Original Article

Glimpse on Hemostatic Changes Produced By Plasmapheresis

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Summary:

Background: Aphaeresis is a term that means to separate or to take away. The basic idea of aphaeresis is efficient removal of a circulating cellular blood component, either cells (Cytopheresis) or plasma solute (plasmapheresis, plasma exchange).Thus, the treatment goal of aphaeresis is to remove the circulating cell or substance directly responsible for the disease process. Acceleration and development of aphaeresis applications had taken place with the arrival of automated cell separators in 1970s that ensure selectively removal of one or more of blood components from the blood and return the remainder to the individual. Plasmapheresis is separation of plasma from blood cells which are returned to the body. It is accompanied by multiple changes in haemostatic system. As many coagulation factors are removed during procedure, changes in selective parameters: Prothrombin Time (PT), Partial Thromboplastin Time (PTT), Thrombin Time (TT), Fibrinogen (FNG) & platelets count are found when the replacement fluids devoid from coagulation factor are used.

Patients and Methods: This clinico-haematological study conducted during a period of six months, from February 2004 to July 2004 at the National Blood Transfusion Center (NBTC) in Baghdad & 50 patients underwent Therapeutic Plasma Exchange (TPE) for various disorders with the use of two types of automated blood cell separators (Haemonetics MCS + which represent an intermittent flow centrifugation technique – IFC & Fresenius AS. TEC 204 which represent the continuous flow centrifugation technique - CFC) in this study, but no instrument type influenced the coagulation screening tests.

Results: The changes in all selective parameter: Prothrombin Time (PT), Partial Thromboplastin Time (PTT), Thrombin Time (TT), Fibrinogen (FNG), Platelets count, Haemoglobin (Hb) and Packed Cell Volume (PCV) were significant after Therapeutic Plasma Exchange (TPE). There was no significant difference in changes in crystalloid group from that in Fresh Frozen Plasma group. In crystalloid group, significant correlation was observed between Prothrombin Time (PT), Activated Partial Thromboplastin Time (APTT), Thrombin Time (TT) & volume of Plasma Exchanged (PE) /session, while spacing between sessions and the number of sessions is significantly correlated with Thrombin Time (TT). Plasma fibrinogen concentration and platelets count were decreased in the patients included in our current study.

Conclusion: There is no significant difference in changes in haemostatic system whether crystalloid or diluted Fresh Frozen Plasma (FFP) was used as replacement fluid. Thus, crystalloid, solution devoid of coagulation material can be used as a replacement fluid in the Therapeutic Plasma Exchange (TPE) if the volume of Plasma Exchanged (PE) is small. These results are of vital importance from the practical & public health point of view in minimizing the usage of blood components((i.e. Fresh Frozen Plasma (FFP) which is a potential source of Transfusion Transmissible Infections (TTIs) worldwide)) & replaced by crystalloid solution as a safer replacement fluid substitute in Therapeutic Plasma Exchange (TPE) process.

Keywords*:* fresh frozen plasma, therapeutic plasma exchange.

Introduction:

The primary objective of aphaeresis is efficient removal of a circulating blood component, either cells (Cytopheresis) or plasma solute (plasmapheresis, plasma exchange). For most disorders, the treatment goal is to remove the circulating cell or substance directly responsible for the disease process (1, 2) (antibodies, immune complexes, abnormal RBCs, malignant WBCs, platelets, protein-bound drugs or toxins). (3) Current automated aphaeresis instrument use microprocessor technology to administer an anticoagulant, collect the treated blood, separate component either by centrifugation or by filtration, isolate the desired component or recombine the remaining component for return to the patient or donor **(**2). Therapeutic Plasma Exchange (TPE) is generally associated with rapid (and repeated) removal of large quantities of plasma and its associated coagulant proteins (1 , 4 , 5 , 6) .When coagulant protein-deficient replacement fluid such as albumin, saline, or colloidal starch are used, an acute fall in clotting factor activity, varying from 40% to 70% of baseline, can be observed immediately after exchange. This depletion

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is usually associated with a small prolongation in measured prothrombin time (PT) and activated partial thromboplastin time (PTT) (1,5,6) . The total amount of PE, spacing in days between sessions and number of sessions in the full course of exchange are the three factors directly related to the procedure of plasmapheresis & are expected to affect the outcome of procedure especially the part related to derangement of coagulation parameters (19) .

