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Association of donor characteristics with coagulation factor levels in fresh frozen plasma

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Abstract:

BACKGROUND: Coagulation factors are essential to maintain normal hemostasis. Plasma for transfusion can be obtained from whole blood donation or plasma apheresis. Plasma obtained from whole blood donation is termed as fresh frozen plasma (FFP). The quality of FFP can be influenced by several factors including donor variables (such as age, gender, diet, genetic profile), environmental factors, collection methods, processing methods, storage temperature, etc. This study was done to assess the association of donor characteristics such as donor age, blood group, and smoking with coagulation factor levels in FFP units.

MATERIALS AND METHODS: The screening of donors for collection of whole blood units was done as per the national guidelines. A total of 144 FFP units were assessed for coagulation factors. The FFP units were tested for prothrombin time (PT), activated partial thromboplastin time, fibrinogen, coagulation factor VIII, and coagulation factor IX (CF IX) on coagulation analyzer.

RESULTS: A total of 144 FFP units were tested for coagulation parameters. The value of PT was highest in units prepared from donors in more than 45 years of age group. The value of CF IX was significantly lower in O blood group as compared to non-O blood group. The value of fibrinogen was significantly higher in smokers as compared to nonsmokers.

CONCLUSION: The findings of the present study further add evidence to the fact that donor factors such as age, blood group, and smoking have an impact on coagulation factor levels in FFP units.

Keywords:

Age, coagulation factors, fresh frozen plasma, O blood group, smokers

Introduction

Plasma is the acellular part of blood and comprises water, proteins, electrolytes, lipids, and carbohydrates. Of these, proteins are of great interest in terms of therapeutic uses of coagulation factors, albumin, and immunoglobulins. Coagulation factors are essential to maintain normal hemostasis. For transfusion, plasma can be obtained by centrifugation of whole blood or by plasma apheresis and then subjecting it to freezing temperatures.[1] Fresh frozen plasma (FFP) is human donor plasma prepared from whole blood donation and frozen within 6–8 h of phlebotomy at a defined temperature, typically <−18°C.[2] The use of FFP has been explained in actively bleeding patients and multiple factor deficiencies as in liver diseases; disseminated intravascular coagulation; massive transfusion; thrombotic thrombocytopenic purpura; factor V deficiency; and deficiency of factor II, V, IX, and X.[1] Although the literature provides evidence of transfusion-related acute lung injury as an adverse effect of FFP transfusions, the incidence has decreased with restriction of the use of female plasma for transfusion. The constituents of FFP can be influenced by several factors including

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donor variables (such as age, gender, diet, genetic profile), environmental factors, collection methods, processing methods, storage temperature, etc.[1] All these factors modify the levels of individual proteins present in FFP. This leads to heterogeneity and reflects both biological variation and variation in methods of collection, processing, storage, and preparation for administration.

Materials and Methods

This was a prospective study conducted for a period of 1 year in a tertiary care institute in North India. The screening of donors for collection of whole blood units was done as per the guidelines recommended in DGHS and NACO guidelines for screening of voluntary and replacement donors.[3,4] Informed consent was taken from accepted donors that blood components prepared would be used for research purpose. All ABO blood group units including O, A, B, and AB were taken. The FFP units from female donors were excluded as institutional policy of using only male plasma for transfusion. Whole blood was collected by single venepuncture in 450-ml CPD/SAGM quadruple blood bags. The flow of blood was constant during donation and only those units were taken for this study where blood collection was completed within 8 min. The FFP units prepared from outside blood donation camps were not taken in the study. Whole blood bags were processed as per department standard operating procedure (SOP). Whole blood bags were given hard spin using Cryofuge at 3100 rpm for 9 min at 4°C or at 3550 rpm for 9 min at 22°C (if platelet concentrates were prepared), followed by separation by buffy coat method using an automated component separator. The volume of FFP units was recorded, and units were labeled as per SOP. FFP units were then frozen at −80°C within 6 h of phlebotomy. Tests for coagulation parameters were performed on an automated coagulation analyzer which was calibrated routinely. The reagents were stored at a specified temperature and were used before the expiry date of reagents. Calibrators provided by the manufacturer were used with each new lot of reagents. Controls (normal and abnormal) provided by the manufacturer were included in the test run each day. The following coagulation parameters were tested on 144 FFP units: prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen, coagulation factor VIII (CF VIII), and coagulation factor IX (CF IX).

