Comparison of ICU Outcomes between Intravenous Immunoglobulin and Plasma Exchange in Treatment of Mechanically Ventilated Patients with GuillainBarré Syndrome in a Neuro-Intensive Care Unit in a Govt. Hospital of Bangladesh: A Observational Cohort Study

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Abstract

Background: The management of Guillain-Barré Syndrome is very crucial for the outcome of the patient. **Objective:** The aim of the study was to compare efficacy of IvIg(Intravenous Immunoglobulin) versus PE(Plasmaexchange) in treatment of mechanically ventilation adults with GBS in neuro-intensive care unit of Bangladesh. **Methodology:** Thiswas a prospective, observationalcohort study, in a Neuro-ICU from 2017 to 2018. We included all patients with GBS who required mechanical ventilation (MV). We defined two groups: group 1 (group treated by IvIg: 0.4 g/kg/day for 5 days) and group 2 (group treated by PE: 5 PE during 10days, every alternate day). We collectedclinical and therapeutic aspects and outcome. **Results:** A total number of 49 patients (34 in group 1 and 15 in group 2) were enrolled. The mean age was 37.4±9.2 years, with a male predominance (65.3%). on electrophysiological findings, in 4(32.7%) patients had acute inflammatory demyelinating polyradiculoneuropathy (AIDP) and acute motor axonal neuropathy (AMAN) in 26 (53.1%) patients and acute motor-sensory axonal neuropathy (AMSAN) was 3(6.1%)and NCS was not done in 4(8.2%) cases. The mean length of ICU stay was 20±19.10 days and 46.60±30.02 days in IVIG and PE group respectively. The ICU stay was significantly shorter (p = 0.001) in the IvIg group than PE group. Patients receiving IvIg were early weaned of MV (p = 0.002) compared to those receiving PE with a statistical significance. Also, duration of M/V (P=.002), Need of tracheostomy (p=.005) and over all surval rate (p=.007) was significantly in favoue of IvIg group than PE group. Out of 49 patients, total 3 patients were died and they all were AMAN variety. **Conclusion:** Our work reveals a meaningful difference for the MV duration, ICU stay, weaning and excellent recovery in IvIg group compared to PE group in terms of less complcations. *[Journal of National Institute of Neurosciences Bangladesh, 2019;5(2): 118-122]*

Keywords: Guillain-Barré syndrome (GBS), IVIG(Intravenous Immunoglbulin), PE(Plasma Exchange), Nerve conduction study (NCS)

Introduction

Guillain-Barré syndrome (GBS) is a demyelinating polyradiculoneuropathy with an acute paralysing disorder, typically symmetric and ascending and areflexia. Incidence varies between 0.66 and 1.79 cases per 100 000 persons in general population[1-6]. About pathogenesis, the aetiologies of GBS remain unclear; however, several findings suggest that causes such as an infection of the respiratory or gastrointestinal tract, vaccinations, surgery and pregnancy generate an abnormal immune response which leads to a destruction of myelin sheaths and/or axons[7-9].

The treatment is based on two mainstays: supportive care and immunomodulatory treatment. Supportive care prevents complications such as deep vein thrombosis, digestive bleeding and infections especially and physiotherapy. Both plasma exchange (PE) and intravenous immunoglobulins (IvIg) are the two immunomodulative treatment. Several studies demonstrated that IvIg and PE are efficacious treatment for GBS[10]. Collective data on five trials and 582 patients do not reveal a significant improvement in outcome, either improving faster or more completely with the combination of IVIG and plasmapheresis. The combination exposes the patients to the risks of adverse events from both modalities. There is no evidence to support the use of both IVIG and plasmapheresis therapies[11].

The aim was to compare efficacy of IvIg versus PE in treatment of mechanically ventilation adults with GBS in a medical intensive care unit.

Methodology

This was a prospective, observational study, realized in a neuro-ICU in National Institute of Neurosciences & Hospital of Banladesh which is a tertiary referring Neuro centre, during 1 year. We included all patients with GBS who required mechanical ventilation (MV). Data collected included age, sex, antecedent infection, the need for mechanical ventilation, length of stay in the neuro- intensive care unit, clinical outcome of cases during stay in ICU and HDU and investigation performed. Investigations included lumbar puncture and electrophysiological studies for AIDP and axonal forms of GBS, which include AMSAN, AMAN. The diagnosis of acute GBS was based on the criteria of an acute progressive symmetric weakness of the extremities with areflexia or hyporeflexia; the cerebral spinal fluid (CSF) showing albumin-cytological dissociation; and electrophysiological studies revealing features of demyelinating/axonal neuropathy.