Patients and Methods:

From February 2004 to July 2004, a total of 50 patients underwent Therapeutic Plasma Exchange (TPE) for various disorders referred to National Center for Blood Transfusion during this study period were included. The study groups included 22 females and 28 males, with age range from 6 years to 64 years .Those patients include the followings: (10) Myasthenia Gravis; (25) Guillian Barre Syndrome (GBS) ; (5) Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) ; (1) Pemphigus; (1) Renal failure for transplantation ; (1) Thrombotic Thrombocytopenic Purpura (TTP) ; (1) Multiple Sclerosis (MS) & (6) Rh- isoimmunized pregnants . Two types of automated blood cell separators (Haemonetics MCS + which represent an intermittent flow centrifugation technique – IFC & Fresenius AS. TEC 204 which represent the continuous flow centrifugation technique - CFC) were used in this study. No instrument specific effects on coagulation screening tests were detected in this study. A course of Therapeutic Plasma Exchange (TPE) includes 3 to 12 sessions at 1 to 11 days interval. About 1000 ml of plasma was exchanged each session. A 0.9% Normal saline used as a replacement fluid for 25 patients and FFP was used for remainder 25 patients. Blood samples were collected from the patients before and immediately after the 1st session and immediately after the last session. PT, PTT, TT, fibrinogen, platelets, Hb and PCV performed immediately. The control group consists of 20 age & sex matched individuals, for whom screening tests (Prothrombin Time (PT), Activated Partial Thromboplastin Time (APTT), Thrombin Time (TT), Fibrinogen (FNG), Platelets count, Haemoglobin (Hb) and Packed Cell Volume (PCV) had been performed.

Sampling:

Patient Group: Blood samples were collected from the patients before and immediately after the first session and immediately after the last session. A 5 ml of venous blood was collected by clean venepuncture in two collecting tubes, 1.8 ml dispensed in plain plastic tube containing 0.2 ml of 0.11µ aqueous trisodium citrate dehydrate for coagulation study. A 2.5ml of the remaining blood sample was dispensed in 2.5 ml ethylendiamine tetra-acetic acid (EDTA) containing tube with concentrate of 1.5 mg EDTA per one ml of blood for determination of platelet count, Hb, PCV and antibody titration. The citrated blood was centrifuged at 2000 g for 15 minutes to get platelet poor plasma (PPP), the later was used for performing Prothrombin time(PT), Activated Partial Thromboplastin time(APTT), Thrombin time(TT) and fibrinogen level(FNG). All the tests performed at Quality Control laboratory in National Blood Transfusion Center - Iraq. Control Group**:** This study includes a control group of 20, age and sex matched healthy individuals. Prothrombin Time (PT), Activated Partial Thromboplastin Time (APTT), Thrombin Time (TT), Fibrinogen (FNG) had been performed.

Haematological screening tests**:** All haematological screening tests were done on the study group include Prothrombin Time (PT), Activated Partial Thromboplastin Time (APTT), Thrombin Time (TT), Fibrinogen (FNG), Platelets count, Haemoglobin (Hb) and Packed Cell Volume (PCV) according to the standard technical procedures recommended by the manufacture & consistent with the international references of practical hematology [22]. All coagulation studies were performed immediately after blood collection.

Statistical analysis: Data were translated into a computerized database structure. Statistical analyses were computer assisted using SPSS ver. 10 (Statistical Package for Social Sciences).

Frequency distribution for selected variables was done first. For variables that were assumed to be normally distributed the statistical significance of mean change observed after plasmapheresis was assessed by Paired t-test, while for a non-normally distributed variable like Antibody titer Wilcoxon signed rank test was used. The statistical significance of difference in mean between the 2 groups was assessed by Independent samples t-test. The statistical significance of association between 2 categorical variables in a small sample size was assessed Fisher's exact test. P value less than the 0.05 level of significance was considered statistically significant. Multiple regression model was used to study the independent and net effect of the total amount of plasma exchange, number and spacing between plasmapheresis sessions on the response variable, which is the change in coagulation parameters after the last session compared to baseline.

Results:

According to the type of fluid used to replace the exchanged plasma subtracted by plasmapheresis in this study, our patients were divided into two groups: First group (Crystalloid group): 25 patients were included & for whom the volume of the plasma subtracted by plasmapheresis was substituted by crystalloid while the second group (FFP group): 25 patients were included & for whom the Fresh Frozen Plasma (FFP) was used to substitute the volume of plasma subtracted by plasmapheresis had been utilized.

