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Study of Motor Nerve Conduction in Pre and Post-Immunoglobulin Treatment of Guillain Barré Syndrome

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Abstract
To evaluate the effects of intravenous immunoglobulin (IVIG) treatment on motor nerve conduction in patients diagnosed with Guillain Barré Syndrome (GBS). This observational study, adhering to STROBE guidelines, involved fifty GBS patients from a rural medical college in central India. Nerve conduction studies (NCS) were performed on the median, ulnar, tibial and peroneal nerves at baseline and one week post-IVIG treatment. The parameters assessed included distal motor latency, amplitude and conduction velocity. The study included 50 patients with clinically diagnosed GBS. Significant improvements in motor nerve function were observed post-IVIG treatment, particularly in the amplitude of right median and ulnar nerves, and both amplitude and distal motor latency in the right peroneal and bilateral tibial nerves. The study recorded statistically significant differences in these parameters, suggesting an effective reversal in conduction deficits. IVIG treatment within the first week of GBS symptom onset is crucial and can significantly improve motor nerve function, as evidenced by NCS parameters. This study underscores the importance of timely diagnosis and initiation of therapy to enhance prognosis in GBS patients.

INTRODUCTION

Guillain-Barre Syndrome (GBS) is a disease which causes severe and acute polyneuropathy leading to significant morbidity and mortality. The syndrome is often triggered by an infection, which arouse immune-mediated nerve dysfunction. Patients often experience changes in sensation or develop pain followed by muscle weakness starting in the feet and hands that progresses rapidly. Often during the acute phase, the disorder can be life-threatening and about every fourth patient requiring treatment in intensive care unit for mechanical ventilation. Few patients are affected by variations in the function of the autonomic nervous system which can lead to dangerous abnormalities in heart rate and blood pressure[1-3]. Documented incidence rates for GBS are 1-2 per 100,000 populations and the lifetime chance of any individual getting GBS is 1:1000. The diagnosis of GBS is commonly made by clinical examination supported by features of polyneuropathy on nerve conduction studies and examination of the cerebrospinal fluid[4-6]. Electro physiological studies are especially useful in diagnosis of polyneuropathy and also for classifying GBS into subgroups such as acute motor axonal neuropathy (AMAN) and acute inflammatory demyelinating polyneuropathy (AIDP). High-dose intravenous immunoglobulin (IVIG) and plasma exchange (PE) therapies are effective in alleviating the severity of symptoms associated with GBS. Various multi-centric trials and case series documented that Intra-Venous Immunoglobulin (IVIG) is effective in patients with GBS[7,8]. The findings of first Randomized Control Trial on the use of IVIG in GBS was published in 1992 and concluded that IVIG is effective[9]. The prognosis of patients depends on prompt diagnosis and treatment. Therefore, investigating motor nerve conduction studies (MNC) in GBS patients is pertinent to provide comprehensive findings into the mechanisms, correlations and timing of treatment.

Thus, the use of immunoglobulin therapy requires careful consideration, specific to the patient's condition and needs. Basically, the study of MNC in Pre- and post-immunoglobulin treatment of GBS is certain to address a notable gap in current GBS research. The essential need to address significant gaps in the current knowledge and study the nerve conduction parameters of GBS before and after the IVIG protocol prompted this research, especially focused toward motor nerves.

MATERIALS AND METHODS

Study Design and Setting: This was an observational study prepared and reported using Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) principles. The IEC approval was obtained and written informed consent was taken from all study participants. The study was conducted for 18-month duration in the neurophysiology Laboratory of the Department of Physiology. Patients were referred from the Department of Medicine at a rural medical college in central India.

Study Participants: Fifty clinically diagnosed patients of the central Indian population with GBS were referred from the Department of Medicine to the Department of Physiology for the nerve conduction study (NCS). The patients were between the ages of 18-60 years. For the prevalence of 2%, with a confidence interval (CI) of 95% and design effect 1, we arrived at a minimum sample size of 31[10,11]. A total of 50 participants were included, further categorized as pre-immunoglobulin therapy and post-immunoglobulin therapy.

