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Regular plateletpheresis increased basal concentrations of soluble P-selectin in healthy donors: Possible involvement of endothelial cell activation?

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ABSTRACT

Background: We explored the effects of repeated plateletpheresis on the platelet P-selectin expression and soluble P-selectin (sP-selectin) concentrations in platelet donors.
Methods: Totally 289 platelet donors and 97 first-time whole blood (WB) donors were enrolled from the blood donor registry at the Fujian provincial blood center, China. The accumulative numbers of plateletpheresis in the last 2 y for participants were recorded, and the basal concentrations of platelet count, sP-selectin and total platelet P-selectin (pP-selectin) were determined.
Results: Platelet donors had significantly higher basal concentrations of sP-selectin compared to WB donors (24.12 ± 7.33 ng/mL vs. 20.74 ± 5.44 ng/mL, $P < 0.0001$), with no difference in platelet count and pP-selectin concentrations. Increased numbers of platelet donation were correlated with a steady increase of sP-selectin ($r = 0.18$, $P = 0.002$). Multivariate regression analysis identified that the frequency of plateletpheresis is an independent factor for the rise of the sP-selectin concentration ($t = 2.64$, $P = 0.009$) while no association was found for pP-selectin and platelet count.
Conclusions: Repeated plateletpheresis could result in an increased basal concentration of sP-selectin in blood donors whereas not an alteration in the concentrations of total platelet P-selectin. It remains to be determined whether this might be a consequence of endothelial activation or platelet activation or some other phenomenon.

1. Introduction

Blood transfusion is required for the clinical hematherapy. Platelet is one of the highly demanded blood components, which can be collected by plateletpheresis directly or be separated from the whole blood after harvested. Of the advantages of high yield and high purity, plateletpheresis has become a more and more popular way of platelet collections in the world.

Plateletpheresis is an extracorporeal circulation process that is complete different from the whole blood (WB) donation. During the apheresis procedures, the blood taken from the donor is exposed to artificial surfaces and external forces such as centrifugation. Therefore, the adverse effects for apheresis donors are largely different from WB donors. So far, the donor safety issues accompanying with the apheresis procedures are more focused on the short-term adverse effects. It has been shown that the interaction of blood with artificial membranes under external forces can result in the activation of the coagulation system [1,2] and various circulating blood cells, such as platelets and leukocytes [3–5]. However, the possible long-term consequences on frequent donors are far beyond fully illustrated.

Plateletpheresis is allowed to be performed 22 to 24 times/year from a single donor, according to the international guideline. The accumulative metabolic effects of plateletpheresis have been implicated with a long-term consequence on healthy donors e.g. reducing bone mineral density or iron storage, or impairment of platelet function [6–8]. P-selectin is an adhesion molecule that can be released from platelets upon activation [9], which occurs during single apheresis procedure [3,4]. It functions in the initial recruitment of leukocytes to the site of injury during inflammation and plays a significant role in the recruitment and aggregation of platelets at areas of vascular injury. Higher concentrations of soluble P-selectin (sP-selectin) were described as a risk factor in a variety of cardiovascular disorders, including coronary artery diseases (CAD) [10,11] and venous thromboembolism (VTE) [12]. Thus, it would be of interesting to know whether repeated stimuli

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Table 1
Demographic information of study subjects.

	WB donors	Platelet donors	*P* value
Number of subjects	97	289	
Leukocyte counts (10^9/L)	6.45 ± 1.53	6.31 ± 1.38	0.46
Platelet counts (10^9/L)	245.7 ± 43.9	245.5 ± 51.7	0.72
RBC counts (10^{12}/L)	4.78 ± 0.53	4.80 ± 0.47	0.74
Hemoglobin (g/L)	142.0 ± 14.2	145.0 ± 14.0	0.04
MCV (fL)	85.5 ± 4.2	86.7 ± 3.7	0.043
Age	28.3 ± 7.3	30.0 ± 7.4	0.025
(Range)	(20–43)	(19–45)	
Male/female	1.9	1.9	

Abbreviation: MCV, erythrocyte mean corpuscular volume.

(plateletpheresis) could have an impact on the platelet physiology response, especially in P-selectin expression, in platelet donors. sP-selectin is suggested as a suitable marker for the detection of circulating activated platelets, particular in clinical settings where more chronic stimuli are present [13].

