Cost analysis of plasma-exchange therapy for the treatment of Guillain-Barre syndrome

Esperou H, Jars-Guincestre M C, Bolgert F, Raphael J C, Durand-Zaleski I

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The use of plasma-exchange (PE) therapy for the treatment of Guillain-Barre syndrome (GBS).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised male and female patients with GBS who were aged over 16 years, who had motor signs that had first occurred less than 1 month before. Pregnant women and patients with atypical forms were excluded, as were those with contraindications to PE. Also excluded were patients with spontaneous improvement over the first 2 days, severe intercurrent disease, any motor sequelae of a prior neurological disorder, and those who could not be exchanged due to technical constraints on the randomisation day.

Setting
The setting was secondary care. The economic analysis was conducted in Paris, France.

Dates to which data relate
The effectiveness and resource data were collected from January 1986 to March 1993. The price year was 1999.

Source of effectiveness data
The effectiveness data were derived from a single prospective study. The effectiveness analysis was published elsewhere (French Cooperative Group on Plasma Exchange, see Other Publications of Related Interest). This paper briefly reported the outcome results and the cost analysis.

Link between effectiveness and cost data
Ten patients were excluded from the economic analysis because no data on resource use were available for them. The costing was carried out prospectively on the remaining 546 patients.

Study sample
Power calculations estimated that 480 patients had to be recruited. Six hundred and eighty-four patients with GBS were eligible, of which 121 were not randomised (6 patients refused) and 7 misdiagnosed patients were excluded. Of the 556 randomised patients, 91 were in the mild group, 304 in the moderate group, and 161 in the severe group.
Study design
The study was a randomised controlled trial that was conducted in 27 centres in France and Switzerland. The trial was not blinded since the observers could easily know the administered treatment. The duration of follow-up was 12 months after discharge. In the mild group, 7 patients were lost to follow-up or had died at one year. In the moderate group, 7 patients were misplaced but were retained in the group for purposes of the analysis.

Analysis of effectiveness
The analysis of the clinical study was conducted on an intention to treat basis. The primary health outcome was the time required to recover the ability to walk with assistance. The secondary end points were:

- the delta score at day 8,
- the proportion of patients with mild and moderate forms of GBS who deteriorated,
- the proportion of patients who required ventilator assistance,
- the time on the ventilator,
- the time required to walk unassisted,
- the time to hospital discharge, and
- the frequency of relapse.

The final end points were the proportions of complete and incomplete recoveries, and the complication and mortality rate. The age of the patients increased from the mild to the severe groups. Some imbalances in mean score value were observed between the two treatment arms in each group. Thus, the treatment effects were examined separately in each group.

Effectiveness results
In the mild group, 2 PEs were more effective for time to onset of motor recovery than none (median: 4 versus 8 days; p=0.0002). The adjusted chance of motor recovery in the 2-PE arm was twice that of the control arm (95% confidence interval, CI: 1.4 - 3.7; p=0.001). Fewer patients in the 2-PE arm deteriorated, (p=0.0001), or required mechanical ventilation, although non significantly, (p=0.11). There was a significant difference in the mean delta score on day 8 between the 2-PE arm and the control arm (-6 versus 3; p=0.005). There was no statistically significant difference in the proportion of patients attaining full muscle strength. There was no significant difference between the two treatment arms in the frequency of complications.

In the moderate group, the time required to walk with assistance was shorter in the 4-PE arm than in the 2-PE arm (24 versus 20 days; p=0.04). The length of ventilation was also shorter in the 4-PE arm than in the 2-PE arm (15 versus 37 days; p=0.005), as was the time to hospital discharge (21 versus 26 days; p=0.04). The frequency of full muscle-strength recovery was higher in the 4-PE arm relative to the 2-PE arm, (p=0.006). Systolic blood pressure instability, (p=0.004), haematomas, (p=0.002), and deaths, (p=0.05), were more frequent in the 4-PE arm than in the 2-PE arm.

In the severe group, 6 PEs were no more beneficial than 4 PEs.

Clinical conclusions
For patients with mild symptoms, 2 PEs were more efficient than none for short-term medical outcomes, but were not statistically better for long-term outcomes. In patients with moderate symptoms, 4 PEs resulted in better short-term and long-term outcomes than 2 PEs. The treatment of patients with severe symptoms was no better with 6 PEs than with 4 PEs.
Measure of benefits used in the economic analysis
The authors noted "because there was no difference in mortality in the three trials and the only differences concerned intermediate endpoints, we undertook a cost-minimization analysis". See 'Other Issues' in the 'Commentary' section.

