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Another year has gone by and the European Journal of Pain has now become an established vehicle for the publication of high quality reports in the field of pain research and treatment. Some changes have occurred during the year that deserve a few comments from the editorial office.

THE EUROPEAN JOURNAL OF PAIN IS NOW PUBLISHED SIX TIMES A YEAR

This is a momentous event for the journal but also one that was expected for a journal that has developed so quickly and that has shown such a healthy rate of growth. The EJP began, like most new journals, as a quarterly publication. From the start we were committed to offering our authors a fast vehicle for publication and we are happy to report that three quarters of the submissions to the journal get a first review answer within 8 weeks of receipt with more than one third in less than 5 weeks. Full electronic handling of all manuscripts has a lot to do with this fast rate of review. As the number of submissions increased we were faced with the situation of having a backlog of accepted papers that had to wait several months before they could be published. I presented this state of affairs to the EFIC Council last year and they approved an increased frequency of publication to six issues per year, starting January 2002. This has dealt effectively with the backlog of accepted papers and will reduce the time between acceptance and publication.

MORE HIGH QUALITY SUBMISSIONS AND A WIDER RANGE OF PAPERS

The need to move from quarterly to bimonthly reflects not only an increased number of submissions but also the fact that many are of high quality and that we also have an increased number of accepted papers. It is rewarding to note the increase in the number of excellent basic science papers from well established laboratories and the wide range of topics dealt with in the clinical submissions. We also receive many good papers dealing with psychological and social aspects of pain treatment as well as some that address questions especially relevant to Europe. This is not to say that the journal is exclusively European, on the contrary, we receive and publish many articles from all over the world, including the United States, Canada, Australia, Japan and many other non-European countries. Our title indicates the base and origin of the journal, our contents show the international character of the publication.

CHANGES AT THE PUBLISHING HOUSE

As you may know, last year our publishing house, Harcourt, was incorporated into the Elsevier publishing group. We are now published by Elsevier Science, the same publisher that also produces PAIN, the official journal of IASP and The Journal of Pain, the journal of the American Pain Society. We look forward to working with our new publishers.

FERNANDO CERVERO
EDITOR-IN-CHIEF
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Neurolytic blockade of the obturator nerve for intractable spasticity of adductor thigh muscles

Eric J. Viel, Dominique Perennou, Jacques Ripart, Jacques Pélissier and Jean J. Eledjam

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Neurolytic blockade is one of the therapeutic possibilities to treat spasticity of various muscles. In patients with spasticity of the adductor thigh muscles, a percutaneous approach to the obturator nerve is often difficult. We describe a new approach to the obturator nerve and we examine its feasibility. The second objective was to assess the efficacy of obturator neurolysis for the management of adductor thigh muscle pain and spasticity associated with hemiplegia or paraplegia. Nerve blocks were performed via a combined approach using fluoroscopy and nerve stimulation to identify the obturator nerve. Neurolysis was performed by injection of 65% ethanol. We performed 27 blocks in 23 patients. Technical evaluation was achieved in terms of number of attempted needle insertions, time to accurate location of the nerve and success rate. The efficacy of the block was assessed using four scores: degree of alleviation of muscle spasm and triple flexion of the lower limb, improvement of gait and facilitation of hygienic care. Success rate of the technique was 100% with a time to accurate nerve location of 130 ± 35 s. Compared with scores measured immediately before the block, all studied parameters were significantly improved. Efficiency was significant on adductor muscle spasticity (p < 0.001 at 1 day and p < 0.01 at 60 and 120 months). Triple flexion was also significantly improved (p < 0.05 from 1 to 120 days), as well as gait (p < 0.02) and hygiene (p < 0.01) scores. No complications occurred. The combined approach of the obturator nerve represents a new technique which proved to be accurate, fast, simple, highly successful and reproducible. Obturator neurolysis was confirmed as an efficient and cost-effective technique to reduce adductor muscle spasm and related pain and to improve gait and hygienic care in patients with neurological sequelae of stroke, head trauma or any lesion of the motor neurone. © 2002 European Federation of Chapters of the International Association for the Study of Pain

KEYWORDS obturator nerve, obturator canal, fluoroscopy, regional anaesthetic technique, stroke, head trauma, multiple sclerosis.

INTRODUCTION

Adductor thigh muscle spasticity is a frequent complication of stroke, cerebral palsy, head and/or spine trauma and multiple sclerosis. Hypertonicity and pain often represent a major source of disability and pain in patients with chronic disorders of the pyramidal tract (Awad, 1972; Loubser, 1997; Kirazli et al., 1998; Viel et al., 2000), especially if we consider gait and hygienic care in patients who are frequently bedridden. In this particular condition, spasticity is usually
non-reducible, frequently painful and prevents patients from having an efficient therapeutic rehabilitation programme.

Obturater neurolysis, using various agents and approaches, is a common treatment to alleviate adductor muscle spasticity (Awad, 1972; Wassef, 1993; Wainapel et al., 1984). The percutaneous approach had been described as early as 1928 by Labat but, surprisingly, this nerve remains difficult to block. Even in healthy patients, where the so-called '3-in-1 block' is defined to include blockade of the obturator nerve, this nerve is usually not sufficiently blocked if the anaesthetic solution is injected near the inguinal ligament (Parkinson et al., 1989). This is even more difficult or even impossible in those spastic patients with anatomical difficulties because, to a variable degree, lower limbs are crossed in front of each other (Magora et al., 1969; Lennard and Shin, 2000). The use of nerve stimulation has been reported to increase the success rate of obturator nerve location (Gasparich et al., 1984; Wassef, 1993; Viel et al., 2000). Therefore, the need for a simplified approach, aiming at improving the identification and success rate of this block, is real. The aims of this study were to evaluate a new simplified and accurate approach to the obturator nerve, based on the combination of fluoroscopy and nerve stimulation, and to assess prospectively its efficacy in the management of adductor muscle spasticity.

ANATOMIC AND TECHNICAL CONSIDERATIONS

The obturator nerve belongs to the lumbar plexus, arising from the ventral branches of L2, L3 and L4 nerve roots, inside the psoas muscle. It emerges from the medial border of the psoas muscle to enter the pelvis. The nerve then passes downward along with the obturator vessels and leaves the pelvis through the obturator canal to enter the thigh. In its course, the anterior branch supplies sensory innervation to the hip joint and to the medial portion of the thigh and motor branches are given off to the external obturator, the gracilis and the anterior adductor muscles. The posterior branch supplies sensory articular innervation to the knee joint and motor innervation to the deep adductor muscles.

In order to improve conditions and success rate of the technique of obturator nerve blockade, we have developed a new technique of nerve location based on the combination of nerve stimulation and fluoroscopy. The patient was placed in the supine position on the radiology table and the radiologist positioned the patient and the X-ray beam in order to obtain an obturator oblique view of the pelvis. This technique allowed a perfect visualization of the obturator canal (Fig. 1). Then, the needle was positioned accurately in front of the foramen and a skin landmark was drawn and infiltrated with 1% lidocaine. We used a 100 mm insulated (Teflon®-coated) needle (Stimuplex®, B.Braun, Melsungen, Germany) connected to a variable amperage nerve stimulator (Stimuplex S®, B.Braun, Melsungen, Europe).

