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Treatment for idiopathic and hereditary neuralgic amyotrophy (brachial neuritis) (Review)

van Alfen N, van Engelen BGM, Hughes RAC

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[Intervention Review]

Treatment for idiopathic and hereditary neuralgic amyotrophy (brachial neuritis)

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ABSTRACT

Background

Neuralgic amyotrophy (also know as Parsonage-Turner syndrome or brachial plexus neuritis) is a distinct peripheral nervous system disorder characterised by episodes (attacks) of extreme neuropathic pain and rapid multifocal weakness and atrophy in the upper limbs. Neuralgic amyotrophy has both an idiopathic and hereditary form, with similar clinical symptoms but generally an earlier age of onset and more episodes in the hereditary form. The current hypothesis is that neuralgic amyotrophy is caused by an underlying genetic predisposition and a susceptibility to mechanical injury of the brachial plexus, and that the episodes are then caused by an immune-mediated response to the brachial plexus. Hereditary neuralgic amyotrophy is genetically heterogeneous and is associated with a point mutation or duplication of the SEPT9 gene on chromosome 17q25 in 55% of the families. In the idiopathic form an underlying but as yet unknown genetic predisposition is also assumed.

Recovery is slow, in months to years, and many patients are left with residual pain and decreased exercise tolerance in the affected limb(s). Anecdotal evidence suggests that corticosteroids may relieve pain or help improve functional recovery. This is an update of a review first published in 2009.

Objectives

The objective was to provide a systematic review of all randomised clinical trials of treatment in neuralgic amyotrophy.

Search methods

We searched the Cochrane Neuromuscular Disease Group Specialized Register (17 May 2011), CENTRAL (*The Cochrane Library* 2011, Issue 2), MEDLINE (January 1966 to May 2011), EMBASE (January 1980 to May 2011), CINAHL Plus (January 1937 to May 2011), and LILACS (January 1982 to May 2011) for randomised controlled trials of treatment for neuralgic amyotrophy.

Selection criteria

Any randomised or quasi-randomised trial of any intervention for neuralgic amyotrophy would be included in the review.

Data collection and analysis

Two review authors extracted the data (RH, NvA) and two authors assessed study quality and performed data extraction independently (NvA, BvE).

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Main results

No randomised or quasi-randomised trials were identified in either the original review or for the update. In 32 articles anecdotal evidence was found on treatment for neuralgic amyotrophy. Only three of these articles contained more than 10 treated cases, with one providing sufficient details to calculate the primary and secondary outcome measures for this review.

Authors' conclusions

There is no evidence from randomised trials to support any form of treatment for neuralgic amyotrophy. Evidence from one open-label retrospective series suggests that oral prednisone given in the first month after onset can shorten the duration of the initial pain and leads to earlier recovery in some patients. Randomised clinical trials are needed to establish the efficacy of treatment with corticosteroids or other immune-modulating therapies.

PLAIN LANGUAGE SUMMARY

Treatment for neuralgic amyotrophy

Neuralgic amyotrophy is a painful disorder of the peripheral nervous system that occurs in episodes. It affects the arms and shoulders, and leads to muscle wasting and weakness. There has been anecdotal evidence that corticosteroids can have a favourable effect on pain and recovery. No randomised clinical trial could be found in either the original 2009 review or when searches were updated in 2011 to validate the effects of this type of treatment, or any treatment. One randomised controlled trial comparing prednisolone to placebo is currently awaiting formal reporting.

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BACKGROUND

The condition

Neuralgic amyotrophy (NA), also called brachial neuritis or Parsonage-Turner syndrome, is a distinct clinical entity (van Alfen 2011)). Core features are episodes ('attacks') of extreme neuropathic pain and a rapid multifocal weakness and atrophy in the upper limb at onset, with slow recovery in months to years. It has both an idiopathic (INA) and autosomal dominant hereditary form (HNA). In this review, the terms HNA and INA refer to specific aspects of either form, while the term NA refers to common characteristics and the disorder as a whole. HNA is genetically heterogenous and has been found to be associated with a point mutation or duplication in the SEPT9 gene on chromosome 17q25 in about 55% of the families affected (Collie 2010). Rarely, a similar clinical phenotype has been described in patients with a point mutation in the PMP22 gene (Russo 2011).

