ISSN NO. 2320-5407

Journal homepage:http://www.journalijar.com
Journal DOI:10.21474/IJAR01

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH

RESEARCH ARTICLE

PLASMAPHERESIS: AN EXPERIENCE AT A TERTIARY CARE HOSPITAL.

Sajad Geelani, Mudasir Qadri, Yasir Bashir, Hilal Bhat, Nadeem Shoukat, Nusrat Bashir, Fahim Manzoor, Shuaeb Bhat, Javid Rasool and Aleem Jan.

Manuscript Info

Manuscript History:

Received: 12 May 2016
Final Accepted: 26 June 2016
Published Online: July 2016

Key words:
Plasmapheresis,Therapeutic plasma exchange,Guillan Bare syndrome..

Corresponding Author

Nusrat Bashir.

Abstract

Objectives:- To analyze our experience with 105 cases who underwent plasmapheresis for various disorders.
Materials and Methods:-Retrospective review of Plasmapheresis(PE) was done over a period of 13 years, from july 2015 to August 2002 in a tertiary care centre.
Results:- The main indication for PE was GuillainBarresyndrome(GBS) (31%) . Age of patients ranged from 18-62 years. The most common complications were paraesthesias and/or cramps (36.1%) and hypocalcemia (7%).There was no mortality related to the procedure.
Conclusion:-The analysis of 105 cases of plasmapheresis in our department showed that the procedure is safe, with only minimal procedure related complications and no mortality.

Introduction:-

The word apheresis is derived from the Greek word “aphaeresis” which means “to separate” “take away by force” or to “remove”. The term was originally used by Abel, Rowntree and turner to describe manual plasma exchange, the removal of units of whole blood anticoagulated with heparin followed by centrifugation to separate the blood in to cellular elements and plasma (1). The cellular elements were then mixed with a replacement for the discarded plasma and reinfused.

In common usage, the terms plasma exchange and plasmapheresis are used interchangeably, although the two procedures are different. Plasmapheresis removes a small amount of plasma, usually less than 15 % of the patients blood volume, and therefore does not require replacement of removed plasma. The most common pharesis procedures performed in the United States are those in which plasma is collected from the healthy donors for transfusion or manufacture in to products such as albumin, IV Ig, factor concentrates, and laboratory reagents.

TPE, through the bulk removal and replacement of plasma, removes pathological substances such as pathological antibodies, immune complexes and cytokines. It has been presumed that the removal of these substances represents the major mechanism of action of TPE. However, this mechanism does not explain the length of response seen in some disorders. Additional evidence that TPE may have immunomodulatory effect beyond the removal of immunoglobulins. Reported effects of TPE on immune function include T-cell modulation with a shift from in the Th1/Th2 balance with a shift towards Th2, suppression of IL-2 and IFN-γ production (2,3), and in vitro cultures demonstrating in concanavalin A-induced suppressor functions . (4)

Devices used to perform TPE can be divided in to two broad categories, those that separate the plasma from the cellular components based on size and those that separate components based on density. TPE-utilizing filters are not widely used in the United States. (5). It is important to realize that there is some mixing that occurs at the interface between the layers in the centrifuge. The implication of this is that some platelets may be present in the plasma layer and, depending upon several factors, there may be a resulting loss of platelets during TPE. (5)

Because of the dilution of the plasma by the replacement fluid, the substance of interest can not be completely removed from the circulation. For each 1-1.5 plasma volume exchanged, approximately 60-70% of the substance present in the plasma at the start of the plasma volume will be removed. As additional volumes are exchanged, the absolute amount removed becomes lower, although removal of a fixed 60-70% still occurs. (6). Treating volumes beyond 1.5 plasma volumes removes smaller, less clinically important amounts of pathological substances present in the plasma while prolonging the procedure and exposing the patient to more replacement fluid and anticoagulant. The result is increasing risk of complications without increasing benefit to the patient. There are diminishing returns in treating beyond 1.5 plasma volumes.

The procedure is non selective, removing both normal and pathological plasma components. Significant declines in factor V (FV), FVII, FVIII, FIX, FX and VWF activity occurs (7-9).Activities of FIII, FIX and VWF return to normal within 4 hours after TPE, whereas the remaining coagulation factors achieve pre TPE levels by 24 hours (7). The exception to this is fibrinogen, which reaches 66% of pre-apheresis levels by 72 hours (8). Theoretically, the removal of inhibitors of coagulation could predispose patients to thrombosis, but this has not been demonstrated definitively. (9-10). TPE may also remove medications. Although the effect of TPE on the majority of medications is unknown due to limited pharmacokinetic studies, some drugs have been reported to have significant removal. (11-12). Drugs that have been reported to be removed by the TPE are listed in table1.

