

Original Research Article

Risk of bleeding after plasmapheresis!

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ABSTRACT

Background: Plasmapheresis is a growing up method used for treatment of many diseases. it is considered as first line therapy for different diseases. During this therapeutic modalities there is an undesirable removal of coagulation proteins particularly fibrinogen. Aim The aim of the present study was to assess the presence or absence of bleeding risk following therapeutic plasmapheresis. This was done by assessment of fibrinogen level pre and post plasmapheresis in different indication including the renal and non-renal disorders.

Methods: The present case control study was conducted on 40 persons from El-Demerdash Hospital in Ain Shams University from the period of May 2019 till November 2019. The study was approved by the hospital's research ethics board. The 40 patients were divided into 2 groups according to presence or absence of renal disordes as renal and non-renal indication for plasmapheresis, Fibrinogen level, aPTT, INR were estimated pre and post session of plasmapheresis. Also, all patients were observed during plasmapheresis session and for 72 hours later for clinical evidence of bleeding tendency.

Results: Fibrinogen levels and aPTT were reduced significantly following plasmapheresis but without increased risk of bleeding.

Conclusions: Fibrinogen level should be assessed in patients undergoing plasmapheresis especially those indicated for invasive maneuvers or surgery following plasmapheresis.

Keywords: Plasmapheresis, Fibrinogen, aPTT, Bleeding risk

INTRODUCTION

Plasmapheresis is a procedure in which extracorporeal separation of blood component results in a filtered plasma product via centrifugation or the use of semipermeable membranes.¹ Plasmapheresis is used when a toxic substance as immunoglobulin present in the plasma and so can be removed.² It is considered as first line therapy for different diseases including the renal and non-renal diseases. Some of the renal causes for plasmapheresis are renal transplant rejection that is antibody-mediated, Goodpasture's syndrome, Recurrent focal segmental glomerular sclerosis, and catastrophic antiphospholipid syndrome. Some of the neurological disorders that need

plasmapheresis as acute Guillain-Barré syndrome, Chronic inflammatory demyelinating polyneuropathy, Myasthenia gravis and paraproteinaemias associated Polyneuropathy. Metabolic indication as Familial hypercholesteremia. Microvascular angiopathy as Thrombotic thrombocytopenic purpura, atypical hemolytic uremic syndrome.³ The replaced fluid during plasma exchange include albumin, electrolyte solutions, hydroxyethyl starch, FFP, and purified protein products such as individual clotting factors or antithrombin III. Albumin is the most commonly used replacement fluid as it has low side-effect widely available. the selection of the replaced fluid depends on the underlying disease, associated disorders, certain laboratory markers (example-

total serum protein, coagulation factors) and the fluid state of the patient so the processour maintain isovolumic stat and a normal oncotic pressure.⁴ When albumin is used as a replacement fluid there is a 30% prolongation of prothrombin time and doubling of partial thromboplastin time after a single plasma exchange.⁵ Fibrinogen is a soluble glycoprotein that act as the substrate for fibrin formation and as the ligand for the platelet receptor promoting platelet aggregation so it has a central role in clot formation.⁶ The reported reduction in fibrinogen level following therapeutic Plasmapheresis session nearly 20 .⁷

Aim of the work

Present study was aiming to assess the effect of therapeutic plasmapheresis on fibrinogen level and risk of bleeding in different indication in renal and non-renal disorders.

METHODS

The present case control study was conducted on 40 patients attended to El-Demerdash Hospital, Ain Shams University from the period of May 2019 to November 2019. The study was approved by the hospital's research ethics board. Any Patients with age ranging 15-45 and undergoing therapeutic plasmapheresis for any indication and willing to participate and giving written consent were involved. Patients with any of the following were excluded from the study Congenital Hypofibrinogenemia, end-stage liver disease severe malnutrition, disseminated intravascular coagulation (DIC), Patients known with solid tumors and, Pregnant females. The 40 patients were divided into 2 groups according to presence of renal cause for plasmapheresis or non renal cause for plasmapheresis. Renal Group Included 20 patients undergoing therapeutic plasmapheresis for renal cause, they were 4 males and 16 females with age ranges from 15 to 45 years. Non renal Group: Included 20 patients undergoing therapeutic plasmapheresis for non-renal indications, they were 5 males and 15 females with age ranges from 15 to 45 years. All participants were subjected to history taking including age, sex, occupation, special habits, drug history and history of other chronic illness, indication of plasmapheresis and frequency of session. Clinical examination and monitoring before plasmapheresis session including blood pressure measurement, heart rate, respiratory rate and BMI, examination of any signs of bleeding tendency, abdominal examination to exclude those with enlargement of liver or spleen. Laboratory studies including renal function tests, liver function tests, CBC were performed for all patient. INR, aPTT and fibrinogen level were assessed before and after plasmapheresis session. Patients were monitored during plasmapheresis session and for 72 hours later for any clinical evidence of bleeding.