Clinically, INA and HNA are very similar disorders with only a few established differences (van Alfen 2006). On a group level HNA patients are usually younger when they suffer their first attack and have more frequent involvement of nerves outside the brachial plexus, a more severe paresis and a less favourable overall outcome. Otherwise the initial pain, possible course and distribution of symptoms within the brachial plexus, recovery, complications such as shoulder joint pathology and response to treatment are the same. For this reason, and because HNA is rare and it is unlikely that significant trials will become available for this group alone, both forms of the disorder will be included in this review but considered separately.

The current hypothesis is that NA is caused by an underlying predisposition and a susceptibility to mechanical injury of the brachial plexus; the episodes are then caused by an immune-mediated response to the brachial plexus (van Alfen 2011). In HNA the underlying predisposition is genetic, while in INA this is plausible but still uncertain as no causative mutations have been found in the idiopathic form of the disorder yet. In all, NA can best be defined as a disorder with a complex pathophysiological mechanism in which autoimmune, genetic and external factors all seem to play an interwoven role.

Anecdotal observations suggest that early treatment with corticosteroids might abort the attack, relieve pain or positively influence the course and outcome (see, for example, van Alfen 2006), but there has been no systematic review of this or other treatments such as analgesics or paramedical interventions. This is an update of a review first published in 2009.

Epidemiology

The minimum incidence of idiopathic NA is estimated at two to four per 100,000 per year (Beghi 1985; MacDonald 2000). The HNA form is thought to be about 10 times rarer. Neuralgic amyotrophy is more common in men (68%). The median age of onset of INA is in the early fourth decade (range: neonatal to seventh decade) and for HNA in the second decade.

Clinical relevance of the treatment and rationale for review

Neuralgic amyotrophy often goes unrecognised by physicians, with an average delay of three to nine months before the diagnosis is made. The initial pain lasts four weeks on average and is very difficult to control with conventional analgesics. The prognosis is not as optimistic as previously assumed, with persistent pain and paresis affecting half to two-thirds of the patients (van Alfen 2006; van Alfen 2009). With an estimated incidence of 3 per 100,000 per year, there are a minimum of about 500 cases in the Netherlands and 7000 cases each year in the USA. On the assumption of a loss of about USD 100 per day (240 days a year) for a sick employee and about 25% of the patients still being unable to return to work after three years, NA would cost society in the Netherlands EUR 2.5 million per year and in the USA (with around 150,000,000 employees) USD 42 million each year just for lost productivity. Healthcare costs have not been included in this estimate.

Corticosteroids have occasionally been used for NA but there has been no systematic review of these or of any other pharmacological or paramedical treatment. A systematic review of the evidence would be a valuable guide to clinical practice and designing trials of treatment. If treatment were found to be beneficial, such a review would be a much needed incentive to convince the medical community that early identification of patients is essential for optimal care and prevention of long-term sequelae. Such a review might also provide an indication of the existence of subgroups that are either more or less likely to benefit from treatment. A systematic review might provide important clues concerning the most appropriate drugs to try and the optimal schedules and routes of dosing.

OBJECTIVES

To provide a systematic review of all randomised trials of treatment for neuralgic amyotrophy.

METHODS

Criteria for considering studies for this review

Types of studies

We planned to include all randomised or quasi-randomised trials of any intervention for neuralgic amyotrophy. Since we expected that there would be few or no randomised controlled trials to allow adequate conclusions, we planned to also assess and summarise observational studies in the Discussion section.

Types of participants

We aimed to include all participants who had been diagnosed as having INA or HNA and to accept the authors' diagnosis provided that it corresponded to the spirit of the preferred diagnostic criteria as put forward in a 1999 European Neuromuscular Centre (ENMC) workshop report (Kuhlenbaumer 2000), described in Table 1, with addition of known variations of the phenotype (van Alfen 2011). We would have included people with both the idiopathic and hereditary variant but considered them separately. We would have compared outcome measures only with other people of the same neuralgic amyotrophy subtype after any intervention. Although nerves outside the brachial plexus are affected in 56% of HNA patients and 17% of INA patients (van Alfen 2006), we only accepted case descriptions when brachial plexus involvement had been documented. We did not include reports on isolated individual nerve lesions or solely lumbosacral plexus involvement, with the exception of the long thoracic nerve as idiopathic long thoracic neuropathy is an accepted part of the NA spectrum.

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Types of interventions

We planned to include any intervention or combination of interventions compared with no treatment, placebo or another treatment or combination of treatments.

