https://doi.org/10.36570/jduhs.2019.3.693

JDUHS

ORIGINAL ARTICLE

Plasma Exchange Versus Intravenous Immunoglobulin in Children with Guillain Barre Syndrome

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ABSTRACT

Objective: To compare the outcome of plasma exchange versus intravenous immunoglobulin among children with Guillain Barre Syndrome.

Methods: A comparative experimental study was conducted at department of Pediatrics, National Institute of Child Health, Karachi from August 2016 to February 2017. All patients of age ranged from 2-15 years of either gender having duration of Guillain Barre Syndrome not more than 14 days were included. The children were divided into plasma exchange or intravenous immunoglobulin group. Intravenous immunoglobulin was administered for five days in a dose of 0.4 g/kg/day/ while a daily one-volume plasma exchange was given to patients in the plasma exchange group for five days. Duration of mechanical ventilation and the pediatric intensive care unit stay in days were noted.

Results: Of 78 children, the mean age was 6.64 ±3.06 years. There were 47 (60.3%) males and 31 (39.7%) females. A significantly higher length of intensive care unit stay was noted among children who received plasma exchange (9.45 ±4.59 days) as compared to the children who received intravenous immunoglobin (4.97 ±2.84 days) (p-value <0.001, 95% CI -6.23 to -2.73). Similarly, the mean duration of ventilator stay was significantly higher among children who received plasma exchange (7.33 ±3.44 days) as compared to the children who received intravenous immunoglobin (2.01 ±0.01 days) (p-value <0.001, -7.91 to -2.74).

Conclusion: The outcome of intravenous immunoglobin founds better than that of plasma exchange in treating children with Guillain Barre syndrome.

Keywords: Plasma exchange, Intravenous immunoglobulin, Children, Guillain Barré syndrome.

INTRODUCTION

The occurrence of Guillain-Barre syndrome is frequently observed due to neuromuscular paralysis at all ages with 1.2-2.3 per 100,000 occurrences per year.[1] Globally, the disease is emerged as a post-infectious disorder, which is mostly recognized as Campylobacter jejuni infection.[2] In addition, Haemophilus influenza, Epstein-Barr virus, Mycoplasma pneumonia, and cytomegalovirus are also other infections associated with Guillain Barre Syndrome. It has been found that the incidence of Guillain Barre Syndrome is reported after operations, stressful events or vaccinations, but the pathophysiology and causality are still scarce.[3]

However, it is still not commonly found among children and possess a milder course.[4,5] This is unspecific and there are no identified differences in its pathology or electrophysiology from Guillain Barre Syndrome among adults so that there are no anticipated differences in treatment response.[6,7] In addition, including intravenous immunoglobulin did not make a substantial difference to any outcome after plasma exchange in the largest trial. Corticosteroids are ineffective in spite of the effectiveness of intravenous immunoglobulin as well as plasma exchange even though other coincident medical conditions are not effective.[8,9]

The rationale of the study is there is dearth of randomized controlled trial locally as well as internationally and secondly having conflicting results.[10] Therefore the present study is designed to assess the outcome between Plasma exchange and intravenous immunoglobulin. The better of the two modalities is used in future considering the resource-poor settings and limited facilities available in our country.

METHODS

This comparative experimental study was conducted at department of Pediatrics, National Institute of Child

Health Karachi, from August 2016 to February 2017. The study was conducted after obtaining approval from the research evaluation unit of College of Physician and Surgeon of Pakistan. Signed informed consent was also obtained from the parents/guardians after explaining the purpose, procedure, risk and benefits of the study and confidentiality was ensured.

The presence of progressive weakness in both arms and legs assessed on MRC sum scores and score less than 5 was taken as progressive weakness along with areflexia (or decreased tendon reflexes) was labeled as Guillain Barre syndrome positive.

All patients of age ranging from 2-15 years of either gender having Guillain Barre Syndrome with muscle weakness and had duration of Guillain Barre Syndrome not more than 14 days were consecutively enrolled. Children with history of myasthenia for >14 days prior to mechanical ventilation, intravenous immunoglobulin or plasma exchange started prior to inclusion in the study, injury to >6 muscle groups and non-consenting parents were excluded.

