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Therapeutic Plasma Exchange in Neurological Disorders: A Retrospective Study of 24 Cases and 112 Procedures

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ABSTRACT

Background- Therapeutic Plasma Exchange (TPE) is a procedure of removing circulating autoantibodies from the patient's blood. In this procedure, patient's blood is passed through apheresis machine, where plasma and red blood are separated and filtered plasma is removed and discarded and red blood cells are reinfused along with replacement fluid such as plasma or albumin in to the patient. In our study, the role of TPE in treatment of various neurologic disorders is presented as a retrospective study.

Material and Method -The present study was conducted in the Department of Transfusion Medicine, M. Y. H. hospital, a tertiary care center, Indore.In this study, 24 cases were included who have undergone 112 procedures. TPE was done through a central venous access in all the patients. Human albumin and fresh frozen plasma were used as replacement fluid.

Result- Maximum number of cases was in the age range of 21-40 years with male to female ratio of 1.4:1. Total 112 procedures were done on 24 patients. Neurological indications included Guillain-Barre` syndrome (n =09), transverse myelitis (n =06), chronic inflammatory demyelinating polyneuropathy (n =04), neuromyelitis optica (n = 02), HTLV induced myeloneuropathy (n = 01), acute disseminated encephalomyelitis (n =01) and polymyositis (n =01). Out of 24 patients, TPE was frontline therapy in 66.66% of the patients (n =16). During the procedures, complications were recorded in about 5.35% patients. Most of the complications were mild and could be easily managed.

Conclusion- TPE is a safe and effective treatment in neurologic diseases where removal of antibodies from plasma gives immediate improvement to the patient's condition.

Keywords: Therapeutic plasma exchange, Guillain Barre Syndrome.

INTRODUCTION

Therapeutic plasma exchange (TPE) is defined by the American Society for Apheresis (ASFA) 2019 guidelines as "A therapeutic procedure in which the blood of the patient is passed through a medical device which separates plasma from the other components of blood....". Unlike plasmapheresis, TPE involves plasma removal and replacement with a solution such as a colloid solution (e.g., albumin and/or plasma) or a combination of a crystalloid/colloid solution [1].

Therapeutic Plasma Exchange (TPE) is a procedure of removing circulating autoantibodies from the patients blood. In this procedure, patient's blood is passed through apheresis machine, where plasma and red blood are separated and filtered plasma is removed and discarded and red blood cells are

reinfused along with replacement fluid such as plasma or albumin in to the patient.

TPE was first performed in a patient with hyperviscosity syndrome due to multiple myeloma in 1952 [2]. By the 1970s TPE was beginning to be used for immune mediated neurological disorders [3,4]. A number of studies across the world revealed that more than one third of TPE procedures were performed for neurological disorders [5–8] . The American Society for Apheresis (ASFA) publishes regular guidelines on the indications for TPE [9]. In our study, the role of TPE in treatment of various neurologic disorders is presented. Studies performed over the last three decades showed that myasthenia gravis (MG), Guillain-Barre syndromé (GBS) and chronic inflammatory demyelinating polyneuropathy (CIDP) were the most frequently cited indications for TPE followed by multiple sclerosis (MS) [6,8,10–19]

Material and Method - The present study was conducted in the Department of Transfusion Medicine, M. Y. H. hospital, Indore. In this study, 24 cases were included who have undergone 112 procedures of Therapeutic plasma exchange between 2018 to 2019. All the patients were properly analyzed for detailed clinical history, personal (drug intake and adjuvant therapy recieved like IV immunoglobulins and corticosteroid) and past history, indications and need of TPE as front line or second line therapy. Patients not willing to undergo the procedure were excluded.The result and complications of each procedure were recorded. TPE was done through a central venous access in all the patients. Continuous flow cell separator spectra Optia and intermittent flow cell separator Haemonetics MCS 300Plus were used for the procedure. For a single patient, TPE was done every alternate day. Human albumin and fresh frozen plasma were used as replacement fluid and acid citrate-dextrose solution was used as anticoagulant during procedure. Around 1 to 1.5 volume plasma was exchanged depending on patients' heights, weights, genders and hematocrit values.