Types of outcome measures

We aimed to measure all outcome variables after up to 12 weeks (short-term), after six months, or long-term, defined as one year to a maximum of five years after the intervention. For the primary outcome measure the primary time of interest was the long-term outcome. Our preferred outcome measures were as follow.

Primary outcomes

Change in disability from baseline as measured by an appropriate, validated scale such as the upper limb scale of the Overall Disability Sum Score (ODSS) (Merkies 2002). We would have scaled results from publications using different follow-up periods to the same follow-up period before pooling the results in a meta-analysis, and investigated the implications of the necessary assumptions.

Secondary outcomes

1. Reduction of pain from baseline, measured with a validated scale. We could also have used a dichotomised version of this outcome, for example a decrease by three points or more on the numerical rating scale or a decrease by 30% of the visual analogue scale score from the McGill Pain Questionnaire (Melzack 1975).
2. Change in weakness from baseline, preferably expressed as the change in the mean Medical Research Council strength grade sum score from baseline (Brain 2000). The sum score was preferably constructed from the six most affected muscle groups selected from the list attached (see Table 2). If this was not available, then we would have used the muscle groups and scales reported by the authors. In that case, for synthesis of the results of more than one trial, we would have used standard deviations of the changes from baseline for all the participants as the units and calculate a weighted standardised mean difference with its 95% confidence interval.
3. Return to work.
4. Health-related quality of life as measured by a validated scale, e.g. the Short Form 36 (McHorney 1993).
5. Adverse events due to treatment.

Search methods for identification of studies

Electronic searches

We searched the Cochrane Neuromuscular Disease Group Specialized Register (17 May 2011) for randomised trials using the following search terms: 'brachial neuropathy or brachial plexitis or brachial radiculitis or brachial neuritis or brachial plexopathy or scapulohumeral paralysis or shoulder neuritis or shoulder amyotrophy or shoulder neuropathy or amyotrophic neuralgia or neuralgic amyotrophy or amyotrophic neuritis or parsonage turner syndrome or plexus neuropathy or brachial predilection or winged scapula or plexus neuritis or plexus radiculoneuritis or idiopathic polyneuritis'.

We also searched CENTRAL (*The Cochrane Library* 2011, Issue 2), MEDLINE (January 1966 to May 2011), EMBASE (January 1980 to May 2011), CINAHL Plus (January 1937 to May 2011) and LILACS (January 1982 to May 2011). A combination of MeSH and keyword searching was used for searching these databases.

For the search strategies see: Appendix 1 (MEDLINE), Appendix 2 (EMBASE), Appendix 3 (CINAHL Plus), Appendix 4 (LILACS) and Appendix 5 (CENTRAL).

Searching other resources

We would have reviewed the bibliographies of the randomised trials identified, and contacted the authors and known experts in the field and pharmaceutical companies to identify additional published or unpublished data.

Data collection and analysis

Selection of studies

Two review authors (NvA, RH) identified all those studies which were potentially relevant from all the titles and abstracts of the articles retrieved by the search. There were no disagreements. We retrieved the full text for all the selected articles and we would have obtained English translations of articles if necessary.

Data extraction and management

The review authors prepared a data extraction form which included the type of study; the quality criteria, described below; number, age and sex of participants; diagnostic criteria; type of intervention used including dosage, duration and administration route details for drugs and therapeutic schemes for paramedical interventions; outcome measures and results.

Two review authors independently extracted the data onto the data extraction sheet from the selected studies, assessed their methodological quality and decided whether they should be included in the review, and in any meta-analysis arising in the course of the review. There were no disagreements. One review author entered data into the Review Manager (RevMan) computer package and a second author checked the data entry.

Assessment of risk of bias in included studies

No trials were identified but in future updates of the review we will assess risk of bias according to the methods promulgated in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2008). We will separately assess sequence generation; allocation concealment; blinding of participants, those administering treatment and assessors; completeness of outcome data; selective outcome reporting; other sources of bias and overall risk of bias as high, low or unclear.

In addition, we will consider whether important differences in demographic or other factors between the intervention groups at baseline were either absent or adequately taken into account in the analysis. If the analysis does not take account of such differences, we will consider those differences which are not significant at the five per cent level as adequate, and those which are significant at this level as having a high risk of bias.

