PLASMAPHERESIS IN NEUROLOGICAL DISORDERS: EXPERIENCE FROM A TERTIARY CARE HOSPITAL IN NORTHWESTERN PAKISTAN

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ABSTRACT

Background: This study assesses plasmapheresis use for neurological disorders in a Northwestern Pakistan hospital, highlighting its efficacy for Guillain-Barre Syndrome (GBS) and Neuromyelitis Spectrum Disorder (NMOSD) in the local context. Further research is warranted to explore its long-term outcomes in diverse neurological conditions.

Objective: The study aimed to evaluate the utilization, indicators, and prevalence of plasmapheresis as a therapeutic intervention in a tertiary care hospital in Northwestern Pakistan.

Methods: A retrospective analysis was conducted on the medical records of patients who underwent plasmapheresis for neurological disorders for six months, from 1st March 2022 to 31st August 2022. Data regarding demographic characteristics, clinical diagnosis, indications for plasmapheresis, treatment outcomes, and prevalence rates were collected and analyzed.

Results: A total of 59 patients with various neurological disorders were included in the study. The most common neurological disorders were Guillain-Barre Syndrome (GBS) and Neuromyelitis Spectrum Disorder (NMOSD), accounting for 82% of the cases. Moreover, 54 % of patients were male, and 46 % were female. It was also observed that while around 13 % of the patients belonged to Peshawar, the rest of the patient population was from outside the local community.

Conclusions: A variety of neurological disorders require plasmapheresis as a treatment option, with Guillain-Barré Syndrome and Neuromyelitis Optica Spectrum Disorder being the most common cases in our setting. This emphasizes the significance of plasmapheresis as an effective treatment for these conditions, especially in comparison to immunoglobulin therapy, which is more commonly used in high-income countries. Further research and prospective studies are needed to explore the long-term outcomes and efficacy of plasmapheresis in managing various neurological disorders.

Keywords: Plasmapheresis, Neurological diseases, Guillain Barre Syndrome, Neuromyelitis Optica Spectrum Disorder, Autoimmune diseases, Therapeutic plasma exchange

INTRODUCTION

Neurological disorders can pose significant challenges for individuals, their families, and healthcare systems worldwide.[1] These disorders encompass a range of conditions that can result in substantial physical, cognitive, and emotional impairments.

Some of the most prevalent neurological disorders include autoimmune conditions such as Guillain-Barré syndrome and multiple sclerosis, as well as neuromuscular disorders like myasthenia gravis and chronic inflammatory demyelinating polyneuropathy[2,3].

A recent neurology study conducted at the University Clinical Centre Tuzla sheds light on the prevalence of different neurological diseases. According to the study, Guillain-Barré syndrome was the most common condition, affecting 37.7% of patients, followed by chronic inflammatory demyelinating polyneuropathy (CIDP) at 23.4%, multiple sclerosis (MS) at 11.7%, and myasthenia gravis at 10.4%. The study found that male patients slightly outnumbered females, accounting for 54.5% of cases, with an average age of 51[2].

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Another study conducted in Europe and North America has highlighted the incidence of Guillain-Barré syndrome (GBS) in different populations. The study found that GBS affects 1 to 2 cases per 100,000 adults annually and 0.4 to 1.4 cases per 100,000 children. The incidence of the condition increases with age and is slightly more common in males than females[4].

In recent years, plasmapheresis has emerged as a promising adjunctive therapy in the management of complex neurological disorders. This treatment involves removing and replacing a patient's blood plasma in order to eliminate harmful antibodies that contribute to the progression of the disease. Plasmapheresis has shown great promise in improving symptoms and outcomes for patients whose symptoms have not responded to traditional treatments[3].

This process is designed with the objective of eliminating pathogenic antibodies and inflammatory mediators that play a pivotal role in driving the disease process. This makes it an effective and focused treatment option for patients[2,3]. This technique has shown promise in not only ameliorating acute neurological exacerbations but also in inducing long-term remission in certain cases[4-9].

Although plasmapheresis is widely recognized as an important treatment, we still lack a clear understanding of how it is used, when it is needed, and how common it is in different regions. Factors like location, genetics, and the environment add complexity, affecting both disease patterns and treatment choices. Therefore, it is essential to conduct local studies to better understand how plasmapheresis works in real-life settings for neurological disorders. This will help create more tailored and effective treatment approaches.[10,11].Northwestern Pakistan, with its distinct demographic and environmental characteristics, represents a unique backdrop to study the utilization of plasmapheresis in neurological disorders.[11,12]

It was the first time that plasmapheresis services were started in the hospital. We aim to study the variety and burden of diseases requiring plasmapheresis, as well as report any adverse complications related to the procedure.

