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Plasma exchange for chronic inflammatory demyelinating polyradiculoneuropathy (Review)

Mehndiratta MM, Hughes RAC, Pritchard J

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Plasma exchange for chronic inflammatory demyelinating polyradiculoneuropathy.

Cochrane Database of Systematic Reviews 2015, Issue 8. Art. No.: CD003906.

DOI: 10.1002/14651858.CD003906.pub4.

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Plasma exchange for chronic inflammatory demyelinating polyradiculoneuropathy

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Editorial group: Cochrane Neuromuscular Group.

Publication status and date: Edited (no change to conclusions), published in Issue 11, 2017.

Citation: Mehndiratta MM, Hughes RAC, Pritchard J. Plasma exchange for chronic inflammatory demyelinating polyradiculoneuropathy. *Cochrane Database of Systematic Reviews* 2015, Issue 8. Art. No.: CD003906. DOI: 10.1002/14651858.CD003906.pub4.

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ABSTRACT

Background

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is an uncommon progressive or relapsing paralysing disease caused by inflammation of the peripheral nerves. If the hypothesis that it is due to autoimmunity is correct, removal of autoantibodies in the blood by plasma exchange should be beneficial.

Objectives

To assess the effects of plasma exchange for treating CIDP.

Search methods

On 30 June 2015, we searched the Cochrane Neuromuscular Disease Group Specialized Register, the Cochrane Central Register for Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL Plus, and LILACS. We also scrutinised the bibliographies of the trials, contacted the trial authors and other disease experts, and searched trials registries for ongoing studies.

Selection criteria

Randomised controlled trials (RCTs) or quasi-RCTs in participants of any age comparing plasma exchange with sham treatment or no treatment.

Data collection and analysis

Two review authors independently selected the trials, extracted the data, and assessed risk of bias. Where possible the review authors combined data according to the methods of the Cochrane Neuromuscular Disease Review Group.

Main results

Primary outcome measure: one cross-over trial including 18 participants showed after four weeks, 2 (95% confidence interval (CI) 0.9 to 3.1) points more improvement on an 11-point disability scale with plasma exchange (10 exchanges over four weeks) than with sham exchange. Rapid deterioration after plasma exchange occurred in eight of 12 who had improved.

Secondary outcome measures: when we combined the results of this cross-over trial and a trial with 29 participants treated in a parallel-group design, there were 31 points (95% CI 18 to 45) more improvement on an impairment scale (maximum score 280) after

plasma exchange (six exchanges over three weeks) than after sham exchange. There were significant improvements in both trials in an electrophysiological measure, the proximally evoked compound muscle action potential, after three or four weeks. Non-randomised evidence indicates that plasma exchange induces adverse events in 3% to 17% of procedures. These events are sometimes serious. Both trials had a low risk of bias. A trial that showed no significant difference in the benefit between plasma exchange and intravenous immunoglobulin is included in the Cochrane review of intravenous immunoglobulin for this condition.

Authors' conclusions

Moderate- to high-quality evidence from two small trials shows that plasma exchange provides significant short-term improvement in disability, clinical impairment, and motor nerve conduction velocity in CIDP but rapid deterioration may occur afterwards. Adverse events related to difficulty with venous access, use of citrate, and haemodynamic changes are not uncommon. We need more research to identify agents that will prolong the beneficial action of plasma exchange.

PLAIN LANGUAGE SUMMARY

Plasma exchange for chronic inflammatory demyelinating polyradiculoneuropathy

Review question

What are the benefits and harms of plasma exchange for chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)?

Background

CIDP is an uncommon paralysing disease caused by inflammation of the peripheral nerves. Plasma exchange, also called plasmapheresis, removes blood from one vein, passes it through a machine, and then returns it into another vein. The machine replaces the plasma, which is the fluid part of the blood, with a substitute and preserves the red blood cells. The procedure removes potentially harmful substances, including antibodies. It takes several hours and is usually repeated about five times over two weeks. We wanted to discover whether plasma exchange is helpful in CIDP.

Study characteristics

We found two randomised controlled trials. Both studies compared plasma exchange with sham exchange (in which blood was removed and returned but not exchanged). One trial aimed to compare four weeks' plasma exchange with sham exchange. The 18 participants received both treatments, being randomised to either treatment in the first period of the trial, crossing over to the other treatment for the second period. The other trial compared three-weeks' plasma exchange in 15 participants with sham exchange in 14 participants. We considered both trials at low risk of bias, which means largely free of flaws that could have influenced the results.

Study funding sources

A charitable grant supported the cross-over trial. The other did not report any support.

Key results

The cross-over trial showed on average two points more improvement on an 11-point disability scale with plasma exchange than sham exchange. This was unlikely to have occurred by chance. The parallel-group trial did not report this outcome. When we combined the results of both trials, plasma exchange produced significantly more improvement in severity of disease signs measured by neurologists than sham exchange. The results reported were short term. In practice, people with CIDP receive repeated courses or combinations of plasma exchange with additional agents. Another Cochrane review includes a trial showing similar improvement after plasma exchange to that after intravenous infusion of immunoglobulin (the antibody portion of blood). According to non-randomised evidence, plasma exchange causes adverse events in 3% to 17% of procedures. These are sometimes serious.

Quality of the evidence

Because of the small size of the only trial reporting changes in disability, the quality of the evidence that plasma exchange reduces disability is moderate. The quality of the evidence that plasma exchange improves the signs of disease measured by a neurologist is high.

The evidence is up to date to 30 June 2015.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [\[Explanation\]](#)

Plasma exchange versus sham exchange for chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)						
Patient or population: people with CIDP Settings: inpatient Intervention: plasma exchange versus sham exchange						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Sham exchange	Plasma exchange				
Change in disability after 4 weeks disability grade change. Scale from: 0 to 10; lower is better	The mean change in disability after 4 weeks in the control period was 0.4 disability grade	The mean change in disability after 4 weeks in the intervention period was 2 grades lower (3.08 to 0.92 lower)		36 (1 study)	⊕⊕⊕○ moderate ¹	Cross-over study and both treatment periods have been included: sham exchange group worsened by a mean of 0.4 and PE group improved by a mean of 1.6 grades
Change in impairment (NIS) after 4 weeks NIS score points. Scale from: 0 to 280; lower is better	The mean change in impairment (NIS) after 4 weeks in the control period was 3.3 NIS score points	The mean change in impairment (NIS) after 4 weeks in the intervention period was 30.6 lower (44.85 to 17.57 lower)		59 (2 studies)	⊕⊕⊕⊕ high	Cross-over studies and both treatment periods have been included
Change in mean compound muscle action potential amplitude after 4 weeks mA	The mean change in compound muscle action potential amplitude after 4 weeks in the control period was -0.9 mA	The mean change in compound muscle action potential amplitude after 4 weeks in the intervention period was 4.6 mA higher (1.4 to 7.8 higher)		30 (1 study)	⊕⊕⊕○ moderate ¹	Cross-over trial and both treatment periods have been included

Serious adverse events - not measured	See comment	See comment	Not estimable	-	See comment	In one study, 1 of 29 participants had a stroke 1 day after PE. No events in controls. In another study 1 of 30 participants had catheter-related myocarditis, not stated whether this was after PE or sham treatment
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*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **NIS:** neuropathy impairment score (formerly known as neurologic disability score, NDS); **PE:** plasma exchange

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹ Only 1 trial.