Statistical analysis

All the statistical tests were two-sided and were performed at a significance level of $\alpha = 0.05$. The statistical analysis was conducted using SPSS 23 (IBM Corp. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp).

Results

A total of 144 FFP units were tested for coagulation parameters. The donors in the study population comprised 18–57 years of age. The mean age of donors was 31.05 ± 8.19 years, and the median age was 30 years. The donors were divided into subgroups of age of donors. The median of values obtained for coagulation parameters of FFP units was compared in subgroups of age of donors [Table 1].

The PT value in subgroups of age of donors was compared using Kruskal–Wallis test (nonparametric tests). The *P* value was statistically significant ($P = 0.012$), with the median PT being highest in the samples with donors more than 45 years of age group [Table 1].

The comparison of values obtained for coagulation parameters in O blood group and non-O blood group is depicted in Table 2 and of smokers and nonsmokers is shown in Table 3.

The value of fibrinogen in smoker and nonsmoker groups was compared using Wilcoxon test and *P* value was found to be significant ($P < 0.001$), with a mean value being maximum in history of smoking present group [Figure 1].

The mean value of CF VIII in O type was lower as compared to non-O type, with the highest value being in non-O type. Wilcoxon test (nonparametric) was used to compare the two groups and *P* value was 0.106 which was not statistically significant. The mean value of CF

Table 1: Comparison of coagulation parameters [median (interquartile range)] in donor subgroups

Parameters	18-25 years	25-35 years	35-45 years	>45 years	*P*
PT (s)	11.1 (0.95)	10.85 (0.8)	10.9 (0.95)	11.3 (0.7)	0.012
INR	0.96 (0.09)	0.94 (0.07)	0.94 (0.08)	0.98 (0.07)	0.012
aPTT (s)	28.35 (2.97)	28.5 (4.42)	29.5 (3.3)	30 (3.65)	0.730
Fibrinogen (mg/dl)	273.5 (68.25)	290.1 (85.3)	299 (74.83)	379.4 (91.5)	0.192
CF VIII (U/dl)	229.02 (43.22)	207.05 (16.22)	216.56 (29.65)	171.56 (21.2)	0.931
CF IX (U/dl)	247.59 (23.45)	203.30 (29.92)	202.83 (18.85)	168.33 (44.45)	0.533

PT=Prothrombin time, aPTT=Activated partial thromboplastin time, CF VIII=Coagulation factor VIII, CF IX=Coagulation factor IX

Table 2: Comparison of coagulation parameters (mean ± standard deviation) between O and non-O blood group FFP

Parameters	O type	Non-O type	*P*
PT (s)	10.95±0.72	11.07±0.72	0.49
INR	0.95±0.07	0.97±0.11	0.47
aPTT (s)	29.71±4.36	29.0±4.13	0.27
Fibrinogen (mg/dl)	288.38±64.28	291.27±71.47	0.97
CF VIII (U/dl)	197.98±172.64	217.17±172.22	0.10
CF IX (U/dl)	210.80±236.85	213.88±125.72	0.02

PT=Prothrombin time, aPTT=Activated partial thromboplastin time, CF VIII=Coagulation factor VIII, CF IX=Coagulation factor IX

Table 3: Comparison of coagulation parameters (mean ± standard deviation) between FFP obtained from smokers and nonsmokers

Parameters	Smokers	Nonsmokers	*P*
PT (s)	11.02±0.71	11.07±0.73	0.70
INR	0.97±0.13	0.96±0.07	0.78
aPTT (s)	29.03±4.47	29.26±3.94	0.33
Fibrinogen (mg/dl)	338.42±62.57	249.20±43.93	<0.001
CF VIII (U/dl)	200.26±94.60	223.61±216.95	0.66
CF IX (U/dl)	196.25±113.49	227.54±184.52	0.27

PT=Prothrombin time, aPTT=Activated partial thromboplastin time, CF VIII=Coagulation factor VIII, CF IX=Coagulation factor IX

IX in O type was lower as compared to non-O type. The *P* value was 0.022 which was statistically significant with CF IX levels highest in non-O type.