2. Materials and methods

2.1. Study subjects

The study protocol was approved by the local institutional review board and signed informed consent was obtained from all participants. All study subjects were voluntary donors of the community blood donation program of the Fujian Provincial Blood Center, Fuzhou, China; they fulfilled the Chinese national standard eligibility criteria for blood donation. Before inclusion in the study, all participants underwent a detailed medical questionnaire. Individuals with a family history of thrombosis, or subjects taking hormonal contraceptives or drugs known to interfere with platelet activation were excluded.

As a case-controlled study, altogether 289 plateletpheresis donors with no mixed whole blood donation after being enrolled as platelet donors were enrolled. Their platelet donation histories in the last two years were retrieved from the donor's registry. Additionally, 97 first-time whole blood (WB) donors were recruited as controls.

Platelet collections were usually conducted with single-needle apheresis devices (MCS+, Hemonetics Corp.; Trima Accel, Terumo BCT). The minimal interval between each collection was 30 days. Other apheresis-related settings were as followed: ACD-A was used as the anticoagulant at a citrate to blood ratio of 1 to 9 (Hemonetics). During a single apheresis, the maximal number of platelets harvested was set to 4×10^{11} platelets; maximal apheresis time was 80 min per procedure.

2.2. Sample collection and preparation

Blood sampling was conducted prior to any apheresis procedure or whole blood donation. EDTA-anticoagulated blood was obtained from each participant using a 21-gauge butterfly needle. During sampling, blood was drawn without using a blood pressure cuff to avoid artificial platelet activation. A minimum time interval between the last blood donation and blood sampling was 30 days. Blood count was performed immediately after sample collection. Within 1 h of sampling, blood samples were further processed to obtain the platelet-free supernatants and platelet lysates, according to a previously published protocol [14].

2.3. Laboratory measurements

The circulating platelet counts were analyzed with an automated hematology analyzer (K-4500, Sysmex Corp,). Total platelet P-selectin (pP-selectin) in platelet lysates and soluble plasma P-selectin (sP-selectin) in platelet-free supernatants were determined by Human sP-Selectin/CD62P ELISA reagent set (R&D Systems). In the present analysis, the pP-selectin concentration was expressed as the total amount of P-selectin (ng) per 5×10^7 platelets.

2.4. Statistical analysis

The analysis was performed by GraphPad Prism 5.0 and SPSS 17.0 software. Data was expressed at mean ± standard deviation or median (interquartile range), as appropriated. The statistical significance of differences between the means of 2 study groups was evaluated by Mann–Whitney *U* test for categorical data or unpaired *t*-test for continuous data. When three or more groups were analyzed, the one-way ANOVA test was applied. Multivariate regression and Pearson or Spearman correlation analysis was conducted as appropriate. A 2-tailed *P*-value < 0.05 was considered significant.

3. Results

3.1. Demographic information and donation history of the study subjects

The demographic information of study subjects was shown in Table 1. Both groups were comparable in peripheral platelet, leukocyte, and red blood cell counts and with a similar male to female ratio; differences exist regarding mean age ($P = 0.025$), erythrocyte mean corpuscular volume (MCV, $P = 0.04$) and hemoglobin concentrations ($P = 0.04$).

The overall distribution of the two-year's platelet donation history among platelet donors was as follows: Donation times were ranged from 1 to 22, with a median of 6 donations (IQR 3 to 11 times). The majority of donors (68.5%) had the accumulative platelet donation frequency of <10 times while 21.5% of subjects had ≥12 donations. The control group includes only first-time WB donors with no history of previous plasma or blood component donations.

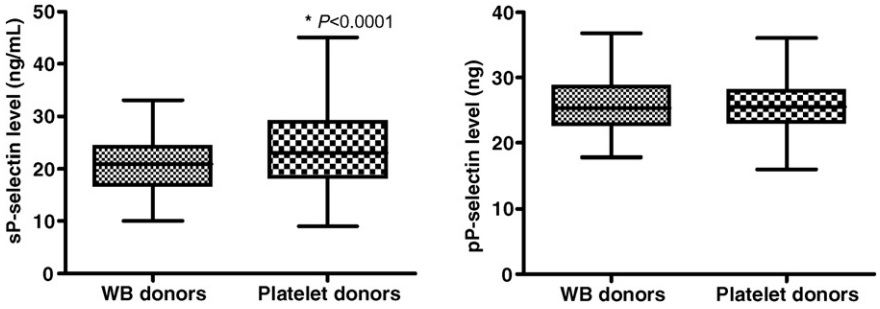

Fig. 1. Comparison of sP-selectin and pP-selectin levels between platelet donors and WB donors. sP-selectin level was higher in platelet donors (*$P < 0.0001$) compared to WB donors, while pP-selectin level showed no significant difference between two groups($P = 0.69$).