BACKGROUND

Chronic inflammatory demyelinating polyradiculoneuropathy (CIPD) causes progressive or relapsing weakness or numbness of the limbs. It affects males and females of all ages and has a population prevalence of two to three per 100,000 people (Mahdi-Rogers 2014; Vallat 2010). Early reports of large series (Barohn 1989; Dyck 1975; Dyck 1985; McCombe 1987; Prineas 1976; Thomas 1969) described the clinical picture but did not precisely define the disease. An expert committee proposed research criteria for the diagnosis in 1991 (Ad Hoc 1991). These included clinical, electrophysiological, cerebrospinal fluid, and histopathological criteria. The clinical criteria consisted of progressive or relapsing motor or sensory dysfunction, or both, of more than one limb, developing over at least eight weeks. Strict electrophysiological criteria failed to capture all the people accepted as cases of CIPD in subsequent case series. Fulfilment of the clinical and electrophysiological criteria are sufficient for a diagnosis of 'probable' CIPD according to these criteria. A diagnosis of 'definite' CIPD requires additional fulfilment of pathological criteria. However, nerve biopsies often show only nonspecific changes or loss of axons in CIPD and they are commonly not performed. We considered it inappropriate to insist on pathological confirmation for the diagnosis in this review. This is in line with the criteria of the European Federation of Neurological Societies/Peripheral Nerve Society guideline (EFNS/PNS CIPD 2010), which has acceptable specificity and higher sensitivity (Breiner 2014). Since there is no absolute diagnostic test it is always necessary to exclude alternative diagnoses, such as hereditary, metabolic, vasculitic, paraneoplastic, and paraproteinaemic neuropathies. There is a debate about whether some cases of neuropathy associated with diabetes mellitus, systemic lupus erythematosus, and monoclonal gammopathy are due to CIPD. Because of the uncertainty we excluded such cases from this review.

The aetiology of CIPD is presumed to be autoimmune (Köller 2005; Vallat 2010). Peripheral nerve biopsies and autopsy studies often reveal characteristic histopathologic features of nerve oedema, scarce lymphocytic infiltrates, and macrophage-mediated segmental demyelination and remyelination (Prineas 1976). Similar histological appearances are seen in the chronic form of experimental autoimmune neuritis (Hahn 1996a). Humoral and cell-mediated responses against a variety of myelin-derived autoantigens have been detected in some people with CIPD (Fredman 1991; Ilyas 1992; Köller 2005; Koski 1985; Lehmann 2011; Querol 2014; van Doorn 1987; Yan 2001). However, no consistent or diagnostically helpful immune response has been identified.

CIPD is a heterogeneous disorder. It is usually symmetrical with motor and sensory dysfunction, but asymmetrical (Lewis 1982; Saperstein 2001) and predominantly sensory forms (Oh 1992) have also been described. We planned to include variants that fulfil the Ad Hoc 1991 criteria in this review. However, multifocal motor neuropathy (MMN) with conduction block is considered

a separate condition (Lewis 1982; Parry 1988). Electrophysiological features of multifocal partial conduction block with almost complete sparing of sensory nerve fibres characterise MMN. Unlike CIPD, MMN may worsen following treatment with corticosteroids, and may have a different pathogenesis (Nobile-Orazio 2013). Consequently, MMN has been excluded from this review and has appeared in another (Umaphathi 2012).

The findings that sera of people with CIPD caused demyelination or functional peripheral nerve deficits following intraneural or systemic transfer provided a rationale for use of plasma exchange (PE) in CIPD (Heininger 1984; Pollard 1983). The observation of temporary improvement following PE in CIPD supported this evidence. PE (also called plasmapheresis) involves removing blood from the person with CIPD, separating the plasma by filtration or centrifugation, and then re-infusing the red blood cells with a plasma substitute. It requires the insertion of two cannulae into veins, one to remove the blood and the other to re-infuse the red blood cells and plasma substitute. The plasma substitute is usually a mixture of human albumin solution and saline. It is customary to exchange about one plasma volume at a time, which is sufficient to reduce the plasma IgM concentration by about 45% and the IgG concentration by about 60% (Khatri 1985). PE has been extensively used for removal of abnormal proteins in haematological disorders and for the treatment of autoimmune diseases (Cortese 2011).

Current treatments for CIPD aim to modulate the abnormal immune response with the intention of suppressing the ongoing activity. The treatments used in CIPD include corticosteroids (Hughes 2015), intravenous immunoglobulin (IVIg) (Eftimov 2013), immunosuppressive agents such as azathioprine, cyclophosphamide, methotrexate or ciclosporin (Mahdi-Rogers 2013), as well as PE (Dyck 1986; Hahn 1996b), combinations of steroids, PE and IVIg (Briellmann 1998), or PE followed by IVIg (Walk 2004). Case series and case reports have reported other agents like rituximab, interferons, fludarabine, mycophenolate, and etanercept to benefit some people with CIPD (Brannagan 2009; Vallat 2010).