Selection Criteria: Inclusion criteria included clinically diagnosed GBS patients of the age group between 18-60 years and of both genders who gave written informed consent. Patients with a recent history of fever, respiratory or gastrointestinal infection, surgery and symptoms such as inability to walk for >10 minutes independently, rapid progression of weakness, severe autonomic or swallowing dysfunction, or respiratory insufficiency and their progression within one week from the time of diagnosis of GBS post-admission to the hospital were selected[10,11]. Exclusion criteria excluded patients with cardiac pacemakers or cardiac pathology, myelopathy, myopathy,

Neuromuscular junction disorders like myasthenia gravis and those who did not give consent and were not willing to participate in the study.

Data Sources and Measurement of Variables: Basic sociodemographic information was collected from each patient, along with clinical history, such as recent history of fever, surgery, weakness of limbs and infection. The RMS EMG EP Mark-II machine used to record the NCV parameters in the neurophysiology laboratory of the Physiology Department at a rural medical college in central India. To reduce the number of errors, the same researcher conducted all of the tests at a constant room temperature (30°C)

Electro Physiological Evaluation of Guillain Barre Syndrome: Nerve conduction studies (MNCS) involve stimulation of motor nerve at two different sites with maximum stimulus and calculation of conduction velocity. Nerves tested were median, ulnar, tibial and peroneal nerves. Setting was kept at sweep speed 5 ms/D, intensity 2 mV, frequency 2 Hz, filter between 2 Hz to 5 Hz and stimulus strength duration was 100 µs[13]. MNCS was conducted on bilateral median, ulnar, tibial and peroneal nerves of GBS patients within one week from the time of diagnosis. The standard GBS therapy protocol was followed to treat the patients

after the initial NCS test reports and a follow-up NCS was performed one week following the immunoglobulin infusion[14,15].

Motor Nerve Conduction Study (MNCS): Motor nerve conduction studies involves stimulation of motor nerves at two different sites with maximum stimulus and calculation of distal motor latency, amplitude and conduction velocity. Setting was kept at sweep speed 5ms/D, intensity 2 mV, Frequency 2Hz, filter between 2 Hz and 5 Hz and stimulation strength duration was 100 μs[13]. MNCS was conducted on bilateral median, ulnar, tibial and peroneal nerves of GBS patients within one week from the time of diagnosis. The standard GBS therapy protocol was followed to treat the patients after the initial NCS test reports and a follow-up NCS was performed one week following the immunoglobulin infusion[14,15].

Statistical Analysis: A standardized data collection form was used for thein formation that was gathered. After the data was collected, it was tabulated, and SPSS software version 27 (SPSS Inc., Chicago, US) was used for the necessary statistical tests and statistical analysis. The values of the research parameters are shown as mean±standard deviation (SD) and the means were compared using an unpaired Student's t-test. Statistics indicate that a P-value below 0.05 is considered statistically significant.

RESULTS AND DISCUSSIONS

The current research included 50 diagnosed GBS patients between the age group of 18 and 60 years, satisfying the inclusion criteria.

The mean and SD of right and left median nerve distal motor latency at pre-treatment were 3.86±2.25 ms and 3.84±2.16 ms., at post-treatment, they were 3.08±0.47 ms and 3.44±1.41ms, respectively. The mean and SD of right and left median nerve amplitudes at pre-treatment were 7.32±4.31mV and 7.27±5.2 mV., at post-treatment, they were 10.5±5.07 mV and 9.89±5.57 mV, respectively. The mean scores of right and left median nerve conduction velocities at pre-treatment were 49.43±10m/s and 47.1±10.84m/s; at post-treatment, they were 51.58±6.84 m/s and 47.56±7.86 m/s, respectively. By using Student's paired t-test, statistically significant difference was found in right median Amplitude before and after IVIG treatment whereas in other parameters no statistically significant difference was found.

The mean and SD of right and left ulnar nerve distal motor latency at pre-treatment were 2.88±1.02 ms and 3.34±2.05 ms., at post-treatment, they were 2.77±1.08 ms and 2.86±1.07ms, respectively. The mean and SD of right and left ulnar nerve amplitudes at pre-treatment were 6.69±5.27mV and 6.11±4.42 mV; at post-treatment, they were 9.35±4.99 mV and 7.46±5.05 mV, respectively. The mean scores of right and left ulnar nerve conduction velocities at pre-treatment were 54.63±15.42 m/s and 53.56±13.26 m/s., at post-treatment, they were 54.43±12.9m/s and 54.43±14.69 m/s, respectively. By using Student's paired t-test, statistically significant difference was found in right ulnar Amplitude before and after IVIG treatment whereas in other parameters no statistically significant difference was found.