FIG. 1. Obturator oblique view of the pelvis showing correct placement of the needle into the obturator canal.
gave informed consent. Twenty-three patients, presenting with unilateral or bilateral adductor thigh muscles spasm, consented to the procedure and entered the study. In chronically comatose patients, consent was obtained from their family. Obturator nerve blocks were performed as described in the previous section, using 65% ethanol as a neurolytic agent. This concentration was obtained by dilution of a 95% solution with normal saline. The injected volume of alcohol was 8–9 ml for each nerve. Results were evaluated considering technical aspects on the one hand and functional aspects on the other hand.

Technical parameters included number of attempted needle insertions, time to accurate location of the nerve and success rate.

Functional evaluation included four different scores:

- **Adductor thigh muscle spasticity** was assessed by passive mobilization of the thigh in abduction, at slow, medium and high speed. We used a four-point score: 0 = ability to abduct the thigh easily to 45°; 1 = ability to abduct the thigh to 45° with mild effort; 2 = ability to abduct the thigh to 45° with major effort; 3 = inability to abduct the thigh to 45°.

- **Triple flexion** of the lower limb, consecutive to the flexor muscle spasm, was assessed using a four-point scale: 0 = hip and/or knee flexion <30°, with or without mild gait disability; 1 = hip and/or knee flexion between 30° and 45° with moderate gait disability; 2 = hip and/or knee flexion between 45° and 60° with severe gait disability; 3 = hip and/or knee irreducible flexion with gait inability.

- **Gait** was assessed, when possible, using a four-point score, representing the effect of obturator neurolysis on spasm and leg crossing: 0 = the patient is able to walk with mild difficulty; 1 = the patient is able to walk with moderate difficulty; 2 = the patient is able to walk with severe difficulty; 3 = the patient is unable to walk.

- **Hygiene** was assessed using a four-point scale, considering the ability of the patient to perform perineal hygiene care, related to the degree of adductor muscles spasticity: 0 = hygienic performance with relative ease;

**PATIENTS AND METHODS**

The study was approved by our University Hospital's Institutional Review Board and Ethics Committee and all patients and/or their family

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**FIG. 2.** Anatomical drawing of an oblique view of the pelvis showing the site of needle placement into the obturator canal.
1 = hygienic performance with mild difficulty; 2 = hygienic performance with moderate difficulty; 3 = hygienic performance with severe difficulty.

All these four scores, reflecting the degree of alleviation and relief of muscle spasm, were evaluated before ($T_0$: control time) and immediately after the obturator nerve block (day 1) and then at 30, 60 and 120 days. Data of various parameters were calculated as medians ± SEM. Student's t-test and χ² analysis were used for statistical analysis where appropriate. A value of $p < 0.05$ was considered significant.

RESULTS

Patients' characteristics and technical parameters

Twenty-three patients (six female, 17 male), presenting with adductor muscle spasm, underwent an obturator neurolytic nerve block. Mean age was 42 ± 17 years (range: 19–71 years). Diseases causing adductor muscle spasm were stroke (10 patients), cerebral palsy (four patients), spine and/or head trauma (seven patients) and multiple sclerosis (two patients). Mean duration of the causative disease was 9.5 ± 7 years (range: 3 months–27 years). The total number of obturator blocks was 27, as 19 patients received a single unilateral block (eight on the right obturator nerve, 11 on the left side) and four patients bilateral blocks.

Number of attempts for needle insertion was 1.2 ± 0.3. Time to adequate location, representing the time elapsed from correct positioning on the table to the end of nerve location procedure, was 130 ± 35 s (range: 70–550 s). Success rate in nerve location was 100%.

Adductor muscle spasm (Fig. 3)

Main score for adductor muscle spasm, quoted as 3 before the block, dramatically decreased to 1 immediately after neurolytic block ($p < 0.001$). This result was confirmed at 1 month, and increased to 1.5 ± 0.3 at 2 and 4 months ($p < 0.01$) (Fig. 2).

Triple flexion, gait and hygiene scores (Figs 4 and 5)

Triple flexion score also decreased significantly from 1.6 to 0.8, 0.5, 0.8 and 0.9 at 1, 30, 60, 120 days respectively ($p < 0.05$) (Fig. 3). Differences were also significant for gait score ($p < 0.02$) (Fig. 4) and hygiene score ($p < 0.01$) (Fig. 5). This improvement resulted in a simplified degree of nursing and physiotherapeutic care as compared with the situation before the block.
DISCUSSION

Traditional approaches to the obturator nerve are quite unsuitable in patients presenting with spastic conditions of the lower limbs, because of major difficulties in achieving adequate positioning. In this study, the high success rate (100%) of obturator nerve blocks we obtained could be attributed to a more accurate approach, thanks to the combination of X-ray and nerve stimulation. This is to be compared with more traditional approaches, with a success rate of approximately 60% or less (Magora et al., 1969), or even with a modified technique (Wassef, 1993) with an 80% success rate.

Technical issues

The obturator nerve can be blocked using the ‘3-in-1’ block technique, also known as the paravascular inguinal block of the lumbar plexus (Winnie et al., 1973). However, it is likely that the obturator nerve is frequently not blocked in this technique (Magora et al., 1969; Parkinson et al., 1989), as its deep situation makes its location difficult to reach. A direct approach to the obturator nerve has been shown to be significantly more effective in producing motor block (Atanassof et al., 1995). Single blockade of the obturator nerve, seldom used in surgical anaesthesia, was advocated during transurethral endoscopic surgery (Gasparich et al., 1984), in order to prevent accidental stimulation of the nerve during electrocautery and, consequently, unwanted adductor contraction that can lead to a bladder perforation.

In the traditional approach, the patient lies supine with the lower limbs slightly spread. The main bony landmark is the spine of the pubic bone. Although well described, the blind percutaneous approach remains difficult even in expert hands (Magora et al., 1969), with a relatively high failure rate. Then, alternative approaches have been described in order to improve its success rate, based for example on the use of nerve stimulation (Gasparich et al., 1984) that allows visible and palpable twitch contractions of the...
adductor muscles to be elicited. In our patients, the additional problem was that they could not be placed in a suitable position, as opening lower limbs was markedly difficult or even impossible to achieve because of the scissoring effect of adductor spasm (Lennard and Shin, 2000). In an attempt to go round these technical difficulties, Wassel (1993) described a variant approach, called the interadductor approach. In a patient lying supine, the surface landmark was located 1–2 cm medial to the femoral artery, immediately below the inguinal ligament. The adductor longus muscle tendon was identified at its pubic insertion and the needle was introduced behind it, directed laterally and slightly posterior and superior toward the skin landmark. The needle was connected to a nerve stimulator and successful location was obtained when adductor muscle contractions resulted. In this series, Wassel obtained a significantly higher success rate, with fewer needle attempts as compared with the traditional approach, both using a nerve stimulator.

