

ORIGINAL ARTICLE

Guillain-Barré Syndrome: Outcome of Treatment by IVIG vs. Methylprednisolone in Pediatric Intensive Care Unit of a Tertiary Care Hospital

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Abstract

Background: Guillain-Barré Syndrome (GBS) deserves a serious attention in children. The treatment of GBS consists of supportive and immune-modulator treatments, among which intravenous immunoglobulin (IVIG) is considered as most effective. But IVIG is costly and many patients cannot afford.

Objective: To document the outcome of treatment of GBS patients by IVIG and Methylprednisolone.

Methods: This is a retrospective study conducted in the Pediatric intensive care unit of Dhaka Shishu Hospital from January 2013 to December 2016. Data was collected from the admission record file in pediatric intensive care unit of Dhaka Shishu Hospital. A total of 36 patients up to the age of 15 years presenting with Guillain-Barré Syndrome were included in the study. Treatment modalities including supportive, Intravenous Immunoglobulins (IVIG) and steroids were selected in patients with GBS depending upon indication and facilities available. Those who were unable to provide IVIG due to financial constrain were treated with Methylprednisolone. Results were analyzed using SPSS (version 16) for Windows.

Results: During the study period, a total of 36 patients were diagnosed and treated as GBS in pediatric intensive care unit. Among those, 34 (94.4%) patient were classical GBS. Most patients were in the age range of 3-5 years (21, 58.3%). Total 19 (52.8%) patients were treated with IVIG and rest was treated with steroid (17, 47.2%). 16 (44.4%) patient needed mechanical ventilation and among the patient needed mechanical ventilation 9 (56.3%) got treatment with IVIG and 7 (43.7%) got treatment with Methylprednisolone. After treatment 31 (86.2%) patients were improved and 5 (13.8%) were expired. Among the improved patient 16 (84.2%) were treated with IVIG and 15 (88.2%) were treated with Methylprednisolone.

Conclusion: Treatment outcome of GBS patient with Methylprednisolone is comparable with IVIG and can be considered in case of financial constrain.

Key words: Guillain-Barré syndrome, IVIG, methylprednisolone, outcome.

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Introduction

Guillain-Barré syndrome is a post infectious polyneuropathy presumed to be immune mediated and manifests as Acute Flaccid Paralysis involving mainly motor, sometimes also sensory and autonomic nerves. It affects people of all ages including pediatric age group. The paralysis usually follows a nonspecific viral infection such as respiratory tract infection and acute gastroenteritis by one to two weeks. It is the commonest cause of acute flaccid paralysis (AFP) after eradication of poliomyelitis.^{1,2} An incidence of 0.5-5/100000 children/year has been reported worldwide.³

GBS is characterized by muscle weakness and areflexia. Weakness usually begins in the lower extremities, progressively involves the trunk, the upper limbs and finally the bulbar muscles. Bulbar involvement occurs in about half of the cases that results respiratory insufficiency. This interferes with eating and increase the risk of aspiration. Respiratory effort must be monitored to prevent respiratory failure and respiratory arrest. Urinary incontinence or retention is a complication in about 20% of cases.^{4,5} The autonomic nervous system is also involved in some cases where cardiovascular monitoring is important. Patients in early stages of this acute disease should be admitted to the hospital for observation because the ascending paralysis can rapidly involve respiratory muscles during the next 24hours & may need mechanical ventilation.⁶

With regard to clinical course and prognosis, classical Guillain-Barré Syndrome has to be differentiated from variants with accompanying central nervous system inflammation and from chronic inflammatory demyelinating polyneuropathy.⁷

AFP includes Guillain-Barré Syndrome, transverse myelitis, viral syndromes, spinal cord compromise (low back trauma, abscesses or tumors), toxins (lead, botulism etc.), metabolic neuropathies (hypokalemia, hypokalemic periodic paralysis, hypophosphatemia, polymyositis and dermatomyositis and tick bite).⁸ GBS still remains the leading cause of AFP in developed as well as developing countries.

Diagnosis of GBS is usually clinical. In addition to routine investigations, CSF examination, electrophysiological and nerve conduction studies and plasmapheresis are usually done. CSF shows no pleocytosis and protein is variably normal or mildly elevated.

Rapidly progressive ascending paralysis is treated with intravenous immunoglobulin. Plasmapheresis and/or immunosuppressive drugs are alternatives if IVIG is ineffective. Supportive care such as respiratory support, treatment of secondary bacterial infection is important.

