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Original Research Paper

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A COMPARATIVE STUDY OF CLINICAL PROFILE AND THERAPEUTIC OUTCOME OF 50 PATIENTS OF GUILLAIN BARRE SYNDROME TREATED WITH IVIg AND PLASMAPHERESIS

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ABSTRACT Guillain-Barré Syndrome (GBS) is an acute autoimmune polyneuropathy characterized by progressive muscle weakness and areflexia. This prospective interventional study aims to evaluate the clinical profiles of GBS patients and compare the safety, efficacy, and outcomes of Intravenous Immunoglobulin (IVIg) and plasmapheresis treatments. Conducted at a tertiary care centre, the study included 50 patients diagnosed with GBS based on the Brighton criteria, randomly assigned to receive either IVIg (0.4g/kg/day for 5 days) or plasmapheresis (five exchanges over alternate days). Clinical outcomes were assessed using the Medical Research Council (MRC) muscle grading, Modified Rankin Scale (MRS), and Single Breath Count (SBC). The study included 33 males and 17 females with a mean age of 35.61 years. Both treatments significantly improved MRC, MRS, and SBC scores. IVIg showed greater improvement in MRC (1.58 vs. 1.33; p=0.072) and MRS (1.25 vs. 0.86; p=0.026) compared to plasmapheresis, although the difference in SBC improvement was not significant (11.13 vs. 8.05; p=0.0613). Subgroup analysis indicated comparable efficacy of both treatments in demyelinating and axonal neuropathies. Patients with mixed neuropathy showed significant improvement in both treatment groups, with a slight advantage observed in the IVIg group. The study concluded that both IVIg and plasmapheresis are effective in treating GBS, with IVIg demonstrating a slight advantage in overall disability improvement. Treatment choice should be individualized based on patient-specific factors and resource availability. Further research is warranted to optimize treatment strategies and to explore the long-term outcomes of these therapeutic interventions.

KEYWORDS : Guillain-Barré Syndrome, autoimmune polyneuropathy, Intravenous Immunoglobulin, plasmapheresis, clinical outcomes, Medical Research Council, Modified Rankin Scale, Single Breath Count.

INTRODUCTION:

Guillain Barre' Syndrome (GBS) is an acute, poly radiculo-neuropathy of autoimmune nature.[1] GBS occurs throughout the world with a median annual incidence of 1.3 cases per population of 100, 000 with men being more frequently affected than women. Typical clinical features of GBS are progressive, symmetrical muscle weakness associated with absent or depressed deep tendon reflexes. The weakness is very variable ranging from mild difficulty in walking to complete paralysis of all four extremities, motor cranial weakness to life-threatening respiratory muscle weakness. The later develops in 10 to 25% of patients necessitating ventilatory support.[2] GBS also affects autonomic nervous system and dysautonomia may occur in up to 70% of patients.

A considerable body of evidence points to an organ specific autoimmune disorder mediated by auto reactive T cell sand humoral antibodies to still incompletely characterized peripheral nerve antigens.[3] A preceding infection may trigger an autoimmune response through molecular mimicry in which the host generates an immune response against an infectious organism that shares epitopes with the host's peripheral nerves. Campylobacter jejuni, cytomegalovirus, Epstein-Barr virus and Mycoplasma pneumoniae are commonly identified antecedent pathogens. Acute Inflammatory Demyelinating Polyneuropathy (AIDP) is by far the most common form of GBS in Europe and North America.

Acute Motor Axonal Neuropathy (AMAN) and Acute Motor Sensory Axonal Neuropathy (AMSAN) subtypes constitute 30–40% of cases in Asia and South America but are rare in the Western world. The Miller-Fisher syndrome (MFS), which accounts for 5% of cases, is characterized by ophthalmoplegia, ataxia, and areflexia. Patients present with diplopia followed by gait and limb ataxia. Diagnosis of GBS is usually clinical.