Whatever the block, accurate placement of the needle is critical to success (Kirazli et al., 1998). In our technique, cutaneous and osseous landmarks no longer appeared essential for the accuracy of nerve location. The technique allowed (a) the tip of the needle to be placed easily in the upper part of the obturator foramen, where the obturator nerve usually lies (Fig. 2), and (b) the accurate placement of the needle to be identified by eliciting the corresponding motor response. Then, as soon as correct placement was achieved, therapeutic neurolytic block could be immediately performed. This improved accuracy could, at least in part, explain the high success rate, as compared with more traditional approaches, in which needle tip positioning is seldom as accurate. Furthermore, this technique allowed the injection of the neurolytic agent within the obturator canal before its division and, consequently, guaranteed blockade of both the anterior and the posterior branches of this nerve. Therefore, spasticity can be relieved on all three adductor thigh muscles (adductor brevis, longus and magnus muscles). Finally, the time to accurate nerve location was shortened.

**Efficiency issues**

Spasticity of the lower limb, especially adductor muscle spasm, is a major source of long-standing disability and pain in neurological patients. Several therapeutic approaches have been proposed to treat spasticity (Young and Dewade, 1981; Myers and Katz, 1992), including physiotherapy, systemic drugs (dantrolene sodium, baclofen, ...), surgery (Gros, 1979) and, more recently, botulinum toxin (Snow et al., 1990; Mémin et al., 1992) and cryoanalgesia (Kim and Ferrante, 1998). The efficacy of neurolytic blocks in reducing skeletal muscle spasm has been reported in several studies (Awad, 1972; Wainapel et al., 1984; Myers and Katz, 1992; Wassel, 1993; Serrie et al., 1994; Kirazli et al., 1998; Viel et al., 2000), using glycerol, high-concentration local anaesthetics, alcohol (Labat, 1928; Myers and Katz, 1992) or phenol (Awad, 1972; Wainapel et al., 1984; Wassel, 1993; Loubser, 1997; Kirazli et al., 1998). Alcohol (35–90%) and phenol (5–12%) are sometimes associated with the development of neuritis, but whether one of these agents may be responsible for a higher incidence of this complication is not definitely clear cut. The primary goal of functional rehabilitation of these neurological patients was to obtain conversion from a bedridden or chairbound status to an improved ability to walk. Obturator nerve blockade, together with physiotherapy and rehabilitation exercises, favored the development of a more efficient gait pattern. Enhancing the interankle distance and reducing triple flexion also contributed to improve gait. In patients with spastic conditions, hip flexion results from the bending action of adductor thigh muscles, while knee flexion results from the flexor role of the gracilis muscle and the hamstrings. The dramatic improvement of triple flexion in our population confirmed the first-line role of adductor muscle block to treat the consequences of spasticity of the lower limbs. Another goal in the nursing care of spastic patients, too often chairbound or bedridden, was to allow adequate hygienic care. Again, the obturator nerve blockade, by reducing thigh adduction, led to the suppression of a significant source of strain and discomfort in performing daily perineal hygienic care.
In some patients, it could also facilitate specific care, such as self-catheterization of the bladder.

**Cost-effectiveness issues**

We did not perform in our study any economic comparison between our technique (regional neurolytic blocks) and other treatments of spasticity. If we only consider direct costs, we have already reported a cost of 8.23€ for the Tellon®-coated needle and 2.44€ for 10 mL of alcohol. In contrast, systemic treatment with dantrolene sodium (200–400 mg per day) ranges from 4.22€ to 8.44€ per day and from 1.44€ to 1.92€ per day with baclofen (30–40 mg per day). In addition, in the long term, one must consider the limited efficacy of these oral treatments and the risks of adverse effects (generalized weakness, hepatotoxicity) and their decreasing efficiency with time. Other regional approaches include intramuscular injections of botulinum toxin type A (500 U: 251.54€) and, exceptionally, intrathecal infusion of baclofen via indwelling catheters and pumps (mean cost: 6500–7000€). Then, considering our patients suffering from definite sequelae and the simplicity and the efficiency of our technique, cost-effectiveness appeared as an additional advantage.

**CONCLUSION**

In conclusion, this study proved obturator neurolysis to be an efficient technique to reduce adductor muscle spasm and, by allowing a new rehabilitation programme to be started, to improve gait and hygienic care in patients with neurological sequelae of stroke, head trauma or any lesion of the motor neurones. Our combined approach appeared accurate, simple and rapid. Its simplicity and its efficacy suggest that this procedure should be indicated more often and earlier in patients with spastic conditions to maximize the functional benefits of the rehabilitation programme.

**ACKNOWLEDGEMENTS**

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**REFERENCES**


Treatment of complex regional pain syndrome type I

Tymour Forouzanfar, Albere J. A. Köke, Maarten van Kleef and Wilhelm E. J. Weber

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Reflex sympathetic dystrophy (RSD), also known as complex regional pain syndrome type I (CRPS I), is a disabling neuropathic pain syndrome. Controversy exists about the effectiveness of therapeutic interventions for the management of RSD/CRPS I. In order to ascertain appropriate therapies we conducted a review of existing randomized controlled trials of therapies for this disabling disease. Eligible trials were identified from the Cochrane, Pubmed, Embase and MEDLINE databases from 1966 through June 2000, from references in retrieved reports and from references in review articles. Twenty-six studies concerning treatment modalities were identified. Eighteen studies were randomized placebo-controlled trials and eight studies were randomized active-controlled trials. Three independent investigators reviewed articles for inclusion criteria using a 15-item checklist. Seventeen of the trials were of high quality according to the 15-item criteria. There was limited evidence for the effectiveness of these interventions because of the heterogeneity of treatment modalities. The search for trials concerning prevention of RSD/CRPS I resulted in two eligible studies. Both were of high quality and dealt with different interventions. There is limited evidence for their preventive effect. © 2002 European Federation of Chapters of the International Association for the Study of Pain

KEYWORDS: complex regional pain syndrome type I, reflex sympathetic dystrophy, randomized controlled trials, treatment, review.

