Original Article

Intravenous Immunoglobulins in Severe Guillian-Barre Syndrome in Childhood

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Abstract. ***Objective :*** This is a retrospective analysis of 25 children with severe Guillain-Barre syndrome admitted to our PICU. ***Method :*** All children were treated with intravenous immunoglobulins (IVIG) in a dose of 2 g/kg body weight over 2-5 days in addition to supportive and respiratory care. Seventeen children were elective admissions to the PICU whereas 8 children were transferred from other hospitals in a critical condition. Five of 8 of the late referrals died as compared to none of the elective admissions. ***Result :*** All 8 of the late referrals required mechanical ventilation as against 3 of the 17 elective admissions. Mean duration of PICU stay in the late referrals was 27 days as compared to 15 days in the elective admissions. ***Conclusion :*** The authors concur with previously published reports, that early use of IVIG could reduce the mortality and the need for intubation and mechanical ventilation. **[Indian J Pediatr 2003; 70 (7) : 541-543]** ***E-mail : pshanbag@yahoo.com***

Key words : *Guillain-Barre syndrome; Intravenous immunoglobulins*

Guillain-Barre syndrome (GBS) is an acute demyelinating polyradiculoneuropathy which is caused by inflammatory cell infiltration and destruction of peripheral nerve myelin. It is characterized by areflexic weakness of all the limbs.[1] Though there are no large controlled randomized trials in children and adolescents, numerous reports over the last decade conclude that high-dose intravenous immunoglobulins (IVIG) are effective in pediatric GBS.[2-10] Use of IVIG in severe GBS has been shown to reduce the need for intubation and mechanical ventilation and substantially shorten the length of PICU stay and time to recovery of ambulation.[11] The authors present their experience with severe GBS in children particularly with respect to the efficacy of IVIG and effect of elective admission to the PICU as against late referral.

MATERIALS AND METHODS

Records of children admitted with severe acute Guillain-Barre syndrome in the Pediatric Intensive Care Unit (PICU) of Lokmanya Tilak Municipal Medical College & General Hospital, Mumbai, between October 1997 and December 2001, were studied. Patients who conformed to the internationally-accepted diagnostic criteria for acute GBS as published by Asbury and Cornblath[12,13] were included in the study. The degree of disability was coded in ten levels as described by Korinthenberg and Monting[14] since this was a retrospective study. Patients with mild GBS are admitted to the general ward and are transferred to the PICU only if there is progression of the disease to Grade 5 i.e. inability to walk. Information regarding the preceding illness and the course of the disease was noted. Signs and symptoms at admission and at the height of the disease were recorded. All children received infusions of IVIG (Gamma IV – Bharat Serums and Vaccines) in the total dose of 2 g/kg over 2-5 days (unless death supervened). IVIG was administered within a week of onset of motor weakness in all patients. As per PICU protocol, routine monitoring included daily determination of muscle power grade, ventilatory status as assessed by single breath count, respiratory rate, chest movements and use of accessory respiratory muscles. The ability to protect the airway was also assessed by the gag reflex, pooling of secretions in the throat, and nasal speech. Patients were also monitored for evidence of autonomic dysfunction like hypo- or hypertension and arrhythmias. Complications were noted. Side-effects of IVIG therapy, if any, were aso noted.

The following outcome measures were also recorded (1) the need for endotracheal intubation and the duration. (2) the need for mechanical ventilation and the duration. (3) the number of days in the PICU. (4) the number of days from the nadir to independent walking. (5) the presence of sequelae or death.

The children were discharged from the PICU on being able to sit upright and to swallow normally. Patients were followed up on an out-patient basis and physiotherapy was continued till the child had no disability.

Statistical Analysis

The proportion of deaths and of children requiring mechanical ventilation in the two groups (i.e. elective admissions and late referrals) was compared using the

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Student t-test for unpaired data. A value of $p<0.05$ was taken to be statistically significant.

RESULTS

Twenty-five children with severe acute Guillain-Barre syndrome (GBS) were admitted to the PICU between October 1997 and December 2001. The age of the patients ranged from 1-10 years with a mean of 4.5 years. There was a preponderance of males (n=15). A history of preceding illness was present in 16 ot 25 children: upper respiratory infections in 10 children, vaccines in 2 (oral polio vaccine 1, tetanus toxoid 1), diarrhea in 1, measles in chicken-pox in 1 and egg allergy in 1.