Levy and Server et al. were the first to report improvement with PE in CIPD (Levy 1979a; Levy 1979b; Server 1979). Since then many papers reported benefit in individual case reports or small uncontrolled series, which are subject to bias (Abe 1986; Bromberg 1992; Choudhary 1995; Donofrio 1984; Gibbels 1986; Gross 1981; Hanaoka 1998; Iwatsubo 1989; Kumazawa 1995; Kumazawa 1998; Maas 1981; Pollard 1983; Tanaka 1998; Toyka 1982; van Nunen 1982). The people with CIPD in these reports also received treatment with immunosuppressive drugs, which could have influenced the clinical response (Dyck 1982). We knew of only two randomised, double-blind, controlled studies comparing PE with sham when the protocol for this review was written (Dyck 1986; Hahn 1996b). Both reported short-term benefit. It is important to know the long-term outcome but there is paucity of information

in the published literature. Another randomised study compared PE with IVIg infusion and found no difference between the two treatments (Dyck 1994). The Cochrane review of IVIg for CIDP included this trial (Efimov 2013). Another randomised study compared immunoabsorption, an alternative technique to PE for removing antibodies, with IVIg (Zinman 2005). The authors of the Cochrane review of IVIg for CIDP considered this study but assessed it as at high risk of bias and excluded it (Efimov 2013). We know of no other systematic review of PE for treating CIDP, but there have been many nonsystematic reviews of treatment for CIDP (Lehmann 2008; Saperstein 2001; Vallat 2010; Van den Bergh 2001). There are completed Cochrane reviews of corticosteroid treatment (Hughes 2015), IVIg (Efimov 2013), and cytotoxic and immunomodulatory drugs (Mahdi-Rogers 2013).

OBJECTIVES

To assess the effects of PE for treating CIDP.

METHODS

Criteria for considering studies for this review

Types of studies

We included all randomised controlled trials (RCTs) or quasi-RCTs comparing any form of PE treatment with sham exchange, no treatment, or another treatment for CIDP.

Types of participants

We included all people who had been diagnosed by the trial authors as having CIDP according to defined criteria, which are similar to those of the Ad Hoc Subcommittee (Ad Hoc 1991). Participants had to have symptoms and signs of polyradiculoneuropathy characterised by progressive or relapsing motor and sensory dysfunction of more than one limb, of more than eight weeks' duration. The diagnosis must have been confirmed by an electrophysiological diagnosis of demyelinating polyneuropathy based on reduced nerve conduction velocities or partial motor nerve conduction blocks. The diagnosis was usually to have been confirmed by the finding of a raised cerebrospinal fluid protein. It might, but need not, have been confirmed by the demonstration of inflammation and macrophage-associated demyelination in a nerve biopsy. We excluded people with clinical features or investigations suggestive of hereditary neuropathy, paraproteinaemia, or systemic diseases.

Types of interventions

We included any method or dose of PE treatment. If PE had been combined with another treatment and compared with no exchange or sham exchange and then some other treatment, we would have included the results in the analysis of the effects of PE. If PE had been combined with another treatment and compared with no exchange or sham exchange and no other treatment, we would have reported the results separately and not combined them with the results of PE alone. If PE had been compared with another treatment we would also have reported this comparison separately. We excluded the comparison of PE with intravenous immunoglobulin, which had already been reviewed (Efimov 2013).

Types of outcome measures

Primary outcomes

The primary outcome measure was the change in disability measured by a validated scale at least four weeks after treatment onset. We intended to convert the scale used by the authors to the Modified Rankin Scale (van Swieten 1988).

Secondary outcomes

The secondary outcome measures were:

1. Change in impairment, at least four weeks after the start of treatment, measured by a validated impairment scale such as the Neuropathy Impairment Score (NIS), formerly called the Neurology Disability Score (NDS) (Dyck 1980), which is an impairment scale according to the World Health Organization (WHO) definition (WHO 1980; WHO 1997). The scale ranges from zero, being normal, to 280, being maximally affected.
2. Change in proximal compound muscle action potential amplitude measured after at least four weeks. Where this had been measured in more than one nerve, we would have used the average of all the nerves studied.
3. Change in disability after at least 12 weeks measured by a validated scale as for the primary outcome measure. For this and the next outcome we wanted to consider separately the long-term effect of initial treatment with PE and of repeated treatments.
4. Change in impairment after at least 12 weeks measured as for secondary outcome measure 1.
5. Serious adverse events during and for one week after PE, sham exchange, or the control period under consideration. We defined serious adverse events as any of the following: death, hypotension requiring rapid volume infusion, infection requiring treatment with antibiotics, or any other event which was life-threatening, or required or prolonged hospital admission.

Search methods for identification of studies

Electronic searches

On 30 June 2015, we searched the Cochrane Neuromuscular Disease Group (CNMDG) Specialized Register, CENTRAL (2015, Issue 6 in *The Cochrane Library*), MEDLINE (January 1966 to June 2015), EMBASE (January 1980 to June 2015), CINAHL Plus (January 1937 to June 2015), and LILACS (January 1982 to June 2015). We also scrutinised the bibliographies of the trials, and contacted the trial authors and other disease experts. There were no language limitations.

The detailed search strategies are in the appendices: [Appendix 1](#) (MEDLINE), [Appendix 2](#) (EMBASE), [Appendix 3](#) (CNMDG Specialized Register), [Appendix 4](#) (CENTRAL), [Appendix 5](#) (CINAHL Plus), and [Appendix 6](#) (LILACS).

Searching other resources

We checked the bibliographies of the trials identified and contacted their authors and other experts to identify additional published or unpublished data. We also searched ClinicalTrials.gov (www.clinicaltrials.gov) and the WHO international Clinical Trials Registry Platform (www.who.int/ictcp/en/).

Data collection and analysis

Two review authors (MMM and RACH) checked the titles and abstracts identified. The review authors obtained the full text of all potentially relevant studies for independent assessment. The review authors independently decided which trials fitted the inclusion criteria and graded their risk of bias using the Cochrane 'Risk of bias' methods, described in the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011](#)).

Two review authors performed data extraction independently. They did not obtain missing data from the trial authors.

We calculated a treatment effect across trials using the Cochrane statistical package, Review Manager (RevMan) 5. We expressed results as risk ratios (RR) with 95% confidence intervals (CI) and risk differences with 95% CI for dichotomous outcomes, and mean differences (MDs) and 95% CI for continuous outcomes. If the results had indicated heterogeneity, we would have undertaken these tests with a random-effects model, but we used a fixed-effect model. If there had been heterogeneity, we would have investigated its source by repeating the analysis after elimination of trials which we judged to have a high risk of bias. We initially treated the data from cross-over trials as if they were parallel-group trials without taking into account the possibility of a cross-over effect. As a sensitivity analysis, we repeated the analyses with the generic inverse variance (GIV) method considered more appropriate for cross-over trials.

We intended to undertake subgroup analyses but appropriate information was not available and the numbers were too small to permit a meaningful analysis. The planned subgroups were participants:

1. with an illness duration less than 12 months and with a illness duration longer than 12 months;
2. with chronic relapsing and chronic progressive forms of CIDP;
3. 50 years old or less and over 50 years old;
4. with symmetrical and asymmetrical (multifocal acquired demyelinating sensory and motor neuropathy) forms of CIDP.

