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Role of Therapeutic plasma exchange in various medical disorders: An Experience from SMS hospital, Jaipur, Rajasthan

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Abstract

Background: Therapeutic plasma exchange (TPE) is the treatment of choice in many neurological, nephrological, hematological and various other disorders.TPE is used either standalone therapy or in conjunction with other modalities of treatment according to their category of indications. Even though it is safe in experienced hands, there is a major concern about its safety among physicians.

Objectives: To analyze our experience with patients who underwent TPE for various diseases admitted in SMS hospital Jaipur.

Materials and Methods: A Retrospective study of Therapeutic plasma exchange procedures done during a period of 3 years, from Jan 2014 to Dec 2016 by Dept. of Immunohematology and Transfusion medicine in SMS hospital Jaipur. TPE was performed by HAEMONITICS MCS+. Indications, clinical results and technical factors are discussed.

Results: The main indication for TPE were Neurological disorders Guillain-Barré syndrome 13,(25.4%), Myasthenia Gravis, 10,(19.6%), Neuromyelitis optica 11,(21.5%),Chronic Inflammatory Demyelinating Polyneuropathy 2, (3.9%), Longitudinally Extensive Transverse Myelitis 2,(3.9%), TPE was performed for 12 cases of for Antibody mediated transplant rejection (23.5%) and 1 case of Thrombotic Thrombocytopenic Purpura (1.96%) . Age of patients ranged from 13-65 years. Most common age group of patient were (20-40 year).The most common complications were mild allergic reactions (7.8%), paresthesia and/or cramps (3.9%), and hypotension(3.9%) .There was no procedure related mortality.

Conclusion: The analysis of 51 patients and 187 procedures of TPE done by our department shows that the procedure is safe, with only minimal procedure related complications and no mortality.

Introduction

Therapeutic Apheresis is the treatment of diseases through removal or extracorporeal manipulation of blood components or specific blood substances. The process of removing plasma is termed plasmapheresis. Even though plasmapheresis and therapeutic plasma exchange (TPE) often used synonymously in the literature, TPE involves the separation and removal of plasma from corpuscular blood and the replacement of it with various fluids, while plasmapheresis only refers to the removal of plasma [(1)].

It was first employed in 1952 in patients with multiple myeloma to control the hyper viscosity. By the 1970s TPE had evolved as a treatment modality in a number of neurological disorders[2].

The goal of TPE is to remove a pathogenic molecule, protein, or high-molecular-weight complex from plasma. In addition, TPE may be used to provide a deficient normal substance, such as an enzyme or coagulation factor. The frequency and duration of treatment are guided by clinical judgment, although laboratory testing may be helpful for some indications[3].

A variety of possible mechanisms for the actions of therapeutic PE have been proposed, including removal of antibody, alloantibody, immune complexes, monoclonal protein, toxin or cytokine(s) and the replenishment of a specific plasma factor.[(4,5,6,7)]

For most indications, albumin is the preferred replacement fluid, because it is isosmotic with blood and has a smaller risk of adverse reactions and infectious disease transmission than plasma. Plasma is indicated for thrombotic thrombocytopenic purpura (TTP) or if coagulopathy is a concern.

Although there are many case reports of successful treatment of a variety of diseases and conditions by apheresis, there have been few high-quality clinical trials. ASFA(American Society for Apheresis) has published clinical guidelines categorizing the indications for apheresis in various disease states.[(3)]

1.Category I: Disorders for which apheresis is accepted as first-line therapy, either as a primary stand-alone treatment or in con- junction with other modes of treatment.

2. Category II: Disorders for which apheresis is accepted as second-line therapy, either as a stand-alone treatment or in conjunction with other modes of treatment.

3. Category III: Disorders in which the optimal role of apheresis therapy is not established. Decision making for patients should be individualized.

4. Category IV: Disorders in which published evidence demonstrates or suggests that apheresis is ineffective or harmful. Institutional review board approval is desirable if apheresis treatment is undertaken in these circumstances.

In experienced hands, TPE is extremely safe. Although mild allergic reactions, hypotension and fluid-electrolyte imbalance may occur either during or following the procedure, most of these problems are rapidly recognised and reversed. The present paper is based on retrospective study conducted in Dept. of Immunohematology and Transfusion medicine from 2014 to 2016 on TPE procedures done by our department.