Frequency distribution of the study sample with different diagnoses for plasmapheresis in crystalloid & FFP groups was tabulated (Table 1 (A**)**). In addition to that, the frequency distribution of the study sample by reported reason for plasmapheresis, age , sex & the type of replacement fluid used was tabulated (Table 1 (B)) In this study , patients within the crystalloid group having abnormally prolonged PT, PTT, TT after a course of TPE were as follows: 12(60%), 6(25%), 1(4%) respectively, versus 11(50%) of patients showing abnormally prolonged PT with no change in PTT & TT in FFP group (Table 1 (C)). On the other hand, patients within the crystalloid group of this study having abnormally low value of fibrinogen, platelets count, Hb and PCV were as follows: 2(8%), 2(9.5%), 3(21.4) and 3(15.8) respectively versus 1(4%), 4(17.4%), 4(19%) and 7(31.8%) patients respectively in FFP group (Table 1 (D)). The changes in all selective parameters (PT, PTT, TT, fibrinogen, platelets count, Hb and PCV) were significant after TPE in crystalloid group with a P value of ≤ 0.001 but they are minimal and many values remain with normal range in FFP group. There was no significant difference in the changes in crystalloid from that in FFP group in this study (Table 2 (A-C) & table 3 (D – G)). The underlying reasons for the inability to test all the parameters for all groups members included in this study was due to many reasons mainly due to insufficient preliminary blood samples, needs for additional blood samples for repetition of tests due to technical errors & others with impossibility to recall the patients within the proper time limits because of poor compliance of the patients & the real difficulties due to the current situation of the country. In crystalloid group there was a significant correlation between total amount of plasma exchanged in the full course of PE and PT, PTT, TT with a P value 0.004, 0.008 and <0.001 respectively. There was a significant difference between spacing between sessions in days and number of sessions with TT only with a P value 0.04 and 0.01 respectively. In FFP group all the three factors (total amount of PE, spacing between sessions and number of sessions) had no significant correlation with the coagulation screening tests. No bleeding or thrombotic sequel reported in this study. (Table 4) Coagulation screening tests:-Control group: A 20age and sex matched control group were selected as volunteers. Their PT ranged between 12-14 seconds, PTT ranged between 30-40 second, the TT ranged between (13-21 sec.) while fibrinogen ranged between (1.5-4.0 g/L).These represented a normal values of the control group to which the study groups were compared statistical calculation whether significant or not. Study group: The changes in PT after plasmapheresis after first and last session were tabulated. In both crystalloid group and FFP group the mean of acute change was increased by 1.5s versus 1.4s, while the mean of chronic change was 1.9s versus 1.3s, these changes were statistically significant [P=<0.001] however they were clinically not significant. The mean of acute & chronic changes in PT in the crystalloid group was not significant from that of FFP group with P value = 0.81, 0.2 respectively. (Table 2 (A)) The mean of acute change and chronic change in PTT in the crystalloid group was not significant from that of FFP group with P value =0.07, 0.09 respectively. In crystalloid group the relative frequency of subject in whom the PTT increased by more than 7s after last session compared to baseline was 5 (20%) (3 patients PTT increased by 8s, 1 patient by 9s and 1 patient by 10s). Patients who received FFP as replacement fluid show no significant increase in the PTT. The change in PTT after plasmapheresis after first (acute change) and last session (chronic change) in both crystalloid group & FFP group was tabulated (Table 2(B)).In both crystalloid and FFP group the mean of acute change was increased by 2s versus 1.4s, while the mean of chronic change was 3.4s versus 1.6s, these changes were statistically significant with a P value of <0.001 however they were clinically not significant. The change in TT after plasmapheresis after first (acute change) and last session (chronic change) in both crystalloid group and FFP group were tabulated. In both crystalloid and FFP groups the mean of acute change was increased by 1.5s versus 1.4s, while the mean of chronic change was 2.6s versus 2.2s, these changes were statistically significant with P value<0.001 however they were clinically not significant. The mean of acute and chronic changes in TT in the crystalloid group was not significant from that of FFP group with P value =0.86 and 0.59 respectively (Table 2(B)). In crystalloid group the relative frequency of subject in whom the TT increased by more than 5s after last session compared to baseline was 5 (20%) patients (2 patients TT increased by 6s, 2 by 7s and 1 patient by8s), while in FFP group 2 patients increased more than 5s (2patients increased by 6s).(Table 2(C)). The change in fibrinogen after plasmapheresis after first (acute change) and last session (chronic change) in both crystalloid group and FFP group were tabulated. In both crystalloid and FFP group the mean of fibrinogen concentration of acute change was reduced by 0.4gm/l versus 0.2gm/l respectively while the mean of chronic change was reduced by -0.9 versus -0.7, these changes were statistically significant with P value<0.001 however they were clinically not significant. The mean of fibrinogen concentration of acute and chronic change in fibrinogen in the crystalloid group was not significant from that of FFP with P valve of 0.1 and 0.36 respectively. (Table 3(D)). The change in platelets count after plasmapheresis after first (acute change) and last session (chronic change) were tabulated. In both crystalloid and FFP group the mean of acute change