RESULTS

Description of studies

Results of the search

In this update, we found 109 papers in MEDLINE (18 new), 94 in EMBASE (15 new), 11 in the Cochrane Neuromuscular Disease Group Specialized Register, 10 in CENTRAL, 18 in CINAHL Plus (2 new) and 0 in LILACS. After deduplication 37 new references remained.

These searches identified the two trials which were included in the original version of this review ([Dyck 1986](#); [Hahn 1996b](#)), but no new trials. Inspection of the reference lists in the trials and other references in this review did not reveal any further RCTs, nor did enquiry from the first authors of each identified trial or direct contact with more than six other disease experts. We found no ongoing studies in trials registries.

Included studies

The first trial had a parallel-group design comparing PE with sham exchange twice weekly for three weeks and took place at the Mayo Clinic in the USA ([Dyck 1986](#)) (see [Characteristics of included studies](#)). The study recruited 34 participants but investigators removed five; four due to possible incorrect diagnosis and one for myocarditis possibly related to an indwelling subclavian catheter. The trialists measured impairment using the NIS and neurophysiological parameters after the first, second and third weeks. Of the 29 participants, 15 were assigned to PE, and 14 to sham exchange. The second trial was a Canadian multicentre study with a cross-over design ([Hahn 1996b](#)). Of the 18 participants recruited one did not receive PE because she wished to leave the trial during the first (SPE) phase of the trial, one did not receive PE because of failed venous access, and one did not receive SPE because of a stroke at the end of the first (PE) phase of the trial. The authors

included all three participants in their analyses using the last observation carried forward. The participants received 10 PE or sham exchanges over four weeks and after an intended washout period of five weeks, participants crossed over to their alternate treatments. Outcome measures were NIS, functional clinical grade, grip strength, and electrophysiological studies at the end of each treatment compared with the start.

Excluded studies

The MEDLINE search for the first version of this review identified three other trials, which on scrutiny of the full text were not randomised (Baba 1996; Kumazawa 1998; Mori 2002). A trial comparing PE with IVIg reported no significant difference in beneficial effect between a regimen of PE and a regimen of IVIg

of similar cost (Dyck 1994). Another trial compared immunoabsorption, which is a form of PE, with IVIg (Zinman 2005). We excluded both these trials according to our criteria for selecting studies for this review. See [Characteristics of excluded studies](#).

Risk of bias in included studies

Both included trials were of high quality but small in size, reflecting the rarity of people with CIDP for whom PE might be considered. Both trials used concealed randomisation to allocate participants and went to the length of sham exchange to disguise the nature of the true treatment from the observers and participants. Both trials had a low risk of bias according to our criteria (Figure 1). However, neither trial stipulated which of their measured outcomes was primary.

Figure 1. Review of bias summary: review authors’ judgements about each risk of bias item for each included study.

Effects of interventions

See: [Summary of findings for the main comparison](#) Plasma exchange versus sham exchange for chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)

Primary outcome measure: change in disability measured by a validated scale at least four weeks after treatment onset

[Dyck 1986](#) did not include a measure of disability. [Hahn 1996b](#) showed significantly more improvement in a novel ad hoc 11-point functional grading scale after the PE than the sham period. The difference in grade was 2 points in favour of the PE compared with the sham group (95% CI 0.9 to 3.1 points, see [Analysis 1.1](#)). Although we do not know the scale used to have been formally validated, it has excellent face validity and is simple, and so likely to have a high inter-rater reliability. We could not convert the scale used by the trial authors to the Modified Rankin Scale ([van Swieten 1988](#)), because the information was not available.

Secondary outcome measures

I.Change in impairment, at least four weeks after the start of treatment, measured by a validated impairment scale such as the Neuropathy Impairment Score (NIS) ([Dyck 1980](#))

This outcome measure was available for both trials. [Dyck 1986](#) made the assessment after three weeks but we included it in a meta-analysis with the result of [Hahn 1996b](#), in which the measurement was made after four weeks. For [Dyck 1986](#), we calculated the data from the published graph. For [Hahn 1996b](#), we imputed the standard deviations from the P values. In both trials, there was significantly more improvement in the PE group or after the PE period than after sham exchange. The MD was 31 NIS points (95% CI 18 to 45, 280 point score) in favour of PE (see [Figure 2](#)).

Figure 2. Forest plot of comparison: I Plasma exchange versus sham exchange, outcome: I.2 Change in impairment (NDS) after 4 weeks.

We repeated this analysis multiplying the change in [Dyck 1986](#) by 4/3 to give an adjusted rate for four weeks. With this adjustment the MD became 36 NIS points (95% CI 23 to 50) more improvement with PE than with sham exchange, a slightly larger difference but with more uncertainty.

2. Change in proximal compound muscle action potential amplitude measured after at least four weeks

There were significant improvements in this outcome in both trials, after three weeks in [Dyck 1986](#) and after four weeks in [Hahn 1996b](#). The raw figures for inclusion in the meta-analysis were not available from [Dyck 1986](#). In [Hahn 1996b](#) there was significantly more improvement in the PE than the sham exchange group: the MD was 4.6 (95% CI 1.4 to 7.8) mV in favour of PE.

3. Change in disability after at least 12 weeks

This outcome was not available for either study but the authors of [Hahn 1996b](#) drew attention to the deterioration of eight of the 12

participants who improved (out of 15) after the initial benefit from PE. We considered the short duration of benefit from PE and need for repeated and supplementary treatments in the [Discussion](#).

4. Change in impairment after at least 12 weeks measured as for secondary outcome measure I

This outcome measure was not available for either study.

5. Serious adverse events during and for one week after PE or sham exchange

In [Dyck 1986](#), the investigators withdrew one participant because of myocarditis, probably related to an indwelling catheter. The study authors did not state whether this participant was in the PE or sham exchange group. In [Hahn 1996b](#), an 84-year-old man had a stroke one day after his ninth (otherwise uneventful) PE treatment. There was no obvious connection between the PE and

the stroke; the participant had been improving from his CIDP until the time of the stroke. Since these were the only serious adverse events reported, we did not construct a comparison table. Further consideration of serious adverse events appears in the [Discussion](#).

Sensitivity analysis

In this update, we repeated the analyses with the GIV method, which made almost no difference to the means and only minor changes to the CIs (see [Analysis 1.4](#), [Analysis 1.5](#), and [Analysis 1.6](#)).

