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Therapeutic Plasma Exchange and Cytapheresis in Various Disorders – Experience from a Tertiary Care Centre in East India

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ABSTRACT

Therapeutic plasmapheresis or plasma xchange has been used to treat a variety of renal, neurological, hematological and autoimmune disorders. The present communication describes our short experience in plasma Exchange in a tertiary care multispeciality hospital in eighty-five cases where two hundred ninety-six procedures in total have been done over 57 months using Cobe Spectra (USA) pheresis machine. The age of the patients varied from 15 to 85 years. The replacement fluid used was mixture of Fresh Frozen Plasma (FFP) and Normal saline. There was no procedure related death. The spectrum of disorders includes cases of antibody mediated rejection after kidney transplant, cases of removing is agglutinin for renal transplantation across Blood Group barrier, Gullian Barre Syndrome, Myasthenia Gravis, TTP, Autoimmune Hemolytic Anemia, Waldenstroms Macroglobulinemia, SLE etc. The safety and Efficacy of plasmapheresis has been reassured. It was also found to be less expensive compared to other modalities of management. Two cases of red cell cytapheresis in sickle cell anaemia during crisis has been described where it is very effective.

Keywords: Plasmapheresis, Theraputic Plasma exchange, Red cell cytapheresis

INTRODUCTION

Plasmapheresis or Therapeutic Plasma Exchange (PE) is a well-established procedure for treating many neurological, renal, haematological and autoimmune disorders [1-3]. This procedure is safe and efficacious in a broad spectrum of diseases starting from neurological to toxic and metabolic disorders. In recent years the scope of plasmapheresis has been broadened with modern application of some modified techniques [4]. The present communication describes our experience in 85 patients from January, 2015 to September, 2019 i.e. over a period of 57 months in therapeutic plasmapheresis largely and a two cases of red cell cytapheresis.

In India, there is increasingly use of plasmapheresis or plasma exchange (PE) is seen in different centres. There have been 3-fold increases in PE between 2005–2009 compared to 2000-2004 [5]. Training and expertise and guidelines have also been published [3]. The safety of the procedure is also due to efficient machines, techniques used and on the top of it clinical response. However, there is paucity of published data from India. This prompted us to report our experience in the present paper.

MATERIALS & METHODS

The total number of eighty-seven patients (85 plasmapheresis and 2 cases of red cell cytapheresis) are included in this study who are investigated, and final diagnosis established in our Apollo Hospitals, Bhubaneswar. The follow up of the cases are done in respective departments. Ten cases of ABO incompatibility for renal Transplantation were also plasmapherosed repeatedly before transplantation and their titres of Anti A and Anti B determined from time to time [6] and when the titre reached 1:16 the patients were taken up for transplantation. This present series also includes 39 cases of plasmapheresis done in renal transplant cases with imminent

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rejection. Informed consent was obtained from every patient prior to the procedure. Serology for HIV, Hepatitis B and C and blood grouping was done for each patient before the procedure. Two cases of sickle cell crisis were also taken up for red cell cytapheresis.

The age of the patient ranged from 15 to 85 years. COBE Spectra (Gambro) was utilised for all the plasmaphereis and Optia (Terumo Penpol) was utilised for red cell cytapheresis. A hematocrit control program based on the patient's height, weight and hematocrit is entered. Inlet flow rates from the

Double lumen catheter was used under local anaesthesia. Serology for HIV, Hepatitis B and C and blood grouping was done in all cases and cardiac and respiratory statuses were assessed by ECG and ECHO and x-ray. Patients were preloaded with 1.5-2L of normal saline for proper hydration, calcium was given by I.V. injection slowly in one peripheral vein. Usually 1 volume to 1.5 volume of plasma was removed each time on alternate day by plasmapheresis. Blood pressure, pulse were monitored every 15-30 min intervals during the sessions and patients were closely observed for changes in symptoms like light headedness,

Double lumen catheter was used under local anesthesia. Serology for HIV, Hepatitis B and C and blood grouping patients were 60-70 ml/min in all patients. This never exceeded 80 ml/min in order to avoid symptoms of alkalosis from citrate toxicity. Blood volume was calculated as a function of body weight, height and body type (fat, thin, normal or muscular). The blood pump speed was set at of 10 ml/min and increased to 60 ml/min gradually.

The central access was obtained by subclavian vein in 92 cases and femoral vein catheterization was performed in 3 cases. A chest x-ray was routinely taken after subclavian catheterization to assure proper placement of the catheter.

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RESULTS

A total of 296 procedures were performed on 85 patients of different disorders **(Figure 1)**.

