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Indications and Long Term Outcomes of Plasmapheresis in Neurological Disorders

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Abstract

Background: Plasmapheresis is the treatment of choice in several immune mediated neurological disorders such as Guillain-Barré syndrome and myasthenia gravis. There are only a few studies from India that have looked in to the outcomes and complications related to therapeutic plasmapheresis in neurological disorders. This study was done to examine the indications, complications and outcomes of plasmapheresis in neurological disorders. *Materials & Methods:* A retrospective study of patients who underwent plasmapheresis for neurological disorders during last five years was done. Demographic, clinical data, indications, complications related to the procedure, clinical outcome and long term follow up data were collected and analyzed. *Results:* Data of sixty patients, who underwent a total of 276 sessions of plasmapheresis were analyzed. Fifty two percent were males and mean age was 45 years. Twenty nine patients (49%) had Acute Inflammatory Demyelinating Polyradiculoneuropathy, 14 (23%) had Myasthenia Gravis and four patients had Acute Disseminated Encephalomyelitis (7%). Other indications were Chronic Inflammatory Demyelinating Polyradiculoneuropathy, transverse myelitis, polymyositis, autoimmune encephalitis, muscular dystrophy, neuromyeltis optica and Febrile infection related epilepsy syndrome. In patients with AIDP, 26 patients (89%) improved. In patients with MG 11 patients (78%) improved. All patients with Autoimmune encephalitis, Polymyositis, Transverse myelitis and Neuromyelitisoptica showed improvement. There was no improvement in patients with Muscular dystrophy and FIRES. Allergic reactions to plasma, intravascular hemolysis and hypotension were the side effects noted which were managed efficiently during procedure. Mild coagulopathy was observed in three patients, but there were no bleeding complications. There were no other significant complications related to procedure. After a mean follow up period of 3 years, 35 patients had complete remission, 10 patients had relapse, 2 patients died whereas 13 patients lost to follow up. *Conclusion:* Plasmapheresis is an effective and safe treatment modality in various immune mediated neurological disorders.

Keywords: Plasmapheresis; AIDP; Myasthenia Gravis.

Introduction

There is increasing evidence for a steady rise in the frequency of autoimmune diseases in the last couple of decades, especially of autoimmune neurological disorders [1]. Reports from India also have shown a significant rise in the prevalence of neuroimmunological disorders in the last decade [2,3]. Although that can be partly explained by the advances in the neuroimaging facilities, studies have shown an increase in admissions related to autoimmune neurological disorders such as Multiple Sclerosis [3] and the spectrum of neuroimmunological disorders is widening [2,4]. Immune mediated encephalitis, acute disseminated encephalomyelitis, myelopathies, and cranial neuropathies like optic neuritis are some of them [4]. The Swedish registry report which retrospectively analysed around 20,000 plasmapheresis sessions for multiple indications stated a very low complication rate of 4.3% [5] The Canadian apheresis registry which reviewed around 1.5 lakh plasmapheresis sessions, stated adverse events occurring in 12% of procedures (mostly minor). Severe events occurred in only 0.4%of procedures [6]. Reports from India have

also shown that therapeutic plasma exchange is an effective and safe modality in neuroimmunological disorders [7,8]. This study was done to examine the outcomes of plasmapheresis in neurological disorders at Amrita Institute of Medical Sciences, a university teaching hospital in Kochi, Kerala, India.

Objectives

To study the clinical outcomes and safety of plasmapheresis in neurological disorders.

Inclusion criteria

All patients who underwent plasmapheresis for neurological disorders during study period (2010-2016) in Amrita Institute of Medical Sciences (AIMS), Kochi.

Materials and Methods

We conducted a retrospective study of patients who underwent plasmapheresis for neurological disorders during 2010-2016 period. Patients were admitted in Neurology department at AIMS. Neurological diagnosis was made by clinical examination and appropriate supporting investigations. Informed consent was obtained patients prior to the procedure. The femoral vein dual lumen temporary catheter was inserted under aseptic precautions. All plasmapheresis procedures were done by dialysis technicians under the supervision of a Nephrologist. Fresenius Medical Care (4008 B) dialysis machines and Plasmaflux PSu 2S (Fresenius Medical Care) plasma filters were used for the procedure. In each session 40 ml/kg plasma was removed. Blood flow was 130ml/minute and intravenous heparin was given at 250 U every 15 minutes to prevent clot formation in the extracorporeal circuit. If there was any contraindications with heparin infusion, procedure was done with intermittent saline push. Blood pressure (BP) and pulse were monitored every 15-30 minute intervals during the sessions and adverse effects were documented. Clinical responses of the patient to plasmapheresis and investigation parameters pre and post procedure were reviewed. Patients were followed up till their last hospital visit. Collected data was analysed using SPSS software version 17.

