Plasmapheresis in Neurological Disorders: Frequency and Type of Adverse Effects Associated with this Procedure in Atertiary Care Hospital in Pakistan

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ABSTRACT

Objective: To determine the frequency and type of adverse effects associated with plasmapheresis among the patients with neurological disorders at a tertiary care hospital in Pakistan.

Study Design: Prospective longitudinal study.

Place and Duration of Study: Pak Emirates Military Hospital, Rawalpindi Pakistan, from Jan to Jun 2019.

Methodology: The sample population comprised 150 patients with various neurological disorders requiring plasmapheresis at a tertiary care hospital in Rawalpindi, Pakistan. The consultant neuro physician diagnosed the underlying disorder, and a management plan of plasmapheresis was given after the departmental meeting. The presence of adverse effects was observed during the session of plasmapheresis till 48 hours after the session.

Results: Out of 150 patients with neurological illness undergoing plasmapheresis at our department, 18 (12%) developed one or more adverse effects due to the procedure, while 132 (88%) did not experience any adverse effects. The mean age of the patients was 30.2 ± 2.698 years. GB syndrome 61 (40.6%) was the commonest disease for which plasmapheresis was done. Allergic reaction 4 (2.6%) was the commonest side effect among the patients undergoing plasmapheresis, followed by abdominal pain 3 (2%). 146 (97.4%) patients were shifted toward, and 4 (2.6%) required intensive care unit admission after the procedure due to complications. Mortality due to this procedure was nil in the given period.

Conclusion: Plasmapheresis is a relatively safe procedure for neurological illnesses with an immunological basis. Patients should be told about the common adverse effects they could face during the procedure especially allergic reactions and abdominal pain. The treating physician should also have detailed knowledge regarding the untoward effects of this procedure.

Keywords: Adverse effects, Neurology, Plasmapheresis.

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INTRODUCTION

Neurological diseases have been passing through the phase of evolution from a diagnostic point of view and the management aspect.[1] Many disorders that previously remained underdiagnosed or hidden have been diagnosed routinely due to the advent of advanced radiological modalities and sophisticated laboratory investigations available.[2] Same is the case with management plans for these disorders. Due to advancements in understanding the aetiology of illnesses, targeted therapies have evolved for various illnesses. Plasmapheresis is one of these modalities that has been in practice for years.[3]

Sometimes basis of neurological illness is purely neurological or involves the nervous system, but in many cases, there are other etiopathogenic explanations of neurological disorders. They may be vascular, immune-based, drug-induced, infective or neoplastic. In each case, in addition to the management of neurological manifestations, exact treatment of the underlying aetiology is necessary to achieve the desired results. Various methods have evolved during the past few years in this aspect. Steroid therapies, plasmapheresis and intravenous immunoglobulin have been a few methods which have been used in this regard to managing the disorders with an immunological basis, either autoimmune or secondary to some other process.[4-6]

Plasmapheresis has been in clinical use for various disorders for years now. Despite its efficacy in immune-based disorders and quick response in the acute phase of many illnesses, it has certain untoward effects, which should be in knowledge by the treating physician and the patient to manage them effectively. A recent study done in the west revealed that neurological disorders were the second most commonest group of disorders for which this modality was used as treatment. Only 4.3% of the patients had adverse effects, and serious adverse effects were even less common.[3] A study done in India, which is our neighbour and a developing country like us, concluded that

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therapeutic plasma exchange is an efficacious treatment for patients of myasthenia gravis and overall safety is also acceptable.[7] Another similar study on patients with neuromyelitisoptica produced positive results stating this treatment is safe and reliable.[8] A large study on both neurological and non-neurological patients revealed that adverse reactions occurred only in 9% of the patients and were not very severe or alarming.[9] All of the literature analysis done in this regard from the studies done in other countries conclude that this therapeutic procedure has high efficacy in most immune-based disorders, and the side effect profile is acceptable.

Plasmapheresis is an operator dependent and relatively expensive technique, especially for a third world country like Pakistan. However, it is less costly than intravenous immunoglobulin but still far more expensive than steroids.[10] Usually the institution has to pay the cost of it if the patient is entitled or the patient himself in case of non-entitlement. An enthusiastic physician is usually interested in the response of illness to this illness and can ignore the adverse effects. However, both patient and physician can also relate some untoward effects of this procedure to the primary illness, worsening the situation. Unfortunately, no data has been available on the local population regarding this aspect of plasmapheresis. Therefore, we planned this study to look for the frequency and type of adverse effects related to this procedure among the neurological patients of our set-up.