The sample size calculated using WHO sample size calculator using significance level=5%, power=80%, reported mean pediatric intensive care unit stay in patients with intravenous immunoglobulin: 16.5 ± 2.1, reported mean intensive care unit length of stay in patients with plasma exchange: 15.0 ± 2.6.[6] The final sample size came out to be 78 patients, i.e. 39 in each group.

Brief history regarding the duration of disease along with demographics details was taken from the parents. The children were divided into two groups by asking the parents to pick one sealed opaque envelop bearing a card of plasma exchange or intravenous immunoglobulin, at the time of inclusion. Endotracheal mechanical ventilation was used to ventilate all patients. If children were not able to protect their airway, they had increased work of breathing, showed CO_2 retention, had PaO_2 as compared to 70 mmHg in room air requiring extra FiO_2 they were intubated. A "T" piece was used for 2 hours to perform a daily spontaneous breathing trial, if intact was reflexed by airway and secretions were managed. If SBT was successful, patients were extubated. If there was increased working of breathing, SpO_2, pH, and $PaCO_2$ remained close to pre-SBT value, and tachycardia, the SBT was observed to be successful. The attending consultant having based on his 5 years of experience make an independent decision regarding the initiation, weaning, and terminating mechanical ventilation.

Intravenous immunoglobulin was administered for five days in a dose of "0.4 g/kg/day". One-volume plasma exchange for 5 consecutive days was offered to patients in the plasma exchange group on a regular basis. The duration of mechanical ventilation and the pediatric intensive care unit in days were included in the primary outcome. This information was observed with the demographics, which include weight, duration of symptoms, gender, height, and age.

SPSS version 21 was used to enter and analyze the data. Quantitative variables like age, weight, height, length of stay in intensive care unit, and duration of mechanical ventilation were calculated through Mean ± standard deviation. The two groups plasma exchange and intravenous immunoglobulin were compared in terms of pediatric intensive care unit stay in days and duration of mechanical ventilation by applying unpaired t test. p-value less than or equal to 0.05 was taken as significant.

The study was conducted as per the national and International ethical standards as described in the Helsinki Declaration of 1975, as revised in 2008. Moreover, study protocol was approved by the institutional committee.

RESULTS

Majority of the patients 47 (60.3%) were presented with ≤7 years of age (Mean age 6.64 ±3.06 years) years. There were 47 (60.3%) males and 31 (39.7%) females. Mean height, weight and BMI of the patients were 111.82 ±19.92 cm, 21.05 ±7.32 kg and 16.28 ±1.52 kg/m^2. Most of the patients 50 (64.1%) had ≤18.5 kg/m2 BMI. Mean duration of symptoms was 2.18 ±2.20 days. Majority of the patients 74 (94.9%) were presented with ≤5 days of duration of symptoms.

Significant difference of age (p-value <0.001), height (p-value <0.001), weight and duration of symptoms (p-value 0.006) was observed in between both groups. (Table 1)

Mean duration of stay in pediatric intensive care unit was 7.09 ±4.37 days. The mean duration of pediatric intensive care unit stay was significantly higher among children who received plasma exchange (9.45 ±4.59 days) as compared to the children who received intravenous immunoglobin (4.97 ±2.84 days) (p-value <0.001, 95% CI -6.23 to -2.73). Similarly, the mean duration of ventilator stay was significantly higher among children who received plasma exchange (7.33 ±3.44 days) as compared to the children who received intravenous immunoglobin (2.01 ±0.01 days) (p-value <0.001, -7.91 to -2.74). (Table 2, 3)

Table 1: Clinical characteristics of the patients (n=78)

Clinical characteristics	IVIG mean ±SD	PE mean ±SD
Age, years	4.10 ±1.69	9.17 ±1.20
Height, cm	95.33 ±13.78	128.31 ±7.49
Weight, kg	15.30 ±4.02	26.79 ±4.95
Duration of symptoms, days	1.51 ±0.51	2.86 ±2.93

IVIG: Intravenous immunoglobulin, PE: Plasma Exchange
All data presented as mean ± SD. Independent t-test applied, p-value <0.05 taken as significant

Table 2: Mean difference of duration of PICU stay in both group (n=78)