DISCUSSION

The two available trials have shown that between 33% and 66% of people with CIDP have significant short-term improvement in disability, impairment and nerve conduction from PE. In observational studies, [Pollard 1987](#) reported improvement in 8 of 12 people with CIDP (66%) and [Gorson 1997](#) reported improvement in 11 of 27 people (41%) ([Gorson 1997](#)). [Bromberg 1992](#) reported one person who responded to regular PE after failing to respond to vigorous immunosuppressive regimens. Various other open-label studies have reported benefit ([Abe 1986](#); [Choudhary 1995](#); [Cocito 2010](#); [Donofrio 1984](#); [Gibbels 1986](#); [Gross 1981](#); [Hanaoka 1998](#); [Iwatsubo 1989](#); [Kumazawa 1995](#); [Maas 1981](#); [Pollard 1983](#); [Tanaka 1998](#); [Toyka 1982](#); [van Nunen 1982](#)).

Neither included trial examined the long-term effects of PE, but in a follow-on study, [Hahn 1996b](#) documented the short duration of effect, which is a feature of most observational studies. Eight out of 12 PE responders (66%) relapsed. In seven, relapse occurred within seven to 14 days after stopping PE. In six participants the deterioration was rapid and severe. Observational studies in which PE has been combined with steroids or immunosuppressive drugs have not reported this abrupt deterioration. For instance, [Donofrio 1984](#) treated 11 participants with PE in combination with steroids (except in one case) for two weeks and noted sustained improvement three months later in seven participants.

Several observational studies have documented the beneficial effect of repeated PE in order to maintain improvement. The authors of [Hahn 1996b](#) evaluated the duration of effect and long-term implications of PE prospectively. Eight out of 12 PE responders (66%) relapsed within seven to 14 days after stopping PE. All these participants improved with subsequent open PE. Fourteen participants were monitored monthly for six months while being treated with prednisone alone or, in seven participants, in combination with PE. Ten recovered almost completely but four needed repeated treatment with PE or, in one case IVIg. In a retrospective follow-up study ([Choudhary 1995](#)), 33 of 105 participants underwent treatment with PE, and 23 responded. Of these 23, seven

participants required repeated treatment for between eight months and five years. These participants were eventually transferred to IVIg, but one did not respond to IVIg and continued to receive PE for six more years. In this participant, an n-of-1 trial showed that PE was more effective than immunoabsorption ([Hadden 2002](#)).

[Hahn 1996b](#) proposed that because of the frequency of rebound worsening after treatment, PE should be repeated and tailed off slowly and that PE should be used in combination with immunosuppressive drugs. Another Cochrane review considered the available evidence concerning immunosuppressive drugs but there is a paucity of randomised trials and no clear preferred agent ([Mahdi-Rogers 2013](#)).

IVIg was introduced for the treatment of CIDP soon after PE and another Cochrane review has confirmed that it produces short-term benefit in disability and impairment ([Efimov 2013](#)). The same review included [Dyck 1994](#), which showed that the amount of improvement following IVIg was not significantly different from that following treatment with a course of PE of similar cost.

The pathogenesis of CIDP is not well understood ([Vallat 2010](#)). According to one hypothesis, it is due to an antibody directed against a component of myelin, which causes demyelination and conduction block. However, no diagnostically helpful antibody has been discovered and the removal of a harmful antibody has not been demonstrated, although antibodies to the myelin glycoprotein P0 are possible candidates ([Yan 2001](#)). A treatment response to PE is not necessarily due to an effect on antibody reduction, since it might alternatively be due to a removal of complement components or alteration of cytokines or T cells. In support of the last is a report that PE in CIDP induces a restoration of suppressed nonspecific T cell suppressor function to normal ([De Luca 1999](#)).

The usefulness of PE is limited by its inconvenience, requirement for hospital attendance and specially trained staff, and the occurrence of adverse events. In [Dyck 1986](#), reactions complicated 12 (6.8%) out of 174 procedures (real or sham), eight arising from hypocalcaemia due to citrate toxicity and four from hypotension. In an open follow-up of [Hahn 1996b](#), one participant had a myocardial infarction within minutes of being connected to the cell separator. In a series of PE procedures for various indications, complications, usually from the use of a central venous catheter, were reported in 17% of 381 procedures. There were two deaths: one from arterial haemorrhage caused by the insertion of a central venous catheter and one from cerebral haemorrhage thought to be due to the underlying disease (thrombotic thrombocytopenic purpura) ([Couriel 1994](#)). In a larger series, adverse reactions occurred in 3.9% of 17,940 procedures on 3583 people ([Kiprov 2001](#)). Events included citrate toxicity (3%), vasovagal reactions, vascular access complications, cardiac arrhythmia, haemolysis, hepatitis B, and fresh frozen plasma reactions. There was one death unrelated to the procedure.

In addition to the risks, the benefits of PE have to be balanced

against the costs. Although the cost is considerable, PE now costs less than IVIg in most countries. For people who require repeated procedures, these costs are additive. Furthermore, the costs of providing repeated venous access with the possible need for an indwelling intravenous line and the attendant risks of sepsis need careful consideration. For these reasons, IVIg is usually the preferred treatment option (EFNS/PNS CIDP 2010). A comparative trial showing no significant difference in the efficacy of the two treatments supported its preferential use (Dyck 1994; Eftimov 2013).

The small number of trials and participants limited this review. We based its analyses on the assumption that there was no cross-over effect in the trial with a cross-over design (Hahn 1996b). This assumption may be justified by the theoretical expectation that the duration of effect of PE is limited, as was shown to be the case in Hahn 1996b.

An expert panel of the European Federation of Neurological Societies and Peripheral Nerve Society considered references retrieved from MEDLINE and the Cochrane Systematic Reviews published between August 2004 and July 2009. Based on this evidence the panel gave its highest level of recommendation to the statement that if IVIg and corticosteroids are ineffective, PE should be considered (EFNS/PNS CIDP 2010).

AUTHORS' CONCLUSIONS

Implications for practice

Plasma exchange produces significant short-term improvement in disability and motor nerve conduction velocity (both moderate-quality evidence) and in clinical impairment (high-quality evidence) in chronic inflammatory demyelinating polyradiculoneuropathy but rapid deterioration may occur afterwards. According to observational studies, adverse events related to difficulty with venous access, use of citrate and haemodynamic changes occur in 3% to 17% of procedures.

Implications for research

More research is needed to identify agents which will prolong the beneficial action of plasma exchange.