It is important to realize that one third of the replacement fluid administered at the beginning of the PE will be present by the end, with the majority having been removed. Administering plasma as a replacement fluid at the beginning of a PE results in exposure of the patient to blood products without benefit.

The most commonly replacement fluid is 4%-5% human albumin in physiological saline. The solution has the advantage of avoiding disease transmission and transfusion reactions (e.g. Transfusion related acute lung injury), both of which can occur with plasma. The main disadvantage of albumin is its expense relative to plasma. This replacement fluid is slightly hypertonic compared with plasma and may therefore expand intravascular volume. This effect can be beneficial in avoiding hypovolemia. Because the albumin replacemt fluid is the most expensive component of the TPE procedure and the use of 100% albumin as a replacement does expand intravascular, some practitioners will use lower albumin concentrations, such as70% albumin and 30% saline. When this is done the, the albumin and saline are alternated, with the majority of albumin being given at the end of the procedure to avoid hypovolemia from redistribution of the crystalloid. It should be noted that the use of albumin and saline has been associated with a greater frequency of hypovolemic reactions compared with using albumin alone (15). The removal of antibodies from the patient can result in false negative tests for infectious diseases, autoantibodies, alloatibodies, and enzyme and coagulation factor activity. Samples for

such testing should be collected before the initiation of TPE. Plasma is used as a replacement fluid in a limited number of disorders, for example, to replace ADAMTS 13 when treating thrombotic thrombocytopenic purpura, to treat coagulation factor deficiencies, and to prevent dilutional coagulopathy in patients with active bleeding (16).

Plasmapheresis is theoretically of greater value than hemodialysis or hemoperfusion in treating poisoning / overdose by substances that are highly bound to proteins or lipids. The successful treatment of poisoning / overdose with plasmapheresis has been reported for a number of agents. Protein bound toxins and drugs for which pheresis has been reported useful include: methylparathion (organophosphate herbicide), Amanita phaloides (mushroom) toxin, L-thyroxine, vincristine and cisplatin. (21). All of the reports evaluating treatment with plasmapheresis are case reports or case series in which many of the patients were treated concurrently with dialysis and /or specific antidotes. There has been no randomized controlled trial comparing plasmapheresis with other treatment modalities. Therefore, recommendations for the treatment of poisoning and overdose are difficult. Plasmapheresis may be used in exceptional cases or under a research protocol . Drugs and toxins for which plasmapheresishas been shown to provide little or no benefit include: barbiturate, tricyclic antidepressants, benzodiazepines, quinine, phenytoin, digoxin, prednisone, tobramycine and propanolol (21).

To perform TPE, it is necessary to obtain vascular access. The Canadian Apheresis study group found that 67% of 5234 TPE procedures could be completed successfully with peripheral venous access alone. (17)

Complications of TPE:-

The frequency of complications associated with TPE reported in the literature is variable and is dependent upon what is or what is not considered a reaction or an expected physiological response. Table 2 summarizes the reported types of reactions and their frequencies in these patients. The reactions reported are, for the most part, mild and easily treated. Risk factors for reactions include the use of plasma as are replacement fluid, (15,18,19) central venous access (18,19) and the presence of neurological disease.(18)

To provide practical evidence based guidance to the apheresis, practitioner and to encourage crititical science in the field of apheresis medicine, ASFA (American society of Apheresis) has published guide lines on the use of therapeutic apheresis in clinical practice. The latest guidelines, published in 2010, are the fifth edition. (20).

Materials and methods:-

We retrospectively reviewed all the Plasmapheresis procedures performed over a period of 13 years, from August 2002 to july 2015 in the department of hematology at a tertiary care centre.

The indications for plasmapheresis were established by proper clinical and laboratory evaluation. Informed consent was obtained from every patient prior to the procedure. ECG, Chest X ray, Serology for Hepatitis B and C, HIV and blood grouping was done. The goal was to perform five exchanges on an alternate day schedule to reach a therapeutic target of 150-200 ml of plasma removed per Kg of body weight.

We did Plasmapharesis on cell separator COBE spectra version 6.5(Fig.1) and all TPE procedures were completed successfully with peripheral venous access alone. Cubital vein was mostly used for access and in only few patients femoral vein was used as an access. All TPE procedures done were dual needle and replacement fluid used was plasma. The procedure was continuous and automated and the anticoagulant used was ACD (activated citrate dextrose).Patients were preloaded with 1.5-2 L of normal saline to get an adequate hydration status before the procedure. The blood pump speed was set at of 60-80 ml/min . Blood pressure (BP) and pulse were monitored at frequent intervals during the sessions and patients were closely observed for development of any complications and overall status The initial part of PE was done with ringer lactate fluid replacement followed by fresh frozen plasma in majority of patients as it is available free of cost at our centre. However, approximately 35 patients received human albumin 20% as replacement fluid. Plasma associated infections were not reported in our unit as patient would be shifted to respective department after completion of PE and could not maintain follow up with our unit.

