The natural history of the Guillain-Barré syndrome in 18 children and 50 adults

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SUMMARY Plasma exchange (PE) is indicated in adult patients with a severe Guillain-Barré syndrome (GBS). For children this has not been proven. If the disease runs a milder course in children, the problems experienced with PE might outweigh the benefit. In order to evaluate the need for such a specific treatment in children, we compared the severity of the disease between 18 children and 50 adults; no significant differences were found. The mean duration of hospitalisation of all children was 84 days, four children needed artificial ventilation for a mean of 21.5 days and two children died. We conclude therefore that PE is indicated in children with a severe GBS. The final decision, however, depends also on the practical feasibility of the procedure.

The Guillain Barré syndrome (GBS) is a monophasic polyneuropathy from which many patients ultimately recover satisfactorily. However, artificial respiration is necessary in 10–20% of the patients in the acute phase of the disease, 10–22% finally remain disabled and there is a mortality of 3–5%.^{1–3} For these reasons, an effective treatment has been sought and at present plasma exchange (PE) is generally accepted as such, early in the course of the GBS.⁴

In all trials leading to the acceptance of PE, children were excluded.^{5–7} Although the effect of PE in children is not really known, there is no reason to assume that it would not be effective. Case studies have shown that treatment related improvement does occur in children⁸ (one of three cases has recently been published⁹).

The practical problems of PE, however, especially in small children, make us reluctant to apply this treatment. Moreover, it has been suggested that the outcome of GBS in children might be more favourable,¹⁰ making such a specific treatment unnecessary.

To enable us to take the clinical decision about treatment with PE in children, it seems necessary to have more knowledge about the natural history of the GBS in children compared with adults. Systematic

studies on this subject are, however, not available. Several reports on the severity of the GBS in children are difficult to interpret because of variable methodology between and within the studies.^{10–13} They suggest, however, that the acute phase might be more severe and clinical outcome worse than generally thought, but patient selection prevents conclusions about children in general.

To evaluate the need for specific treatment in children we therefore studied retrospectively the clinical course of all children and adults admitted to our clinic from 1975 until the introduction of PE in 1985.

Patients and methods

Eighty four patients with a GBS according to the generally accepted criteria¹⁴ and admitted between 1975 and the time we started treating these patients with PE or immunoglobulin⁹ (for adults 1985, for children 1987) were screened for inclusion in the study. Patients with predominant involvement of the cranial nerves (two children and four adults) or the sensory system (one adult) were excluded as well as patients with severe concurrent medical disorders interfering with functional abilities (three adults: one with severe asthma, one with disabling rheumatoid arthritis and one patient with multiple myeloma). Six patients (one child, five adults) lived too far away for follow-up in our hospital and were therefore excluded. From four adults we know, however, that they recovered between six months and three years after onset of the disease. The only child in this group had already considerably recovered at the time of discharge. We could not obtain any further information about one adult who could at least walk some distance unaided at the time he left hospital.

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Received 29 November 1988 and in revised form 10 March 1989.
Accepted 22 March 1989

Ultimately, 68 patients were studied: 18 children and 50 adults. None of these patients was treated with PE or immunoglobulin. The clinical characteristics that were used to delineate the clinical course were: duration of the disease until maximum disability, duration of artificial ventilation, duration of hospitalisation, and functional outcome one and two years after onset of the disease.

The functional status was assessed according to the grading system used in the North American trial,² which we modified slightly (table 1).

A clear distinction between grades 0 and 1 could not be made in retrospect, and so these grades have been combined, implying good recovery.

In the final analysis, the patients were split into two groups: patients who had made a good recovery (0/1) and patients who had a residual handicap or had died (grades 2–6). The great majority of the information was available in the medical records: sometimes the general practitioner was consulted in order to complete the follow-up data.

Results

In the 18 children studied the age varied between 1 and 14 years (median 7) whereas in the 50 adults, the age range was 16 to 74 years (median 32).

Severity of the disease (table 2)

Time until nadir was similar in both groups. Four (22%) children required artificial ventilation versus 15 (30%) in the adult group (not significant, Fisher exact test). Median duration of artificial ventilation was 21.5 days in children and 32 days in adults (not significant, Mann Whitney U Test). Duration of hospitalisation (including rehabilitation centre) was equal in the two groups, 84 and 86 days respectively.