Clinical Features

All 25 children had weakness of the lower limbs at admission. Areflexia was present in 13 of 25 children at admission but was present in all at maximum disability. Cranial nerve involvement (7th nerve) was present in 11 children at admission and 16 children at maximum disability. Bilateral facial nerve involvement was present in 13 children. Bulbar involvement in the form of an absent gag reflex was present in 15 children at maximum disability.

The children were admitted to the Pediatric Intensive Care Unit after a median of 4 days after the onset of weakness (range 1-8 days). The disease progressed over a median duration of 3 days (range 1-10 days) from the onset of weakness to maximum disability. Seventeen children were direct admissions to the hospital whereas 8 children were transferred from other hospitals within and outside the city in a critical condition. Six of these 8 children had been intubated before transfer and were hand-ventilated during transport, for durations ranging from 1-6 hours, often by the relatives of the patient while 2 more required immediate endotracheal intubation at admission. None of the children were hand-ventilated after admission to the PICU.

Ventilator-associated pneumonia was seen in 6 of 8 late referrals and 1 of the elective admissions. Autonomic dysfunction was noted in 4 late referrals as against 2 of the elective admissions.

Table 1 shows the outcome. There were no deaths in children who were transferred electively whereas all 5 deaths occurred in patients who had been referred late ($p<0.01$). These children were all hand-ventilated during transfer. The deaths occurred between 2 and 48 hours of admission. One child died of massive pulmonary hemorrhage within 2 hours of admission.

Eleven children required mechanical ventilation. All 8 late referrals required endotracheal intubation and mechanical ventilation whereas of 17 elective admissions, only three required intubation and mechanical ventilation ($p<0.01$). Four of the elective admissions required endotracheal intubation alone. The median duration of ventilation and the median time from maximum disability to full ambulation and median duration of PICU stay was much longer in the late referrals as compared to the elective admissions (see table). All children recovered without any sequelae. There were no side-effects of IVIG therapy. Follow-up ranged from 5-12 months after discharge. None of the patients had a relapse during this period.

DISCUSSION

This being a retrospective study, we had to choose definitions of outcome variables and disability, which could be obtained from the hospital charts with a reasonable degree of reliability. However the authors accept that not all variables would have the same high reliability. Due to limited resources in terms of availability

Table 1. Outcome

	Elective admissions (n=17)	Late referrals (n=8)	Total (n=25)	
Number of deaths	0/17	5//8	5	CR=3.644 P<0.01
Number requiring mechanical ventilation	3/17	8/8	11	CR=3.564 P<0.01
Median duration of ventilation in survivors	10 days (2-11 days)	13 days (3 survivors) (11-14 days)	11 days (2-14 days)	
Number requiring endotracheal intubation alone	4	0	4	
Median duration of endotracheal intubation alone	3 days (2-6 days)	-	3 days (2-6 days)	
Median duration of PICU stay	15 days (5-51 days)	27 days (3 survivors) (25-27 days)	18.5 days (5-51 days)	
Median time from maximum disability to full ambulation	41 days (18-135 days)	57 days (41-57 days)	44 days (18-135 days)	

CR: Critical ratio

of PICU beds, ventilators and the high cost of IVIG therapy, children with GBS are admitted to the PICU only if there is evidence of ventilatory insufficiency or if they are unable to walk. Children with GBS are admitted to the general ward, where they are given only supportive therapy and monitored for progression. Children are transferred to the PICU for IVIG therapy, if progression occurs i.e. the disability score rises to 5 or greater. Thus our study included only children with severe GBS. Because of the high cost of IVIG therapy, Singhi and coworkers also used it only in patients with severe GBS and reported a good outcome.[11]

In patients who were electively transferred to the PICU, timely administration of IVIG, i.e. before the onset of respiratory weakness, resulted in a better outcome with respect to mortality. The need for intubation and mechanical ventilation as well as duration of PICU stay and the time from maximum disability to full ambulation was also less in this group. Eight patients were referred from other hospitals in a critical condition. It is important that children with GBS should be transferred to a hospital with facilities for ventilation especially if they are unable to walk or if the disease progression is rapid. This is crucial in the absence of trained transport teams and transport ventilators. Five of the late referrals were hand-ventilated for durations ranging from 1-6 hours before admission, often by the relatives and ventilation was probably sub-optimal. Mortality was thus high, since patients had already progressed to ventilatory insufficiency and secondary complications. The findings suggest that timely referral of patients with GBS to a tertiary centre, before respiratory insufficiency and other complications supervene, improves the outcome in terms of decreased mortality and a reduced need for endotracheal intubation and mechanical ventilation.

Acknowledgements

The authors would like to thank our Dean, Dr. Armida Fernandez, for granting us permission to publish this article.

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