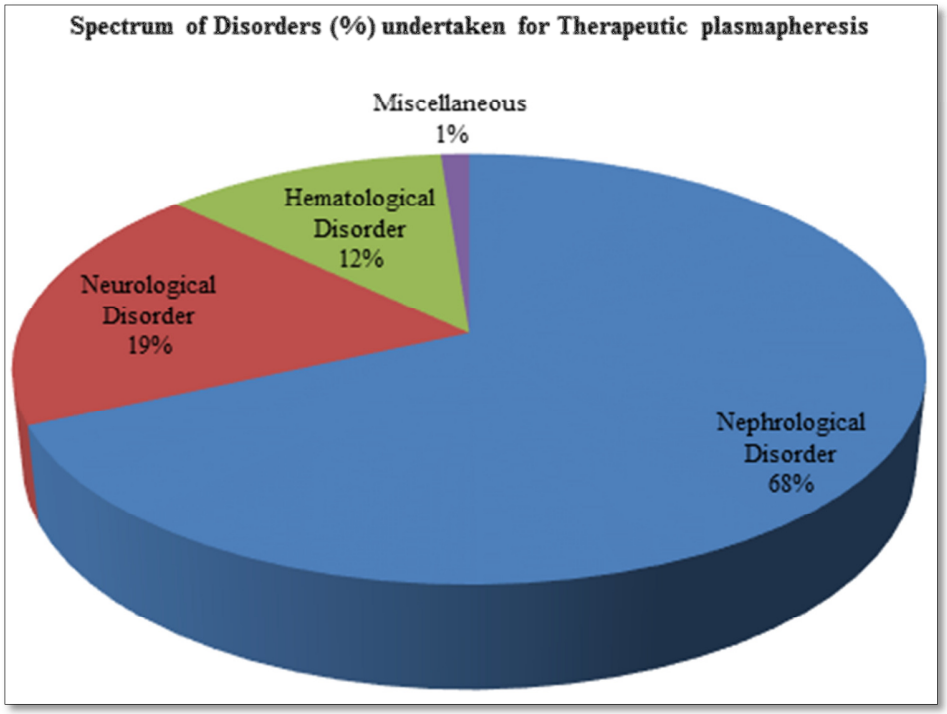

Figure 1. Spectrum of Disorders (%) undertaken for Therapeutic plasmapheresis.

The age of the patients varied from 15 to 85 years. There are 71 males and 14 females. The indications for plasmapheresis in different disorders have been shown in **Table 1**. It appears that majority of cases belong to kidney transplantation rejection and transplantation across the blood group barrier (**Table 1**).

Furthermore, it is interesting to note that the cases of Gullian Barre syndrome improved with TPE alone after 4 to 5 times. The maximum TPE in those cases was 10. The other neurological cases include CIDP and AIDP also showed improvement with TPE.

Table 1. Details of plasma exchange in different disorders.

Disorders		**No. of Patients**	**No. of Procedures**	**Frequence of Plasma Exchange**	**Average Volume**
Nephrological Disorder					
	AKI on CKD	5	14	Alternate day	1.5 L to 3.5 L
	Rejection of graft	41	139	Alternate day	1.5 L to 3.5 L
	ABO imcompatable Transplant	11	35	Alternate day	1.5 L to 3.5 L
	MPGN	1	1	Alternate day	1.5 L to 3.5 L
	Total	58	189		
Neurological Disorder					
	G.B.S.	5	26	Alternate day	1.5 L to 3.5 L
	CIDP	4	18	Alternate day	1.5 L to 3.5 L
	AIDP	4	13	Alternate day	1.5 L to 3.5 L
	M. Gravis	3	15	Alternate day	1.5 L to 3.5 L
	Total	16	72		
Hematological Disorder					
	HUS / TTP	6	21	Alternate day	2 to 3.5 L
	Waldenstrom's Macroglobulinemia	1	6	Alternate day	2 to 3.5 L
	Multiple Myeloma	1	1	Alternate day	2 to 3.5 L
	AIHA	2	4	Alternate day	2 to 3.5 L
	Total	10	32		
Miscellaneous					
	SLE	1	3	Alternate day	2 to 3.5 L

Furthermore, it is interesting to note that the cases of Gullian Barre syndrome improved with TPE alone after 4 to 5 times. The maximum TPE in those cases was 10. The other neurological cases include CIDP and AIDP also showed improvement with TPE.

Out of six cases of TTP/HUS five cases had very successful outcome after plasmapheresis. One case died after two days of hospital stay although improved initially with rise of platelet count. But succumbed to death after two days. Rest 5 cases are on follow up for last 3 to 4 yrs with no recurrence till date. The Waldenstrom's macroglobulinemia and multiple myeloma cases also were subjected to plasmapheresis (TPE) for hyperviscosity and enhanced free light chain respectively. There are two patients of AIHA in our series with high titre cold antibody. They were given in

addition to TPE Wyselone (prednisolone) after the Plasma Exchange.

DISCUSSION

TPE is used to treat a number of disorders such as neurological, haematological, renal and autoimmune. This procedure is based upon controlled trials, case series and case reports describing efficacy. In the most recent guideline ASFA (American Soc of Apheresis) has provided on the use of TPE in 100 clinical situations in 65 diseases [7,8]. ASFA has published guidance for TPE and provides the ASFA category and recommendations [2]. Complications from TPE were minimal and included nausea, vomiting, allergic reaction and temporary allergic reaction.