ACKNOWLEDGEMENTS

We thank Tony Swan for help with statistical advice and Mr and Mrs Lazari for financial support.

This project was supported by the National Institute for Health Research via Cochrane Infrastructure funding to the Cochrane Neuromuscular Disease Group. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, NHS or the Department of Health. The Cochrane Neuromuscular Disease Group is also supported by the MRC Centre for Neuromuscular Disease.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Dyck 1986

Methods	Double-blind randomised controlled trial	
Participants	N = 34, number removed from the study = 5. Analysis done in 29 participants who completed the study. PE group = 15 Sham exchange = 14	
Interventions	PE and sham exchange	
Outcomes	Change in impairment (neurology disability scale, NDS)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	“restricted randomization according to age (< 50 or = or > 50 years), sex, neurologic disability score (< 100 or = or > 100 points)”
Allocation concealment (selection bias)	Low risk	“Only the patient coordinator, statistician and personnel of the apheresis laboratory knew which treatment schedule was being used.”
Blinding (performance bias and detection bias) All outcomes	Low risk	“Only the patient coordinator, statistician and personnel of the apheresis laboratory knew which treatment schedule was being used.”
Incomplete outcome data (attrition bias) All outcomes	High risk	34 participants entered the trial. Investigators withdrew 4 because of doubt about the diagnosis and 1 because of the development of myocarditis possibly related to the intervention. The trial authors did not report outcomes for this participant nor the group to which this participant had been assigned
Selective reporting (reporting bias)	Low risk	We detected no selective reporting
Other bias	Low risk	We detected no other sources of bias

Hahn 1996b

Methods	Double-blind, sham-controlled, cross-over study
Participants	N = 18
Interventions	PE and sham exchange
Outcomes	Change in disability and impairment scale
Notes	Three participants only completed one phase of the trial: one did not receive PE because she wished to leave the trial during the first (SPE) phase of the trial, one did not receive PE because of failed venous access, and one did not receive SPE because of a stroke at the end of the first (PE) phase of the trial. The authors included all three participants in their analyses using the last observation carried forward

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Patients were randomly assigned to either a series of plasma exchanges or sham plasma exchanges."
Allocation concealment (selection bias)	Low risk	"The participating patients and evaluating neurologist remained blinded throughout the entire trial; only the study coordinator and the plasma exchange personnel were non-blinded. The code was broken at the time of data analysis."
Blinding (performance bias and detection bias) All outcomes	Low risk	"The participating patients and evaluating neurologist remained blinded throughout the entire trial; only the study coordinator and the plasma exchange personnel were non-blinded. The code was broken at the time of data analysis."
Incomplete outcome data (attrition bias) All outcomes	Low risk	"Three patients did not complete the trial: one because of failed access for the second treatment arm (plasma exchange); one because of a stroke at the end of the first treatment arm (plasma exchange) and there was one drop-out during the first treatment series (sham plasma exchange)." There were 18 participants altogether in this cross-over trial and 15 (83%) completed both trial periods. We decided that this was unlikely to have such a large effect on the results as to affect the conclusion from the trial. The

Hahn 1996b (Continued)

		authors state “All patients were included in an intention to treat analysis” but the three participants who did not complete the trial were not included
Selective reporting (reporting bias)	Low risk	We detected no selective reporting
Other bias	Low risk	We identified no other sources of bias

PE: plasma exchange

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Baba 1996	Observational study of 14 people. Not a RCT
Dyck 1994	Comparison of PE with IVIg not placebo Reviewed in Efimov 2013
Kumazawa 1998	Observational study of 14 people. Not a RCT
Mori 2002	Review, not a RCT
Zinman 2005	Comparison of immunoabsorption not PE with IVIg not placebo. Authors of the Cochrane review of IVIg for CIDP considered and excluded this trial because of a high risk of bias (Efimov 2013)

IVIg: intravenous immunoglobulin

PE: plasma exchange

RCT: randomised controlled trial

DATA AND ANALYSES

Comparison 1. Plasma exchange versus sham exchange

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Change in disability after 4 weeks	1	36	Mean Difference (IV, Fixed, 95% CI)	-2.0 [-3.08, -0.92]
2 Change in impairment (NDS) after 4 weeks	2	65	Mean Difference (IV, Fixed, 95% CI)	-31.21 [-44.85, -17.57]
3 Change in mean compound muscle action potential amplitude after 4 weeks	1	36	Mean Difference (IV, Fixed, 95% CI)	4.60 [1.41, 7.79]
4 Change in disability after 4 weeks (generic inverse variance method)	1		Mean Difference (Fixed, 95% CI)	-2.0 [-3.08, -0.92]
5 Change in impairment (NDS) after 4 weeks (generic inverse variance method)	2		Mean Difference (Fixed, 95% CI)	-30.76 [-45.09, -16.43]
6 Change in mean compound muscle action potential amplitude after 4 weeks (generic inverse variance method)	1		Mean Difference (Fixed, 95% CI)	4.6 [1.09, 8.11]

Analysis 1.1. Comparison 1 Plasma exchange versus sham exchange, Outcome 1 Change in disability after 4 weeks.

Review: Plasma exchange for chronic inflammatory demyelinating polyradiculoneuropathy

Comparison: 1 Plasma exchange versus sham exchange

Outcome: 1 Change in disability after 4 weeks

Analysis 1.2. Comparison 1 Plasma exchange versus sham exchange, Outcome 2 Change in impairment (NDS) after 4 weeks.

Review: Plasma exchange for chronic inflammatory demyelinating polyradiculoneuropathy

Comparison: 1 Plasma exchange versus sham exchange

Outcome: 2 Change in impairment (NDS) after 4 weeks

Analysis 1.3. Comparison 1 Plasma exchange versus sham exchange, Outcome 3 Change in mean compound muscle action potential amplitude after 4 weeks.

Review: Plasma exchange for chronic inflammatory demyelinating polyradiculoneuropathy

Comparison: 1 Plasma exchange versus sham exchange

Outcome: 3 Change in mean compound muscle action potential amplitude after 4 weeks

Analysis 1.4. Comparison 1 Plasma exchange versus sham exchange, Outcome 4 Change in disability after 4 weeks (generic inverse variance method).

Review: Plasma exchange for chronic inflammatory demyelinating polyradiculoneuropathy

Comparison: 1 Plasma exchange versus sham exchange

Outcome: 4 Change in disability after 4 weeks (generic inverse variance method)

Analysis 1.5. Comparison 1 Plasma exchange versus sham exchange, Outcome 5 Change in impairment (NDS) after 4 weeks (generic inverse variance method).