Diagnostic criteria for GBS from the Brighton criteria[4] have an important role in research and are widely used in clinical practice. Cerebrospinal fluid (CSF) analysis show cytoalbuminologic dissociation at one week after onset of symptoms. Nerve conduction studies when available should be performed to confirm diagnosis.

Treatment of GBS is subdivided into: (i) the management of severely paralyzed patients with intensive care and ventilatory support; and (ii) specific therapeutic interventions aimed at mitigating the harmful effects of autoantibodies, such as IVIg infusion and plasma exchange that shorten the progressive course of GBS and aid rapid resolution of the disease.[5]

Therapeutic plasma exchange/plasmapheresis is recommended for patients with moderate to severe weakness (defined as the ability to walk only with support or worse). Benefits are clearest when plasma exchange is begun within 2 weeks of onset. The recommended plasmapheresis schedule entails a series of five exchanges (40-50 mL/kg) with a continuous flow machine on alternate days using saline and albumin as replacement fluid. The Cochrane review confirmed the value of plasma exchange over supportive therapy in hastening the recovery from GBS when started within 30 days after disease onset. Three randomized trials comparing IVIg with plasma exchange demonstrated the benefit of five daily infusions of IVIg (0.4 g/kg/day) given in the first 2 weeks of the disease. There was no advantage of using both together. These findings were confirmed by another Cochran systematic review.[6]

The prognosis of GBS is generally favourable. Approximately 80 and 84 percent patients with GBS walk independently at six months and one year after diagnosis, respectively.[7]

AIMS AND OBJECTIVES:

1. To evaluate the clinical profile in patients of GBS
2. To evaluate IVIg on the basis of safety, efficacy and outcome
3. To evaluate Plasmapheresis on the basis of safety, efficacy

and outcome
4. To know the complications of IVIg and plasmapheresis in studied population

MATERIALS AND METHODS:

The study was conducted in Department of General Medicine, in a tertiary care centre.

Study Type: A Prospective Interventional Study

Sample Size: 50

Randomization In Each Group: Simple Randomization

Patient Selection:

Inclusion Criteria:

1. This study consists of patients who are aged 12 and above and give consent for participation who presented with features of GBS based on Brighton criteria

Exclusion Criteria:

1. Early and prominent bladder and bowel dysfunction
2. Marked and persistent asymmetry of symptoms and signs
3. Presence of persistent sharp sensory level
4. Features of other diseases like myasthenia gravis, botulism, poliomyelitis, porphyria and diphtheria
5. Drug or toxin induced acute neuropathy
6. Acute exacerbation of CIDP (Chronic Inflammatory Demyelinating Polyneuropathy)
7. Those who unwilling to give consent

Method:

The study was approved by the Institutional ethics committee (Ethics committee registration no. ECR/72/Inst/2013/RR-2019; reference no. 111/2021).

50 patients diagnosed as Guillain Barre Syndrome (GBS) fulfilling the Brighton criteria, admitted in the medical wards of Civil Hospital Ahmedabad from June 2019 to August 2021 were included in this study.

This was a prospective interventional study. In this study 50 consecutive patients who fulfilled the inclusion and exclusion criteria and who gave a written informed consent were recruited over a period of 2 years. A detailed history and physical examination were carried out in every patient. History of preceding illnesses and clinical symptoms were recorded. Every patient was assessed initially by Medical Research Council[2] (MRC) Grading of muscle weakness, Modified Rankin's scale[3] (MRS) and SBC (Single Breath Count). Routine investigations like Hb, CBC, RFT, LFT, blood sugars were recorded. Details of specialized investigations nerve conduction studies and cerebrospinal fluid findings were recorded. Patients were investigated and treated as per the treating physicians' decision. In group A (25 patients) IVIg was given in a dose of 0.4g/kg/day for 5 days. In group B (25 patients) five cycles of plasmapheresis was done on alternate days. Patients were followed up regularly during the hospital stay. Patient outcome was assessed using the MRC, MRS and SBC. End points of the study was either death during hospital stay or discharge from the hospital.