In the absence of adequate randomised trials concerning a particular intervention we considered observational studies in the Discussion. No search strategy exists to reliably identify all such studies but we aimed, at a minimum, to identify from MEDLINE and EMBASE all studies which included consecutive cohorts of at least 10 participants and in whom the number of people treated was

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described with the results of follow-up for at least 12 weeks in 80% or more of the participants.

Data synthesis

Where more than one study had addressed the same comparisons, we would have used the Cochrane RevMan statistical package to undertake meta-analyses. We would have reported risk ratios (RRs) for dichotomous data and mean differences (MDs) for continuous data with their 95% confidence intervals (CIs). If the results from the different studies were homogeneous, we planned to use a fixed-effect model for meta-analysis. If they were heterogeneous, we planned to use a random-effects model and to inspect the forest plots and trial characteristics to identify the reasons for the heterogeneity. We planned to perform sensitivity analyses by omitting trials with lower methodological quality to discover whether our conclusions from all the trials were robust, had there been sufficient trials addressing the same intervention. We would have created and inspected a funnel plot to seek evidence of publication bias.

As randomised trials are often short term, they may not adequately capture information about side effects of drugs. To overcome this, we would have considered non-randomised evidence about side effects in the Discussion, using as a minimum the non-systematic review "Meyler's Side Effects of Drugs" (Dukes 2000). Finally, we also planned to address in the Discussion costs and cost effectiveness, also taking into account the non-randomised literature.

RESULTS

Description of studies

The results of the current search strategies are: MEDLINE, 394 (68 new papers); EMBASE (new filter), 81 (43 new papers); EMBASE (old filter), 292 (40 new papers); CINAHL Plus, 94 references; LILACS, 14 (2 new papers); Cochrane Neuromuscular Disease Group Specialized Register, 22 (1 new paper); CENTRAL, 44.

From a total of 616 references we identified 18 articles describing therapy in patients with neuralgic amyotrophy. A further 14 articles containing mention of therapy were found in a personal database of papers on neuralgic amyotrophy previously used for a thesis. No randomised studies were found, so no studies could be included in the review.

Risk of bias in included studies

Not applicable

Effects of interventions

Not applicable

DISCUSSION

No randomised controlled study on any treatment for neuralgic amyotrophy was found. From 32 articles we found anecdotal evidence on treatment for neuralgic amyotrophy. Only three observational studies contained more than 10 cases with treatment (Tsairis 1972; van Alfen 2006; van Eijk 2009). Neither of the first two studies (Tsairis 1972; van Alfen 2006) contained sufficient details to calculate the primary or secondary outcome measures of this review. In a consecutive case series of 99 patients (70 males, age range 3 months to 74 years), Tsairis et al mention 15 patients treated with corticosteroids (10 oral prednisolone, 5 intramuscular adrenocorticotropic hormone (ACTH)), 15 patients treated with cortisone injections into the shoulder, and 22 patients receiving physical therapy (Tsairis 1972). Steroids were prescribed "in moderate doses early in the course of their illness" and physical therapy was given "for prolonged periods", but further treatment details are not given. The authors report that there was no evidence that early systemic corticosteroid treatment altered the course of the disease, although a few patients reported relief of pain. Additionally 8 of the 15 patients injected in the shoulder reported pain relief. Physical therapy did not seem to speed up recovery. The study by van Alfen et al (van Alfen 2006) describes 41 patients treated with corticosteroids in a case series of 246 patients; clinical details are given for 29 patients (16 male). The median time to start of treatment was 13 days. In 18 patients the same dosage regimen of a two-week course of oral prednisolone, 60 mg daily in the first week and tapering to 10 mg per day in the second week, was used; in the other patients the dose and duration varied. Four out of 20 patients (25%) subjectively felt treatment had had a positive influence on their symptoms. The median time to a decrease in pain was five days compared to 20 days in the untreated group. In 8% (3/37) of treated patients a full recovery was documented within one month from onset, compared to 5% (11/203) in the untreated group. After a mean follow-up of 1.3 years, only the time to start of the recovery from paresis was statistically significantly shorter in treated patients. Side effects were reported by 31% (8/26) of the patients, and four patients had stopped corticosteroid therapy because of them. There were no other reports with sufficient information on side effects. The third study by van Eijk and co-workers (van Eijk 2009) did contain information on several of the secondary outcome measures of this review. It reports a retrospective analysis of 50 patients (24% HNA) treated with oral prednisone within one month from onset compared to a historical cohort of 203 untreated patients (19.2% HNA). Clinical details of 16 patients were also described earlier, but less extensively, in the study by van Alfen et al (van Alfen 2006). A shorter median time to pain relief was found in the treated group (12.5 days) compared to the untreated patients (20.5 days), and more patients recovered strength in the first month (18% versus 6.3%) in the treated group. After one year, full recovery was found in 12% of the treated patients and in only 1% of the controls, while good (but not complete) recovery was also more frequent in the treated group (44% versus 10.7%). Side effects of oral prednisone were found in 20% of the patients but did not lead to discontinuation of treatment. It was concluded that oral prednisone seems effective when initiated in the acute phase of neuralgic amyotrophy.