Group	Duration of PICU stay (in days)		
	Mean ±SD	p-value	95% CI
IVIG	4.97 ±2.84	<0.001	-6.23 to -2.73
PE	9.45 ±4.59		

IVIG: Intravenous immunoglobulin, PE: Plasma Exchange
All data presented as mean ± SD. Independent t-test applied, p-value <0.005 taken as significant

Table 3: Mean difference of duration of ventilator stay in both group (n=78)

Group	Duration of ventilator stay (in days)		
	Mean ±SD	p-value	95% CI
IVIG	2.01 ±0.01	<0.001	-7.91 to -2.74
PE	7.33 ±3.44		

IVIG: Intravenous immunoglobulin, PE: Plasma Exchange
All data presented as mean ± SD. Independent t-test applied, p-value <0.005 taken as significant

DISCUSSION

It has stated in literature that plasma exchange and intravenous immunoglobulin are effective immunotherapies for patients with Guillain Barre Syndrome, if both immunotherapies are provided within the first few weeks of disease.[11] Plasma exchange is mostly administered as one plasma volume for Guillain Barre Syndrome patients over 1 to 2 weeks on 5 separate occasions.[12] This study was conducted to assess the individual role of both therapies in terms of length of intensive care unit and mechanical ventilation stay.

The finding of this study showed that the mean duration of pediatric intensive care unit stay was significantly higher among children who received plasma exchange as compared to the children who received intravenous immunoglobin. Similarly, the mean duration of ventilator stay was significantly higher among children who received plasma exchange as compared to the children who received intravenous immunoglobin. Somewhat similar finding was reported in a study conducted by Gajjar et al.[13] The author stated that in children with Guillain barre Syndrome, plasma exchange was demonstrated to be efficient as first line or adjunctive therapy. It is secure if quantity changes, supplementation of calcium and access to veins are taken care of.[13] However, Hughes et al in their systematic review has reported no obvious difference between plasma exchange and intravenous immunoglobulin.[14]

Several studies suggested that children affected by Guillain Barre Syndrome should receive a normal intravenous immunoglobulin course, as well as a normal plasma exchange course of five successive days.[15-17] A study by Ye et al conducted in China has reported that after plasma exchange treatment, nerve function defect appeared to improve better than as compared to patients who received intravenous immunoglobulin group. Moreover, the clinical effect was also better than the immunoglobulin group. The author also stated that both plasma and intravenous immunoglobulin exchange have an elevated therapeutic reaction and are sensible therapeutic choices for Guillain Barre Syndrome.[17] Gajjar et al has reported inadequate vascular access as the common complication of plasma exchange.[13] However, in a study conducted by Rekha *et al*, the most common complication was allergic reactions to fresh frozen plasma.[18] In spite of this, plasma exchange is reported to be more curative as it can enhance the symptoms efficiently and help patients in their early rehabilitation.[13,19,20]

A study investigated complications among adults with neurological disorders who received plasma exchange. According the study findings, hypotension, allergic reactions, and vomiting were some the findings and the frequency ranged from 11-2%.[21] In another study, complication during plasma exchange procedure reported as 18.3%. These complications were catheter placement procedure, hypotension, hypocalcaemia, and allergic reactions.[22] However, in the current study, we failed to collect the information regarding complications.

This study has certain limitations, firstly the sample size of the study was small. Secondly, the study has not reported certain important variables like complications, outcomes. Future research should conduct randomized controlled trials well as appropriately designed cohort studies for comparing the outcome after several treatment regimens undertaking significant numbers of patients. Despite of the mentioned limitations, this study has given local insight of plasma exchange in children with GBS. Although literature search has reported, previously most of the studies were conducted on adult patient with GBS. In these studies, no significant difference in the outcome was noted among GBS patients receiving plasma exchange versus the intravenous immuno-globulin.[23,24]

CONCLUSION

The outcome of intravenous immunoglobin found better than that of plasma exchange in treating children with Guillain Barre syndrome.

AUTHORS' CONTRIBUTION: EE, MA, BUN substantially contributed to the conception and design of the study. EE, SA has worked in the acquisition, analysis and interpretation of the data also drafted the manuscript. MA, BUN revised it critically for intellectual content and gave final approval.

CONFLICT OF INTEREST: None

FUNDING: None

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