Results

Data of sixty patients, who underwent a total of 276 sessions of plasmapheresis, were analyzed. Thirty one patients (51%) were males. Mean age was 45 years with a range of 20 to 64 years. Twenty nine patients (49%) had Acute Inflammatory Demyelinating Polyradiculoneuropathy, 14 patients (23%) had Myasthenia Gravis and four patients (7%) had Acute Disseminated Encephalomyelitis. Other indications were Chronic Inflammatory Demyelinating Polyneuropathy, Transverse myelitis, Polymyositis, Autoimmune Encephalitis, Muscular Dystrophy, Neuromyeltis Optica, and Febrile Infection Related Epilepsy Syndrome. Thirty four patients (56%) had no significant co-morbidities at the time of presentation. Twenty two patients (36%) had systemic hypertension and twelve patients (20%) had type 2 diabetes mellitus. Other co morbidities noted were Coronary artery disease, Cerebrovascular

Table 1: Frequency of neurological disorders in the study population

Disease	Number
Guillain-Barré Syndrome	33 (55%)
Acute inflammatory demyelinating polyneuropathy	29(49%)
Acute motor axonal neuropathy	2(3%)
Acute motor and sensory axonal neuropathy	2(3%)
Myasthenia gravis	13(22%)
Acute disseminated encephalomyelitis	4(6%)
Chronic inflammatory demyelinating polyneuropathy	2(3%)
Autoimmune encephalitis	2(3%)
Neuromyelitisoptica	1(1.5%)
Muscular dystrophy	1(1.5%)
Polymyositis	1(1.5%)
Transverse Myelitis	1(1.5%)
Febrile infection-related epilepsy syndrome	1(1.5%)
Multiple Sclerosis	1(1.5%)

Table 2: Complications related to plasmapheresis in the study group

Complications	Rate
Allergic reactions	6 (10%)
Intravascular haemolysis	4 (6%)
Hypotension	2 (3%)
Muscle cramps	2 (3%)
Prolongation of Prothrombin time	3 (4.5%)
Access complications	1 (1.6%)
Death	None

Table 3: Long-term outcome of the study population

Outcome	Number (%)
No relapse	35 (58%)
Relapse	10 (16%)
Lost to follow up	13 (21%)
Death due to various causes	2 (3%)

accident, chronic liver disease, bronchial asthma and seizure disorder.Twenty eight patients (46%) received three sessions of plasmapheresis and twenty nine patients (47%) received six sessions. Plasma was removed on an average of 1600 ml per session. Fifty six patients (93%) received fresh frozen plasma as replacement fluid and four (6%) patients received human albumin. Heparin anticoagulation was used in 52 patients (87%) and heparin free plasmapheresis was done in eight patients (13%).Twelve patients (20%) received IVIG prior to plasmapheresis. Fifteen patients (25%) had a history of past episodes of the disease prior to this hospital admission. Two patients had received plasmapheresis earlier. Four patients (6%) developed seizure during hospital stay. Three patients (5%) developed altered sensorium. During hospital stay 19 patients (31%) needed mechanical ventilation Forty eight patients (80%) had significant clinical improvement after plasmapheresis therapy. There were no deaths during hospital stay. In patients with AIDP, 26 patients (89%) improved. In patients with Myasthenia gravis 11 patients (78%) improved. All patients with Autoimmune encephalitis, Polymyositis, Transverse myelitis and Neuromyelitisoptica improved. There was no improvement in patients with Muscular dystrophy and FIRES. All patients with Myasthenia gravis underwent plasmapheresis for myasthenic crisis. Mild coagulopathy was observed in three patients with mean INR of 1.7. There were no bleeding complications. One patient had access complication as femoral catheter block. None of our patients had hypocalcaemia related major adverse events. There were no other significant complications related to procedure. After a mean follow up period of 3 years, 35 patients (58%) had complete remission, 10 patients (16%) had relapse, 2 patients (3%) passed away due to various reasons whereas 13 patients (21%) were lost to follow up. Relapse rate was low in AIDP (10%), Myasthenia gravis (21%) and ADEM (25%). Relapse rate was high in CIDP (50%) and Autoimmune encephalitis (50%).