INTRODUCTION

Complex regional pain syndrome (CRPS) types I and II are neuropathic pain syndromes accompanied by sudomotor and vasomotor disturbances. CRPS I, which corresponds to the common image of reflex sympathetic dystrophy (RSD) is defined as a painful, disabling syndrome (Merskey and Bogduck, 1994). The Consensus Conference of the International Association for Study of Pain defined CRPS I as a post-traumatic syndrome that presents with spontaneous pain that is not related to the territory of a single nerve and is disproportionate to the inciting event (Merskey and Bogduck, 1994; Schurmann et al., 1999). The diagnostic criteria include (a) pain, allodynia, or hyperalgesia, (b) evidence at some time of oedema, vasomotor and sudomotor change in the pain region and (c) no other conditions that would otherwise account for the degree of pain and dysfunction. CRPS II is a pain syndrome that starts after a nerve injury and is not necessarily limited to the distribution of the injured nerve (Baron, 2000; Woolf and Mannion, 1999). The diagnostic criteria are the same as those of CRPS I. CRPS is differentiated from other neuropathic pain syndromes by the existence of oedema, vasomotor and sudomotor disturbances. Some authors previously used a positive response on sympathetic blockade and diffuse or patchy osteopenia as an important diagnostic criterion for RSD (Davidoff et al.,
1989; Kozin et al., 1981; Schwartzman and McLellan, 1987). In CRPS I the role of sympathetic block in diagnosis has been minimized. Consequently, each category under the term CRPS could be divided into patients responsive and unresponsive to sympathetic blocks (Stanton-Hicks et al., 1995).

Currently practised treatments of RSD/CRPS I include radical scavengers (Zuurmond et al., 1996), regional intravenous sympathetic blocks (Jadad et al., 1995) and neuromodulation (Kemler et al., 2000). Kingery et al. (Kingery, 1997) reviewed existing trials for RSD/CRPS management in 1997 and demonstrated that there is limited support for the effectiveness of topical dimethylsulphoxide (DMSO), epidural clonidine, intravenous regional blocks and intranasal calcitonin. Jadad et al. (1995) showed that there is no evidence for the efficacy of regional intravenous sympathetic (RIS) blockade. We conducted a systematic review of published trials for the treatment and prevention of this disease with an emphasis on randomized controlled trials (RCTs).

MATERIAL AND METHODS

Selection of studies

A computer-assisted search of the Cochrane, Pubmed, Embase and MEDLINE databases from 1966 through June 2000 was conducted using the keywords ‘complex regional pain syndrome type I’, ‘reflex sympathetic dystrophy’ in combination with ‘trial’ or ‘randomized trials’ or ‘random allocation’ or ‘prospective studies’ or ‘double/single blind’ and ‘prevention’. Additional reports were identified from reference lists in retrieved reports and in review articles. In 1994 the term CRPS was introduced (Merskey and Bogduk, 1994; Schuurman et al., 1999). Because of the differences in diagnostic criteria between RSD and currently used CRPS I, studies about RSD and CRPS I were reviewed separately.

Two investigators independently reviewed all identified trials to determine whether a study should be included. Studies were included if they were double- or single-blinded RCTs with patients suffering from RSD or CRPS I using pain intensity as the main outcome measure. Only studies from the Dutch, German and English literature were included. We excluded non-randomized studies. Case reports and clinical observations were also excluded.

Methodological quality of the studies

Trials concerning treatment effectiveness were scored using a 15-item check list (de Vet et al., 1997) (Table 1), which included selection and restriction of the study group, treatment allocation, study size, prognostic comparability, drop-outs, interventions, extra treatments, blinding procedure, outcome measurements, follow-up period, side-effects and analysis and presentation of data. Each criterion was weighted, resulting in a maximum score of 100 for each study. The essence of a good clinical trial is the (statistical) comparability of the different treatment groups. Thus allocation procedure and drop-out rates are key elements in controlled trials. Therefore, these criteria received the highest possible scores in the check list. Three independent investigators (T. Forouzanfar and W. E. J. Weber reviewed the placebo-controlled studies; T. Forouzanfar and A. J. A. Köke reviewed active-controlled studies) assessed the methodological quality of the trials. Disagreements were resolved by consensus between the two investigators. If no agreement could be reached a third investigator was consulted. The assessment resulted in a hierarchical list in which higher scores indicate studies with a higher methodological quality. Trials dealing with prevention of RSD or CRPS I were scored using the same methodology.

Outcome of the studies

We considered a study to be positive if the pain intensity was significantly reduced by the therapeutic intervention described when compared with placebo or a control group. A study was classified as ‘negative’ if no difference in pain was achieved by the intervention when compared with the placebo. If the therapeutic intervention under
### Table 1: Methodological 15-item criteria score.

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<th>Answers</th>
<th>Scores</th>
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<td>Restriction to a homogeneous study population</td>
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<tr>
<td>2</td>
<td>Smallest group bigger than 50 subjects</td>
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<td>3</td>
<td>Smallest group bigger than 75 subjects</td>
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</tr>
<tr>
<td>D</td>
<td>Prognostic comparability</td>
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<tr>
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<td>Type of diagnosis</td>
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<td>Baseline scores for outcome measures</td>
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<td>Duration of the complaint</td>
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<td>E</td>
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<td>Number of drop-outs given in each group</td>
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<td>Reasons for withdrawal (of drop-outs) given in each group</td>
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<td>Drop-outs not leading to bias (less than 5%)</td>
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TABLE 1. (Continued)

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<table>
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<th>O</th>
<th>Analysis and presentation of data</th>
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<tbody>
<tr>
<td>1</td>
<td>Frequencies/mean and standard deviation/median and quartiles</td>
</tr>
<tr>
<td>2</td>
<td>Intention to treat analysis, or</td>
</tr>
<tr>
<td>3</td>
<td>Adequate correction for baseline differences or drop-outs</td>
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study was more effective, but not significant, the study was classified as 'positive not significant'.

A similar categorization was used for preventive treatments. These studies were classified positive if RSD/CRPS I was prevented significantly compared with placebo. If no prevention was achieved, then the study was classified as 'negative'. If the intervention applied in the study prevented the development of RSD/CRPS I more than placebo, but not significantly so, it was classified as 'positive not significant'.

We also investigated the influence of sponsorship of the reviewed studies on the methodological quality of the selected studies.

Statistics

Studies with similar interventions were pooled. A study was regarded as relevant if either pain intensity or prevention of CRPS I was the outcome measure. For methodological quality score we used a cut-off point of 50 as mentioned in the study of van Tulder et al. (1997). A trial was considered to be of high quality if the methodological score was 50 points or more and of low quality if the score was less than 50 points. The level of evidence for therapeutic intervention effectiveness was graded into four levels based on the quality, outcome and relevance of the studies (van Tulder et al., 1997). The four levels were strong evidence, moderate evidence, limited evidence and no evidence. Strong evidence was based on multiple relevant, high quality trials; moderate evidence on one relevant, high quality trial and one or more relevant low quality trials. Limited evidence was classified as one relevant, high quality trial or multiple relevant, low quality trials whereas no evidence was classified as one relevant, low quality trial, no relevant trials or contradictory outcomes.