During each examination, the following were noted:

1. Medical Research Council (MRC) Grading Of Muscle Weakness.

0- No muscle contraction visible
1- Flicker of contraction but no movement
2- Joint movement when effect of gravity eliminated
3- Movement against gravity but not against examiner's resistance
4- Movement against resistance but weaker than normal
5- Normal power

2. Modified Rankin scale (MRS) Score description

0. No symptoms at all
1. No significant disability despite symptoms; able to carry out all usual duties and activities
2. Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3. Moderate disability; requiring some help, but able to walk without assistance
4. Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5. Severe disability; bedridden, incontinent and requiring constant nursing care and attention
6. Dead

3. Bedside Autonomic Function Tests -

Resting Heart rate, Resting Blood Pressure, Postural Hypotension, Blood pressure changes at the end of one minute and 3 minutes on standing from lying position, wherever possible. In addition, complaints suggestive of autonomic dysfunction such as excessive sweating, urinary retention and constipation, palpitations, postural giddiness was also noted.

Data Analysis:

Recorded information was entered in Microsoft Excel Worksheet. Data was analysed and compared by using appropriate statistical test- paired and unpaired t-tests. P value of <0.05 was considered to be statistically significant.

RESULTS

All patients were hospitalized and the average duration of hospital stay was 17.72 ± 6.19 days. Out of all 33 patients (66%) were males and 17 (34%) were females. The age of patients ranged from 12 to 60 years (Mean age 35.61 years) with the maximum number (34%) of patients in 21 to 28 years age group. Out of 50, 23 patients showed Cytoalbuminologic Dissociation in cerebrospinal fluid routine micro report. Five patients (10%) died in this study.

Disability at discharge was assessed according to mMRC grading. Most of the patients (42%) were discharged at Grade 2; 17 patients (34 %) were discharged at grade 3 whereas no or minimal improvement was seen in 4 patients (grade 1). Three patients recovered almost completely (grade 4) and discharged

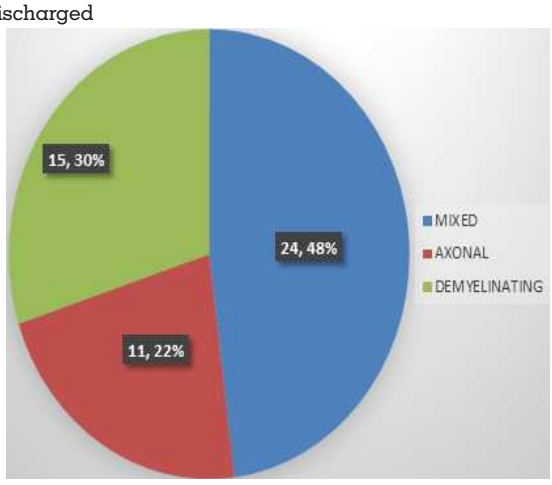

Chart 1. Nerve Conduction Studies Pattern

Table 1: Mean Change In mMRC (combined, N=50)

TREATMENT	ON ADMISSION	ON DISCHARGE	P VALUE
IVIg	0.96	2.54	0.00001 (>0.05)
PLASMAPHERESIS	0.90	2.23	0.00001 (>0.05)

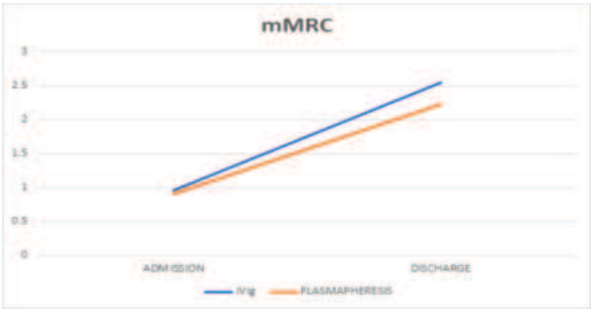

Chart 2: Mean Change In mMRC (combined, N=50)

Thus, mMRC improved by 1.58 in IVIg group and by 1.33 in plasmapheresis group in case of combined neuropathy. Which was compared by unpaired t-test and P value was 0.072(>0.05) thus difference was not significant.