ABO-incompatible renal transplant has been done in ten cases in the present series. TPE has been employed in our cases to remove significant level of isoagglutinin and IVIG to restrict its production. As it appears from our small study it is quite effective **(Table 2)**.

Table 2. Details of plasma exchange and follow up in cases of renal transplant across blood group barrier.

Sl. No	Age/ Sex	Recipient	Donor	HLA Matching	Cross Match	Starting Titre		No. of Plasma-pheresis	Before Transplant, After Plasma-pheresis		The titre after Transplant		Remarks
		Blood group	**Blood Group**										
						Anti A	**Anti B**		**Anti A**	**Anti B**	**Anti A**	**Anti B**	
1	58/M	A	AB	0/6	Negative		16	3		4		4	HD
2	58/M	O +ve	A -ve	2/6	Negative	128	128	3	8	8	8	16	Fungal infection death
3	37/M	O +ve	A +ve	0/6	Negative	32	32	3	4	4	2	4	HD
4	46/M	O +ve	A +ve	0/6	Negative	256	256	5	16	16	16	32	good
5	44/M	A +ve	AB +ve	4/6	Negative		256	3		8		2	death
6	47/M	O +ve	B +ve	3/6	Negative	128	256	4	8	16	8	4	good
7	31/M	A +ve	AB +ve	3/6	Negative		32	3		4		4	good
8	53/M	B +ve	AB +ve	3/6	Negative	32		3	4		4		Good
9	38/M	O +ve	B +ve	6/6	Negative	128	256	5	8	16	4	8	Good
10	42/M	O +ve	A +ve	4/6	Negative	>512	>512	3 (glycol sorb)	16	32	32	64	Good

We are in agreement with earlier report [9]. In one case the titre of the is agglutinin did not come down (Case No.10). Therefore, we have to use Glycosorb to bring down the level of the ABO antibody before transplant. We have in this study limited follow up of 3 to 4 years. However, the rates of complications and survival seems to be almost similar to ABO-Compatible transplantation. So, the present study is in agreement with other published reports [9-12].

Earlier reports of antibody mediated rejection (AMR) of kidney allografts reported to be 23% of unselected low-risk recipients [13] and 60% of high-risk recipients. Along with PE high dose of IVIG (2 g/kg) was used therefore to suppress antibody production. A metaanalysis of uncontrolled data show full or partial remission with early TPE [14].

Antibody mediated rejection (AMR) still occurs in approximately 5% of compatible kidney transplant and incidence seems to be higher in incompatible kidney transplant recipients, as high as 40% [15]. According to some reports TPE remains therefore the mainstay in the management of these cases [16,17]. DSAs (donor specific antibodies) to HLA antigens can cause acute AMR after kidney transplant. Densensitization protocols typically include TPE or intravenous immunoglobulin or both and rituximab to reduce the process. We have used the same combination of treatment in our transplanted cases. In the present series 39 cases are plasmapherosed for AMR.

After transplantation, a correlation between postoperative rebound of AB abs to titres $\geq$ 1:32 and AMR has been observed, occurring in approximately 15-17% of patients [18,19]. In our study the rebound after transplant was observed in 2 cases (case No. 10 and case No.4) out of ten.
In GBS, the recommended treatment options of PE or IVIg therapy are equally effective. However, in our Indian set up PE is a cheap procedure compared to IVIg therapy. This is extremely safe in experienced hand. It must be stressed that PE therapy in patients in other neurological disorders is the first line therapy along with corticosteroids. So, these are add on therapy along with immunosuppressive therapy for other neurological disorders.

Efficacy of therapeutic plasma exchange for the treatment of autoimmune haemolytic anemia has been reported earlier [20]. The use of TPE is effective due to the removal of autoimmune antibodies from the intravascular space. Regarding PE in TTP, ASFA has put this under Category I, where this procedure is the primary modality of management and so also in Waldenstrom's macroglobulinemia and multiple myeloma with excess free light chain.

CYTAPHERESIS

Only in two cases of sickle cell crisis red cell cytapheresis have been undertaken. These two cases had severe vaso-occlusive crisis. The cases did not respond to Nitric acid inhalation therapy which we administer to our cases for VOC and also to other measures like maintaining electrolyte fluid balance, antibiotics and opioid analgesic. One patient had priapism also. Therefore, one volume of red cell cytapheresis was done with replacement using group compatible packed RBC. After consecutive 2 days of cytapheresis the patients improved.

Erythrocytapheresis is an important procedure in the management of certain complications of sickle cell disease, including acute stroke, stroke prevention, acute chest syndrome and multi organ failure. It simply entails the remedial of the patient's red blood cells containing abnormal sickle haemoglobin and replacing them with normal RBC having normal haemoglobin [21].

CONCLUSION

Our small series of plasma exchange in various disorders reaffirmed the safety and efficacy of the procedure in an appropriate set up. It may be stressed here that this procedure is the need of the hour in treating various neurological, renal, haematological and renal transplant cases and is comparatively cheaper and effective compared to other modalities of management.

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