METHODS

This retrospective observational study utilized medical records from Neurology department, with the approval of the Ethical Review Board, in a tertiary care hospital in Peshawar, Pakistan, to evaluate the utilization, indicators, and prevalence of plasmapheresis as a therapeutic intervention for neurological disorders. The study period spanned from 1st March 2022 to 31st August 2022 for a total of 6 months. A sample size of 59 was calculated based on a confidence interval of 95%, 7% margin of error, and expected burden of neurological disease as 5%. The data collection process involved the extraction of relevant information from the medical records, including demographic characteristics, clinical diagnoses, indications for plasmapheresis, treatment outcomes, and prevalence rates. A standardized data collection form was used to ensure consistency and accuracy in the data extraction process.

The inclusion criteria for this study encompassed all patients who underwent plasmapheresis for neurological disorders during the six months period. Ethical considerations were followed diligently, adhering to the guidelines and regulations of the research institution. Patient confidentiality and privacy were given utmost importance throughout the study. Individuals who were pregnant or lactating, had severe cardiovascular complications, coagulation disorders, uncontrolled infections, or hypersensitivity to plasma or replacement solutions were excluded.

Once the data were collected, a descriptive analysis was conducted to summarize the demographic characteristics of the patients, such as age and gender distribution. The clinical diagnoses and indications for plasmapheresis were reported in percentages to provide an overview of the neurological disorders and their respective indications for plasmapheresis. The prevalence of plasmapheresis utilization in neurological disorders was calculated by dividing the number of patients who underwent plasmapheresis by the total number of patients with neurological disorders during the six-month study period. We evaluated the mean age of each disorder, along with geographical distribution. The gender ratio, and percentage distribution was also evaluated for the said disorders.

RESULTS

A detailed analysis of the data showed the frequency of autoimmune diseases, with one case reported for Marburg's syndrome, Acute Disseminated Encephalomyelitis (ADEM), and Thrombotic Thrombocytopenic Purpura (TTP) each. N-methyl-D-aspartate (NMDA), Multiple Sclerosis (MS), Sequential Optic Neuritis, and Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) each had just two cases reported, whereas four were reported for Myasthenia Gravis. Myasthenic Crisis, Neuromyelitis Optica Spectrum Disorder (NMOSD), and Longitudinally Extensive Transverse Myelitis (LETM) had five, nine, and eleven patients, respectively. GBS had the highest number of them all, with nineteen reported cases.

Table 1: The frequency (in numbers), percentage, and mean age (in years) for all the neurological disorders found in this study

Diseases	Frequency	Percentage	Gender		Mean Age (years)
			Male	Female	
Marburg's Syndrome	1	1.69%	0	1	55
Acute Disseminated Encephalomyelitis (ADEM)	1	1.69%	0	1	27
Thrombotic Thrombocytopenic Purpura (TTP)	1	1.69%	1	0	17
N-methyl-D-aspartate (NMDA)	2	3.34%	0	2	18
Multiple Sclerosis (MS)	2	3.34%	2	0	22
Sequential Optic Neuritis	2	3.34%	0	2	53.5
Chronic inflammatory demyelinating polyneuropathy (CIDP)	2	3.34%	2	0	60
Myasthenia Gravis	4	6.78%	1	3	39.3
Myasthenic Crisis	5	8.47%	3	2	43.3
Neuromyelitis optica spectrum disorder (NMOSD)	9	15.25%	2	7	36.9
Longitudinally Extensive Transverse Myelitis (LETM)	11	18.64%	4	7	36.3
Guillain-Barre Syndrome (GBS)	19	32.2%	16	3	39.3

Table 2: Complications of plasma exchange/adverse effects

Local Complications	patients (%)	Systemic Complications	patients (%)
D/L site infection	2 (3.39%)	Fever	2 (3.39%)
D/L site bleeding	2 (3.39%)	Hypotension	3 (5.08%)
DVT	2 (3.39%)	Respiratory arrest (requiring ventilatory support)	4 (6.78%)
Pneumothorax	1 (1.69%)	Hypocalcemia	2 (3.39%)
		Seizures	1 (1.69%)
		Renal failure	1 (1.69%)
		Death	3 (5.08%)