Table 3: Mean Change In MRS (combined, N=50)

TREATMENT	ON ADMISSION	ON DISCHARGE	P VALUE
IVIg	4.12	3	0.00001 (< 0.05)
PLASMAPHERESIS	4.12	3.72	0.00001 (< 0.05)

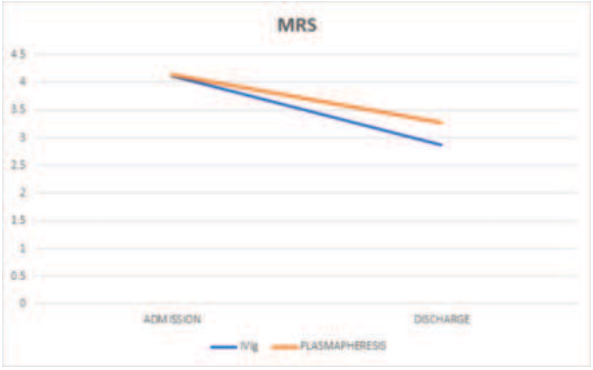

Chart 4: Mean Change In MRS (combined, N=50)

Thus, MRS improved by 1.25 in IVIg group and by 0.86 in plasmapheresis group in case of combined neuropathy. This improvement was compared by unpaired t test and P value was 0.026 means IVIg is **significantly better** than plasmapheresis for overall prognosis.

Table 4: Mean Change In SBC (Single Breath Count) (combined, N=50)

TREATMENT	ON ADMISSION	ON DISCHARGE	P VALUE
IVIg	19.33	30.46	0.00001 (< 0.05)
PLASMAPHERESIS	20.47	28.52	0.00001 (< 0.05)

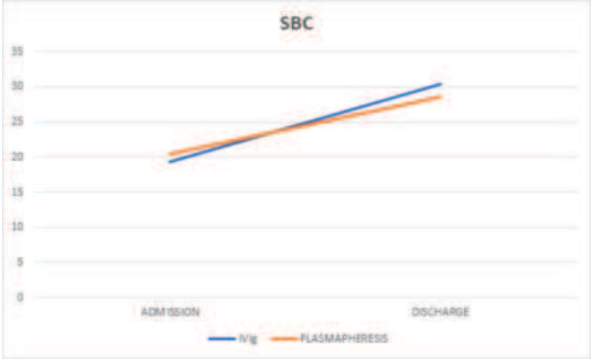

Chart 5: Mean change in SBC (combined, N=50)

Thus, SBC improved by 11.13 in IVIg group and by 8.05 in plasmapheresis group in case of combined neuropathy, which was compared by unpaired T test and P value was 0.0613 and difference in improvement in SBC was not significant.

Table 5: Mean Change In mMRC (demyelinating, N=15)

TREATMENT	ON ADMISSION	ON DISCHARGE	P VALUE
IVIg	1.14	2.28	0.0046 (< 0.05)
PLASMAPHERESIS	0.71	2.33	0.0016 (< 0.05)

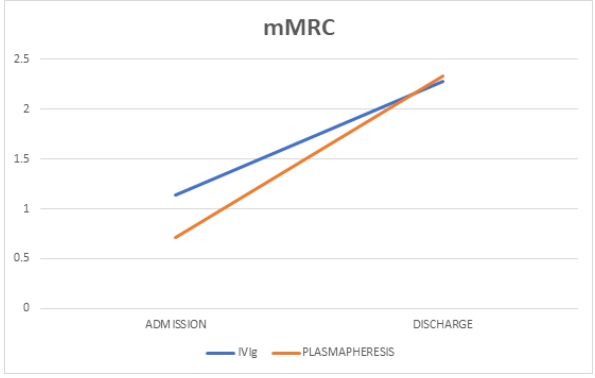

Chart 6: Mean change in mMRC (demyelinating, N=15)

Thus, mMRC improved by 1.14 in IVIg group and by 1.62 in plasmapheresis group in case of Demyelinating neuropathy. This improvement was compared by unpaired T test and calculated P value was 0.2804 (>0.05) meaning both treatments are equally effective.