Study design

The study was conducted using a descriptive cross-sectional design. This study was conducted on 40 patients divided into 2 groups containing both renal and non-renal.

Renal group included 20 patients undergoing therapeutic plasma exchange for renal indication, they were 4 males and 16 females with age ranges from 15 to 45 years.

Sample size and sampling technique

A sample size of 40 was calculated using the sample size formula for a single proportion. The sample size was proportionally allocated to various units including the medical and nursing services, laboratory, morgue, theatre, environmental health unit. The cleaners were also involved in the study. The respondents in these subgroups were enrolled until the allocated numbers of respondents were enrolled. The enrolment was spread across different shifts to ensure adequate representation of staff in various units that operate based on shift systems.

Statistical analysis

Statistical analysis was conducted using the Statistical package for social sciences (SPSS software version 25).

RESULTS

The present study involved 40 patients divided into 2 gropes according to presence of renal cause of dialysis.

Table 1: Demographic data of the study groups.

	Renal n=20	Non-renal n=20	P value
Age			
Mean±SD	6.1±29.2	6.7±26.2	0.147
Range	(41-19)	(44-19)	
Gender			
Male	(20.0%) 4	(%25.0) 5	0.99<
Female	(%80.0) 16	(%75.0) 15	
Smoking			
Yes	(%5.0) 1	(%10.0) 2	0.99<
No	(%95.0) 19	(%90.0) 18	
Weight			
Range	83-53	88-53	0.43
Mean±SD	8.06±69.9	8.4±69.9	
Hight			
Range	180-150	177-150	0.12
Mean±SD	8.04±163.8	7.4±162.3	
BMI			
Range	29.4-21.5	29.4-20.2	0.55
Mean±SD	1.9±26.02	1.8±26.4	

* P significant at level > 0.05 ,BMI = body mass index SD = standard deviation

Renal group included 80% (16) female, with mean age was 29.2±6.1 years, mean BMI was 26.02±1.9 while group B consisted of 75% (15) female, their mean age was 26.2±6.7 years and mean BMI was 26.4±1.8 (Table 1). There was a significant prolongation of the INR in both groups (renal and non-renal group) post plasmapheresis as INR was initially 1.2±0.2 and changed post-session to 1-1.6 in the renal group and in the non renal group it changed from 1.3

to 1.9. Also there was a prolongation of APTT post plasmapheresis significantly in both groups post plasmapheresis this can be explained by use of heparin as anticoagulant (Table 2,3). The fibrinogen level also significantly reduced in both groups post plasmapheresis. Its median level was 310 pre plasmapheresis and reduced to 212 post plasmapheresis in the renal group. Similarly its level was reduced significantly in the non renal group of plasmapheresis with a median level reached to 114 post plasmapheresis (Table 4). This changes in coagulation profile occurred in both renal and non renal indication of plasma pheresis without significant increase in bleeding risk in both groups post plasmapheresis.

Table 2: Changes in lab data in renal group.

The mean value for	Pre n=20	Post n=20	P value
aPTT			
INR			
Median	1	0.2±1.2	0.001
Range	(1.2-1)	(1.6-1)	
aPTT			
Mean±SD	1.8±37.5	9.3±76.5	*0.001>
Range	(40-33)	(90-54)	

Table 3: Changes in lab data in non-renal group.

	Pre n=20	Post n=20	P value
INR			
Median	1	0.2±1.3	*0.002
Range	(1.3-1)	(1.9-1)	
APTT			
Mean±SD	3.5±39.7	9.9±65.1	*0.001
Range	(48-34)	(87-48)	

Table 4: Changes in fibrinogen level in both groups.