AUTHORS' CONCLUSIONS

Implications for practice

No studies were found that could provide evidence for a particular form of treatment in neuralgic amyotrophy. Anecdotal evidence and a single unblinded, uncontrolled retrospective case series show some evidence to suggest that early corticosteroid therapy may have a positive influence on pain in some patients, and possibly speed up recovery in a few.

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Implications for research

There is a need for randomised controlled treatment trials that evaluate the effect of immune-modulating and rehabilitation therapy for neuralgic amyotrophy. The results of a randomised controlled trial on the effect of oral prednisolone are awaited.

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CHARACTERISTICS OF STUDIES

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

Study	Reason for exclusion
Allanore 2002	Single case description, in retrospect not compatible with diagnostic criteria for NA
Amato 1997	Single case description, multiple interventions, not compatible with diagnostic criteria for NA
Antoniou 2000	Case series with mixed diagnoses, insufficient clinical details, statistical interpretation questionable
Ardolino 2003	Single case description, no control or placebo
Dierckx 1990	Single case description, treatment details unclear
Foo 1983	Case series without treatment
Guillozet 1973	Single case description, no control or placebo
Hershman 1989	Case series, insufficient clinical and treatment details, no controls or randomisation
Iceton 1987	Case series with just one NA patient, insufficient details
Klein 2002	Case series, variable treatment regimens, no randomisation or controls
Koski 2002	Review without original data, unclear if NA patients were included
Lederman 1996	Case series, insufficient clinical and treatment details
Martin 1974	Case series, insufficient clinical and treatment details, no randomisation or controls
Martinelli 1997	Single case, unclear diagnosis, insufficient treatment details
Nakajima 2006	Single case, no placebo or control
Poffenbarger 1968	Case series, insufficient treatment details
Russell 1994	Review without original data
Rühmann 2001	Case series, no NA patients included
Sabato 2005	Case series, insufficient details on diagnosis and treatment, no randomisation or controls
Schollen 2007	Case series, insufficient clinical details, no randomisation or controls
Spillane 1964	Case series, insufficient clinical and treatment details
Steinmann 2003	Case series, no NA patients included
Stolk 2000	Case series, no randomisation

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Study	Reason for exclusion
Suarez 1996	Case series, insufficient clinical details, varying treatment modalities, no randomisation or controls
Taylor 1960	Case series, insufficient clinical and treatment details
Tonali 1983	Case series, insufficient clinical and treatment details, varying treatment modalities, no randomisation or controls
Tsairis 1972	Case series, insufficient clinical and treatment details, no randomisation or controls
van Alfen 2006	Case series, varying treatment modalities, no randomisation or controls
van Alfen 2009	Description of symptoms but does not provide therapy details for individual patients
van Eijk 2009	Not a randomised controlled trial. A retrospective case series of treatment with historical controls
Versteegh 2007	Case series, insufficient clinical details, outcome after treatment unclear
Watson 1995	Single case description, no control or placebo

NA: neuralgic amyotrophy

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

van Alfen - RCT

Trial name or title	Prednisolone treatment for acute neuralgic amyotrophy
Methods	Randomised placebo-controlled trial
Participants	Adult patients with idiopathic or hereditary neuralgic amyotrophy within 4 weeks from onset
Interventions	13-day oral course of prednisolone; 60 mg during first 7 days, tapering with 10 mg every subsequent day and finally 5 mg on day 13
Outcomes	A significant difference in numerical rating scale pain score after 48 hours and a significant difference in the mean MRC sumscore of the two most affected muscles 12 weeks after treatment
Starting date	October 2004
Contact information	Nens van Alfen, MD PhD. RU Nijmegen Medical Centre, Dept. of Neurology 920 KNF, PO Box 9101, 6500 HB Nijmegen, The Netherlands. Phone: =31-24-3613491. Email: n.vanalfen@neuro.umcn.nl.
Notes	Inclusion stopped early in October 2007 because of logistic problems due to the slow inclusion rate; only 38 out of the intended 80 patients could be included. Results awaiting analysis