RESULTS

Methodological flaws

The major methodological flaws in the reviewed studies included poor description of the inclusion and the exclusion criteria, restriction to a homogeneous study population, small study size, lack of details about previous medications and inadequate patients' compliance description (Tables 2-4). In most studies it was not clear whether the therapist or the observer was blinded. Moreover, only one study tested whether the blinding procedure was adequate (Wu et al., 1999). In 21 studies the treatment was defined as successful when the pain after intervention was significantly reduced compared with baseline (Adami et al., 1997; Bickerstaff and Kanis, 1991; Bonelli et al., 1983; Bounamaux et al., 1984; Fialka et al., 1993; Geertzen et al., 1994; Gobelet et al., 1992; Hanna and Peat, 1989; Jadad et al., 1995; Kemler et al., 2000; Kettler and Abram, 1988; Kho, 1995; Korpam et al., 1999; Oerlemans et al., 1999; Ramamurthy and Hoffman, 1995; Rauck et al., 1993; Rocco et al., 1989; Uher et al., 2000; Varennana et al., 2000; Wallace et al., 2000; Wu et al., 1999; Zuurmond et al., 1996). Only in five studies was a pain reduction of 30% or more compared with baseline defined as a successful
### TABLE 2. Hierarchical list of the quality score of the RCTs with a placebo group.

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### TABLE 3. Hierarchical list of the quality score of randomized active-controlled trials.

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<th>J</th>
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<th>M</th>
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<td>Rocca et al.</td>
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<td>Bonelli et al.</td>
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<td>Geertzen et al.</td>
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<td>Uher et al.</td>
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<td>Wallace et al.</td>
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<td>0</td>
<td>0</td>
<td>8</td>
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<td>49.5</td>
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### TABLE 4. Hierarchical list of RCTs on the prevention RSD.

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<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
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<th>H</th>
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<th>J</th>
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<td>Zollinger et al.</td>
<td>4</td>
<td>15</td>
<td>6</td>
<td>7</td>
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<td>3</td>
<td>2</td>
<td>5</td>
<td>2</td>
<td>76</td>
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<td>Geschwind et al.</td>
<td>4</td>
<td>15</td>
<td>4</td>
<td>7</td>
<td>12</td>
<td>4</td>
<td>4</td>
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<td>0</td>
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<td>70</td>
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</table>

*European Journal of Pain (2002)*
Randomized placebo-controlled trials

A total of 18 articles were included in this review. Tables 5 and 6 list these studies according their quality score. Fifteen studies used RSD criteria. From these studies five were published after 1994 (Adami et al., 1997; Jadad et al., 1995; Kho, 1995; Varenna et al., 2000; Zuurmond et al., 1996). Three studies used the diagnostic criteria for CRPS I (Korpan et al., 1999; Price et al., 1998; Wu et al., 1999). The two investigators managed to resolve disagreements by consensus and the third investigator was never involved. Three trials investigated the effectiveness of acupuncture and used sham acupuncture as placebo. These studies were classified as placebo-controlled trials (Hanna and Peat, 1989; Kho, 1995; Korpan et al., 1999) because it was not clear whether sham acupuncture was an active control or a placebo.

The quality score of the reviewed papers for RSD ranged from 26.5 to 79. Ten RCTs had a methodological quality score of 50 points or more (Adami et al., 1997; Bickerstaff and Kanis, 1991; Blanchard et al., 1990; Gobelet et al., 1986; Jadad et al., 1995; Kettler and Abram, 1988; Rauck et al., 1993; Varenna et al., 2000; Verdugo and Ochoa, 1994; Zuurmond et al., 1996). These articles were considered to be of high quality. Three studies had a crossover design (Blanchard et al., 1990; Jadad et al., 1995; Kettler and Abram, 1988). The study populations varied between 6 and 66 patients. Treatment modalities included elodine (Rauck et al., 1993), calcium (Bickerstaff and Kanis, 1991; Gobelet et al., 1986), clonodine (Varenna et al., 2000), alendronate (Adami et al., 1997), DMSO cream (Zuurmond et al., 1996), phenolamine (Verdugo and Ochoa, 1994), phenylephrine (Verdugo and Ochoa, 1994), reserpine (Blanchard et al., 1990), guanethidine (Blanchard et al., 1990; Jadad et al., 1995), droperidol (Kettler and Abram, 1988), prednisolone (Christensen et al., 1982), acupuncture (Fialka et al., 1993; Kho, 1995) and ketanserin (Bounameaux et al., 1984; Hanna and Peat, 1989).

The methodological quality score of the CRPS I studies ranged between 41.5 and 64.5 and the study population between seven and 26 patients (Price et al., 1998; Wu et al., 1999; Korpan et al., 1999). The studies of Price et al. (1998) and Wu et al. (1999) had scores of 64.5 and 59 respectively. These studies were considered to be of high quality. The treatment modalities included sympathetic ganglion blocks (Price et al., 1998), qigong (Wu et al., 1999), and acupuncture (Korpan et al., 1999).

RSD

Sympathetic block. The study performed by Rauck et al. (1993) was classified as high quality. Epidural clonidine 700 mg and 300 mg both decreased pain significantly more than placebo.

The high quality study of Verdugo and Ochoa (1994) demonstrated that neither intravenous phentolamine 35 mg nor phenylephrine 500 mg given to achieve regional sympathetic block were effective for the treatment of RSD.

One study (Blanchard et al., 1990) tested intravenous reserpine (0.5 mg for the upper extremity; 1 mg for the lower extremity) and intravenous guanethidine (20 mg for the upper extremity; 30 mg for the lower extremity). One further trial (Jadad et al., 1995) on RSD investigated only intravenous guanethidine (10 mg and 30 mg for the upper extremity; 20 mg and 30 mg for the lower extremity). Both articles were of high quality and did not find any improvement compared with placebo.

The high quality study of Kettler and Abram (1988) showed that administration of intravenous droperidol (2.5 mg in 30 ml saline for the upper extremity and 2.5 mg in 30 ml saline for the lower extremity) did not result in any improvement in RSD patients.