The cost-effectiveness of plasmapheresis as a therapy varies greatly from disease to disease. For some diseases, plasmapheresis is the only effective front- line therapy treatment, and it significantly improves patient quality of life. For other diseases, plasmapheresis is only of limited utility and does not significantly improve patient quality of life. There may also be alternative therapies available to treat certain diseases. In our center the cost per session of plasmapheresis was approximately rupees 10,000 to 15,000 per session. However, those patients were plasma was used instead of albumin, the cost per session was rupees 7,500.

Results:-

A total of 549 plasmaexchange(PE) procedures were performed on 105 patients. There were (68)male patients and (37)female patients. Age ranged from 18 to 62 years . Age distribution of patients is given in the Table 3.

Various indications for plasmapharesis in our setup is given in Table 4.Most of our patients have been from neurology and nephrology departments. Common indications have been Guillan Bare syndrome (31%),Myasthenia Gravis (23%)Rapidly progressive glomerulonephritis (22%)

The target of our Plasmapheresis protocol was five exchanges in most of our patients, however some of the patients could complete all the five sessions(Table 5) . Various reasons for incomplete PE sessions were significant improvement after less number of exchanges (n = 5,), significant hemodynamic instability during procedure (n = 1), and allergic reactions (n = 4).In some patients seven (15 cases)and six exchanges (5 cases) were also done.All of these patients were more than five sessions of plasmapharesis were done were GBS on ventilatorysupport,however 2 of these case died 2 weeks after last session and 1 patient died 1 month after last session due to ventilator associated pneumonia.

Average volume of plasma removed was 1.5 Liters per session.
Complications related to procedure are given in Table 6.Most common complication was paresthesias(36%) followed by hypocalcemia(7%).

Table 1:- Medications reportedly removed by TPE. (12,13,14,)

Basiliximab	Ceftriaxone	Ceftizidime
Chloramphenicol	Verapam	Diltiazim
IFN-α	IVIG	Pavilizumab
Tobramycin	Propranolol	Rituximab
Propoxyphene	Cisplatin	Vincristine

Table 2:- Reactions due to TPE

Reaction	Couriel and Weinstein (18)	Basic-Jukic (19)	Basic-Jukic (19)
No of TPE procedures	381	4857	4857
Paresthesias	5.5%	2.7%	2.7%
Urtricaria	0.26%	1.6%	1.6%
Hypofibrinogenemia	3.67%	NR	NR
Hypotension	2.1%	NR	NR
Vasovagal reactions	0.5%	NR	NR
Nausea	2.9%	NR	NR
Others	0.5%	NR	NR
Hemothorax	0.26%	NR	NR
Catheter siteinfection	0.26%	0.04%	0.04%
Bleeding/hematoma	0.26%	2.46%	2.46%
Pneumothorax	0.26%	0.06%	0.06%
Vomiting	NR		

NR indicates not reported

Table 3:- Age distribution of patients.

Age group	**No.of cases**
<20 yrs	**10**
21-40	**22**
41-60	**63**
>60	**10**
Total	**105**

Table 4:- Indications for plasmapheresis.

Disease	**No. of patients**
GBS	**32**
MG	**24**
RPGN-	**23**
HUS/TTP	**21**
Myeloma	**4**
Renal graft rejection	**1**

Table 5:-Number of exchanges.

No. of exchanges	**No.of patients**
7	**15**
6	**5**
5	**75**
4	**7**
2	**2**
1	**1**
Total	**105**

Table 6:-Complications of plasmapheresis

Complications	No.ofpatients(%)
Partesthesias	36%
Hypocalcemia	7%
Hypotension	3%
Hypothermia	2%
Urticaria	1%

Fig.1:-Cobe spectra at our center

Discussion:-

First plasma pharesis was done on 30th august 2002. Till date 549plasmaexchanges have been done on 105 patients. Most of our patients have been from neurology and nephrology departments. Common indications for the procedure was Guillan Bare syndrome (31%) followed by Myasthenia Gravis (23%),Rapidly progressive glomerulonephritis (22%),Haemolytic uremic syndrome, Thrombotic thrombocytopenic purpura (20%),Multiple myeloma (4%)&Renal graft rejection (1%). 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 PE is extremely safe in experienced hands.[16] .Majority of patients were adults in age range of 18-62 years.