Table 6: Mean Change In MRS (demyelinating,N=15)

TREATMENT	ON ADMISSION	ON DISCHARGE	P VALUE
IVIg	4	3.14	0.143(>0.01)
PLASMAPHERESIS	4.14	3.57	0.217(>0.01)

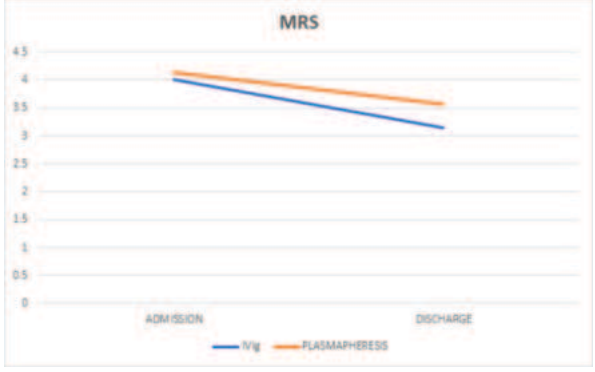

Chart 7: Mean Change In MRS (demyelinating, N=15)

Thus, MRS improved by 0.86 in IVIg group and by 0.57 in plasmapheresis group in case of Demyelinating neuropathy. Both treatments were compared by unpaired T test, calculated P value was 0.8339 (>0.05).

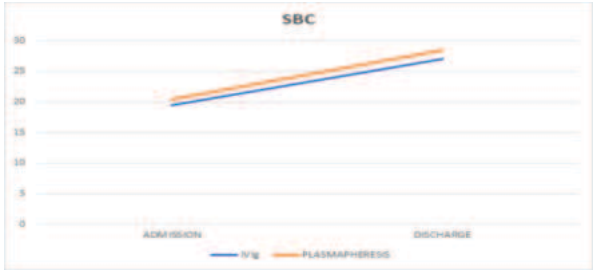

Chart 8: Mean change in SBC(demyelinating, N=15)

Table 7: Mean Change In SBC (Single Breath Count) (demyelinating, N=15)

TREATMENT	ON ADMISSION	ON DISCHARGE	P VALUE
IVIg	19.43	27	0.099(>0.05)
PLASMAPHERESIS	20.43	30.67	0.019(>0.05)

Thus, SBC improved by 7.57 in IVIg group and by 10.24 in plasmapheresis group in case of Demyelinating neuropathy. On comparing improvement by unpaired T test p value was 0.5617 (>0.05)

Table 8: Mean Change In mMRC (axonal, N=10)

TREATMENT	ON ADMISSION	ON DISCHARGE	P VALUE
IVIg	1.6	3	0.051(>0.01)
PLASMAPHERESIS	0.5	2.33	0.0018(<0.01)

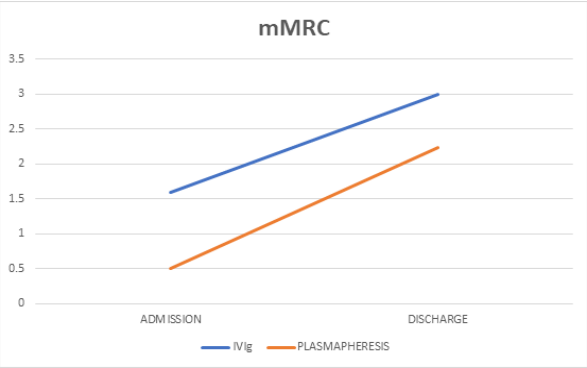

Chart 9: Mean change in mMRC(axonal, N=10)

Thus, mMRC improved by 1.4 in IVIg group and by 1.83 in plasmapheresis group in case of Axonal neuropathy. This was compared by unpaired T-test which brought p value of 0.1866 (>0.05) meaning both treatments are equally effective.