Materials and Methods

A retrospectively study was done for all the TPE procedures performed during a period of 3 years from 1st Jan 2014 to 31st Dec 2016 by Dept. of Transfusion medicine SMS hospital Jaipur. Total 51 patients were included in the study after taking consent, who were admitted in SMS hospital for various medical disorders and undergone TPE procedures .Diagnosis and indication for TPE were established with proper clinical and laboratory evaluation. Informed consent was obtained from every patient prior to the procedure.Pre procedural work- up as CBC, coagulation profile, ABG analysis, specific disease markers, ECG, Chest X ray, Serology for mandatory Transfusion transmitted infections (TTI) , blood grouping were done and cardiac and respiratory statuses were assessed.Patients were catheterized the with 12/11.5 no. French dialysis catheter in Internal Jugular, Sub-clavian, Femoral vein in aseptic conditions. Hemonitics MCS+ machine was used for TPE in all patients which is based on intermittent flow centrifugation.Total plasma volume of patient was calculated. Plasma exchange dose was calculate by using

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Plasma volume, Total blood volume, Red cell volume (PV, TBV, RCV). Size of TPE procedure was recorded in terms of patients plasma volume typically 1 to 1.5 plasma volume. ACD- A was used as Anticoagulant. 5% albumin, and group compatible & crossed matched FFP and 0.9% Normal saline was used as replacement fluid in most of the cases.Optimal withdrawal rate was maintained around 60-80 ml/ minute, vitals were monitored regularly during procedure and patients were closely observed for changes in appearance, develop-ment of symptoms (e.g., lightheadedness, nausea, paresthesia, itching etc.), and overall status.Altogether 187 PE procedures were performed on 51 patients. There were 33 male patients and 18 female patients. Age ranged from 13 to 65 years. Number of patients in different age-groups is given in the Table 1.

<20 years	9 (17.6%)
20-40 years	27(52.9%)
40-60 years	11 (21.5%)
>60 years	4 (7.8%)
TOTAL	51

Out of total 51 patients, most common age group of patient was 20-40 years (52.9%) followed by 40-60 years (21.5%) ,< 20 years (17.6%) and > 60 years (7.8%) respectively. (Table-1)

Table-2 : Diseases for which Therapeutic Plasma Exchange was done.

Disease	NO of patient
GBS	13 (25.4%)
NMO	11 (21.5%)
MG	10 (19.6)
AMR	12 (23.5%)
CIDP	02 (3.9)
LETM	02 (3.9)
TTP	01 (1.96)

GBS-Guillain-Barré syndrome, MG-Myasthenia Gravis, NMO-Neuromyelitis optica, CIDP (Chronic Inflammatory Demyelinating Polyneuropathy) LETM-Longitudinally Extensive Transverse Myelitis, AMR- Antibody mediated rejection TTP-Thrombotic Thrombocytopenic Purpura.

Out of total 51 patients who had undergone TPE, the most common indication was GBS 13/51 (25.4%) followed by AMR 12/51 (23.5%), NMO 11/51(21.5% ,Myasthenia Gravis 10/51(19.6%), and less common indications for TPE were (CIDP 2/51),LETM (2/51), and TTP(1/51) which were 3.9%,3.9% and 1.96% respectively.(Table-2)

Complications of TPE

Overall TPE procedures were well tolerated, some procedure related complications were reported like mild allergic reactions, paraesthesia/ cramps, hypotension, thrombophlebitis etc.

Table-3: Complication of TPE

Complication	Patient
Allergic reactions /urticaria	4 (7.8%)
Paresthesia / cramps	2 (3.9%)
Hypotension	2 (3.9%)
Others (Thrombophlebitis)	1 (1.96%)

Among the systemic complications, allergic reactions/ urticaria were most common. 4 patients (7.8%) developed urticarial rash which was managed with IV antihistamines and corticosteroids.

Perioral and/or limb paraesthesia, and muscle cramps were the second most common, occurred in 02 (3.9%) patients. These were mild and transient and never resulted in termination of the procedure.