Discussion

We studied sixty patients who underwent plasmapheresis for various neurological diseases in our hospital. There was a slight male preponderance (52%). AIDP was the most common cause (48%) followed by Myasthenia gravis (23%) and ADEM (6%). Similar patient profiles were reported by earlier studies done in south India [9,10]. GBS, especially AIDP variant remains the most common neuroimmunological disorder requiring plasmapheresis.

In our study, twenty six patients with AIDP (89%) showed significant clinical improvement after plasmapheresis. The mean number of sessions required was 4.9 (range 3-9). Majority of the patients (55%) required six sessions of plasmapheresis for improvement. Plasmapheresis and IVIg are effective treatment modalities for GBS if given during the first few weeks of disease. Although several studies in the late 1990s showed a slight superiority of IVIg over Plasmapheresis in the treatment of GBS in terms of complications and overall outcomes, recent evidence suggest that plasmapheresis may be cheaper, but equally effective and safe as IVIg [11-14]. It is also interesting to note the two Cochrane reviews published in 2012. Raphael et al in their review opined that there was moderate quality evidence showing significantly more improvement with plasma exchange than supportive care alone in adults with Guillain-Barré syndrome without a significant increase in serious adverse events [15]. Another review suggested that the mean difference (MD) of change in a seven-grade disability scale after four weeks was not significantly different between the two treatments [16]. There was no benefit in using a combination of IVIg and Plasmapheresis [16]. Although IVIg is an easier treatment option, the cost of therapy is also prohibitively high for a large majority; especially in a country like India. Hence plasma exchange still remains treatment of choice for them. Plasma exchange has been accepted as a relatively cheaper and effective treatment for myasthenic crisis, especially in India [17,18]. Like other studies, the second most common cause in our study was was MG, which accounted for 23% of our study group. All of our patients had undergone plasmapheresis for myasthenic crisis. Seventy nine percent of the patients with myasthenic crisis recovered. Average number of sessions required was 3.6. Although mild prolongation of prothrombin time was observed in three patients, there were no major bleeding complications. The third common condition in the study group was ADEM, which accounted for 6.7%. ADEM is often treated with high-dose intravenous corticosteroids, to which it usually responds. However, therapeutic plasma exchange has been found to be useful in severe cases of ADEM that is not amenable to medical management [19]. The response rate was 50% in this study, but the sample size is too small to reach any meaningful conclusions. Among two patients with CIDP one patient showed clinical improvement. Only 10 patients (16%) in the whole study group showed relapse in 3 year follow up. We observed lower rates of relapse in AIDP (10%), Myasthenia gravis (21%) and ADEM (25%). However, the rate of relapse was high in CIDP (50%) and Autoimmune encephalitis (50%).There was no improvement in patients with Muscular dystrophy and FIRES. We

did not encounter any major complications during the procedures. Allergic reactions to plasma were found in 10% of patients and hemolysis in 6% of patients. Hypotension was found in 3% of patients and coagulopathy was found in 4% of patients. There were no deaths related to procedure. Our study thus support that fact that plasmapheresis is a safe procedure.

Conclusion

Plasmapheresis is an effective and safe treatment modality in various immune mediated neurological disorders. There was high rate of remission followed by plasmapheresis in common neurological conditions like GBS and Myasthenia crisis. Although not as effective as the above procedures, it was also found to be effective in CIDP and ADEM. We did not encounter any major complications and even the rates of minor complications were very low. We suggest that plasmapheresis is a safe and effective procedure in neuroimmunological disorders.

Limitations of the study

This was a retrospective study done by record review. Moreover, the sample size was also limited to reach a concrete conclusion especially in rare disorders.

Conflicts of interest

The authors declare no conflict of interest.

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