Short report

Treatment of the Guillain-Barré syndrome by plasma exchange

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SUMMARY Twelve consecutive patients with Guillain-Barré syndrome were treated with plasma exchange. Examination two weeks after treatment was commenced showed that three had not improved. Five showed only a minimal improvement, which was considered to be compatible with the natural history of the disease. The remaining four patients showed a more substantial improvement which could have been related to the plasma exchange.

The aetiology and pathogenesis of acute polyneuropathy (Guillain-Barré syndrome) is still incompletely understood. Both humoral and cell mediated immunological mechanisms have been implicated. The former are suggested by the finding of immunoglobulin in nerves,¹ circulating immune complexes,²⁻⁴ complement fixing antibodies against neural tissue in 50% of cases,⁵ and demyelination in tissue culture by cell free serum⁶ or when injected intraneurally.⁷ Pathological examination of the peripheral nerves in this condition shows infiltration with mononuclear cells associated with demyelination suggesting a cell mediated component.⁸ Brettle *et al*⁹ were the first to use plasma exchange in the treatment of acute polyneuropathy on the basis of the humoral immunological abnormalities. Since then several reports of uncontrolled series have produced favourable results,^{4,10-14} although others have been less impressive.^{15,16} We report our results in a series of 12 consecutive cases of Guillain-Barré syndrome treated with plasma exchange. The aim of the study was to determine whether plasma exchange produced improvement in the condition or arrested the rate of deterioration.

Methods

Plasma exchange was performed using an Aminco con-

tinuous flow-cell separator (Celltrifuge). Venous access was by 16 gauge butterfly needles in the antecubital fossa, although internal jugular lines were used occasionally. The patients were heparinised before the procedure and continuously throughout.¹⁷ A mean of seven (range 5-10) plasma exchanges, usually of 4 litres each, over a period of 10-22 days (see table), were performed and replacement fluid consisted of 1.5 l normal saline, 1 l Haemmacel and 1.5 l plasma protein fraction with added calcium and potassium supplements.

Patient assessment Of the 12 patients studied seven were males and five were females whose ages ranged from 27 to 75 years (mean 52 years). Diagnosis of Guillain-Barré syndrome was made according to established criteria.¹⁸ All patients had obvious motor involvement. No treatment other than supportive measures or assisted respiration was given except in one case (12) in which methylprednisolone, 1 g daily was given intravenously for five days before plasma exchange was commenced. A full clinical assessment was carried out before treatment was commenced, and motor function was tested every 2-3 days thereafter to ascertain any immediate effect. A further full assessment was made two weeks after the start of plasma exchange. A 2 week interval was chosen to try and minimise the effect which spontaneous improvement might have on the outcome of the study. Clinical assessment was made using muscle strength graded according to the standard 0-5 MRC scale. Sensory testing for light touch, pin prick, position and vibration were recorded as were the state of the reflexes. The overall functional state of the patients was also graded according to the following scale.¹⁹

Grade 0—healthy, Grade 1—minor symptoms or signs of neuropathy, Grade 2—able to walk 5 m without assistance, walking frame or stick, Grade 3—able to walk 5 m with assistance, walking frame or stick, Grade 4—confined to bed or chairbound, Grade 5—requiring assisted ventila-

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Table Details of patients and their treatment

Case	Sex	Age (yr)	Time from onset to reaching lowest grade (days)	Time from onset to entry (days)	Disability grade at entry	Number of exchanges	Volumes (litres)	Period during which exchange performed	Functional grade after two weeks	Functional grade after follow-up
1	F	37	14	16	3	7	7 × 4.0	13	1	1
2	F	47	2	3	5	8	7 × 4.0 1 × 2.0	22	4	2 at ½
3	M	70	3	8	5	7	7 × 4.0	10	5	4 at ½
4	M	26	6	5	3	5	3 × 4.0 1 × 3.0 1 × 1.9	7	1	1
5	F	66	36	45	5	10	10 × 4.0	17	5	3 at ½ relapsed
6	F	75	20	38	4	7	2 × 3.7 3 × 3.2 2 × 2.0	17	3	1 at ½
7	M	72	15	29	4	6	3 × 3.7 1 × 3.2 2 × 2.2	12	2	1 at ½
8	M	27	5	13	4	6	2 × 4.0 3 × 3.7 1 × 2.5	12	4	3 at ½
9	F	75	20	35	4	5	4 × 3.8 1 × 2.0	12	3	—
10	M	50	2	3	4	7	7 × 4.0	15	2	1 at ½
11	M	44	7	7	4	6	6 × 3.8	12	4	2 at ½
12	M	38	10	10	5	6	1 × 1.2 2 × 2.0 2 × 3.6 1 × 4.0	7	4	2 at ½

tion. All patients have been followed up for between 2–18 months.