Final outcome

The functional outcome was assessed after one and two years (table 3) using the functional grading scale (table 1). As mentioned before, functional grades 0 and 1 have been combined, indicating good recovery. In both groups the majority of patients had already recovered completely or nearly completely after one year; there was a slight increase in the number of recovered patients after two years in both groups. Two children died from cardiac arrest, one in the acute phase, one early in the plateau phase. In both cases death had been preceded by severe fluctuations in

Table 2 Severity of the disease

	Children (n = 18)	Adults (n = 50)
Mean time, 2 SE until nadir in days	9.6, 3.2	11.0, 1.6*
Artificial ventilation; percentage of patients, between brackets 95% confidence limits	22% (7–45%)	30% (18–45%)*
Duration of artificial ventilation (days) mean:	21.5	32*
range:	16–48	1–126
Duration of hospitalisation (incl. rehabilitation centre) (days) mean:	84	86*
range:	7–449	7–551

*not significant: Mann Whitney U-test.

†not significant: Fisher exact test.

heart rate and blood pressure. One other child, a 10 year old boy, had not made a good recovery within two years; he was in functional group 2. In the adult group, four patients were found to have made an incomplete recovery after two years; one was confined to a wheelchair (38 years) and three were in functional group 2 (23, 39 and 46 years respectively). When patients in grade 2–6 are considered together, three (17%) children had not recovered completely after 2 years (this included two deaths), versus four (8%) adult patients (table 4).

Discussion

Using artificial ventilation, length of hospitalisation and functional outcome after one and two years as parameters for the severity of the disease, we have not been able to demonstrate statistically significant differences between 18 children and 50 adults. The 95% confidence limits are, however, rather large reflecting the relatively small number of patients. Therefore no definite conclusions regarding the similarity of the two groups can be drawn; in fact, either group may be more severely affected. Recently it has been demonstrated that the prognosis is worse for adults over 40 years of age¹⁵ compared with younger adults. It might thus be reasonable to consider children and adults under 40 years of age as a single group having a better prognosis than the older patients.

It has recently been shown that the duration of the

Table 1 Functional grading system

0 = healthy
1 = minor symptoms and signs, fully capable of manual work
2 = able to walk > 10 m without any assistance
3 = able to walk > 10 m with a walker or support
4 = bed or chair-bound (unable to walk > 10 m with a walker or support)
5 = assisted ventilation required for at least part of the day
6 = dead

Table 3 Outcome

Functional grade	One Year		Two Years	
	Children	Adults	Children	Adults
0/1	14 (77%)	43 (86%)	15 (83%)	46 (92%)
2	1 (6%)	4 (8%)	1 (6%)	3 (6%)
3	1 (6%)	1 (2%)	—	—
4	—	2 (4%)	—	1 (2%)
5	—	—	—	—
6	2 (11%)	—	2 (11%)	—

Table 4 Outcome (continued)

Functional grade	One Year		Two Years	
	Children	Adults	Children	Adults
0/1	14 (77%)	43 (86%)	15 (83%)	46 (92%)
2/6	4 (23%)	7 (14%)	3 (17%)	4 (8%)

disease before the lowest point is reached is of prognostic importance.¹⁶ Again this parameter did not differ between the two groups. The percentage of patients who needed artificial ventilation is somewhat larger than generally mentioned in the literature, presumably because our hospital is also a secondary referral centre for more severely affected patients. In both groups the percentage of patients who finally made a complete recovery is in agreement with the literature.³

For a description of the severity of the GBS, we chose to focus not only on the final outcome but also on the duration of artificial ventilation, and the duration of hospitalisation. These latter parameters concerning disease severity are frequently not mentioned when discussing the need for treatment, and only the final outcome is taken into account.¹⁰ The duration of hospitalisation and artificial ventilation with its complications, are also important factors influencing the decision whether or not to apply PE, especially since these latter factors can be influenced by PE.⁵

From our data, we conclude that specific treatment should also be considered in children with GBS and not only in adults. Although the ultimate outcome is often excellent, it would certainly not seem superfluous to attempt to influence the clinical course: the mean duration of hospitalisation of all children has been 84 days and the mean duration of artificial ventilation in four children 21.5 days.

Although plasma exchange has proved its beneficial effects in clinical trials performed exclusively in adults, there is no reason to believe that it would be less effective in children. Case reports, including our own observations⁹ suggest beneficial effects. Plasma exchange, however, is a cumbersome procedure with practical difficulties especially in smaller children. It should therefore be reserved for more severely affected children, in whom the beneficial effect of PE will outweigh the technical difficulties.

In the near future, high dose immunoglobulins might be an alternative, even for the smallest children. Recently, we described the promising experience with this treatment in eight GBS patients, including one 11 year old child.⁹ Application of this treatment must, however, await the results of the ongoing Dutch multicentre trial, (in which children are also included)

to compare the effect of plasma exchange with immunoglobulin infusion.

We thank Dr P I M Schmitz for statistical advice and Ms R M van den Hoven for secretarial help.

Preliminary results have been presented on the first conference of the European Neurological Society in June 1988.¹⁷

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