Upon further analysis we found that the Marburg's Syndrome, Acute Disseminated Encephalomyelitis (ADEM), and Thrombotic Thrombocytopenic Purpura (TTP) each accounted for 2% of the total cases. N-methyl-D-aspartate (NMDA), Multiple Sclerosis (MS), Sequential Optic Neuritis, and Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) were 3% of the total patients each. Furthermore, Myasthenia gravis reported 7% of cases. Myasthenic Crisis, Neuromyelitis OpticaSpectrumDisorder (NMOSD), and Longitudinally Extensive Transverse Myelitis (LETM) each accounted for 9%, 15%, and 19% of the total patients, respectively. GBS had the highest percentage, i.e., 32%

Out of 59 patients, 46% (27) were females, whereas 54% (32) were males.

Patients came to our facility from different regions ranging from Afghanistan in the far west to Chitral in the northeast. We had only one patient from Tirah valley, two from Bannu, Dara, Swabi, Karak, and Chitral each. Kohat, Charsadda, Bara, and Malakand had three patients each. We had four patients each from Kurram agency, Dir, and Mardan, five from Afghanistan, six from Khyber agency, and thirteen from Peshawar.

DISCUSSION

The findings of our study provide crucial insights into the utilization and prevalence of plasmapheresis in the management of neurological disorders at our tertiary care hospital in Northwestern Pakistan. Among the 59 patients included in the study, we observed a diverse array of neurological conditions, with Guillain-Barre syndrome and Neuromyelitis Spectrum Disorder (NMOSD) emerging as the most common, jointly accounting for an impressive 82% of the cases. The gender distribution revealed a slight male predominance, with 54% of the patients being male and 46% female. Intriguingly, a substantial proportion of patients, approximately 87%, sought treatment from outside the local community, underscoring the significance of our hospital as a regional referral center for complex neurological cases. Our study also brought to light the unique clinical presentations of certain disorders, with Marburg's syndrome and Acute Disseminated Encephalomyelitis (ADEM) being particularly rare, represented by only one female patient each. Additionally, we observed specific gender disparities in diseases such as Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), Multiple Sclerosis (MS), and Thrombotic Thrombocytopenic Purpura (TTP), where male patients constituted the entirety of reported cases. This comprehensive exploration of the patient population and disease distribution significantly contributes to our understanding of plasmapheresis utilization in Northwestern Pakistan and holds paramount implications for optimizing treatment strategies, enhancing patient outcomes, and furthering neurologic care in our region.

Several major randomized-controlled trials have shown Therapeutic Plasma Exchange (TPE) as an effective treatment modality in Guillain-Barre Syndrome (GBS) patients[14]. The treatment modality also has a strong level of established effectivity according to the American Academy of Neurology (AAN)[15] and American Society for Apheresis (ASF)[16] guidelines. In our patients, the Acute Inflammatory Demyelinating Polyneuropathy (AIDP) variant showed good response to TPE, compared to the Acute Motor Axonal Neuropathy (AMAN) and Acute Motor Sensory Axonal Neuropathy (AMSAN) variants. Also, the young patients and the patients without bulbar symptoms responded better as compared to those who were older or developed bulbar symptoms at the onset of the disease process. Our study showed about 32 % of our patients underwent Therapeutic Plasma Exchange for the treatment of Guillain-Barre Syndrome while studies at other international centers mention the percentage to be 34 % and 66 %[17,18].

The patients with Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) presented late in their disease but still showed some improvement with Therapeutic Plasma Exchange (TPE) and were discharged on immunosuppressants. The effectivity of TPE in patients with CIDP was documented in a randomized double-blind placebo-controlled trial[19,20]. Around two-thirds of patients suffer a relapse after plasma exchange and hence require a maintenance form of plasma exchange or other long-term immune modulatory medications[21]. Our study showed about 3.4 % of patients underwent plasma exchange therapy for the treatment of Chronic Inflammatory Demyelinating Polyneuropathy while studies at other international centers mention the percentage to be around 4.3 % and 11 %[17].