was reduction by -31.1×10^9/L versus -32.4×10^9/L, while the mean of chronic change was a reduction by -74.4×10^9/L versus -82×10^9/L, these changes were statistically significant with a P value<0.001 however they were clinically not significant. The mean of acute and chronic change in platelet count in the crystalloids group was not significant from that of FFP with a P value of 0.85 and 0.5 respectively. (Table3) (E). the change in Hb concentration after plasmapheresis after first (acute change) and last session (chronic change) were tabulated. In both crystalloid and FFP groups the mean of acute change was reduction by -0.3gm/L versus -1.5gm/L while the mean of chronic change was reduction by - 4.4gm/L versus -4gm/L, these changes were statistically significant with a P value<0.001 however they were clinically not significant. The mean of acute and chronic change in Hb concentration in the crystalloid group was not significant from that of FFP with P value of 0.35 and 0.76 respectively. (Table 3 (F))

The change in PCV after plasmapheresis after first (acute change) and last session (chronic change) were tabulated. In both crystalloid and FFP group the mean of acute change was reduction by -0.004L/L versus -0.014L/L while the mean of chronic changes was reduction by -0.023L/L versus -0.037L/L, these changes were statistically significant with P value≤0.001 however they were clinically not significant (except acute change in crystalloid group which was statistically and clinically not significant). The mean of acute and chronic change in PCV in the crystalloid group was not significant from that of FFP with P value of 0.9 and 0.06 respectively. (Table 3 (G)).

Table 1: A. Frequency distribution of the study sample with different diagnoses for plasmapheresis in crystalloid & FFP groups.

	Crystalloids group		FFP group	
	No.	**%**	**No.**	**%**
Diagnosis (reason for plasmapheresis)				
Guillian Barre Syndrome	12	48	13	52
Myasthenia Gravis	3	12	7	28
Chronic Renal Failure	0	0	1	4
TTP	0	0	1	4
Pemphigus	0	0	1	4
Polyneuropathy	3	12	2	8
Multiple sclerosis	1	4	0	0
Isoimmunization	6	24	0	0
Total	**25**	**100**	**25**	**100**

B. Frequency distribution of the study sample for plasmapheresis by age and sex in crystalloid & FFP groups.

Children (<15)	3	12	0	
Young Adults (15-49)	17	68	20	80
Older adults (50+)	5	20	5	20
Gender				
Female	15	60	7	28
Male	10	40	18	72
Total	**25**	**100**	**25**	**100**

C. Abnormal prolonged coagulation times with a baseline normal value for PT, PTT & TT parameters after the first and last session of plasmapheresis in crystalloid & FFP groups.

	Crystalloids group					**FFP group**				
Subjects with normal parameter	Total	Abnormally prolonged after the first session		Abnormally prolonged after the last session		Total	Abnormally prolonged after the first session		Abnormally prolonged after the last session	
	No.	**No.**	**%**	**No.**	**%**	**No.**	**No.**	**%**	**No.**	**%**
PT	20	11	55	12	60	22	9	40.9	11	50
PTT	24	1	4.2	6	25	25	0	0	0	0
TT	25	2	8	1	4	25	0	0	0	0

D. Abnormal low value for Fibrinogen, Platelet count, Hb & PCV selected parameters after the first and last session of plasmapheresis in crystalloid & FFP groups.