Intravenous ketanserin was investigated in two studies (Bounameaux et al., 1984; Hanna and Peat, 1989). Bounameaux et al. (1984) administered ketanserin 10 mg in one bolus. There was no significant improvement in pain intensity. Hanna and Peat (1989) did the same. However, they
<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Score</th>
<th>Crossover</th>
<th>Patients</th>
<th>Treatment¹</th>
<th>Treatment²</th>
<th>Measurements</th>
<th>Outcome for success</th>
<th>Follow-up (months)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rauck et al.</td>
<td>1993</td>
<td>77</td>
<td>No</td>
<td>26</td>
<td>Clonidine 700 µg (epid)</td>
<td>Clonidine 300 µg (epid)</td>
<td>VAS, MPQ pain reduction scale</td>
<td>Significant differences improvement between groups ($p &lt; 0.05$)</td>
<td>—</td>
<td>Positive significant</td>
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<tr>
<td>Gobelet et al.</td>
<td>1992</td>
<td>76</td>
<td>No</td>
<td>66</td>
<td>Calcitonin 100 U thrice daily for 3 weeks (i.n.)</td>
<td></td>
<td>Pain scale at rest, pain scale during movement, ROM, oedema scale</td>
<td>Significant differences between groups ($p &lt; 0.05$)</td>
<td>2</td>
<td>Positive significant</td>
</tr>
<tr>
<td>Varemma et al.</td>
<td>2000</td>
<td>75</td>
<td>No</td>
<td>32</td>
<td>Clodronate 300 mg daily for 10 days (i.v.)</td>
<td></td>
<td>VAS, global measure of improvement global assessment, ROM, laboratory tests</td>
<td>Significant differences in improvement between groups ($p &lt; 0.05$)</td>
<td>6</td>
<td>Positive significant</td>
</tr>
<tr>
<td>Adami et al.</td>
<td>1997</td>
<td>74.5</td>
<td>No</td>
<td>20</td>
<td>Alendronate 7.5 mg/day for 3 days (i.v.)</td>
<td></td>
<td>VAS, motor score, DXA</td>
<td>Significant differences in improvement between groups ($p &lt; 0.05$)</td>
<td>12</td>
<td>Positive significant</td>
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<tr>
<td>Zuurmond et al.</td>
<td>1996</td>
<td>64.5</td>
<td>No</td>
<td>32</td>
<td>50% DMSO cream for 2 months</td>
<td></td>
<td>RSD score, VAS</td>
<td>Significant change of the median (between baseline and after 2 months) compared between both groups</td>
<td>2</td>
<td>Negative</td>
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<tr>
<td>Authors</td>
<td>Year</td>
<td>Score</td>
<td>Crossover</td>
<td>Patients</td>
<td>Treatment a</td>
<td>Treatment a</td>
<td>Measurements</td>
<td>Outcome for success</td>
<td>Follow-up (months)</td>
<td>Result</td>
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<td>-------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------</td>
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<tr>
<td>Verdugo and Ochoa</td>
<td>1994</td>
<td>61</td>
<td>No</td>
<td>77</td>
<td>First phase: i.v. placebo followed by i.v. phentolamine 35 mg for 30 min</td>
<td>Second phase: i.v. placebo was followed by i.v. phentolamine 35 mg or phenylephrine 500 μg in random order</td>
<td>Pain, quantitative somatosensory thermotest, laser Doppler capillary flowmetry, hyperalgesy Chororimetry, pain questioner, hand volume, grip strength, finger stiffness VAS</td>
<td>Significant improvement within patients; change by 50% of more was considered as significant. Significant differences in improvement between groups.</td>
<td>—</td>
<td>Negative</td>
</tr>
<tr>
<td>Bickerstaff and Kanis</td>
<td>1991</td>
<td>54</td>
<td>No</td>
<td>40</td>
<td>Calcitonin 200 IU twice daily for 4 weeks (i.n.)</td>
<td>UE, guanethidine 20 mg 30–40 ml; LE, guanethidine 30 mg 40–50 ml (i.v.)</td>
<td>UE, guanethidine 20 mg 30–40 ml; LE, guanethidine 30 mg 40–50 ml (i.v.)</td>
<td>Significant differences in improvement between groups; change by 50% of more was considered as significant. Significant differences in improvement between groups.</td>
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<td>Negative</td>
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<tr>
<td>Blanchard et al.</td>
<td>1990</td>
<td>53.5</td>
<td>Yes</td>
<td>21</td>
<td>UE, reserpine 0.5 mg 30–40 ml; LE, reserpine 1 mg 40–50 ml (i.v.)</td>
<td>UE, guanethidine 20 mg 30–40 ml; LE, guanethidine 30 mg 40–50 ml (i.v.)</td>
<td>UE, guanethidine 20 mg 30–40 ml; LE, guanethidine 30 mg 40–50 ml (i.v.)</td>
<td>Significant differences in improvement between groups; change by 50% of more was considered as significant. Significant differences in improvement between groups.</td>
<td>3</td>
<td>Negative</td>
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<tr>
<td>Kettler and Abram</td>
<td>1988</td>
<td>53</td>
<td>Yes</td>
<td>6</td>
<td>UE, droperidol 2.5 mg and heparin 500 U in 30 ml of normal saline (i.v.); LE, droperidol 2.5 mg and heparin 1000 U in 50 ml of normal saline (i.v.)</td>
<td></td>
<td>UE, guanethidine 20 mg 30–40 ml; LE, guanethidine 30 mg 40–50 ml (i.v.)</td>
<td>VAS, total pain relief, mood, verbal rating scale</td>
<td>Significant differences in improvement between pre- and afterblock between treatment and placebo, and time that pain returned to preblock intensity as determined by VAS</td>
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<td>Jadad et al.</td>
<td>1995</td>
<td>51.5</td>
<td>Yes</td>
<td>16</td>
<td>UE, 10 mg guanethidine in 25 ml saline (i.v.); LE, 20 mg guanethidine in 50 ml saline (i.v.)</td>
<td>UE, 30 mg guanethidine in 25 ml saline (i.v.); LE, 30 mg guanethidine in 50 ml saline (i.v.)</td>
<td>UE, 30 mg guanethidine in 25 ml saline (i.v.); LE, 30 mg guanethidine in 50 ml saline (i.v.)</td>
<td>Significant differences in improvement between groups.</td>
<td>—</td>
<td>Negative</td>
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<td>Study</td>
<td>Year</td>
<td>Group</td>
<td>Sample Size</td>
<td>Treatment</td>
<td>Endpoint Description</td>
<td>Outcome</td>
<td>Statistical Significance</td>
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<td>Christensen et al.</td>
<td>1982</td>
<td>45</td>
<td>23</td>
<td>Prednisone 10mg (p.o.) thrice daily until clinical response was obtained (maximum 12 weeks)</td>
<td>Clinical scale 75% improvement in the clinical scale was classified as cured</td>
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<td>Positive significant</td>
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<td>Bounameaux et al.</td>
<td>1984</td>
<td>41</td>
<td>9</td>
<td>Ketanserin 10 mg (i.v.)</td>
<td>Scales for pain and cold sensation, skin temperature, blood flow VAS</td>
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<td>Negative</td>
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<td>Fialka et al.</td>
<td>1993</td>
<td>38</td>
<td>14</td>
<td>Acupuncture 5 times/week for 3 weeks</td>
<td>Sham VAS Comparison of mean pain reduction in both groups as measured by VAS</td>
<td>0.8</td>
<td>Positive not significant</td>
<td></td>
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<td></td>
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<tr>
<td>Hanna and Peat</td>
<td>1999</td>
<td>34.5</td>
<td>16</td>
<td>Ketanserin 10 mg (i.v.)</td>
<td>VAS, temperature Significant differences in improvement between groups</td>
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<td>Positive significant</td>
<td></td>
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<tr>
<td>Kho</td>
<td>1995</td>
<td>26.5</td>
<td>28</td>
<td>Acupuncture 5 times a week for 3 weeks</td>
<td>Sham VAS, sensory abnormality, temperature Comparison of improvement between the groups</td>
<td>0.8</td>
<td>Positive not significant</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*epid, epidural; i.n., intranasal; i.v., intravenous; UE, upper extremity; LE, lower extremity; p.o. per os.
| Authors       | Year | Score | Crossover | Patients | Treatment                                                                 | Treatment | Measurements                  | Outcome for success                                                                 | Follow-up (months) | Result                        | Result          |
|--------------|------|-------|-----------|----------|-----------------------------------------------------------------------------|-----------|------------------------------|-----------------------------------------------------------------------------------|-------------------|-------------------------------|----------------|-----------------|
| Price et al. | 1998 | 64.5  | Yes       | 7        | Sympathetic ganglion block by 1% lidocaine                                 | VAS, alldynia | Significant differences between groups in peak analgesic effect and block duration (peak analgesic effect = VAS differences between baseline and the lowest VAS in the first hour of the block; block duration = time that the pain intensity returned to 50% of the difference between baseline and peak analgesic effect) | 0.5 | Positive | not significant                  |
| Wu et al.    | 1999 | 59    | No        | 26       | Qigong 40 min twice a week for 3 weeks and 7 weeks at home Acupuncture 5 times a week for 3 weeks | VAS, medication usage, SCL90, behaviour, bone scan | Significant differences in improvement between groups | 2.5 | Positive | significant                  |
| Korpan et al.| 1999 | 41.5  | No        | 14       | Acupuncture 5 times a week for 3 weeks                                     | Sham VAS, functional impairment, volumetric measurement, goniometry, temperature | Significant differences in improvement between groups | 6   | Negative                          |                |
found significant improvement by ketanserin compared with placebo.

