Immunotherapy for Guillain-Barre syndrome: a systematic review
Hughes R A, Swan A V, Raphael J C, Annane D, van Koningsveld R, van Doorn P A

CRD summary
The authors concluded that plasma exchange increases the speed of recovery and improves outcomes in patients with Guillain-Barre syndrome, and that intravenous immunoglobulin and plasma exchange appear to have similar effects, but further research is required. It is difficult to assess the reliability of these conclusions given the diversity of the studies and the lack of a study quality assessment.

Authors' objectives
To evaluate the effectiveness of immunotherapy for Guillain-Barre syndrome (GBS).

Searching
The Cochrane Library (including the specialised register of the Cochrane Neuromuscular Disease Group), MEDLINE and EMBASE were searched to June 2006; the search terms were reported. In addition, the references from RCTs were screened, and authors and other experts were contacted for information about additional published and unpublished trials.

Study selection
Study designs of evaluations included in the review
Quasi-randomised and randomised controlled trials (RCTs) were eligible for inclusion in the review.

Specific interventions included in the review
Although inclusion criteria for the interventions were not specified, it was clear that studies that evaluated immunotherapy were eligible for inclusion. The included studies compared plasma exchange (PE), intravenous immunoglobulin (IV Ig) and corticosteroids with supportive care, no treatment, placebo, immunoabsorption, or each other; some studies evaluated combinations of interventions.

Participants included in the review
Although inclusion criteria for the participants were not specified, it was clear that studies of patients with GBS were eligible for inclusion. Some of the included studies were in adults or children only, while others were in all age groups. The participants varied in the severity of GBS: some studies only included patients with severe or mild disease and others included all forms of the disease.

Outcomes assessed in the review
Inclusion criteria were not specified in terms of the outcomes. Most of the studies assessed outcomes using the 7-point GBS disability scale (see Other Publications of Related Interest). For patients who were unable to walk independently (GBS disability grade 3 or more), the primary review outcome was the mean improvement in disability grade at 4 weeks after randomisation. Secondary outcome measures included the number of patients improved by one or more grades at 4 weeks, duration of ventilation, time to recover independent walking, death and residual disability, and death. For patients who were able to walk without assistance (GBS grade 2 or less), the primary review outcome was the time until the start of motor recovery (defined by an improvement of at least 2 items of a muscle strength score or 1 item plus improvement in cranial nerve function or trunk or respiratory involvement). The review also assessed safety and relapses.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected the studies and resolved any disagreements by discussion.

Assessment of study quality
Studies were apparently assessed for adequacy of randomisation and allocation concealment. The authors did not state how the validity assessment was performed.
Data extraction
Two reviewers independently extracted the data and resolved any disagreements by discussion. Some missing data were obtained from the authors. Standard deviations were imputed where required.

Methods of synthesis
How were the studies combined?
The studies were grouped by the drugs evaluated and compared. They were combined using meta-analysis, where possible, otherwise a narrative synthesis was used. Pooled relative risks (RRs) and 95% confidence intervals (CIs) were calculated for dichotomous data and pooled weighted mean differences (WMDs) and 95% CIs for continuous data. Fixed-effect methods were used in the absence of significant heterogeneity and random-effects models in its presence.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the chi-squared and I-squared statistics. Potential sources of heterogeneity were explored and other differences between the studies were discussed.

Results of the review
According to the text, the review included 8 studies that evaluated PE, 10 studies that evaluated IV Ig and 8 studies that evaluated corticosteroids. However, the data extraction tables presented 10 comparisons (n=1,179) listed under PE, 12 comparisons (n=933) listed under IV Ig and 8 studies (n=623) listed under corticosteroids. Some studies were listed under more than one treatment. It is unclear why not all studies included in these tables were included in the review.

Eighteen trials reported adequate randomisation and concealment methods.