Table 9: Mean Change In MRS(axonal, N=10)

TREATMENT	ON ADMISSION	ON DISCHARGE	P VALUE
IVIg	4	3	0.034(>0.01)
PLASMAPHERESIS	4.17	3	0.013(>0.01)

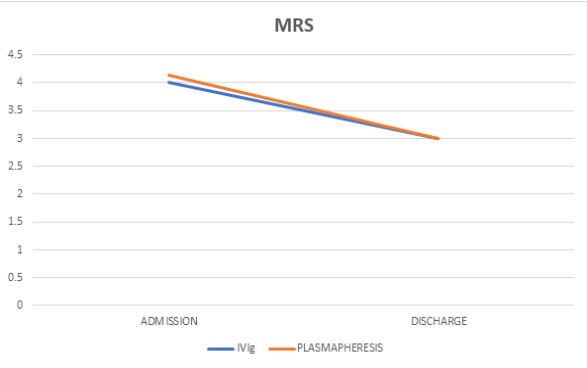

Chart 10: Mean Change In MRS(axonal, N=10)

Table 10: Mean Change In SBC (Single Breath Count) (axonal, N=10)

TREATMENT	ON ADMISSION	ON DISCHARGE	P VALUE
IVIg	18.8	30.6	0.001 (<0.01)
PLASMAPHERESIS	20.83	29.33	0.0002 (<0.01)

Thus, MRS improved by 1 in IVIg group and by 1.17 in plasmapheresis group in case of Axonal neuropathy. Both results were compared by unpaired T-test and calculated P value was 1 (>0.05) which suggests both the treatment are of same efficacy.

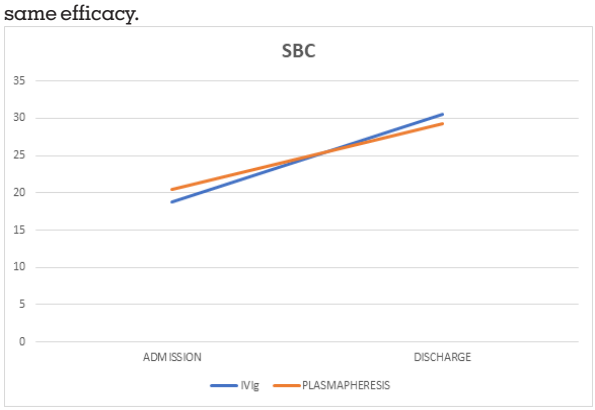

Chart 11: Mean Change In SBC(axonal, N=10)

Thus, SBC improved by 11.8 in IVIg group and by 8.5 in plasmapheresis group in case of Axonal neuropathy. Both results were compared by unpaired T-test and calculated P value was 0.623 (>0.05) which suggests both the treatment are of same efficacy.

DISCUSSION

This study is a prospective interventional study with the objective to analyse the clinical profile of Guillain-Barré Syndrome (GBS) patients and conduct a comparative evaluation of treatment efficacy. Specifically, we compared the effectiveness of Intravenous Immunoglobulin (IVIg) and Plasmapheresis, the two primary treatment modalities for GBS. The number of patients in each group was the same.

When comparing the effects of IVIg and Plasmapheresis, we found that both treatments significantly improved the Modified Rankin Scale (MRS) and Single Breath Count (SBC). However, the Modified Medical Research Council (mMRC) score improved to a greater extent with IVIg treatment, suggesting its potential superiority in enhancing patients' respiratory function and overall disability.