Direct costs
The perspective of the health care system was adopted. Only the direct costs were included. These covered initial hospitalisation in the intensive care unit (ICU), PEs, treating complications (using the increase in the diagnosis-related groups payment), and the ambulatory costs (including rehabilitation after discharge). The costs of the ICU covered medical and non medical salaries, housekeeping expenses, supplies, biological and imaging tests, drugs and overheads. The costs of PE also considered the method (infiltration or centrifugation) and replacement fluids used. The unit cost of hospitalisation was obtained from the hospital accounting charts. The cost of replacement fluid was obtained using the purchase prices from the hospital blood bank. The ambulatory costs were from the French health care financing administration cost schedule. The resource quantities and the costs were not reported separately. All the costs were adjusted to year 1999. The costs were not discounted since the follow-up period was less than 2 years.

Statistical analysis of costs
No statistical analysis of the costs was performed.

Indirect Costs
Production costs were estimated through the number of workdays lost and the ability of the patients to resume work. However, these indirect costs were not included in the final computations. The total production costs were estimated from the French minimum wage ($1,000 per month) and the daily compensation provided by Social Security to persons unable to resume their occupation. The resource quantities and the unit costs were reported separately. The costs were computed for the year 1999. The costs were not discounted since the follow-up period was less than 2 years.

Currency
Euros (Euro). French costs were converted into Euros using the exchange rate at January 2000, 1 Euro = approximately 1 US dollar.

Sensitivity analysis
One-way sensitivity analyses were performed for the total costs related to the changes in practice patterns for PEs, and for the cost of filtration (+50%).

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
For a patient with mild symptoms, the average health care cost was Euro 38,753 with no intervention versus Euro 21,353 for the 2-PE arm. The total production cost was Euro 9,149 with no intervention versus Euro 5,961 for the 2-PE arm.

For a patient with moderate symptoms, the average health care cost was Euro 80,737 for the 2-PE arm versus Euro 59,480 for the 4-PE arm. The total production cost was Euro 10,007 for the 2-PE arm versus Euro 9,519 for the 4-PE arm.

For a patient with severe symptoms, the average health care cost was Euro 57,621 for the 4-PE arm versus Euro 61,056 for the 6-PE arm. The total production cost was Euro 11,161 for the 4-PE arm versus Euro 11,633 for the 6-PE arm.
The cost analysis appeared to be robust when the PE costs increased by roughly 50%.

**Synthesis of costs and benefits**
Not applicable.

**Authors' conclusions**
The treatment of Guillain-Barre syndrome (GBS) by plasma exchange (PE) at the onset of disease appears to have been medically justified. There were dominant strategies in two severity groups with a better efficacy and lower costs, the 2-PE arm in the mild group and the 4-PE arm in the moderate arm. In the severe group, 4-PEs were as efficient and somewhat less expensive than 6-PEs.

**CRD COMMENTARY - Selection of comparators**
The reason for the choice of the comparators appears to have been clear. You should consider whether these are widely used technologies in your own setting.

**Validity of estimate of measure of effectiveness**
The basis of the analysis was randomised prospective study, which was appropriate for the study question. Power calculations were reported. It is likely that the study sample was representative of the study population. The patients were shown to be comparable at analysis, so confounding should be low. Selection bias was likely to have been low due to randomisation. The reader should refer to the parent clinical study for more details of the methods and analysis undertaken in relation to effectiveness.

**Validity of estimate of measure of benefit**
There was no summary measure of benefit.

**Validity of estimate of costs**
The costs and the quantities were not reported separately. Adequate details of the methods of cost estimation were given. The cost estimates were likely to be specific to the French setting. These factors would hinder the reproducibility of the results in other settings. A potentially good feature of the cost analysis was that the authors evaluated both direct and indirect costs. However, the indirect costs were not included in the final results. Consequently, the study lacked a comprehensive cost analysis relating to both direct and indirect costs. The price year was reported, thus aiding reflation exercises. The cost estimates were treated deterministically. A limited sensitivity analysis on the filtration costs was performed.

**Other issues**
This study cannot be considered a cost-minimisation analysis (except in terms of equal mortality between the groups, as the authors stated) because the effectiveness analysis showed statistically significant differences between treatment strategies in at least two groups. It would therefore be more appropriate to consider the study a cost-consequences analysis. The generalisability of the results was discussed. The findings were compared with those from one other study. The authors reported further limitations of their study and do not appear to have reported their results selectively.

**Implications of the study**
The authors recommended that patients with mild initial symptoms should be treated with 2 PEs, and patients with moderate or severe initial symptoms should be treated with 4 PEs.

**Source of funding**
Supported by a grant from the Delegation a la Recherche Clinique (Assistance Publicque-Hopitaux de Paris).

**Bibliographic details**

**PubMedID**
11030166

**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Adolescent; Adult; Cost-Benefit Analysis; France; Guillain-Barre Syndrome /rehabilitation /therapy; Humans; Outcome Assessment (Health Care) /economics; Plasma Exchange /economics; Sensitivity and Specificity; Severity of Illness Index; Statistics, Nonparametric

**AccessionNumber**
22000001444

**Date bibliographic record published**
31/08/2004

**Date abstract record published**
31/08/2004