Results

The results of the study are shown in the table. Clinical improvement after the first plasma exchange has been reported by others^{4,12} but did not occur in any of the 12 patients we studied. However, one patient (1) did show improved nerve conduction after the first exchange as previously reported.²⁰

Cases were analysed according to the rate of progression of the neuropathy. Five patients (2, 3, 8, 10, 11) had a rapid progression of the disorder reaching grade 4 or 5 within 5 days. These patients received plasma exchange within a few days of onset of the neuropathy. After two weeks, two of these patients (3, 8) showed no improvement, two showed improvement by one functional grade (2, 11) and one by two functional grades (10). Three patients (1, 4, 12) had a less acute progression reaching their maximum disability between 6–14 days after onset. Two of these cases (1, 4) had improved two grades at two weeks and one (12) by one grade. The latter patient had initially been treated with intravenous methylprednisolone 1 g daily for five days during which time he steadily deteriorated and needed intubation to aspirate profuse tracheal secretions. The remaining four patients (5, 6, 7, 9) deteriorated more slowly reaching their maximum disability

15–30 days after onset. After two weeks one patient (5) showed no change, and remained on a ventilator for a total of three months. She made a very slow recovery reaching grade 3 after six months, and then relapsed to grade 4. A further course of plasma exchange had had little effect after five weeks. Two of the other patients (6, 9) improved by one grade after two weeks and one patient (7) by 2 grades.

Analysis was also made of whether plasma exchange prevented patients who were deteriorating from reaching the stage when intensive care and assisted ventilation (AV) were necessary, or whether it shortened the period for which these measures were required. Six patients were grade 4 when plasma exchange was commenced, some of whom might have been expected to progress to a stage requiring assisted ventilation. In two patients plasma exchange had little effect in this respect, since one (12) progressed to require assisted ventilation for seven days, and the other (8) had already stopped deteriorating 48 hours prior to commencement of plasma exchange and, therefore, would not have been expected to deteriorate further prior to its commencement. Of the remaining four patients, three (6, 7, 9) had a slow progression, and one (10) a rapid progression but showed no evidence of respiratory difficulty before plasma exchange was commenced. They did not then deteriorate further so it is possible that plasma exchange may have helped in these cases although the natural history of

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the disorder could have accounted for this.

Of the four patients (2, 3, 5, 11) who required assisted ventilation before plasma exchange was commenced, two (3, 5) showed no response and required assisted ventilation for 2 and 2.5 months respectively. The remaining two (2, 11) required assisted ventilation for 12 and 4 days respectively, a period possibly modified by plasma exchange.

COMPLICATIONS OF PLASMA EXCHANGE

Plasma exchange is not a totally benign procedure, and out of 90 exchanges two were associated with allergic reactions to the infused plasma protein fraction. In six there were venous flow problems and 10 vaso-vagal reactions were experienced (in five patients). These responses were no more prevalent in the older aged patients than in the younger.

FOLLOW-UP

Our period of follow-up was only between three and 10 months, as shown in the table. During this time eight patients have made a complete or almost complete recovery (Grade 1 or 2) and three still suffered a significant motor deficit. We have no follow-up on the remaining patient (9).

Discussion

Twelve patients with the Guillain-Barré syndrome were treated with plasma exchange. Examination two weeks after treatment was commenced showed that three had failed to show any improvement and of the nine who did improve, five showed an improvement of one grade only, and four an improvement of two grades. It is debatable whether an improvement of only one grade over a two week period is any better than might be expected from the natural history of the illness and in these cases plasma exchange was considered not to have been of value. Thus in only four of the 12 patients studied was there any suggestion that plasma exchange was beneficial. It was not clear from our results whether or not the exchange had any significant effect in either reducing the period of intensive care and assisted ventilation or preventing deterioration to such a stage.

Some workers have suggested that poor results are due to too little plasma being exchanged, or employing plasma exchange too late in the course of the disease.²¹ The former was not the reason in the present study in which each plasma exchange was of about 4 l unless reduced by technical problems such as poor venous access, and four to five such exchanges were carried out in the first week. Nor did our poor results appear to be due to delay in starting plasma exchange. Four of our five patients with a

rapid progression, reaching grade 4 or 5 within five days of onset, were all treated very rapidly yet failed to make an impressive early improvement. We never observed the dramatic improvement which others have reported to follow the first plasma exchange.^{4 13 14} Five of our patients were aged 66 yr or over and we had hoped that plasma exchange might reduce the duration of their illness since they are so susceptible to other complications such as pulmonary emboli and bed sores. However, only one improved by two functional grades after two weeks, and the others showed little significant improvement, suggesting that there is no special indication for treating elderly patients with plasma exchange.

In conclusion, the present study has failed to show that plasma exchange has any more than a marginally beneficial effect on the course of Guillain-Barré syndrome, and it remains to be seen whether the controlled trials of plasma exchange now underway in Britain and the United States will resolve the present controversy. Meanwhile, we would simply point out that the plasma exchange is a time-consuming, expensive and potentially hazardous technique which should not be allowed to overshadow the need to continue to explore other forms of treatment.

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