ADDITIONAL TABLES

Table 1. Summary of the 1999 ENMC criteria for HNA

Clinical criteria	Electrophysiological	Molecular genetics	Footnotes

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Table 1. Summary of the 1999 ENMC criteria for HNA *(Continued)*

1. Clinical criteria	2. Electrophysiological criteria	3. Molecular genetics	I = Inclusion C = Compatible E = Exclusion
Family history I. Autosomal dominant inheritance with high penetrance (> 90%) C. Isolated cases may be due to de novo mutations Age at onset I. Most commonly in the second or third decade of life C. Earlier or later onset is possible Clinical manifestations I. Acute, recurrent uni- or bilateral brachial plexopathy I. Severe pain precedes the onset of weakness by days to few weeks I. Deficits are predominantly motor I. Number of episodes may vary from one to many (up to 20) C. Lumbar plexus may be affected C. Cranial nerves may be affected (most commonly: facial nerve, recurrent laryngeal nerve) C. Phrenic nerve may be affected C. Dysmorphic features may be present (most commonly: hypotelorism, epicanthal folds) C. Abortive attacks may present with pain not followed by weakness C. Intervals between attacks can be very long (up to many years) E. Absence of pain before or during attacks (absence of pain has never been reported in the first attack but may very rarely occur in one of the following attacks) Clinical examination C. Motor symptoms are prominent compared to sensory loss C. Sensory abnormalities may be present C. Autonomic symptoms may be present (abnormal sweating in affected arm, Horner's syndrome) C. Tendon reflexes are diminished or absent in affected limbs C. Muscle weakness and atrophy may be noted in previously affected limbs C. Hypotelorism, epicanthal folds, short stature may co-segregate E. Signs of a generalized neuropathy Course and severity I. Relapsing/remitting course with symptom-free intervals I. Complete recovery without any residual deficit between attacks I. Recovery occurs within month to 2 years C. Recovery is in many cases incomplete and residual neurologic deficit persists especially after repeated attacks affecting the same limb C. Chronic undulating course without completely symptom-free intervals (especially pain)	I. EMG shows signs of denervation or reinnervation in muscles innervated by affected nerves C. Slightly reduced distal nerve conduction velocities in the affected nerves C. Reduced amplitude of compound muscle action potential in affected nerves C. Reduced amplitudes of sensory nerve action potentials in affected nerves E. Electrophysiological signs of generalized neuropathy	I. Linkage to the HNA locus on chromosome 17q25 C. Absence of linkage to the HNA locus on chromosome 17q25 E. Presence of the HNPP deletion on chromosome 17p11.2 E. Presence of mutations in the PMP22 gene	

EMG: electromyography

Table 2. List of muscles from which the six most affected groups will be selected

Muscle
serratus anterior
rhomboids

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Table 2. List of muscles from which the six most affected groups will be selected *(Continued)*

trapezius and levator scapulae
latissimus dorsi
pectoralis major
supraspinatus
deltoid
infraspinatus and teres minor
subscapularis and teres major
biceps and brachialis
triceps
wrist extensors
wrist flexors
forearm pronators
forearm supinators
finger extensors
thumb extensors
superficial finger flexors
deep flexors of thumb and index finger
deep flexors of 3rd to 5th digit
interosseus muscles
thumb abductors

APPENDICES

Appendix 1. MEDLINE OvidSP search strategy

1 randomized controlled trial.pt.
2 controlled clinical trial.pt.
3 randomized.ab.
4 placebo.ab.
5 drug therapy.fs.
6 randomly.ab.
7 trial.ab.
8 groups.ab.
9 or/1-8
10 exp animals/ not humans.sh.