METHODOLOGY

This Prospective longitudinal study was conducted at the Neurology Department of a Tertiary Care Hospital, Rawalpindi, from January to June 2019. A non-probability consecutive sampling technique was used to gather the sample. The sample size was calculated using the WHO sample size calculator. The population proportion of 4.3%.[3] Screening was performed on all the patients with neurological illnesses undergoing plasmapheresis at our department.

Inclusion Criteria: All the patients between the age of 12-65-years undergoing plasmapheresis for any neurological condition were included in the study.

Exclusion Criteria: Patients with a past or current history of any dementia or delirium or with a past or current history of substance use were excluded from the study. Patients undergoing this procedure due to some illness other than neurological illness were also not included in the study. Pregnant women or patients with uncontrolled co-morbid disorders like DM HTN, IHD etc., were also excluded from the study.

Patients with neurological illnesses admitted to ICU were also not approached to be enrolled in this study. Ethical approval via letter no A/28/EC/106 for the study was obtained from the Ethical Review Board Committee of the hospital. After written informed consent, subjects were provided with a detailed description of the study and were inducted into the study. Before this procedure, proper clinical and laboratory investigations like ECG, chest x-ray, cardio-respiratory status, and serology were carried out. Anti-coagulation with citrate was systematically used. The plasma removed during the session was replaced with isotonic sterile saline to make up one-half of the volume and with 5% purified human albumin and fresh frozen plasma to complete it. Careful monitoring of hemodynamic parameters was done, and complications during or following TPE were rapidly recognised and reverted by rationale interventions of the medical staff that assisted the procedure. Calcium replacement with 10 ml of 10% Calcium Gluconate was infused over 15 min approximately halfway through the procedure to avoid citrate toxicity. Patients were observed and asked about the adverse effects during the procedure till 48 hours after the procedure.[11-13] Outcome was classed as patients returned without any significant event due to this procedure, shifted to ICU, or died during or soon after the procedure due to any lethal complication but not due to underlying illness or any other cause. The socio-demographic data and the adverse effects faced by the patients participating in the research were entered in a structured Performa specially designed for this study.

All statistical analysis was performed using the Statistics Package for Social Sciences version 24 (SPSS-24). Mean and standard deviation for age were calculated for the study participants. In addition, frequency and percentages for gender, type of illness, and all the complications recorded during the study were calculated. Similarly, percentages were calculated regarding the three parameters of outcome already mentioned in the methodology.

RESULTS

A total of 153 patients undergoing plasmapheresis due to the neurological condition were approached to participate in the study. One did not give informed consent to participate in the study. The diagnosis of one patient was not clear. One patient was mentally disabled. A total of 150 participants who had

completion of the plasmapheresis session were included in the final analysis. 99 (66%) were male, while 51 (34%) were females. The mean age of the patients was 30.2 ± 2.698 years. Table-I showed the general characteristics of the patients. Variants of GB syndrome were the commonest disorders (61, 40.6%), for which this procedure was adopted as a management plan in our department.

Table-I: Characteristics of study participants undergoing plasmapheresis due to neurological conditions (n=150).

Characteristics	n (%)
Age (Years)	
Mean ± SD	30.2 ± 2.698
Range (min-max)	12 - 59 (Years)
Gender	
Male	99 (66%)
Female	51 (44%)
Neurological condition	
Variants of Gullian Barre Syndrome	61 (40.6%)
Chronic Inflammatory Demyelinating Polyneuropathy	18 (12%)
Myasthenia Gravis	18 (12%)
Neuro-Myelitis Optica Spectrum Disorders	16 (10.6%)
Transverse Myelitis	13 (8.6%)
Thrombotic Thrombocytopenia Purpura/Haemolytic Uremic Syndrome	11 (7.3%)
Acute Disseminated Encaphlo-Myelitis	08 (5.3%)
Autoimmune Encephalitis	03 (2%)
others	02 (1.3%)

Table-II showed that Allergic reaction 4 (2.6%) was the commonest adverse effect faced by the target population, followed by abdominal pain 3 (2%).

Table-II: Adverse effects faced by the patients during or after the plasmapheresis (n=18).