**Calcium-regulating drugs.** Varenya *et al.* (2000) investigated the efficacy of intravenous clodronate 300 mg given for 10 days. Their trial was of high quality and resulted in a significant improvement in pain reduction in those patients given clodronate compared with the placebo group. Thus there is limited evidence for the efficacy of clodronate. Adami *et al.* (1997) administered intravenous alendronate 7.5 mg or placebo daily for 3 days. This was a high quality trial with a positive significant result.

Two articles (Bickerstaff and Kanis, 1991; Gobelet *et al.*, 1986) were identified using calcitonin (intranasal) as a therapeutic intervention. Both articles were of high quality. In the study with the highest quality score (76), performed by Gobelet *et al.* (1986), significant improvement in pain intensity was achieved after intranasal calcitonin 100 IU thrice daily for 3 weeks, whereas in the trial of Bickerstaff and Kanis (1991) no improvement was found after administering calcitonin 200 IU intranasally twice daily for 4 weeks.

**Radical scavenging.** Topical DMSO was tested by Zuurmond *et al.* (1996) in a high quality study which did not show significant pain reduction.

**Corticosteroids.** We found one trial (Christensen *et al.*, 1982) that investigated the efficacy of prednisolone 10 mg thrice daily for a maximum period of 12 weeks. Christensen *et al.* (1982) found a significant improvement after administering prednisolone. However, this trial was of low quality.

**Complementary therapies.** Two trials (Hanna and Peat, 1989; Kho, 1995) studied the efficacy of acupuncture five times a week for 3 weeks in patients with RSD. They found an improvement compared with sham acupuncture (Hanna and Peat, 1989; Kho, 1995). However, this improvement was not significant. Both articles were of low quality.

**CRPS I**

**Sympathetic block.** Sympathetic ganglion block in CRPS I patients by 1% lidocaine was tested in one high quality study performed by Price *et al.* (1998). The results demonstrated that there was a slight improvement after lidocaine, but this improvement was not significant compared with saline.

**Complementary therapies.** The efficacy of 40 min of qigong exercises twice a week for 4 weeks was investigated by Wu *et al.* (1999) in a high quality study and significant improvement was noted when compared with sham exercises.

One low quality trial investigated the efficacy of acupuncture five times a week for 3 weeks on CRPS I patients and did not find any improvement (Korpan *et al.*, 1999).

**Randomized active-controlled trials**

Eight studies were identified investigating the effectiveness of the treatment modalities by comparing different treatment interventions. The results are shown in Tables 7 and 8. In six studies RSD diagnostic criteria were used. Two of these studies were published after 1994 (Oerlemans *et al.*, 2000; Ramamurthy and Hoffman, 1995). Two studies were identified performing the CRPS I diagnostic criteria (Uher *et al.*, 2000; Wallace *et al.*, 2000).

The quality score of the RSD studies ranged between 35 and 65.5. Three studies proved to be of high quality. The interventions consisted of regional intravenous sympathetic blocks (Bonelli *et al.*, 1983; Hord *et al.*, 1992; Ramamurthy and Hoffman, 1995; Roece *et al.*, 1989), physical therapy (Oerlemans *et al.*, 1999), stellate ganglion block (Bonelli *et al.*, 1983) and DMSO application (Geertzen *et al.*, 1994).