Discussion

In the present study, in O blood group donors, PT, INR, and fibrinogen values were lower as compared to non-O blood group donors. The mean value of CF VIII was 197.98 U/dl and CF IX was 210.80 U/dl which was much lower as compared to non-O blood group samples. There was no statistical significance in the difference between CF VIII values, but there was a significant difference between CF IX values. In a study done by Favaloro *et al*. to study the influence of ABO blood groups on CF, similar results were found.[5] The CF VIII and CF IX were found to be significantly lower in O blood group as compared to non-O blood group individuals. O'Donnell and Laffan further supported the evidence that CF VIII values were significantly lower in O blood group as compared to non-O blood group individuals.[6] In a study done in Indian setup by Dhantole *et al*., CF VIII levels were seen less in O group as compared to non-O group donors, which was similar to the present study.[7]

There was a significant increase in PT and INR in donors with age of more than 45 years in the present study which was similar to the study done by Madla *et al*. where the effect of donor age on the quality of FFP was studied. Madla *et al*. had found an increase in INR, aPTT, fibrinogen, and factor VIII with increasing age of donors.[8] In the present study, an increasing trend was

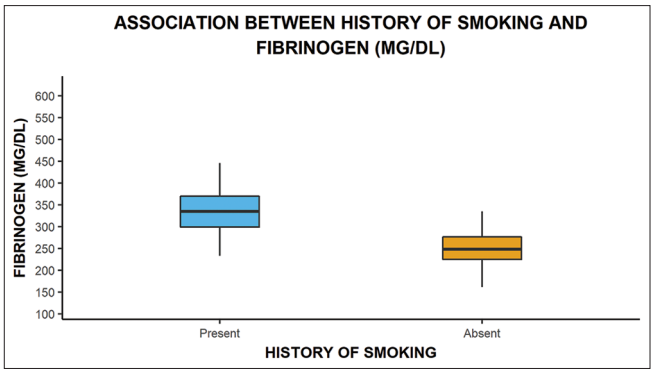

Figure 1: Box and whisker plot representing the distribution of fibrinogen in two groups

observed in aPTT and fibrinogen levels with an increase in age although it was not statistically significant. The correlation could not be established between CF VIII or CF IX with increasing age in donors in the present study.

There was a statistically significant difference in fibrinogen levels in smokers and nonsmokers with fibrinogen levels being higher in smoker group in the present study. Similar results were found in the study done by Yanbaeva *et al*. PT, INR, aPTT, CF VIII, and CF IX were not significantly different in the two groups in the present study.[9]

It is important to know the coagulation factor levels of FFP units being used for transfusion to the patient so as to attain desired improvement in patients. The clinical uses of FFP have been described as prophylactic, therapeutic or for plasma exchange.[3] Peralta *et al*. had described the use of FFP in trauma-induced or drug-induced coagulopathy in surgical patients.[10] Nakae *et al*. conducted a retrospective study in traumatic brain injury patients with coagulopathy and found that outcome was better in patients who had plasma fibrinogen levels of more than 150 mg/dl at 3 h after injury in FFP transfused group.[11] Thus, the levels of coagulation factors in FFP units if known would help to further improve patient outcome.

Conclusion

The findings of the present study further add evidence to the fact that PT and INR values increase with the age of more than 45 years. The fibrinogen levels are higher in smokers as compared to nonsmokers. CF VIII and CF IX levels are lower in O blood group individuals as compared to non-O blood group individuals.

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Conflicts of interest
There are no conflicts of interest.

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