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11 9 not 10
12 exp Brachial Plexus Neuropathies/
13 (brachial adj2 (neuropath$ or plexitis or neuritis or plexopath$)).mp.
14 (shoulder adj2 (neuritis or amyotroph$ or neuropath$)).mp.
15 (amyotroph$ adj2 (neuralgi$ or neuritis)).mp.
16 (parsonage turner or scapulohumeral paralys$ or brachial predilection).mp.
17 (plexus adj2 (neuropath$ or neuritis or radiculoneuritis)).mp.
18 (winged scapula or idiopathic polyneuritis).mp.
19 or/12-18
20 11 and 19

Appendix 2. EMBASE OvidSP search strategy

1 crossover-procedure/
2 double-blind procedure/
3 randomized controlled trial/
4 single-blind procedure/
5 (random$ or factorial$ or crossover$ or cross over$ or cross-over$ or placebo$ or (doubl$ adj blind$) or (singl$ adj blind$) or assign$ or allocat$ or volunteer$).tw.
6 groups.ab.
7 or/1-6
8 exp animals/
9 exp humans/
10 8 not (8 and 9)
11 7 not 10
12 limit 11 to embase
13 brachial plexus neuropathy/
14 neuralgic amyotrophy.mp.
15 (brachial adj2 (plexitis or radiculitis or neuritis or neuropath$ or plexopath$)).mp.
16 (shoulder adj2 (neuritis or amyotroph$ or neuropath$)).mp.
17 (amyotroph$ adj2 (neuralgi$ or neuritis)).mp.
18 (parsonage turner or scapulohumeral paralys$ or brachial predilection or winged scapula or idiopathic polyneuritis).mp.
19 (plexus adj2 (neuropath$ or neuritis or radiculoneuritis)).mp.
20 or/13-19
21 12 and 20

Appendix 3. CINAHL Plus EBSCOhost search strategy

S36 S18 and S35
S35 S19 or S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30 or S31 or S32 or S33 or S34
S34 plexus neuritis
S33 winged scapula
S32 brachial predilection
S31 plexus neuropath*
S30 parsonage turner
S29 amyotroph* N5 neuritis
S28 neuralg* N5 amyotroph*
S27 shoulder N5 neuropath*
S26 parsonage turner
S25 shoulder N5 amyotroph*
S24 shoulder N5 neuritis
S23 brachial plexopath*
S22 brachial neuritis
S21 brachial plexitis
S20 brachial neuropath*
S19 (MH "Brachial Plexus Neuritis") OR (MH "Brachial Plexus Neuropathies")
S18 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17
S17 ABAB design*
S16 TI random* or AB random*
S15 (TI (cross?over or placebo* or control* or factorial or sham? or dummy)) or (AB (cross?over or placebo* or control* or factorial or sham? or dummy))
S14 (TI (clin* or intervention* or compar* or experiment* or preventive or therapeutic) or AB (clin* or intervention* or compar* or experiment* or preventive or therapeutic)) and (TI (trial*) or AB (trial*))

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S13 (TI (meta?analys* or systematic review*)) or (AB (meta?analys* or systematic review*))
S12 (TI (single* or doubl* or tripl* or trebl*) or AB (single* or doubl* or tripl* or trebl*)) and (TI (blind* or mask*) or AB (blind* or mask*))
S11 PT ("clinical trial" or "systematic review")
S10 (MH "Factorial Design")
S9 (MH "Concurrent Prospective Studies") or (MH "Prospective Studies")
S8 (MH "Meta Analysis")
S7 (MH "Solomon Four-Group Design") or (MH "Static Group Comparison")
S6 (MH "Quasi-Experimental Studies")
S5 (MH "Placebos")
S4 (MH "Double-Blind Studies") or (MH "Triple-Blind Studies")
S3 (MH "Clinical Trials+")
S2 (MH "Crossover Design")
S1 (MH "Random Assignment") or (MH "Random Sample") or (MH "Simple Random Sample") or (MH "Stratified Random Sample") or (MH "Systematic Random Sample")