Central venous catheter was inserted through the jugular vein in all patients. All procedures were performed by senior apheresis technicians under direct supervision of faculty of Transfusion Medicine. All the basic investigations like complete blood count, prothrombin time, serum electrolytes, serum calcium levels were done a day before the precedure was performed. Patients relatives were explained about the risk and complications of procedures in detail and written informed consent was taken before the beginning of the procedure. The patients were continuously monitored for the vital signs and for the complications through out the procedure. the beginning and at the end of each procedure. Patient's total blood volume was calculated as per Nadler's formula [20]. A 10 ml of calcium gluconate was given during the procedure to prevent citrate toxicity in patients with low calcium levels [21]. Depending on the amount of plasma exchanged, the duration of procedure varied from 1 to 3 hours. One plasma volume is exchanged with 3 units of FFP. Albumin is the choice of replacement fluid alternate to FFP but of high cost. The dose was 250 ml albumin in 500 ml of normal saline infusion.

Result-

Table no. 1 - Indications and number of procedures of Therapeutic Plasma Exchange

S. No.	DIAGNOSIS	No. of cases	No. of procedures
1	GBS	09 (37.5%)	42 (37.5%)
2	LETM	06 (25%)	31 (27.68%)
3	CIDP	04 (16.66%)	18 (16.08%)

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4	NMO	02 (8.33%)	08 (7.14%)
5	HTLV induced myeloneuropathy	01 (4.17%)	04 (3.57%)
6	ADEMS	01 (4.17%)	04 (3.57%)
7	Polymyositis	01 (4.17%)	05 (4.46%)
	Total	24	112

In this study, (Table no. 1) Total 112 procedures were done on 24 patients. Neurological indications included Guillain-Barre` syndrome (n =09), transverse myelitis (n =06), chronic inflammatory demyelinating polyneuropathy (n =04), neuromyelitis optica (n = 02), HTLV induced myeloneuropathy (n = 01), acute disseminated encephalomyelitis (n =01) and polymyositis (n =01).

Table no. 2 - Age and gender wise distributions, TPE as frontline and second line therapy, no. of procedures, replacement fluid used and response rate in various cases

Diagnosis	GBS	LETM	CIDP	NMO	HTLV induced myeloneuropathy	ADEMS	Polymyositis	Total
Age								
0-20	00	02	00	00	00	00	00	02 (8.33%)
21-40	05	02	02	01	01	01	01	13 (54.17%)
41-60	04	02	02	01	00	00	00	09 (37.5%)
61-80	00	00	00	00	00	00	00	00
total	09	06	04	02	01	01	01	24
Sex								
Male	04	03	03	02	01	01	00	14(58.33%)
Female	05	03	01	00	00	00	01	10(41.66%)
TPE as front	08	04	03	00	00	00	01	16 (66.66%)

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line therapy								
TPE as second line therapy	01	02	01	02	01	01	00	08(33.33%)
Replcement fluid								
Albumin	03	01	02	01	00	01	00	08(33.33%)
FFP	06	06	02	00	01	00	01	16(66.66%)
Response								
Complete	02	01	00	00	00	00	00	03(12.5%)
Partial	06	04	04	01	01	01	00	17(70.83%)
No response	01	01	00	01	00	00	01	04(16.66%)

*Complete response (CR)-If the neurological deficit of the patients improved completely

*Partial response (PR) - If there was some response, but the neurological deficit did not disappear completely after TPE.

*No response (NR) - if there was not any response after TPE

In our study, (Table no.2) Maximum number of cases were in the age range of 21-40 years with male to female ratio of 1.4:1.

Out of 24 patients, TPE was frontline therapy in 66.66% of the patients (n =16) while as adjuvant therapy in 33.33% of patients.

We used albumin as replacement fluid in about 33.33% patients while FFP was used as replacement fluid in 66.66% patients.

Total 83.3% patients responded with TPE. Out of which, 12.5% patient responded completely while 70.8% patients corresponded partially. All the patients showing respons either complete or partial come under ASFA category I.

Table no. 3 - Complications related to TPE.