The mean and SD of right and left peroneal nerve distal motor latency at pre-treatment were 5.48±2.25 ms and 4.85±1.82 ms., at post-treatment, they were 4.1±0.78 ms and 4.49±1.31ms, respectively. The mean and SD of right and left peroneal nerve amplitudes at pre-treatment were 3.24±3.23mV and 3.39±3.54 mV; at post-treatment, they were 4.94±3.21 mV and 4.31±3.41 mV, respectively. The mean scores of right and left peroneal nerve conduction velocities at pre-treatment were 49.05±12.05 m/s and 49.65±13.18m/s; at post-treatment, they were 52±13.06m/s and 52.48±14.87 m/s, respectively. By using Student's paired t-test, statistically significant difference was found in right peroneal Amplitude and distal motor latency before and after IVIG treatment whereas in other parameters no statistically significant difference was found.

The mean and SD of right and left tibial nerve distal motor latency at pre-treatment were 4.62±1.35 ms and 4.75±1.51 ms., at post-treatment, they were 4.01±1.19 ms and 4.22±1.03ms, respectively. The mean and SD of right and left tibial nerve amplitudes at pre-treatment were 4.71±3.85mV and 5.8±5.87 mV., at post-treatment, they were 10.43±6.38 mV and 9.71±5.12 mV, respectively. The mean scores of right and left tibial nerve conduction velocities at pre-treatment were 50.61±17.65 m/s and 49.52±21.79m/s; at post-treatment, they were 49.89±15.15m/s and 48.22±11.16 m/s, respectively. By using Student's paired t-test, statistically significant difference was found in both (Rt and Lt) tibial nerves Amplitude and distal motor latency before and after IVIG treatment whereas no statistically significant difference was found in conduction velocity.

As per our literature search, no definite original research study has been identified that elicits the electrophysiological changes related to motor nerves occurring in GBS patients pre and post intravenous infusion of immunoglobulin. This lack of research hampers the representation of alterations in motor nerve function, impeding an overall understanding of the clinical correlation of the disease. GBS is largely classified as demyelinating and axonal subtypes as per electrophysiological and histopathological observations. Nerve conduction studies are essential in electrodiagnosis and the categorization of subtypes. AIDP is characterized by conduction slowing, conduction block, and temporal dispersion. Axonal

Table 1: Comparison of Median Nerve Score at pre and post IVIG treatment

Median Nerve	Pre Test	Post Test	Mean Difference	t-value	p-value
R Median(Lat) ms	3.86±2.25	3.08±0.47	0.78±2.21	1.97	0.058,NS
R Median(Amp) mv	7.32±4.31	10.50±5.07	3.17±6.28	2.81	0.009,S
R Median(CV) m/s	49.43±10	51.58±6.84	2.14±9.98	1.19	0.241,NS
L Median(Lat) ms	3.84±2.16	3.44±1.41	0.39±2.40	0.90	0.376,NS
L Median(Amp) mv	7.27±5.20	9.89±5.57	2.62±8.34	1.72	0.096,NS
L Median(CV) m/s	47.10±10.84	47.56±7.85	0.46±11.94	0.21	0.831,NS

Table 2: Comparison of Ulnar Nerve Score at pre and post IVIG treatment

Ulnar Nerve	Pre Test	Post Test	Mean Difference	t-value	p-value
R Ulnar(Lat) ms	2.88±1.02	2.77±1.08	0.10±1.29	0.46	0.648,NS
R Ulnar(Amp) mv	6.69±5.27	9.35±4.99	2.66±5.72	2.55	0.016,S
R Ulnar(CV) ms	54.63±15.42	54.43±12.90	0.19±20.75	0.05	0.959,NS
L Ulnar(Lat) ms	3.34±2.05	2.86±1.07	0.47±2.16	1.16	0.254,NS
L Ulnar(Amp) mv	6.11±4.42	7.46±5.05	1.35±5.68	1.26	0.219,NS
L Ulnar(CV) ms	53.56±13.26	54.43±14.69	0.87±17.69	0.26	0.795,NS