Appendix 4. LILACS search strategy

(Mh Brachial Plexus Neuropathies OR Mh Brachial Plexus Neuritis OR brachial neuropath$ OR brachial plexitis OR brachial radiculitis OR brachial neuritis OR brachial plexopath$ OR scapulohumeral paralysis OR shoulder neuritis OR shoulder amyotroph$ OR shoulder neuropath$ OR neuralg$ amyotroph$ OR amyotroph$ neuralg$ OR amyotroph$ neuritis OR parsonage turner syndrome OR plexus neuropath$ OR brachial predilection OR winged scapula OR plexus neuritis OR plexus radiculoneuritis) [Words] and ((Pt randomized controlled trial OR Pt controlled clinical trial OR Mh randomized controlled trials OR Mh random allocation OR Mh double-blind method OR Mh single-blind method) AND NOT (Ct animal AND NOT (Ct human and Ct animal)) OR (Pt clinical trial OR Ex E05.318.760.535$ OR (Tw clin$ AND (Tw trial$ OR Tw ensa$ OR Tw estud$ OR Tw experim$ OR Tw investiga$)) OR ((Tw singl$ OR Tw simple$ OR Tw doubl$ OR Tw doble$ OR Tw duplo$ OR Tw trebl$ OR Tw trip$) AND (Tw blind$ OR Tw cego$ OR Tw ciego$ OR Tw mask$ OR Tw mascar$)) OR Mh placebos OR Tw placebo$ OR (Tw random$ OR Tw randon$ OR Tw casual$ OR Tw acaso$ OR Tw azar OR Tw aleator$) OR Mh research design) AND NOT (Ct animal AND NOT (Ct human and Ct animal)) OR (Ct comparative study OR Ex E05.337$ OR Mh follow-up studies OR Mh prospective studies OR Tw control$ OR Tw prospectiv$ OR Tw volunt$ OR Tw volunteer$) AND NOT (Ct animal AND NOT (Ct human and Ct animal))) [Words]

Appendix 5. CENTRAL search strategy

#1MeSH descriptor Brachial Plexus Neuropathies explode all trees
#2brachial NEAR/2 neuropath*
#3brachial near/2 plexitis
#4brachial near/2 radiculitis
#5brachial near/2 neuritis
#6brachial NEAR/2 plexopath*
#7scapulohumeral NEAR/2 paralysis
#8shoulder NEAR/2 neuritis
#9shoulder NEAR/2 amyotroph*
#10shoulder NEAR/2 neuropath*
#11neuralg* NEAR/2 amyotroph*
#12amyotroph* NEAR/2 neuritis
#13"parsonage turner"
#14plexus NEAR/2 neuropath*
#15brachial NEAR/2 predilection
#16winged NEAR/2 scapula
#17plexus NEAR/2 neuritis
#18plexus NEAR/2 radiculoneuritis
#19(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18)

WHAT'S NEW

Date	Event	Description
21 June 2011	New search has been performed	Searches updated to May 2011. No randomised controlled trials identified.

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HISTORY

Protocol first published: Issue 1, 2008
Review first published: Issue 3, 2009

Date	Event	Description
5 May 2008	Amended	Converted to new review format.
14 November 2007	New citation required and major changes	Substantive amendment

CONTRIBUTIONS OF AUTHORS

N van Alfen and R Hughes revised the text of this update, B van Engelen agreed the final text. N van Alfen and R Hughes identified all potentially relevant studies and extracted the data. N van Alfen entered data into the review computer package and compiled the update. R Hughes checked the data entry.

DECLARATIONS OF INTEREST

N van Alfen and BGM van Engelen have co-authored a study of a large cohort of neuralgic amyotrophy (NA) patients that included a description of a series of open-label treated patients (van Alfen 2006) and are currently involved in a nationwide placebo-controlled randomised controlled trial in the Netherlands, assessing the effect of a 13-day course of oral prednisone in the acute phase of NA.

N van Alfen receives funding from the Dutch Rare Diseases Fund for developing rehabilitation treatment for NA.

RAC Hughes holds consultancies with the following companies which produce intravenous immunoglobulin or immunosuppressive drugs: Baxter, LFB, Novartis, Octapharma and Talecris.

BGM van Engelen is research director of the European Neuromuscular Centre and receives institutional support from the Radboud University Nijmegen Medical Centre and the ENMC, grant support from the Global FSH, Netherlands Organization for Scientific Research, Prinses Beatrix Fonds, and the Dutch FSHD Foundation.

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Internal sources

- Nens van Alfen, Netherlands.

  None
- Baziel GM van Engelen, Netherlands.

  None
- Richard Hughes, UK.

  None

External sources

- None, Not specified.

INDEX TERMS

Medical Subject Headings (MeSH)

Anti-Inflammatory Agents [therapeutic use]; Brachial Plexus Neuritis [*drug therapy]; Glucocorticoids [therapeutic use]; Prednisolone [therapeutic use]

MeSH check words

Humans

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