	Renal n=20	Non-renal n=20	P value
Fibrinogen pre	310.5	337.5	0.291
Median (Range)	(387-256)	(412-260)	
Fibrinogen post	-110) 212	-114) 140	0.189
Median (Range)	(386	(415	
P value (pre vs post)	<*0.001	*0.001	
Reduction in fibrinogen	11-(101 to 234)	-(136.5 58to 252)	0.245
Median (Range)			
%Reduction in fibrinogen	3-(35.7to 68)	-(50.1 19.2to 68.5)	0.152
Median (Range)			
Reduction group			
>20%	9 (45%)	5 (25%)	0.543
20%-40%	2 (10%)	3 (15%)	
<40%	9 (45%)	12 (60%)	

*P significant at level <0.05

DISCUSSION

Therapeutic plasmapheresis is one of the growing therapeutic modalities for different clinical indications.⁸ During The process of plasma removal there is a removal of coagulation factors. This unintended removal of coagulation factors is especially critical when replacement fluids other than donor plasma is used, and has a possibly important hemostatic effect on patients undergoing invasive procedures immediately before or after TPE.⁹ In spite of the potential risk of bleeding associated with this procedure, therapeutic plasmapheresis is generally safe and well tolerated maneuver, with few complications apart of complication of any intravenous procedure.¹⁰

The present study showed that female gender represented 75% of cases. This can be explained that most autoimmune diseases follow a female bias.¹¹

This is consistent with Zollner study in 2014 which was performed on 17 patients undergoing therapeutic plasma exchange for MS, GBS, MG and demonstrated that 59% of participants were females, 41% were males.⁷ The result is not consistent with Hassan study in 2010 which performed therapeutic plasma exchange on 50 patients as 44% were females and 56% were males.¹² The male predominance was explained as 50% of cases were GBS which has a male predominance.¹³

Also the present study showed highly statistical significance reduction in fibrinogen level in both renal and non renal indication of plasmapheresis compared to the pre-session levels. Reduction occurred by 35.7% in renal group versus 50.1% in non-renal group. This is matched with the results of Tholking at 2015 who reported decrease in fibrinogen by 54% in patients performing TPE and none of them dropped below 150 mg.¹⁴

This was also consistent with Zollner et al who reported a significant reduction in fibrinogen levels post plasmapheresis as fibrinogen was reduced by 48.5%.⁷ Also Zainab et al at 2010 reported decrease in fibrinogen levels in patients doing TPE in her study on 25 patients using FFP as replacement fluid versus 25 using crystalloid 8% of cases of crystalloid group versus 4% of FFP showed reduction in their post session fibrinogen levels.¹³ Also Abdel-Monem et al 1992 in his study on 18 neurological patients doing TPE reported decrease in serum fibrinogen levels without clinical bleeding. Fibrinogen reduction wasn't correlated to age or sex changes, also it was not associated with any significant bleeding. This can be explained that serum fibrinogen level never reached below 100 mg/dl. at which risk of bleeding occurs.¹⁵ No significant changes were observed between renal and non renal group as regard fibrinogen reduction or risk of bleeding. Similar result was reported by Zainab et al, who showed no cases of bleeding despite reduction in fibrinogen levels, also Domen et al 1984 recorded reduction in fibrinogen level with two cases of bleeding

and this was explained by drop of fibrinogen levels below 50 mg/dl.^{13,16}

In the study of Zollner 2014; fibrinogen reduction below 100 mg occurred in 17 % with bleeding events in 2.3% of cases treated with TPE. This was explained by difference in plasma volume proceeded during session, spacing between sessions and presence of other risk of bleeding tendency as use of anticoagulants or performing invasive procedures.⁷ Regarding aPTT our results showed that aPTT was prolonged in 100% of cases.

These changes are consistent with Tholking et al, 2015 who reported prolongation of aPTT in 60% of cases.¹⁴ And s consistant with Zeinab 2010 who reported that aPTT levels were prolonged in all patient groups compared with pre session. This could be explained by transient reduction of coagulation factors during session; as well as use of heparin as anticoagulant during session.¹⁵

The limitation of the study was the small sample size and lack of comparison of the different modalities of plasmapheresis as regarede to the effect of different replacing fluid and its effect on bleeding risk.

CONCLUSION

Although there was a significant changes in coagulation profile post plasmapheresis in different patient who were indicated for plasmapheresis this was not associated with increased risk of bleeding.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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