Complications	Albumin	FFP	Total
Allergic reactions	01	01	02
Hypertension	00	00	00
Hypotension	00	00	00
Bradycardia	00	00	00

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Chills	00	00	00
Vomiting	01	00	01
Nausea	00	00	00
Abdominal pain	00	00	00
Dyspnea	00	00	00
Fever	01	00	01
Tachycardia	01	00	01
Anxiety	01	00	01
Total	05 (4.46%)	01 (0.89%)	06 (5.35%)

In our study, (Table no. 3) total 5.35% complications were reported during and after the procedures, in which 4.46% complications were during the use of albumin as replacement fluid while 0.89% complications were during the use of FFP as replacement fluid. Allergic reactions are the common side effects with both the replacement fluid.

Discussion- In 2019, the ASFA guidelines[h]defined specific recommendations for the use of TPE, and GBS, CIDP, MG, and NMO were included among the diseases of interest. Of these diseases, the strongest grades of recommendation were assigned to MG and CIDP, whereas the weakest grades were assigned to NMO and GBS [1].Neurological conditions in general are known to account for 44% of the cases in which TPE is indicated [22]. TPE and IVIG both are equally effective for the neurological diseases like GBS etc. The use TPE for the treatment only depends upon the treatment availability, side effect profile and financial condition of the patients. In this study, TPE was indicated for all the conditions studied with maximum 9 cases of GBS followed by 6 cases of Transverse Myelitis.

GBS is an acute inflammatory demyelinating neuropathy [23]. TPE or IVIG are used in patients with severe GBS [24,25]. In our study, 8 out of 9 patients of GBS showed improvement with TPE, one patient died after 2 procedures. The reason for this mortality was the patient present in late stage of the disease with respiratory muscle involvement and needed ventilator support at the time of presentation.

In this study, we came across 6 cases of Transverse myelitis with 31 procedures. 5 patients showed improvement while 1 patient showed progressive disease. In our study, 4 cases of CIPD were included, in which TPE was used as first line therapy in 3 cases and as second line therapy in 1 case. All the treated cases showed improvement with TPE. We came across 2 cases of NMO, in which TPE was used as second line therapy. Out of these 2 cases, one case show improvement while the other case did not showed any improvement.

One case of each HTLV induced polyneuropathy and ADEMS, showed partial response after TPE used as second line therapy in both of these neurological diseases One case of polymyositis performed TPE as first line therapy which did not show improvement even after 4 procedures.

The number of treatment cycles was average five which is consistent with studies that report a total fluid exchange divided five times in MG [28], GBS [22], and CIDP [26,27]. Jiao et al. reported a slightly different range, 2–7 treatment cycles, in 29 patients with NMO [29].

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In this study, hypotension is the most frequent side effect encountered during the TPE procedures. Allergic reactions are the second most common side effect observed. These results are consistent with studies done by T.Moser et al[30], D.Aguirre-Valencia et al [31], A. Lemaire et al [32] and S.L. Clark et al [33] and I. Kleyman et al [34]

We found that total 83.3% patients responded with TPE. Out of which, 12.5% patient responded completely while 70.8% patients corresponded partially. All the patients showing respons either complete or partial come under ASFA category I.

In our study, we found that TPE is very safe procedure with complication risk of 5.35% and most of the complications were with albumin. This is on contrary to other studies[35]. Greater number of complications with 5% albumin may be due to low body weight of patients. Low body weight or debilitated patients well tolerated FFP as replacement fluid as compared to 5% albumin.

Conclusion- TPE is a safe and effective treatment in neurologic diseases where removal of antibodies from plasma give immediate improvement to the patient's condition. According to our results, we concluded that ASFA category I well responded to TPE as compared to other ASFA categories. So, Therapeutic plasma exchange would be a safe and effective alternative treatment for other neurological and non neurological disorders also. TPE has high tolerance and strong safety profile in various neurological diseases.

Abbreviations - GBS-Guillain-Barre`syndrome,TMtransverse myelitis,CIDPchronic inflammatory demyelinating polyneuropathy, NMO neuromyelitis optica, ADEM acute disseminated encephalomyelitis,TPE therapeutic plasma exchange, IVIG intravenous immunoglobulin, FFP fresh frozen plasma

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