	Crystalloids group					**FFP group**				
Subjects With normal parameter	Total	Abnormally low after the first session		Abnormally low after the last session		Total	Abnormally low after the first session		Abnormally low after session	las
	No.	No.	%	No.	%	No.	No.	%	No.	%
Fibrinogen	25	0	0	2	8	25	0	0	1	4
Platelet count	21	2	9.5	2	9.5	23	0	0	4	17.4
Hb	14	0	0	3	21.4	21	1	4.8	4	19
PCV	19	1	5.3	3	15.8	22	1	4.5	7	31.8

Table 2 (A - C) : The changes in PT, PTT, TT, Fibrinogen, Platelets count, Haemoglobin & PCV after plasmapheresis after the first (acute change) and last session(chronic change) in crystalloid & FFP groups

					Change after the last session compared to	
	Baseline	**After the first session**	**Acute change**	**After the last session**	**First session**	**(Chronic change)-baseline**
A. PT (seconds) in Crystalloid group						
Range	(11 to16)	(12 to 17)	(0 to 4)	(12 to 18)	(-2 to 3)	(-1 to 6)
Mean	13.4	14.9	1.5	15.3	0.4	1.9
SE	0.25	0.27	0.2	0.35	0.3	0.39
***P (Paired t-test)**			<0.001		0.22 *[NS]*	<0.001
FFP group						
Range	(12 to 16)	(13 to 18)	(0 to 3)	(13 to 17)	(-2 to 2)	(0 to 3)
Mean	13.3	14.8	1.4	14.6	-0.1	1.3
SE	0.21	0.28	0.14	0.25	0.2	0.17
***P (Paired t-test)**			<0.001		0.56 *[NS]*	<0.001
****P (Student's t-test)=**	0.72 *[NS]*		0.81 *[NS]*		0.18 *[NS]*	0.2 *[NS]*
B.PTT (seconds)in Crystalloid group						
Range	(30 to 41)	(33 to 42)	(-1 to 4)	(31 to 45)	(- 4 to 7)	(-4 to 10)
Mean	34.2	36.2	2	37.6	1.4	3.4
SE	0.59	0.5	0.27	0.71	0.61	0.74
***P (Paired t-test)**			<0.001		0.031	<0.001
FFP group						
Range	(32 to 37)	(33 to 40)	(0 to 3)	(34 to 39)	(-1 to 2)	(0 to 3)
Mean	34.2	35.6	1.4	35.8	0.2	1.6
SE	0.29	0.33	0.21	0.23	0.19	0.15
***P (Paired t-test)**			<0.001		0.31 {N S}	<0.001
****P (Student's t-test)=**	0.95 *[NS]*		0.07 *[NS]*		0.07 *[NS]*	0.09 {N S}

					Change after the last session compared to	
	Baseline	**After the first session**	**Acute change**	**After the last session**	**First session**	**baseline**
C.TT (seconds) in Crystalloid group						
Range	(11 to 21)	(13 to 22)	(0 to 4)	(12 to 22)	(-3 to 5)	(-3 to 8)
Mean	15	16.4	1.5	17.6	1.1	2.6
SE	0.54	0.53	0.17	0.5	0.49	0.57
***P (Paired t-test)**			<0.001		0.032	<0.001
TT (seconds) in FFP group						
Range	(11 to 18)	(12 to 20)	(0 to 3)	(13 to 21)	(-1 to 4)	(0 to 6)
Mean	13.4	14.8	1.4	15.6	0.8	2.2
SE	0.28	0.33	0.15	0.48	0.28	0.33
***P (Paired t-test)**			<0.001		0.008	<0.001
****P (Student's t-test)=**	0.012		0.86 *[NS]*		0.57 *[NS]*	0.59 *[NS]*

table 3 (D – G) : The changes in PT, PTT, TT, Fibrinogen, Platelets count, Haemoglobin & PCV after plasmapheresis after the first (acute change) and last session(chronic change) in crystalloid & FFP groups.

					Change after the last session compared to	
	Baseline	After the first session	Acute change	After the last session	First session	Baseline
D. Fibrinogen conc. (gm/L) in Crystalloid group						
Range	(1.9 to 3.7)	(1.8 to 3.3)	(-0.7to -0.1)	(1.4 to 2.8)	(-1.1to -0.1)	(-1.7 to -0.2)
Mean	3	2.6	-0.4	2.1	-0.5	-0.9
SE	0.09	0.08	0.03	0.07	0.05	0.07
*P (Paired t-test)			<0.001		<0.001	<0.001
FFP group						
Range	(1.9 to 3.7)	(1.6 to 3.4)	(-0.6 to 0.7)	(1.4 to 3.1)	(-1.9 to -0.1)	(-2.1 to 0)
Mean	2.9	2.7	-0.2	2.2	-0.5	-0.7
SE	0.11	0.09	0.06	0.08	0.08	0.09
*P (Paired t-test)			<0.001		<0.001	<0.001
**P (Student's t-test)=	0.82 [NS]		0.1 [NS]		0.94 [NS]	0.36 [NS]