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Mild transient hypotension (systolic BP < 90 mmHg with only minimal or no symptoms) occurred in 02 (3.9%) patients during at least one of their TPE cycles. This was readily corrected by reducing the pump speed or administering intravenous 0.9% saline. TPE was continued in all of them without any significant symptoms or complications during or after the procedure.

Significant cardiac, renal or hepatic abnormality did not occur during or after the TPE and there was no worsening of associated medical disorders like COPD, diabetes or hypertension in any of the patients. There was no procedure related mortality in any of the 51 patients.

Discussion

We report a series of 51 cases that underwent 187 cycles of TPE over 3 years for various diseases. The major indication for the procedure was GBS (25.4%). In GBS, the recommended treatment options are TPE (ASFA category I indication) or Intravenous immunoglobulin (IVIG) and both have been found to be equally effective and significantly better than the conservative treatment for recovery from the disability[8,9,10]. Because of the ease of administration and less chance of complications, IVIG is preferred by most physicians. According to the report of the therapeutics and technology assessment subcommittee of the American Academy of Neurology on plasmapheresis in 2011, it was found that TPE is extremely safe in experienced hands[11].

Second most common neurologic indication of TPE at our Centre was NMO (ASFA category II).In NMO, TPE is used in steroid resistant cases, if patient is not improving after 5 doses of iv Methyl prednisolone.

Myasthenia gravis is also ASFA category I indication for TPE where results of TPE are superior to other modalities of treatment. The patients with myasthenia gravis (MG) who underwent TPE were in myasthenic crisis and significant improvement has been seen in most of the cases.

In AMR (category II indication) we generally use 1.5 volume of PE to remove around 80-85% of antibodies from plasma.

Although complication can occur, most of these are rapidly recognized and reversed, and are rarely serious. The deaths from TPE have been reported, but have generally been related to underlying or preexisting illness than the procedure itself.

Majority of patients were adults and middle aged (20-40yr age). Old age is also a high risk for the procedure due to higher chance of hemodynamic alterations during the procedure. In a study in patients aged 65 years or older, complications occurred during of treatments, compared to in the younger group.[12]

In our study 4 patients were above 60 years. Of these, 3 patients tolerated the procedure well and in the remaining one the procedure had to be discontinued due to patient refusal.

Allergic reactions, hypotension, nausea-vomiting, paresthesia are the most common complications of TPE which may be seen in around 17% of the procedures. These events are usually mild and resolves with symptomatic treatment or withdrawal of procedure.

The most common complication reported in our study was allergic reactions/ urticarial (7.8%), paresthesia and cramps (3.9%). This is attributed the large fluid shifts between the intra and extra vascular compartments with associated electrolyte imbalances and the citrate content of the anticoagulant which chelates the calcium. Similarly, there was incidence of hypotension in our series in 2 patients (3.9%). First, the vast majority of our patients were having GBS, a disorder prone to have autonomic dysfunction. As we used FFP as the

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replacement fluid which has been associated with higher incidence of hypotension and other adverse events.

The recommended replacement fluid in GBS is 5% albumin in place of FFP [13] but choice of replacement fluid in developing country with limited resource has to strike a balance between what has to be done and how it can be done. so we preferred FFP over albumin owing to the higher cost of the latter. Nevertheless, the high incidence of adverse events in our study is in agreement with some previous studies, including one large study from India [14].

Globally, neurological disorders constitute the leading indication for TPE, followed by hematological, renal and rheumatologic disorders. Hyper viscosity syndrome, cryoglobulinemia, thrombotic thrombocytopenic purpura, hemolytic uremic syndrome and idiopathic thrombocytopenia are some of the leading haematological indications. The complication and mortality rates do not vary significantly among different clinical indications.

Conclusion

Our results shows that TPE is not only a safe and effective treatment but also a cost effective alternative to IVIG, for various immune mediated neurological,hematological, Renal, rheumatological and various other medical disorders.

Most of the patients demonstrated improvement with each cycle of TPE and all procedures were well tolerated with only transient adverse reactions, all of which were successfully resolved with minor or no sequelae. No procedure related mortality was reported in our study.

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