Federal Drug Association (FDA) approved IVIG indications include primary immunodeficiency disease, idiopathic/immune-mediated thrombocytopenic purpura (ITP), human immunodeficiency virus, bone marrow transplanation, Kawasaki disease and chronic lymphocytic leukemia.⁹ High-dose immunoglobulin (hdIVIG) given at dose up to 2g/kg total dose has immunomodulatory actions mediated via a number of different effects like autoantibody neutralization and Interleukin 12 production.¹⁰ Therapeutic IVIG is capable of neutralizing neuromuscular blocking antibodies in GBS by dose dependent, antibody mediated mechanism.¹¹

Cost of IVIG is a major drawback in case of treating poor patient. Although steroids are not effective but chronic GBS patients are treated with high dose Methylprednisolone. Their effectiveness is less predictable. The dose of intravenous Methylprednisolone is usually considered 30mg/kg/dose for 5 consecutive days.¹²

Prognosis is good with complete recovery in more than 95% patients with GBS but it usually takes weeks to months,¹³ 3% mortality due to respiratory & autonomic involvement. It is necessary to have the knowledge regarding practical scenario of critically ill patients of GBS, their treatment in ICU and overall outcome which will ultimately help us to modify the overall management plan in our limited critical care resource.

Materials and Methods

The study was conducted at Pediatric Intensive Care Unit, Dhaka Shishu (Children) Hospital from January 2013 to December 2016. A total of 36 patients up to the age of 15 years were admitted and diagnosed as GBS. Detailed history and clinical examination for distribution of weakness, cranial nerve involvement, sensory loss and autonomic dysfunction and involvement of respiratory muscles and bulbar paralysis was recorded. Routine investigations including CBC, ESR, serum electrolytes, and random blood sugar were done in all patients. CSF examination was done in the second week of illness. Nerve

conduction studies and electromyography were not done due to unavailable resources. Treatment modalities including supportive, Intravenous Immunoglobulins (IVIG) and steroids were selected in patients with GBS depending upon indication and facilities available. Indications for IVIG were rapidly progressive disease, paralysis or impending paralysis of respiratory muscles, dysphagia and involvement of autonomic nervous system. Those who were unable to provide IVIG due to financial constrain were treated with Methylprednisolone. Data was collected and results were analyzed using SPSS (version 16) for Windows. A permission to conduct this study was obtained from Dhaka Shishu Hospital authority.

Results

A total of 39 patients were admitted in ICU with the diagnoses of acute flaccid paralysis and out of them 36 were GBS. Among these GBS patients, 34 (94.4%) were classical GBS and 2 (5.6%) was relapsing case. Most patients in this study were in the age range of 3-5 years (21, 58.3%) and other age group was 6-10 years (6, 16.7%), more than 10 years (5, 13.9%), 1-2 years (4, 11.1%), and no patient were below 1 year age (Table I). In our study, number of male patients was 20 (55.6%) and female was 16 (44.4%).

Age group (Years)	Number	Percentage
1-2	4	11.1
3-5	21	58.3
6-10	6	16.7
>10	5	13.9

Main reason of ICU admission was respiratory muscle and bulbar paralysis (33, 91.7%), and other causes were autonomic involvement, aspiration pneumonia and for close monitoring. In 29 (80.6%) patients the antecedent event was respiratory tract infection and gastrointestinal infection was in 3 (8.3%) cases. In 4 (11.1%) cases there was no significant preceding illness. Regarding clinical assessment areflexia and paraesthesia was present in all cases, autonomic dysfunction in 20 (55.6%) and cranial nerve involvement was in 2 (5.6%) cases (Table II).

Table II
Major clinical findings of the enrolled cases (n=36)

Clinical findings	Number	Percentage
Areflexia	36	100
Autonomic dysfunction	20	55.6
Cranial nerve palsy	02	5.6
Paraesthesia	36	100

Cerebrospinal fluid study was done in 29 (80.6%) patients and albumin-cytological dissociation was found in 25 (86.2%) cases. The criteria for albumin-cytological dissociation were CSF protein more than 80mg/dl and cells less than 10/cmm.

Out of 36 patients, 19 (52.8%) were treated with IVIG and rest (17, 47.2%) were treated with intravenous steroid, as they could not afford IVIG. Mechanical ventilation in course of treatment was needed in 16 cases out of total 36 (44.4%). Respiratory muscle paralysis (13, 81.3%) was the commonest indication of mechanical ventilation and cardiac arrest (3, 18.7%) was another cause.

Out of 16 patients who needed mechanical ventilation 9 (56.3%) were treated with IVIG and among them 6 (66.7%) were improved and 3 (33.3%) expired. Seven (43.7%) patients who needed mechanical ventilation were treated with Methylprednisolone and among them 5 (71.4%) were improved and 2 (28.6%) expired (Table III). Mean duration of ICU stay of patients treated with IVIG was 12.3±4.1 days in comparison to 14.8±6.0 days for Methylprednisolone group. Though the duration of ICU stay was shorter in IVIG group, it is not statistically significant (p=0.15).