There are multiple studies mentioning the beneficial effect of Therapeutic Plasma Exchange (TPE) in Myasthenia Gravis patients[22,23]. Some studies label TPE and intravenous immunoglobulin to be equally efficacious, while other studies suggest TPE to be more effective, with significant improvement in respiratory function[21,24]. Our study revealed that about 8.6 % of our patients underwent TPE for the treatment of Myasthenic crisis while studies at other international centers mention the percentage to be around 15.3 % and 21 %[17,18]. In a study comparing patients treated with TPE before thymectomy with those managed with thymectomy alone, the patients who underwent TPE had a lesser number of crises in the coming months, along with high post-operative remission at 5–7 years[25]. Our study showed about 6.8 % of our patients underwent TPE before thymectomy while studies at other international centers mention the percentage to be 9.8 % and 12 %[18].

New studies indicate the presence of anti-Myelin Oligodendrocyte Glycoprotein (MOG) antibodies in about 50% of the patients with Acute Disseminated Encephalomyelitis (ADEM)[21]. The patient presented to us with an altered mental status and encephalopathy which progressed to coma; however, other patients can also present with hemiparesis, quadriparesis, and ataxia as well[26]. We treated the patient initially with intravenous methylprednisolone. The patient showed a mild response to it. Afterwards, Therapeutic Plasma Exchange (TPE) sessions of the patient were started, to which he showed some improvement. In a case series, some patients with ADEM who did not respond to corticosteroids improved significantly with TPE[27]. Our study showed about 1.7% of our patients underwent TPE for the treatment of Acute Disseminated Encephalomyelitis while studies at other international centers mention the percentage to be 1.09 % and 3.17 %[17.]

In this spectrum of disorders, we received patients who had spinal cord syndrome with positive aquaporin and anti-Myelin Oligodendrocyte Glycoprotein (MOG) antibodies, as well as patients with sequential optic neuritis who had negative serology. The patients initially received intravenous methylprednisolone, which was followed by Therapeutic Plasma Exchange (TPE). Few patients showed a good response, while in some patients, the response was clinically very mild. Studies have shown that early TPE in such patients can yield positive results in terms of recovery[28,29,30]. Our study revealed that about 15.5% of our study group comprised of Neuromyelitis Optica Spectrum Disorder (NMOSD) patients, while the same figure in international studies is around 3.17%[18].

There is evidence about the usefulness of Therapeutic Plasma Exchange (TPE) in Multiple Sclerosis (MS) patients. There were three patients with Multiple Sclerosis treated within our study. Two of the patients were in their acute or relapse phase, while one of the patients had the Marburg variant of Multiple Sclerosis. The patient showed mild improvement with the TPE. According to the American Academy of Neurology (AAN) and American Society for Apheresis (AFSA) guidelines, TPE is probably an effective adjuvant treatment modality for the severe relapsing form and also in the steroid-unresponsive fulminant forms. However, it is not effective in the progressive forms of multiple sclerosis[21]. 3.4 % of our study group labeled as Multiple Sclerosis underwent TPE, compared to around 3.17 % in international studies[18].

We had two female patients with Anti-N-Methyl-D-Aspartate Receptor (NMDAR) encephalitis. The patients were treated with Methylprednisolone initially, which was followed by Therapeutic Plasma Exchange (TPE). Both patients showed improvement. Ovarian teratoma is found in about half of the female patients with this disease and shows a good response to the treatment when the ovarian tumor is removed[21]. After TPE, the treatment can be further escalated to the use of monoclonal antibodies like Rituximab, etc.[31,32,33,]. Our study showed that about 3.4 % of our patient group underwent TPE for the treatment of NMDA encephalitis, while studies at other international centers mention the percentage to be around 2.3%[17.]

It is important to acknowledge that this study has inherent limitations due to its retrospective nature, such as potential incomplete or missing information in the medical records. Furthermore, as the study was conducted in a single tertiary care hospital, the generalizability of the findings to other settings may be limited. Nevertheless, the utilization of plasmapheresis, along with the observed indicators and prevalence rates, will provide valuable insights into its role as a therapeutic intervention for neurological disorders in the specific context of tertiary care hospitals.

CONCLUSION

It is thus concluded that plasmapheresis is an effective treatment modality that can be used in the management of many different neurological diseases that have an autoimmune basis. It is a lifesaving procedure in certain diseases like Guillain-Barre Syndrome and Myasthenia crisis. The management option can be used in poor countries where there is difficulty arranging intravenous immunoglobulins.

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