					Change after the last session compared to	
	Baseline	After the first session	Acute change	After the last session	First session	Baseline
E. Platelets count ($X10^9$/L)in Crystalloid group						
Range	(121 to477)	(113 to 440)	(-97 to -7)	(103 to 401)	(-134 to -3)	(-159 to -11)
Mean	295	263.9	-31.1	220.6	-43.3	-74.4
SE	17.18	15.3	4.34	14.04	5.65	6.67
*P (Paired t-test)			<0.001		<0.001	<0.001
Platelets count ($X10^9$/L) in FFP group						
Range	(132 to 403)	(120 to 388)	(-87 to -8)	(106 to 310)	(-150 to -13)	(-209 to -26)
Mean	284.8	252.5	-32.4	202.8	-49.7	-82
SE	13.76	11.94	3.96	10.07	7.19	9
*P (Paired t-test)			<0.001		<0.001	<0.001
**P (Student's t-test)=	0.65 [NS]		0.83 [NS]		0.49 [NS]	0.5 [NS]

					Change after the last session compared to	
F. Blood Hb conc. (gm/L)	Baseline	After the first session	Acute change	After the last session	First session	Baseline
Crystalloid group						
Range	(104 to 154)	(103 to 155)	(-3 to 3)	(94 to 151)	(-27 to 1)	(-27 to 1)
Mean	127.1	126.8	-1.8	122.7	-4.1	-4.4
SE	3.38	3.32	0.26	3.68	1.26	1.21
*P (Paired t-test)			0.003		0.003	0.001
FFP group						
Range	(71 to 157)	(68 to 157)	(-11 to 4)	(65 to 154)	(-7 to 1)	(-15 to 4)
Mean	133.6	132.2	-1.5	129.7	-2.5	-4
SE	3.76	3.93	0.49	3.99	0.42	0.72
*P (Paired t-test)			0.006		<0.001	<0.001
**P (Student's t-test)=	0.2 [NS]		0.35 (N S)		0.22 [NS]	0.76 [NS]

					Change after the last session compared to	
G. PCV L/ L	Baseline	After the first session	Acute change	After the last session	First session	Baseline
Crystalloid group						
Range	(0.33 to 0.55)	(0.32 to 0.52)	(-0.03 to 0.04)	(0.28 to 0.48)	(-0.1 to 0.02)	(-0.13 to 0.01)
Mean	0.404	0.4	-0.004	0.38	-0.019	-0.023
SE	0.0113	0.0118	0.0034	0.0105	0.0056	0.0062
*P (Paired t-test)			0.25 [NS]		0.002	0.001
FFP group						
Range	(0.22 to 0.55)	(0.2 to 0.55)	(-0.06 to 0.02)	(0.18 to 0.5)	(-0.05 to 0.01)	(-0.09 to -0.01)
Mean	0.429	0.416	-0.014	0.392	-0.024	-0.037
SE	0.013	0.0137	0.0033	0.0131	0.0032	0.0036
*P (Paired t-test)			<0.001		<0.001	<0.001
**P (Student's t-test)=	0.14 [NS]		0.9 (N S)		0.5 [NS]	0.06 [NS]

Table 4: The range and mean or median of selected variables by type of replacement fluid used.

	Crystalloids group		FFP group
	(Rhesus iso-immunization)	(others)Autoimmune disease	Immune diseases
Total amount of plasma exchange (ml) in the full course of exchanges			
Range	(3020 - 6050)	(628 - 5128)	(2420 - 13764)
Mean	4953.3	2746.8	4316.7
SE	542	293	459
Mean amount of plasma exchanged per session (ml)			
Range	(500 - 560)	(188 - 1026)	(600 - 1966)
Mean	512.3	602.6	849.4
SE	10	57	54
Duration of the full course of exchanges(days)			
Range	(30 - 112)	(5 - 11)	(4 - 30)
Median	82	7	7
Spacing between sessions in days			
Range	(5 - 11)	(1 - 3)	(1 - 3)
Median	7	2	1
Number of sessions in the full course of exchange			
Range	(6 - 12)	(3 - 7)	(4 - 12)
Median	11	5	5