PE (8 studies): patients who received PE reported a significant improvement in GBS disability grade at 4 weeks compared with those who did not receive PE (WMD -0.89, 95% CI: -1.14, -0.63, p<0.000001), based on 4 studies (n=585.) One trial included patients with mild GBS who could walk unaided. This study reported a significantly greater number of patients with one or more grades of improvement at 1 month in the PE group compared with control (RR 3.47, 95% CI: 1.45, 8.31, p<0.01).

IV Ig (10 studies): 3 small studies in children reported greater benefits with IV Ig compared with no treatment or placebo. All studies reported significantly greater improvements in the IV Ig groups compared with controls. There was no statistically significant difference in the GBS disability grade at 4 weeks, or for other outcomes assessed, between patients who received PE compared with IV Ig (5 studies, n=582), between IV Ig and immunoabsorption (1 study, n=41), between IV Ig 0.4 mg/kg for 3 days versus 6 days (1 study, n=39), or between IV Ig 0.4 g/kg per day for 5 days versus 1.0 g/kg for 2 days (1 study, n=50).

There was no statistically significant difference in the GBS disability grade at 4 weeks between patients who received PE alone compared with PE followed by IV Ig (1 study, n=249), or between patients who received immunoabsorption followed by IV Ig versus immunoabsorption alone (1 study, n=37).

Corticosteroids (8 studies): there was no statistically significant difference in the GBS disability grade at 4 weeks between patients who received corticosteroids and those who did not (6 studies, n=587). Statistically significant heterogeneity was detected (p=0.0002; I-squared 80%). For the 4 small studies (n=120) that used oral corticosteroids, there was significantly less improvement among patients receiving corticosteroids than among those not receiving corticosteroids (WMD -0.82, 95% CI: -0.17, -1.47, p<0001). Heterogeneity was reduced (p=0.10; I-squared 51%). For the 2 larger studies (n=467) that used intravenous methylprednisolone, there was no significant difference between corticosteroids and no corticosteroids. There was no evidence of heterogeneity (p=0.32; I-squared 0%).

Safety: there was no significant difference in serious adverse events (severe infections, blood-pressure instability, pulmonary embolism or cardiac arrhythmias) between PE and supportive care (3 studies), in adverse events between fresh frozen plasma and albumen as replacement (1 study), or in adverse events between PE and IV Ig (3 studies). One study reported significantly fewer patients with multiple complications in the IV Ig group compared with the PE group (RR 0.31, 95% CI: 0.12, 0.80).

None of the treatments were associated with significant reductions in mortality.
The results for other secondary outcomes were also reported.

**Authors' conclusions**
PE increases the rate of recovery and improves outcomes at 1 year in patients with GBS. There was insufficient evidence for IV Ig compared with no treatment, but IV Ig and PE appear to have similar effects.

**CRD commentary**
The review question was clear with respect to the participants, intervention and study design, although inclusion criteria were not explicitly defined. A number of studies that were included in the tables were not included in the review, and the reasons for this were unclear. It was not clear if the primary outcome was selected before or after reviewing potentially relevant studies. Several relevant sources were searched and attempts were made to minimise publication bias. It was not clear whether any language restrictions had been applied, so the potential for language bias could not be assessed. Only two validity criteria were assessed and the exact criteria on which these were assessed were unclear; this inadequate assessment makes it difficult to judge the reliability of the evidence presented. Methods were used to minimise reviewer error and bias in the study selection and data extraction processes, but it was unclear whether similar steps were taken in the assessment of validity.

Where possible, the data were pooled statistically and potential sources of heterogeneity were examined. It is difficult to assess the reliability of the conclusions given the limited definition of inclusion criteria, the diversity of the studies, the unknown extent to which the data represent all patients with GBS, and the absence of a quality assessment of the included studies. The recommendations for further research appear justified.

**Implications of the review for practice and research**
Practice: The authors did not state any implications for practice.

Research: The authors stated the need for further research to identify more effective treatments for patients with GBS.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.