Albumino-cytological dissociation was defined as CSF with a raised protein and total cell count of ≤10 per cubic mm[9]. Nerve conduction velocity and electromyography were performed at the end of 1st weeks of admission.We defined two groups: group 1 (group treated by IvIg: 0.4 g/kg/day) and group 2 (group treated by PE: 4 PE during 10days, every alternate day). The choice of treatment depends on the economic level of the patient and the presence or not of a contraindication to any of the treatments. We recorded data age, sexof the patient, comorbidities, results of CSF study, Varieties of GBS by NCS, the mean length of ICU stay, duration of ventilation, need of tracheostomy, complications, and specific treatments including plasma Exchange and IvIg. We also registered the findings Survival status by subdividing to survived and non-survived. All patients were ventilated using endotracheal mechanical ventilation then tracheotomised. Patients were intubated if they had SpO_2 less than 90% in room air requiring increasing FiO_2, or showed clinical symptoms of CO_2 retention, laboured breathing and aspiration. When patients were able to trigger spontaneous breathing, they were changed to a pressure-support spontaneous ventilation mode. Pressure support was gradually decreased to 10 cmH_2O. If secretions were manageable with good airway reflexes, a daily spontaneous breathing trial (SBT) was performed using a T-piece for 12 to 24 hours. Patients were extubated if SBT was successful. SBT was declared successful if there was no increased work of breathing or apnea, symptoms of hypercapnia, tachycardia and if SpO_2 remained well compared to pre-SBT value. Tracheostomy was done usually after second week when patient still have poor airway reflexes, excessive secretions, and SBT was unsuccessful.

Statistical analysis:Statistical analysis was performed with SPSSversion 22.0 for Windows. Frequencies, percentages, means and standard deviation (SD) were calculated. The Chi-square test and Fisher's exact test were used for comparison between independent groups of categorical data. The unpaired t-test was used for numerical data and one-way analysis of variance (ANOVA) was used to compare more than two groups. For all statistical tests, values of $p < 0.05$ (two-tailed) were considered statistically significant.

Results

Between January 2017 and December 2018, 74 patients were enrolled, 58 in group 1 (IvIg group) and 16 in group 2 (PE group). The mean age was 30.94 ± 14.96

years, with a masculine predominance (65.3%). There was no significant difference of age, sex, antecedent events, cranial nerve affection, pattern of weakness, MRC scale, comorbidities and NCS between the two groups, representing that two groups are equally distibued best cohort not influencing outcome. Symptoms preceding the onset of GBS were gastro-intestinal infections in 36(79.59%) patients, RTI 13(26.53%) and 1(2.04%) chicken pox. There was no involvement of the cranial nerves in 10 patients (Table 1).

Table 1: Comparison of IVIG and PE groups regarding baseline characteristics

Variables	IVIG group	PE Group	P value
Age Group			
Less than 20 years	7	3	
20 to 40 years	18	10	0.564
More than 40 years	9	2	
Mean age	30.94±14.96		
Sex			
• Male	22	10	0.894
• Female	12	5	
Antecedent events			
• RTI	8	5	
• GI Infection	26	9	0.219
• Chicken pox	0	1	
Cranial nerve affection*			
• VII	14	7	
• Bulber	13	5	0.931
• No	7	3	
Pattern of weakness*			
• Ascending	17	8	0.830
• Descending	17	7	
MRC Sum Score on admission#			
• Only a trace or flicker of muscle contraction is seen	20	10	
• Muscle movement is possible with gravity eliminated	9	3	0.950
• Muscle movement is possible against gravity	2	1	
• Muscle strength is reduced, but movement against resistance is possible	3	1	

*Chi-Square Tests # Fisher's Exact Test; IvIg: intravenous immunoglobulin; PE: plasma exchange

The reason for admission in the ICU was respiratory impairment. Most of the patients were transferred from the department of neurology. CSF study was performed on all patients without increasing CSF cell count.