Review: Plasma exchange for chronic inflammatory demyelinating polyradiculoneuropathy

Comparison: 1 Plasma exchange versus sham exchange

Outcome: 5 Change in impairment (NDS) after 4 weeks (generic inverse variance method)

Analysis 1.6. Comparison 1 Plasma exchange versus sham exchange, Outcome 6 Change in mean compound muscle action potential amplitude after 4 weeks (generic inverse variance method).

Review: Plasma exchange for chronic inflammatory demyelinating polyradiculoneuropathy

Comparison: 1 Plasma exchange versus sham exchange

Outcome: 6 Change in mean compound muscle action potential amplitude after 4 weeks (generic inverse variance method)

APPENDICES

Appendix 1. MEDLINE (OvidSP) search strategy

Database: Ovid MEDLINE(R) <1946 to June Week 3 2015>

Search Strategy:

```
1 randomized controlled trial.pt. (397600)
2 controlled clinical trial.pt. (89726)
3 randomized.ab. (294510)
4 placebo.ab. (153075)
5 drug therapy.fs. (1785057)
6 randomly.ab. (207734)
7 trial.ab. (303892)
8 groups.ab. (1321810)
9 or/1-8 (3370287)
10 exp animals/ not humans.sh. (4061621)
11 9 not 10 (2869219)
12 (inflammatory adj3 demyelinating).tw. (3610)
13 (polyradiculoneuropath$3 or polyneuropath$3).tw. (11624)
14 polyneuropathies/ or Polyradiculoneuropathy/ (7968)
15 (polyneuritis or polyradiculoneuritis).tw. (1704)
16 13 or 14 or 15 (17479)
17 chronic disease.tw. or exp Chronic Disease/ (237714)
18 12 and 16 and 17 (331)
19 Polyradiculoneuropathy, Chronic Inflammatory Demyelinating/ or (chronic adj3 inflammatory adj3 demyelinating adj3 polyradicu-
loneuropathy).tw. (1260)
20 cidp.mp. (1123)
21 18 or 19 or 20 (1718)
22 plasma exchange.mp. or exp Plasmapheresis/ or plasmapheresis.tw. (16464)
23 11 and 21 and 22 (114)
24 remove duplicates from 23 (109)
```

Appendix 2. EMBASE (OvidSP) search strategy

Database: Embase <1980 to 2015 Week 26>

Search Strategy:

```
1 crossover-procedure.sh. (43327)
2 double-blind procedure.sh. (121405)
3 single-blind procedure.sh. (20468)
4 randomized controlled trial.sh. (375311)
5 (random$ or crossover$ or cross over$ or placebo$ or (doubl$ adj blind$) or allocat$).tw,ot. (1154503)
6 trial.ti. (179393)
7 or/1-6 (1295598)
8 (animal/ or nonhuman/ or animal experiment/) and human/ (1378962)
9 animal/ or nonanimal/ or animal experiment/ (3404536)
10 9 not 8 (2831761)
11 7 not 10 (1190541)
12 limit 11 to embase (978188)
13 (inflammatory adj3 demyelinating).tw. (5717)
14 (polyradiculoneuropath$3 or polyneuropath$3).tw. (16402)
15 polyneuropathies/ or Polyradiculoneuropathy/ (13169)
```

16 (polyneuritis or polyradiculoneuritis).tw. (1658)
 17 14 or 15 or 16 (23126)
 18 chronic disease.tw. or exp Chronic Disease/ (172736)
 19 13 and 17 and 18 (127)
 20 chronic inflammatory demyelinating polyneuropathy/ or (chronic adj3 inflammatory adj3 demyelinating adj3 polyradiculoneuropathy).tw. (2572)
 21 cidp.mp. (2087)
 22 or/19-21 (3331)
 23 plasma exchange.mp. or exp Plasmapheresis/ or plasmapheresis.tw. (31181)
 24 12 and 22 and 23 (94)
 25 remove duplicates from 24 (94)

Appendix 3. CNMDG (CRS) search strategy

#1 MeSH DESCRIPTOR Polyradiculoneuropathy, Chronic Inflammatory Demyelinating [REFERENCE] [STANDARD]
 #2 (chronic NEAR3 inflammatory NEAR3 demyelinating NEAR3 polyradiculoneuropathy) or (chronic NEAR3 inflammatory NEAR3 demyelinating NEAR3 polyneuropathy) or cidp [REFERENCE] [STANDARD]
 #3 “inflammatory demyelinating” [REFERENCE] [STANDARD]
 #4 polyradiculoneuropathy or polyneuropathy or polyradiculoneuropathies or polyneuropathies [REFERENCE] [STANDARD]
 #5 polyneuritis or polyradiculoneuritis [REFERENCE] [STANDARD]
 #6 MeSH DESCRIPTOR Polyneuropathies [REFERENCE] [STANDARD]
 #7 MeSH DESCRIPTOR Polyradiculoneuropathy [REFERENCE] [STANDARD]
 #8 #4 or #5 or #6 or #7 [REFERENCE] [STANDARD]
 #9 “chronic disease” [REFERENCE] [STANDARD]
 #10 #3 and #8 and #9 [REFERENCE] [STANDARD]
 #11 #1 or #2 or #10 [REFERENCE] [STANDARD]
 #12 “plasma exchange” or plasmapheresis [REFERENCE] [STANDARD]
 #13 #11 and #12 [REFERENCE] [STANDARD]
 #14 (#11 and #12) AND (INREGISTER) [REFERENCE] [STANDARD]

Appendix 4. CENTRAL search strategy

#1 “inflammatory demyelinating”
 #2 polyradiculoneuropath* or polyneuropath*
 #3 MeSH descriptor: [Polyneuropathies] this term only
 #4 MeSH descriptor: [Polyradiculoneuropathy] this term only
 #5 polyneuritis or polyradiculoneuritis
 #6 #2 or #3 or #4 or #5
 #7 MeSH descriptor: [Chronic Disease] this term only
 #8 chronic next disease
 #9 #7 or #8
 #10 #1 and #6 and #9
 #11 MeSH descriptor: [Polyradiculoneuropathy, Chronic Inflammatory Demyelinating] this term only
 #12 (chronic near/3 inflammatory near/3 demyelinating near/3 polyradiculoneuropathy) or cidp
 #13 #10 or #11 or #12
 #14 (plasma next exchange) or plasmapheresis
 #15 #13 and #14

