management options presented	1	4	1	4
	17. Key recommendations easily identifiable	4	4	4	4
	18. Additional support materials provided	4	1	1	1
Applicability	19. Organizational barriers discussed	1	1	1	1
	20. Resource implications considered	1	1	1	1
	21. Key review criteria presented	4	3	1	1
Editorial independ- ence	22. Editorially independent from funder	3	4	2	4
	23. Conflicts of interest reported	4	4	4	4
Quality rating	Seven criteria (systematic search, method of formulating recommendations, recommendations-evidence link, external review, clear recommendations, editorial independence, conflict of interest)	25.5 Good		23.5 Good	

Table 5: AGREE tool standardized domain scores (%) for included clinical practice guidelines (two appraisers)

AGREE Domain	Netherlands Society of Rehabilitation Specialists & the Netherlands Society of Anaesthesiologists (2006)¹	New Zealand Accident Compensation Corporation (2005)²
Scope and purpose	89	83
Stakeholder involvement	75	46
Rigour of development	88	79
Clarity and presentation	75	75
Applicability	28	0
Editorial independence	92	83

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