Furthermore, we subdivided our patient population into those with demyelinating and axonal neuropathy. In the case of demyelinating neuropathy, both IVIg and Plasmapheresis demonstrated comparable efficacy across all assessed parameters, including mMRC, MRS, and SBC. Conversely, for patients with axonal neuropathy, our results indicated that IVIg and Plasmapheresis exhibited similar effectiveness in improving mMRC, MRS, and SBC.

The primary outcome analyzed in the selected studies, including our own, was the curative effect of IVIG (intravenous immunoglobulin) compared to PE (Plasma Exchange) in patients with Guillain-Barré Syndrome (GBS). Consistently, the studies showed no significant difference in the efficacy between IVIG and PE. Both treatments were equally effective in improving disability scores and reducing the severity of symptoms. Our study reported that IVIG showed greater improvement in MRC (Medical Research Council) muscle grading and Modified Rankin Scale (MRS) scores compared to plasmapheresis, although the difference in Single Breath Count (SBC) improvement was not significant.

Primary Outcomes:

The results consistently showed no significant difference in the efficacy between IVIG and PE in the selected studies. Both treatments were equally effective in improving disability scores and reducing the severity of symptoms. Notably, the study by van der Meché et al. (1992) reported fewer relapses in the IVIG group, with a significant p-value of <0.05, indicating

that IVIG might have a slight edge over PE in reducing relapse rates. In our study, IVIG demonstrated a slight advantage in overall disability improvement, with significant improvements in MRC and MRS scores.

Secondary Outcomes:
Secondary outcomes included hospitalization length, ICU/PICU stay, mechanical ventilation duration, complications, and mortality. Across the studies, including ours:

Hospitalization And ICU/PICU Stay:
There was no significant difference between IVIG and PE in terms of the length of hospital or ICU/PICU stay. Our study showed that both treatments significantly improved hospitalization outcomes.

Mechanical Ventilation Duration:
The duration of mechanical ventilation was similar between the two treatments across the studies. In our study, the improvement in SBC, which reflects respiratory function, was not significantly different between the two treatments.

Complications And Mortality:
The incidence of complications and mortality rates did not differ significantly between IVIG and PE, reinforcing the notion that both treatments are comparably effective and safe for managing GBS. Our study also reported no significant differences in complications and mortality between the two groups.

CONCLUSION:

The findings from our study are in line with the results from the selected studies, reinforcing the conclusion that both IVIG and PE are effective treatments for GBS. The choice between IVIG and PE can thus be guided by other factors such as resource availability, cost, and patient-specific considerations. Our study, along with the selected studies, underscores the importance of personalized treatment decisions and ongoing research to optimize treatment strategies for GBS. While IVIG may offer a slight advantage in terms of reducing relapse rates and improving disability scores, both treatments ultimately provide significant clinical benefits.

Table 11

Name of Study	Type of Study	Regimen and Number of Patients in Each Regimen	Results	Difference Between Groups (IVIG vs PLEX)	Significance (p-value)	PMID
van der Meché FG, Schmitz PI, 1992[8]	Randomized Trial	IVIG: 75, PLEX: 74	IVIG and PLEX had similar efficacy, fewer relapses in IVIG group	Fewer relapses in IVIG group	<0.05	1552913
Bril V, Ilse WK, et al., 1996[9]	Pilot Trial	IVIG: 14, PLEX: 15	No significant difference in outcomes between IVIG and PLEX	No significant difference	>0.05	8559353
PSGBS trial group, 1997[10]	Randomized Trial	IVIG: 121, PLEX: 124, Combined: 115	IVIG and PLEX equally effective, combined treatment not superior	No significant difference	>0.05	9014908
Diener HC, Haupt WF, et al., 2001[11]	Randomized Multicenter Study	IVIG: 11, PLEX: 10, Immune Adsorption: 11	All treatments had similar efficacy, no significant differences	No significant difference	>0.05	11528165
Elahi et al., 2019[12]	Randomized Trial	IVIG: 78, PLEX: 78	No significant difference in outcomes between IVIG and PLEX	No significant difference	>0.05	

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