Appendix 5. CINAHL (EBSCOhost) search strategy

Tuesday, June 30, 2015 11:01:10 AM

S35 S18 and S31 and S34 18
S34 S28 or S32 or S33 503
S33 chronic n3 inflammatory n3 demyelinating n3 polyradiculoneuropathy 121
S32 cidp 192
S31 S29 or S30 65,178
S30 TI chronic disease or AB chronic disease 28,283
S29 (MH "Chronic Disease") 42,544
S28 S21 or S27 465
S27 S22 and S26 364
S26 S23 or S24 or S25 4,616
S25 polyradiculoneuropath* or polyneuropath* or polyneuritis 1,732
S24 (MH "Polyneuritis+") 333
S23 (MH "Polyradiculoneuritis+") or (MH "Polyradiculopathy") 3,241
S22 inflammatory n3 demyelinating 488
S21 S19 and S20 161
S20 TI inflammatory or AB inflammatory 35,362
S19 (MH "Demyelinating Diseases") 1,143
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 755,807
S17 ABAB design* 93
S16 TI random* or AB random* 151,778
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)) 302,796
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*)) 106,572
S13 (TI (meta?analys* or systematic review*)) or (AB (meta?analys* or systematic review*)) 38,221
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*)) 23,532
S11 PT ("clinical trial" or "systematic review") 128,404
S10 (MH "Factorial Design") 946
S9 (MH "Concurrent Prospective Studies") or (MH "Prospective Studies") 266,129
S8 (MH "Meta Analysis") 22,594
S7 (MH "Solomon Four-Group Design") or (MH "Static Group Comparison") 48
S6 (MH "Quasi-Experimental Studies") 7,399
S5 (MH "Placebos") 9,296
S4 (MH "Double-Blind Studies") or (MH "Triple-Blind Studies") 31,919
S3 (MH "Clinical Trials+") 189,073
S2 (MH "Crossover Design") 13,073
S1 (MH "Random Assignment") or (MH "Random Sample") or (MH "Simple Random Sample") or (MH "Stratified Random Sample") or (MH "Systematic Random Sample") 69,703

Appendix 6. LILACS search strategy

((polyradiculoneuropath\$ OR polyneuropath\$ OR polyneuritis OR polyradiculoneuritis) AND chronic AND “inflammatory demyelinating”) OR “chronic inflammatory demyelinating polyradiculoneuropathy” OR cidp) AND (“plasma exchange” OR Mh Plasma-pheresis) AND ((PT:“Randomized Controlled Trial” or “Randomized Controlled trial” or “Ensayo Clínico Controlado Aleatorio” or “Ensaio Clínico Controlado Aleatório” or PT:“Controlled Clinical Trial” or “Ensayo Clínico Controlado” or “Ensaio Clínico Controlado” or “Random allocation” or “Distribución Aleatoria” or “Distribuição Aleatória” or randon\$ or Randomized or randomly or “double blind” or “duplo-cego” or “duplo-cego” or “single blind” or “simples-cego” or “simples cego” or placebo\$ or trial or groups) AND NOT (B01.050\$ AND NOT (humans or humanos or humanos)))

WHAT'S NEW

Date	Event	Description
21 July 2017	Amended	Data for Hahn 1996b corrected

HISTORY

Protocol first published: Issue 4, 2002

Review first published: Issue 3, 2004

Date	Event	Description
30 June 2015	New citation required but conclusions have not changed	New search on 30 June 2015
12 March 2015	New search has been performed	Background and Discussion updated with new references. No new trials. Conclusions not changed. Jane Pritchard became a co-author
22 June 2012	New citation required but conclusions have not changed	New searches performed on 14 May 2012
19 May 2012	New search has been performed	No new trials found from updated searches. Puneet Agarwal withdrew from authorship
12 May 2010	New search has been performed	New searches January 2010. No new trials. Risk of bias has been reassessed according to the 2008 Handbook methods, a sensitivity analysis and 'Summary of findings' table have been added and the wording of the conclusions has been changed
27 July 2008	New search has been performed	Updated with literature search up to September 2007.
1 February 2006	New search has been performed	February 2006 We updated the search of the NMD Group Register (January 2006), MEDLINE (January 1966 to January

(Continued)

		2006), EMBASE (January 1980 to January 2006) and CINAHL (January 1982 to January 2006). We found one new trial, a pilot trial comparing immunoadsorption with IVIg which will be considered in an update of the van Schaik 2002 review of IVIg treatment for CIDP. We updated references to diagnostic guidelines and non-systematic reviews
14 May 2004	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

Man Mohan Mehndiratta and Puneet Agarwal wrote and Richard Hughes edited the first draft. Man Mohan Mehndiratta and Richard Hughes wrote the subsequent drafts. Jane Pritchard edited this update.

DECLARATIONS OF INTEREST

Man Mohan Mehndiratta: no conflicts of interest to declare.

Richard Hughes has or has had consultancies with Baxter, CSL Behring, Grifols, LFB and Octapharma, companies which produce immunoglobulin which is an alternative treatment for CIDP. RACH is also a Member of Medical Advisory Board of GBS CIDP Foundation International and Medical Patron of the inflammatory neuropathy charity, gain.

Jane Pritchard was involved in a trial of interferon in the treatment of Guillain Barré syndrome. Serono provided departmental funding for the trial to the department in which she was working at the time.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- Donation from the late Mr Lazari and Mrs Lazari, UK.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

In the 2010 revision, we reassessed risk of bias according to the *Cochrane Handbook for Systematic Reviews of Interventions* 2008 methods, and added a sensitivity analysis and 'Summary of findings' table. The terminology for the 'Risk of bias' assessments changed in 2012 from yes/no/unclear to high/low/unclear (Higgins 2011).

Puneet Agarwal withdrew from authorship prior to the 2012 update of the review.

NOTES

The authors consider that further trials are unlikely; therefore, the next planned update of this review will be four years from the current date of search rather than the usual two years. If new evidence emerges contrary to this, an earlier update will be scheduled.

In July 2017 the first author of Hahn 1996b pointed out that this review had omitted the three participants who had only completed one period of the crossover trial from the meta-analysis. The authors of Hahn 1996b had included these participants imputing the missing data from the last observation carried forward in their published paper. The analyses and text of the review have now been amended to correct this omission which, however, has not affected the conclusions of the review.

INDEX TERMS

Medical Subject Headings (MeSH)

*Plasma Exchange; Cross-Over Studies; Polyradiculoneuropathy, Chronic Inflammatory Demyelinating [*therapy]; Randomized Controlled Trials as Topic

MeSH check words

Humans