The methodological quality scores of the studies on CRPS I were 55 and 49.5 (Uher *et al.*, 2000; Wallace *et al.*, 2000). The studies investigated the efficacy of lymph drainage (Uher *et al.*, 2000) and intravenous lidocaine (Wallace *et al.*, 2000).
<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Score</th>
<th>Crossover</th>
<th>Patients</th>
<th>Intervention</th>
<th>Intervention</th>
<th>Intervention</th>
<th>Measurement</th>
<th>Outcome for success</th>
<th>Follow-up (months)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hord et al.</td>
<td>1992</td>
<td>60</td>
<td>Yes</td>
<td>12</td>
<td>RIS block by 1.5 mg/kg bretylum and 0.5% lidocaine</td>
<td>RIS block by 40-60 ml of 0.5% lidocaine</td>
<td>VAS, vital signs, skin temperature</td>
<td>Pain reduction of more than 30% was considered as significant</td>
<td>3.5</td>
<td>Maximal bretylum and lidocaine resulted in significantly better improvement than lidocaine alone</td>
<td></td>
</tr>
<tr>
<td>Oeriemans et al.</td>
<td>1999</td>
<td>59.5</td>
<td>No</td>
<td>135</td>
<td>Physical therapy</td>
<td>Occupational therapy</td>
<td>Social work (no therapy)</td>
<td>VAS, MPQ, AROM, skin temperature, volumetry</td>
<td>Differences between baseline and subsequent observations for each group and within groups ($p &lt; 0.05$)</td>
<td>12</td>
<td>Significant improvement compared with baseline and control group</td>
</tr>
<tr>
<td>Ramamurthy and Hoffman</td>
<td>1995</td>
<td>58</td>
<td>Yes</td>
<td>60</td>
<td>UE, 20 mg guanethidine (i.v.) LE, 40 mg guanethidine (i.v.)</td>
<td>UE, 2 ml saline in 0.5%, 30-50 ml lidocaine; LE, 4 ml saline in 0.5%, 40-75 ml lidocaine</td>
<td>MPQ, global evaluation scale, ROM, skin temperature</td>
<td>The primary efficacy variable was the pain rating index of the MPQ between placebo and treatment</td>
<td>6</td>
<td>No significant improvement</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Year</td>
<td>Score</td>
<td>Treatment Details</td>
<td>VAS, NRS, pain diary, skin temperature</td>
<td>Differences between baseline and subsequent observations for each group and within groups</td>
<td>Conclusion</td>
<td></td>
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<tr>
<td>Rocco et al.</td>
<td>1989</td>
<td>47.5</td>
<td>RIS block by 20 mg guanethidine in 50 ml 0.5% lidocaine</td>
<td>50 ml 1.25 mg reserpine in 50 ml 0.5% lidocaine</td>
<td>Differences between baseline and subsequent observations for each group and within groups</td>
<td>24 No significant improvement</td>
<td></td>
<td></td>
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<tr>
<td>Bonelli et al.</td>
<td>1983</td>
<td>38</td>
<td>Stellate ganglion block with bupivacaine 0.5% 15 ml to a total of 8 blocks</td>
<td>20 mg guanethidine (i.v.), every 4 days to a total of 4 blocks</td>
<td>VAS, skin temperature, skin plethysmography</td>
<td>3 Significant improvement compared with baseline, no differences between groups</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Geertzen et al.</td>
<td>1994</td>
<td>35</td>
<td>DMSO 50% in water, 4 times a day for 3 weeks</td>
<td>RIS block twice a week for 3 weeks</td>
<td>VAS, daily activity, oedema, discoloration, ROM, finger function, psychological aspects</td>
<td>3 Significant improvement compared with baseline, no differences between groups</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Authors</td>
<td>Year</td>
<td>Score</td>
<td>Crossover</td>
<td>Patients</td>
<td>Intervention</td>
<td>Intervention</td>
<td>Measurement</td>
<td>Outcome for success</td>
<td>Follow-up (months)</td>
<td>Result</td>
<td></td>
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<tr>
<td>Uher <em>et al.</em></td>
<td>2000</td>
<td>55</td>
<td>No</td>
<td>35</td>
<td>Exercise in combination with manual lymph drainage 3 times a week for 6 weeks</td>
<td>Exercise 3 times a week for 6 weeks</td>
<td>VRS, ROM, skin temperature, volumetry, scintigraphy</td>
<td>Differences between baseline and subsequent observations for each group and within groups ($p &lt; 0.05$)</td>
<td>1.5</td>
<td>Significant improvement compared with baseline, no differences between groups</td>
<td></td>
</tr>
<tr>
<td>Wallace <em>et al.</em></td>
<td>2000</td>
<td>49.5</td>
<td>Yes</td>
<td>16</td>
<td>Plasma concentration of 1, and 2 and 3µg/ml lidocaine were targeted and maintained for 20 min i.v.</td>
<td>Diphenhydramine</td>
<td>Vas, allodynia, neurosensory testing</td>
<td>Differences between baseline and subsequent observations for each group and within groups ($p &lt; 0.05$)</td>
<td>0.25</td>
<td>Significant decreased response to stroking and cool stimuli, and spontaneous pain at high lidocaine plasma level</td>
<td></td>
</tr>
</tbody>
</table>
RSD

Sympathetic block. Three cross over studies have investigated the effectiveness of sympathetic blockade. Hord et al. (1992) administered bretyllium 1.5 mg/kg together with 0.5% lidocaine or only 0.5% lidocaine without bretyllium. They defined a pain reduction of more than 30% compared with baseline as significant. This high quality study demonstrated that the combination of both treatments resulted in significant pain reduction.

Ramarurth and Hoffman (1995) compared the effectiveness of guanethidine in a high quality trial. The patients were enrolled to receive four intravenous regional blocks at 4 day intervals with either guanethidine or 0.5% lidocaine. Each patient was randomized to receive one guanethidine and three lidocaine blocks, two guanethidine and two lidocaine blocks or four guanethidine blocks without any lidocaine block. The sympathetic blocks for the upper extremity were done with either 2 ml (20 mg) guanethidine or 0.5% lidocaine 30–50 ml. For the lower extremity the blocks were performed with 4 ml (40 mg) guanethidine or 0.5% lidocaine 40–75 ml. The results did not demonstrate any significant differences between the interventions. In addition, Rocco et al. (1989), in a low quality randomized cross-over study, investigated the effectiveness of guanethidine and reserpine. All patients successively received 20 mg guanethidine in 50 ml 0.5% lidocaine, 1.25 mg reserpine in 50 ml 0.5% lidocaine and 50 ml 0.5% lidocaine with a 1 week interval between medications. No significant reduction in pain was found with either combination therapy.

Stellate ganglion block using 15 ml 0.5% bupivacaine was compared with regional intravenous sympathetic block using guanethidine 20 mg every 4 days to a total of four blocks (Bonelli et al., 1983) in a low quality study. This study did not demonstrate any differences between these treatments.

Radical scavenging vs Sympathetic block. Geertzen et al. (1994) compared in a low quality study the effectiveness of dermal application of DMSO 50% four times daily for 3 weeks with regional intravenous sympathetic blockade thrice weekly for 3 weeks. No differences were found between these interventions.

CRPS I

Sympathetic block. Wallace et al. (2000) administered lidocaine and compared its effectiveness with diphenhydramine. Plasma lidocaine concentration steps of 1 µg/ml, 2 µg/ml and 3 µg/ml were targeted and maintained for 20 min. In this low quality study lidocaine proved to achieve significant improvement.

Complementary therapies. In a study by Uher et al. (2000) the effectiveness of lymph drainage combined with exercise was compared with exercise alone. This high quality study did not show any differences between these interventions.

Prevention of CRPS I

The search for relevant studies concerned with prevention of RSD/CRPS I resulted in two randomized placebo-controlled studies (Gschwind et al., 1995; Zollinger et al., 1999) that describe preventive modalities in RSD patients (Tables 4 and 9). Both articles were of high quality. In the

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Score</th>
<th>Crossover</th>
<th>Patients</th>
<th>Treatment</th>
<th>Treatment</th>
<th>Outcome</th>
<th>Follow-up (months)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zollinger et al.</td>
<td>1999</td>
<td>75</td>
<td>No</td>
<td>123</td>
<td>Vitamin C 500 mg for 50 days</td>
<td>Placebo</td>
<td>RSD criteria</td>
<td>12</td>
<td>Significantly less incidence of RSD with vitamin C</td>
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<tr>
<td>Gschwind et al.</td>
<td>1995</td>
<td>70</td>
<td>No</td>
<td>71</td>
<td>Guanethidine 20 mg l.v.</td>
<td>Placebo</td>
<td>RSD criteria</td>
<td>1.5</td>
<td>Negative</td>
</tr>
</tbody>
</table>

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