Table 2: Comparison of Comorbidities variance between two groups

Variables	IVIG group	PE Group	P value
Comobidity#			
• Yes	7	1	0.136
• No	27	14	
DM#			
• Yes	7	1	0.219
• No	27	14	
HTN#			
• Yes	8	1	0.158
• No	26	14	
IHD#			
• Yes	3	1	0.643
• No	31	14	
Bronchial asthma#			
• Yes	1	1	0.523
• No	33	14	

*Chi-Square Tests corrected by Fisher's Exact Test

Based on electrophysiological findings, in 4(32.7%) patients had acute inflammatory demyelinating

Table 3: Electrophysiological variance between two groups

Treatment	Types of NCS				P value
	0	AIDP	AMAN	AMSAN	
IVIG	3	11	17	3	
Plasma exchange	1	5	9	0	0.663
Total	**4**	**16**	**26**	**3**	

*Chi-Square Tests corrected by Fisher's Exact Test

Table 4: Comparison of Complications between two groups

Variables	IVIG group	PE	P value
Complications			
• Yes	12	11	0.008
• No	22	3	
Complcation-VAP*			
• Yes	4	8	0.004
• No	30	7	
Complcation-Sepsis*			
• Yes	3	8	0.001
• No	31	7	
Complcation-UTI*			
• Yes	2	8	0.079
• No	32	7	
Complcation-lung Collapse*			
• Yes	1	8	0.000
• No	33	7	
Complcation-Bedsore*			
• Yes	0	4	0.006
• No	34	11	

*Chi-Square Tests corrected by Fisher's Exact Test

polyradiculoneuropathy (AIDP) and acute motor axonal neuropathy (AMAN) in 26 (53.1%) patients and acute motor-sensory axonal neuropathy (AMSAN) was 3(6.1%)and NCS was not done in 4(8.2%) cases (Table 3).

The mean length of ICU stay was 20±19.10 days and 46.60±30.02 days in IVIG and PE group respectively. The ICU stay was significantly shorter (p=0.001) in the IvIg group than PE group. Patients receiving IvIg were early weaned of MV (p=0.002) compared to those receiving PE with a statistical significance. Also, duration of M/V (P=0.002), Need of tracheostomy (p=.005) and over all surval rate (p=0.007) was significantly in favour of IvIg group than PE group (Table 5).

Table 5: Comparison of Outcome between Two Groups

Variables	IVIG group	PE	P value
ICU stay	20±17.104	46.60 ±30.02	0.001
Duration of MV	17.26±12.329	36.60 ±23.451	0.002
Tracheostomy			
• Yes	10	11	0.005
• No	24	4	
Starting of Weaning of M/V (days)	16.67±11.733	36.33 ±22.784	0.002
Final outcome			
• Survived	34	12	0.007
• Non-survived	0	3	

Discussion

In this study, mean age was 30.94 ± 14.96 years, females were affected more than males and this is against most of the previous reports which mention that GBS demonstrates a slight male predominance, with a male/female ratio of approximately 1.2–1.5:1[12,13]. Other researchers in Hong Kong reported a similar predilection between the two sexes[14]. Symptoms preceding the onset of GBS were gastro-intestinal infections in 36 (79.59%) patients, RTI 13(26.53%) and 1 (2.04%) chicken pox. It was reported that respiratory infections are the commonest antecedent infection, occurring in about 40–70% of cases, while 7–20% are gastrointestinal infections[13,15]. The findings of this present study have showed that AMAN is the most common diagnosed subtype by electrophysiological studies which is 46(50.0%) patients followed by AIDP (34.78%), AMASN (6.52%) and no MFS. AMAN pattern was the predominant underlying subtype in China, Japan, and Central and South America[13,15]. Other studies from North America and Europe as most GBS was AIDP variety[13,15]. This different figure supports the large variations in the incidence of different types of

GBS which may be related to seasonal or genetic factors with no support studies explaining this difference until now[15].

This present study showed favourable outcome than PE in terms of shorter ICU stay, early starting weaning from MV, shorter duration of MV, less complications and less mortality. It has been found that the mean duration of ICU stay and duration of mechanical ventilation in patients treated with plasmapheresis are significantly lower than in cases treated with IVIG; this reduced the cost of hospitalization and intensive care unit (ICU) care in these patients.

The results of this present study are supported by some previous studies that recorded a significant decrease in duration of ICU stay and shorter mechanical ventilation duration which compensate for the cost of plasmapheresis; better secondary outcomes were also achieved[15]. However, some studies suggested that patients who received IVIG treatment had more improvement than those with plasmapheresis[16-17]. Some other researchers showed no significant difference between the two treatment groups[18-19]. However, someother studies suggest that patients had IvIg treatment had more improvement than those had PE. Indeed, Koul and Alfutaisi[17] and Van der Meché et al[16] showed that IvIg group had a significant fast evolution than PE group.

There are some limitations of this study. The small number of cases has also made the comparison statistics not valuable enough as significant results.

Conclusion

Although our results are not conclusive, our work reveals that there arepositive recovery of ICU stay, duration of MV, weaning from MV in IvIg group compared to the PE group. IVIG group reduce the duration of hospital stay and hasten the recovery of patients with GBS.These encouraging results would merit to be confirmed by controlled and randomized works.

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