Discussion:

In this study, small volume plasmapheresis (about 500 – 1000 ml / session) was selected instead of a more extensive procedure (i.e. the volume of plasma to be exchanged is more than 1000 ml / session) because this involves minimal risks for patients. Twenty - five patients received fluids devoid from coagulation protein ((0.9 % Normal Saline(NS)) as in other studies [4,5,6,7,8,9,10,11,12]and the other 25 patients received diluted FFP (FFP/NS 1:1) as in many studies [13,14,15,16,17] TPE is generally associated with rapid and repeated removal of large quantities of plasma and its associated coagulant protein. When replacement fluid which is deficient in coagulation protein is used a fall in clotting factors activities can be observed immediately after the exchange (1, 18). In this study, fall in the level of coagulation proteins was observed as a slight prolongation in PT, PTT, TT The prolongation in coagulation screening tests in crystalloid group (e.g. Rh- isoimmunization) was higher but not significant from that in FFP. These minimal changes in coagulation screening tests were most likely due to small volume of PE as a usual practice at the national blood transfusion center.

In this study, the range of exchanged plasma volume per a session of TPE in Rh isoimmunization – crystalloid group - is from 500 to 560 ml). These findings agree with Mark E. Brecher study (1) as the prolongation is slight in the measured PT, PTT and TT, although such values frequently remain within normal range. The total amount of PE, spacing in days between sessions and the number of sessions in the full course of exchange are the three factors directly related to the procedure of plasmapheresis & are expected to affect the outcome of procedure especially the part related to derangement of coagulation parameters (19). In crystalloid group, significant correlation was found between total amount of PE in the full course of plasmapheresis and the coagulation screening tests. These findings are mostly due to increase loss of coagulant proteins with increasing total amount of PE, while spacing between sessions in days and number of sessions show significant correlation with TT only. These findings could be due to the direct relation between TT and fibrinogen level (6).In FFP group, all the three factors (total amount of plasma exchange, spacing between session and number of sessions) have no significant effect on coagulation screening tests (PT, PTT and TT) because there is partial replacement of coagulation material (20, 21) .In this study, it has been found that there is a significant reduction in fibrinogen level in the crystalloid and FFP group. This has been demonstrated by the study of Domen et al (6), Flum et al (9) and Chrinside et al (11) as they demonstrated that fibrinogen was efficiently depleted by plasma exchange and its removal was maximal, where as less efficient removal was seen for other factors. In this study, the consequence of PE is a reduction in circulating platelet but with no significant difference between crystalloid and FFP .This is consistent with the finding of Bracher et al (1) and Strobel (3). The current study shows a minimal reduction in PCV/Hb after a course of PE and this could be probably due to use of developed machines, small volume PE & replacement fluid. The vascular access was obtained from large veins, the free flow of blood from obstruction, the adequately needle bore diameter & the use of FFP & isotonic solution (0.9 % Normal Saline) as a replacement solution. All these measures diminished the risk of hemolysis & dilution. This is consistent with the findings of Foke et al (23) & Susan et al (24). In addition to that, no hemorrhage was observed during or after PE in the patients of this study even after repeated plasmapheresis at short intervals which is most likely due to minimal changes in coagulation screening tests. These minimal changes in coagulation profile were most likely due to small

volume of PE as a usual practice at the national blood transfusion center.

Conclusion:

Crystalloid, solution devoid of coagulation material can be used as a replacement fluid in the TPE if the volume of PE is small as there was no statistical significant difference in changes in hemostatic system whether crystalloid or diluted FFP was used as replacement fluid. These results are of vital importance from the practical & public health points of view in minimizing the usage of blood components (i.e. FFP) which is a potential source of transfusion transmissible infections (TTIs) worldwide & replaced by crystalloid solution as a safer synthetic replacement fluid substitute for the FFP in TPE process. In crystalloid group, statistical significant correlation was observed between PT, PTT, TT and volume of PE/session, while spacing between sessions and the number of sessions was statistically significant correlated with TT. Plasma fibrinogen concentration and platelets count were decreased acutely & over the period of the study, however it was clinically not significant. There was a minimal reduction in PCV/Hb after a course of PE and this could be due to the use of developed machines and small volume PE.

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