Plasma exchange and intravenous immunoglobulin were equally effective for the Guillain-Barré syndrome

Plasma Exchange/Sandoglobulin Guillain-Barré Syndrome Trial Group. **Randomised trial of plasma exchange, intravenous immunoglobulin, and combined treatments in Guillain-Barré syndrome.** Lancet. 1997 Jan 25;349:225-30.

Objective
To evaluate the effectiveness of intravenous immunoglobulin (IVIg), plasma exchange (PE), and the combination of both in the treatment of the Guillain-Barré syndrome.

Design
Randomized, single-blind, controlled trial with 48-week follow-up.

Setting
38 centers in 11 countries.

Patients
383 patients > 16 years of age (mean age 53 y) with severe Guillain-Barré syndrome (required an aid to walk or worse) and had onset of neuropathic symptoms within the previous 14 days. Exclusion criteria were atypical forms of the Guillain-Barré syndrome, other serious diseases, or contraindications to IVIg or PE.

Intervention
121 patients were allocated to PE, five 50 mL/kg exchanges over 8 to 13 days. If the exchange was inadequate, a sixth exchange was given to achieve a total exchange of 250 mL/kg. 130 patients were allocated to IVIg, 0.4 g/kg daily for 5 days starting on the day of randomization. 128 patients were allocated to the PE course immediately followed by the IVIg course.

Main outcome measures
Disability grade, group grade, and vital capacity.

Main results
4 patients were excluded from the analysis; 96% of the remaining 379 were followed for 48 weeks. Analysis was by intention to treat. No difference existed between the treatment groups for mean disability-grade improvement after 4 weeks. The difference in improvement between the PE group and the IVIg group was 0.09 grade (95% CI – 0.23 to 0.42), between the PE plus IVIg and IVIg alone groups was 0.29 grade (CI – 0.04 to 0.63), and between the PE plus IVIg and PE alone groups was 0.20 grade (CI – 0.14 to 0.54). The study had 90% power to detect a true difference of ≥ 0.5 in disability grade between the IVIg and PE groups. No differences existed between the groups for time to ability to walk unaided, time to discontinuation of ventilation, time to hospital discharge, time to return to work, or time to recovery from disability over the 48-week follow-up.

Conclusions
Plasma exchange and intravenous immunoglobulin were similar in improving the symptoms in patients with severe Guillain-Barré syndrome. The combination of the 2 treatments did not confer any additional benefit.

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Commentary

The Plasma Exchange/Sandoglobulin Guillain-Barré Syndrome Trial Group reports the first comparison of PE, IVIg, and combined therapy (PE plus IVIg) for the Guillain-Barré syndrome. The methods of the trial were sound.

The 2 individual treatments for the Guillain-Barré syndrome were found to be equipotent. After 4 weeks, the disability grade improved by 0.9 points with PE and 0.8 points with IVIg. A clinically important effect was assumed to be at least 0.5 disability grade improvement. The authors conclude that "on the grounds of equal therapeutic benefit, greater convenience, and similar overall cost, IVIg may be preferable to PE."

An important issue in this study is the clinical significance of the treatment effect noted with PE and IVIg compared with combined therapy. However, a subgroup of 344 patients (i.e., those with complete neurophysiologic data) showed a statistically greater benefit from combined treatment compared with either treatment alone, after adjustment for prognostic factors that differed between treatment groups. The combined therapy was 0.43 disability grade better than IVIg or PE alone and promoted faster recovery ($P = 0.05$). These findings may be clinically important. Is the marginal cost worth this degree of extra benefit, and might some patients (e.g., those who are refractory to PE or IVIg alone) require the more expensive, dangerous, and potent alternative? Although IVIg is preferable to PE, there may also be a place for PE in patients who cannot tolerate IVIg.

Combined therapy is statistically better, but further clarification of the clinical importance of this difference is required. It is likely that many neurologists will continue to use combined therapy for the most severely ill patients, and many will recognize that these data tentatively support this practice.

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Author's response

Clinicians should note that in our primary analysis before adjustment and in our secondary analysis, no statistically significant differences were found in favor of combined treatment. Only a trend toward faster recovery of unaided walking in the combined treatment group was reported. Therefore, we do not feel that our data support the use of combined treatment.

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