Out of 36 patients, 31 (86.2%) patients were improved and transferred to ward and there average duration of ICU stay was 16.8 days. On the other hand, 5 (13.8%) patients expired during treatment in ICU and there average duration of ICU stay was 5.6 days, which indicates either rapid progression of the disease or delayed transfer to PICU. Total 16 (84.2%) patients were improved those who were treated with IVIG and 3 (15.8%) were expired and 15 (88.2%) were improved those who were treated with Methylprednisolone and 2 (11.8%) expired (Table IV).

Table III
Hospital outcome of the GBS patients admitted in ICU (n=36)

IVIg group (n=19, 52.8%)		Methylprednisolone group(n=17, 47.2%)		p-value
Improved	Expired	Improved	Expired	
16 (84.2%)	3 (15.8%)	15 (88.2%)	2 (11.8%)	0.89 (not significant)

Table IV
Outcome of cases those received mechanical ventilation (n=16)

IVIg group(n=9, 56.3%)		Methylprednisolone group(n=7, 43.7%)		p-value
Improved	Expired	Improved	Expired	
6 (66.7%)	3 (33.3%)	5 (71.4%)	2 (28.6%)	0.73 (not significant)

During treatment in PICU 12 (33.3%) patients developed aspiration pneumonia, cardiac arrest 3 (8.3%) and autonomic involvement was 20 (55.5%) (Figure I). There was no steroid related complication.

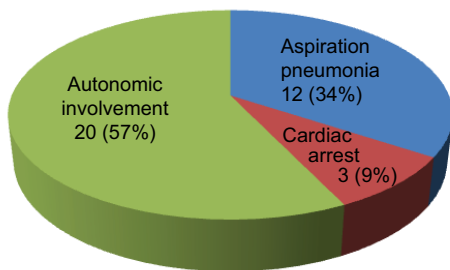


Fig 1 Complications during treatment (n=35)

Discussion

Acute flaccid paralysis in children is defined as acute onset of flaccid paralysis in one or more limbs or of bulbar paralysis in any child less than 15 years of age.¹ GBS is the commonest cause of AFP worldwide. Other causes include transverse myelitis, botulism, Tic bite paralysis and traumatic neuritis. In our study the commonest cause of AFP was also GBS followed by transverse myelitis. In a study from Australia common causes of AFP were GBS (47%) and transverse myelitis (19%) followed by acute disseminated encephalomyelitis, traumatic neuritis, tic bite paralysis and infantile botulism.¹ A study from Hongkong showed GBS 42%, followed by transverse myelitis 15% as the common causes of AFP in children.² Two different studies in Pakistan also describes GBS as the leading cause of AFP.^{14,15}

Among the children with GBS 25 (69.4%) were under 5 years of age. It could be due to high incidence of

infections in young children which is consistent with other studies from Hong Kong and Central America.^{2,16} Male to female ratio in our study was 1.2:1 which also correlates with a study from Malaysia where this ratio was 1.3:1.¹⁷

Involvement of respiratory muscles was present in 27 (75%) patients. It is higher compared to a study from Pakistan where this figure was 55.9%.¹⁸ Cranial nerve involvement was found in 3.6% children which have been found to be 45% and 50% in other studies in pediatric patients.^{19,20} Autonomic dysfunctions were noticed as 55.6% which is comparable with a study in children where it was 51%.¹⁹

CSF albuminocytological dissociation was present in 25 among 29 cases where CSF study was done (86.2%) in our study while in another study it was found in 97.5% of patients.²⁰ We performed CSF examination in second week of illness and our criteria for dissociation was protein >80 mg/dl and cells <10/cmm.

In our patients with GBS mortality was 13.8%. All these patients belong to mechanically ventilated group with or without other treatment modalities. Total 16 (44.4%) patient needed mechanical ventilation during treatment in ICU, which was 15% to 20% in other studies.^{21,22}

It shows that the patients who have severe disease at onset and required mechanical ventilation had poor prognosis. The high mortality in this group also be related to complications like infection, aspiration, autonomic dysfunction and cardiac arrest.

Data on the course of recovery in our patients are better than in the literature. Briscoe et al reported a mean time of recovery after reaching the maximum

disability of the disease of 28 days, where in our study it was 13.5 days (5-28 days).²³

In our study 52.8% patient received IVIG and 47.2% patient was treated with steroid. Patients treated with IVIG improved earlier than those with steroid, though not statistically significant, which is comparable with the study of Gureset al.²⁴ In children, three cases with rapid improvement during administration of intravenous immunoglobulin within four to seven days have been observed which is comparable with other studies.²⁴⁻²⁸

We have the impression that the benefit of intravenous immunoglobulins is better in children for GBS. Although in our study corticosteroids were also shown to be of value, their effectiveness seems to be inferior to immunoglobulins. But can be of lifesaving when IVIG is not available.

Conclusion

Treatment outcome of GBS patient with Methylprednisolone is comparable with IVIG and can be considered in case of financial constrain.

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