Adverse Effects	n (%)
Allergic reactions	04 (22.2%)
Abdominal pain	03 (16.7%)
Chest pain	02 (11.1%)
Dysesthesia	02 (11.1%)
Convulsions	01 (5.6%)
Fever	01 (5.6%)
Hypotension	02 (11.1%)
Nausea/headache/vertigo	02 (11.1%)
others	01 (5.6%)

The overall outcome was satisfactory as 146 (97.4%) patients were shifted to the ward soon after the procedure without any significant event, while 4 (2.6%) needed ICU admission due to complications of this procedure. Not a single patient died due to this procedure in the study period (Table-III).

Table-III: Outcome of patients put underwent plasmapheresis in neurology department (n=150).

Shifted to Ward	Shifted to Intensive Care Unit	Deaths due to Complication of Procedure
146 (97.3%)	4 (2.7%)	None

DISCUSSION

There is hardly any medicine or procedure in medical science which is completely hazard-free. The same is the case with the plasmaphresis.[14,15] Whenever any procedure is introduced in the routine patient management, it goes through many trials. Unfortunately, most medications and procedures have been tried on western samples before being adopted by developing countries like ours, where infrastructure regarding these trials is lacking. The minimum effort which could be done in this regard with limited clinical resources is conducting the studies on patients with various study designs to get the results that could apply to our population. We have been using plasmapheresis extensively in many neurological and non-neurological conditions with some immune basis. However, no effort has been made to determine the number and type of untoward effects and complications faced by the patients during this procedure. This study was an effort to look into this phenomenon. To remain focused on this aspect, response to underlying illness was not part of the study design. Instead, all attention was given to the adverse effects faced by the patients during or soon after the procedure.

Most of our patients suffered from minor adverse effects, and that too vanished with time without much effort. These results were per the studies done in the west regarding this procedure. The allergic reaction was the commonest complication faced by our patients, followed by abdominal pain.

GBS with many variants was the commonest clinical condition for which the patients underwent plasmapheresis in our study. On the other hand, Myasthenia gravis was the second most common disease. This trend was the same in the research available on this subject by Kumar *et al,* in 2017, and Momtaz *et al,* in 2018.[8,16] The response to this treatment has also been positive, so clinicians prefer this mode of treatment for these illnesses worldwide.

Most of the patients were males in our study. The male to female ratio was 1.94:1. Mixed results were reported in the past studies by Bobati *et al,* in 2017 and Som *et al,* in 2012.[9,17] Some immunological disorders are more common in females. However, our hospital is

from a military organisation that primarily offers free treatment to male soldiers, which automatically increases the chances of males enrolling in the study. Therefore, data from the public hospital may be more generalizable in this regard.

The allergic reaction was the commonest side effect faced by our study participants.[4] patients had this complication. Two out of them were shifted to a critical care setting to cater to the severity of the reaction. One patient with hypotension and one with seizures were also shifted to ICU. All of these recovered from the complication, and no one died. Other mild complications were abdominal pain or nausea etc. The nature of most of the adverse effects faced by the patients undergoing plasmapheresis in our study was mild, and they recovered in less than 48 hours. Similar results have been produced in the past as well on studies done on the patients undergoing this procedure for immune-based disorders by Kumar *et al,* in 2017 and 2018.[7,8]

The overall outcome of our study was quite positive. Despite minor side effects, most patients were shifted back toward and did not show any severe morbidity in the next 48 hours due to this procedure. Only four patients had to be shifted to a critical care facility due to life-threatening complications of this procedure. The death rate was zero due to complications related to plasmapheresis in our study. Similar safety profiles and good outcomes of this procedure have been documented in other studies done by Kumar *et al,* in 2018, Bobati *et al,* in 2017 and Batra *et al,* in 2017.[8,9,18]

Our study design posed a few limitations as well. Specific adverse effects of each disease were not mentioned separately, and a link could not be established that either nature of the disease could contribute to the presence of adverse effects during or after the procedure or not. Moreover, the effect of comorbid was not seen as other illnesses of non-neurological or non-immunological origin present in the patients can affect our study variables. Patients were also not followed up for long to look for any delayed complications or adverse effects. Finally, more serious patients admitted to the critical care setting were omitted, making the result less generalizable. Future studies involving patients from public hospitals and addressing these complications may generate more accurate results.

CONCLUSION

Plasmapheresis is a relatively safe procedure for neurological illnesses with an immunological basis. However, patients should be told about the common adverse effects they could face during the procedure especially allergic reactions and abdominal pain. The treating physician should also have detailed knowledge regarding the untoward effects of this procedure.

Conflict of Interest: None.

Authors' Contribution

SSK: WA: AH: AY: KHN: ZH: Direct contribution.

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