The common reaction observed in our patients was Paresthesias (36%) attributed to the large fluid shifts between the intra and extra vascular compartments with associated electrolyte imbalances and the citrate content of the anticoagulant in the FFP .Few of our patients (7%) developed hypocalcemia. Hypotension was seen in(3%) cases which was managed by transiently stopping the procedure. Hypothermia was noted in 2% of patients. None of our patients had procedure related nausea, vomiting, Vasovagal reactions, Pneumothorax, Hemothorax, bleeding, hematoma, pruritis, tachycardia or fever. Urticaria was noted in 1% patients. We did not follow our patient for the development of hypofibrinogenemia.

Conclusion:-

Plasmapheresis is safe, cost effective procedure with only minimal procedure related complications and no mortality.

Conflicts of interest:- None.

References:-

1. Abell JJ, Rowntree LC, Turner BB. Plasma removal with return of corpuscles.JpharmacolExp Ther,1914:5;625-641
2. Kambara C, Matsuo H, Fukudome T, Goto H, Shibuya N. Miller Fischer syndrome and plasmapheresis. TherApher. 2002;6:450-453
3. Shariatmadar S, Nassiri M, Vincek V. Effect of plasma exchange on cytokines measured by multianalyte bead array in thrombotic thrombocytopenic purpura. Am J Hematol.2005; 79:83-88.
4. De Luca G, Lugerasi A, Iarlori C, et al. Prednisone and plasma exchange improve suppressor cell function in chronic inflammatory demyelinating polyneuropathy. J Neuroimmunol.1999; 95:190-194.
5. Burgstaler EA: current instrumentation for apheresis, In: Mcleod BC, szczepiorkowski ZM, Weinstein JL, eds. Apheresis: principles and practice. 3rd Ed. Bethesda, MD: AABB press, 2010:95-130.
6. Derksen RH, schuurman HJ, Myeling FH, et al. The efficacy of plasma exchange in the removal of plasma components. J Lab Clin Med. 1984;104:346-354
7. Flaum MA, Cuneo RA, Appelbaum FR et al. The hemostatic imbalance of plasma-exchange transfusion. Blood.1979; 694-702.
8. Orlin JB, Berkman EM: partial plasma exchange using albumin replacement: Removal and recovery of normal plasma constituents. Blood. 1980: 56:1055-1059
9. Chirnside A, Urbaniak SJ, Prowse CV et al. Coagulation abnormalities following intensive plasma exchange on the cell separator. II. Effects on factors I, II, V, VII, VIII, IX, X and Antithrombin III. Br J of Haematol. 1981; 48: 627-634.
10. Volkin RL, Starz TW, Winkelstein A, et al. Transfusion. 1982; 22:54-58.
11. Ibrahim RB, Liu C, Cronin SM et al: Drug removal by plasmapheresis: An evidence based review. Pharmacotherapy. 2007;27:1529-1549
12. KalePradhan PB, Woo MH: A review of the effects of plasmapheresis on drug clearance. Pharmacotherapy.1997; 17:984-695.
13. Wood GJ, Hall GM: plasmapheresis and plasma cholinesterase. Br. J Anaesth. 1978; 50:945-949.
14. Klintzel PE, Eastlund T, Calis KA. Extracorporeal removal of antimicrobials during plasmapheresis.JClinApher. 2003;18:194-205
15. Shemin D, Briggs D, Greenan M. Complications of therapeutic plasma exchange. A prospective study of 1,727 procedures. J Clin Apher,2007;22:270-276
16. McLeod BC. Therapeutic apheresis.Use of human serum albumin, fresh frozen plasma and cryosupernatant plasma in therapeutic plasma exchange. Best Prac Res Clinical Haematol.2006; 19:157-167.
17. Sutton DM, Nair RC, Rock G. Complications of plasma exchange. Transfusion.1989; 29:124-127.
18. Couriel D, Weinstein R. Complications of therapeutic plasma exchange: A recent assessment. J ClinApher. 1994: 9:1-15
19. Basic-Jukic N, Kes P, Glava-Boras S, Brunetta B, Bubic-Filipi L, Puretic Z. Complications of therapeutic plasma exchange: Experience with 4857 treatments. TherApher Dial. 2005;9:391-395
20. Szczepiorkowski ZM, Winters JL, Bandarenko N. et al. Guide lines on the use of therapeutic apheresis in clinical practice: evidence- based approach from the Apheresis Applications committee of American Society for Apheresis. J Clin Apher.2010,25:83-177
21. Winters JL, Pineda AA, McLeod BC, Grima KM, Therapeutic apheresis in renal and metabolic diseases. J Clin Apheresis 2000;15:53-73.