Table 3: Comparison of Peroneal Nerve Score at pre and post IVIG treatment

Peroneal Nerve	Pre Test	Post Test	Mean Difference	t-value	p-value
R Peroneal(Lat) ms	5.48±2.25	4.10±0.78	1.37±2.01	3.79	0.001,S
R Peroneal(Amp) mv	3.24±3.23	4.94±3.21	1.70±3.30	2.87	0.007,S
R Peroneal(CV) ms	49.05±12.05	52±13.06	2.95±16.42	1.00	0.325,NS
L Peroneal(Lat) ms	4.85±1.82	4.49±1.31	0.35±2.44	0.79	0.435,NS
L Peroneal(Amp) mv	3.39±3.54	4.31±3.41	0.91±4.03	1.24	0.223,NS
L Peroneal(CV) ms	49.65±13.18	52.48±14.87	2.83±17.32	0.89	0.378,NS

Table 4: Comparison of Tibial Nerve Score at pre and post IVIG treatment

Tibial Nerve	Pre Test	Post Test	Mean Difference	t-value	p-value
R Tibial(Lat) ms	4.62±1.35	4.01±1.19	0.60±1.14	2.98	0.006,S
R Tibial(Amp) mv	4.71±3.85	10.43±6.38	5.71±6.17	5.24	0.0001,S
R Tibial(CV) ms	50.61±17.65	49.89±15.55	0.72±21.25	0.19	0.848,NS
L Tibial(Lat) ms	4.75±1.51	4.22±1.03	0.53±1.43	2.06	0.048,S
L Tibial(Amp) mv	5.80±5.87	9.71±5.12	3.91±7.71	2.82	0.008,S
L Tibial(CV) ms	49.52±21.79	48.22±11.16	1.29±19.95	0.36	0.720,NS

neuropathy, on the contrary, lacks demyelinating features and shows a decrease in distal compound muscle action potentials (CMAPs) and SNAPs[10]. In nearly all cases of GBS, there is impairment in MNC, Compound motor action potential was affected in 71-100 % of patients, distal motor latency was affected in 65-100 % of patients and conduction velocity was affected in 52-57% of patients[13,16].

As per our study findings, when clinical intervention occurred inside the first week of the onset of GBS symptoms, intravenous-immunoglobulin (IVIG) infusion, there was a significant improvement seen in the amplitude of right median and ulnar nerves whereas there was significant improvement in amplitude and distal motor latency of right peroneal nerve, additionally notable improvement was seen in amplitude and distal motor latency of bilateral tibial nerves suggesting a recovery in motor nerve function. In a follow-up study conducted after two weeks, Kuwabara *et al.* documented that the electrophysiological changes had returned to normal[17].

The systemic review and meta-analysis conducted in 2023 suggested that both intravenous immunoglobulins (IVIG) and plasma exchange (PE) have similar curative effects, relapse rates, decrease in hospitalization and ventilation duration and the potential risk of complications. However, the analysis suggested that IVIG is easier to use and hence can be preferred for treating patients with severe symptoms of GBS[18]. Our study results are in accordance with this finding wherein we documented statistically significant improvement in amplitude and distal motor latency in motor nerves by nerve conduction studies.

It is observed that improvements in NCS parameters correspond with clinical improvement after IVIG. Usually, the clinical outcome of any GBS patient is likely to be correlated with the results of electrophysiological nerve conduction studies conducted before and after IVIG treatment. This approach brings valuable insights into the percentage of involvement in motor nerves, allowing clinicians to make informed and early treatment decisions for the patient. Timely diagnosis and prompt initiation of treatment have the potential to boost the prognosis for all subtypes of GBS.

Limitations: The GBS patients were not divided into subtypes. The sample size is comparatively less and a larger sample size with serial nerve conduction studies will provide a more accurate estimate of the percentage of motor nerves involved. The study did not cover the pediatric age group patients., But, this can be added in future studies to improve results across a wider age range. Moreover, although it was not used in the study, a different statistical method might be applied to assess a composite score of several indications, which could advance the field.

CONCLUSIONS

The present study highlights the clinical outcome of GBS patients is strongly supported by the findings of

the electrophysiological study. Especially, the treatment protocol involving IVIG initiation within the first week of onset of symptoms shows evidence of reversible conduction in motor nerve's CMAP and DML. This is evident from the improvement observed in the potentials of our motor nerves. In principle, the findings underscore the crucial role of timely diagnosis and the prompt initiation of treatment in enhancing the prognosis for individuals with all subtypes of GBS.

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