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Effects of Plateletpheresis on Hematological Parameters

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Abstract

Apheresis for platelet concentrates has been used more frequently in recent years due to the rising demand for platelet transfusions for patients with various medical and surgical disorders. Studies on the effect of repeated or frequent plateletpheresis on the donor's hematological parameters are still limited. This article will review the effects of plateletpheresis on the donor's hematological parameters to define the proper deferral for repeat donation because this treatment is relatively new and requires early repeat donations. We systematically search the studies and review current evidence about the effects of plateletpheresis on blood parameters in healthy donors. Literature tracking was performed on PubMed, CENTRAL, EbscoHost, and ProQuest databases. There are different effects, and some studies reveal that plateletpheresis can decrease hematological parameters (HB, HCT, PLT, PDW). Some can cause an increase in hematological parameters (HB, HCT). These different effects can be caused by variable cell separator technologies, residual blood volume lost during apheresis, and mechanical hemolysis of blood in tubes by machine pumps.

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Background

Technology-advanced "apheresis" for platelet concentrates has been used more frequently in recent years due to the rising demand for platelet transfusions for patients with various medical and surgical disorders [1]. Due to this development, single-donor platelets acquired through automated blood collection have become increasingly popular. Apheresis is a technique used to extract one or more specific blood components, such as platelets, plasma, and stem cells, to obtain a standardized, high-quality output [2]. In the process of plateletpheresis, whole blood from a donor is processed, platelets are isolated on their own, and the remaining blood components are then given back to the donor [3].

Red blood cells and plasma are returned to the patient together with the platelets suspended in plasma as the final result. One unit of platelet concentrate created from one unit of whole blood typically contains 7.5 x 10^{10} platelets and should boost the platelet count in a 70 kg recipient by 5 to 10 x 10^{9}/L (5,000–10,000/L). Depending on the collection method, apheresis platelet concentrates typically comprise 3–6 x 10^{11} platelets [4]. As a result, apheresis allows for the supply of six times as many platelets as whole blood donation.

The cell separator has been used as a primary tool to collect platelet concentrates. Thus, the productivity and quality of apheresis platelets have significantly increased. Following a donation, plateletpheresis reveals changes in hematological parameters. This modification has significant clinical implications for donors. However, only a few medical facilities offer regular, high-quality plateletpheresis programs and donor follow-up. Data from earlier investigations on the changes in hematological parameters following plateletpheresis are contradictory. In fact, after plateletpheresis, one study found increases in hemoglobin concentration (Hb), hematocrit (Hct), and white blood cell (WBC) count [5]. However, other studies described considerable decreases in these metrics. However, these hematological changes could have clinical effects on the donor, like thrombocytopenia and anemia, the prior findings [6].

Studies on the effect of repeated or frequent plateletpheresis on the donors' hematological profiles are still limited. This article will review the effects of plateletpheresis on the donor's hematological profile and platelet regeneration time to define the proper deferral for repeat donation because this treatment is relatively new and requires early repeat donations.

Materials and Methods

We systematically search the studies and review current evidence about the effects of plateletpheresis on blood parameters in healthy donors. Literature tracking was performed on PubMed, CENTRAL, EbscoHost, and ProQuest databases. The results of the systematic search are described narratively. The keywords used in the research process include: "Plateletpheresis", "apheresis", "apheresis platelet", "blood parameter", "donor platelets". The studies with the available full text published in English will be reviewed further.

Discussion

Platelets are small, enucleated megakaryocytes from the hematopoietic lineage made in the bone marrow and aid in the

maintenance of primary hemostasis, or blood flow in the blood vessel, by platelet adhesion and platelet aggregation, respectively [7]. Transfusions of platelets can be performed either therapeutically or preventively. The majority of transfusions are administered to thrombocytopenic patients to stop bleeding. Single Donor Plateletpheresis (SDP) or a pool of four to six concentrates from different units of whole blood make up the standard dose of platelets [8]. The benefit of SDP is that a single donor can produce an adequate amount for transfusion while reducing the number of donors exposed to transfusion-transmitted infections by 4-6 times [10]. Several studies show that plateletpheresis performed by donors might significantly alter hematological parameters, so it is important to investigate and assess the effects of automatic plateletpheresis on donors' hematological parameters and its implication [9]. Here we will discuss some of the effects of plateletpheresis on the donor's hematological parameters from previous studies.

Table 1. Hematological parameter result after plateletpheresis procedure

Authors	Subject and methods	Results
Suresh et al. [11]	90 plateletpheresis donors on Fresenius Kabi AG(Else-Kröner-Straße 1, Bad Homburg, Germany)	Hb (P=0.002), Hct (P=0.045), and PDW (P=0.039) values decreased significantly in the donors. There was a slight increase in MPV (P=0.067) and a decrease in MCV and RBC (P>0.5), but the results were not clinically significant.
Lazarus et al. [12]	939 plateletpheresis donors on CS3000 Plus equipped with the TNX-6 separation chamber and the PLT- 30 collection chamber (Baxter Healthcare Corp)	Hb, Hct, PLT, MPV, and PDW in the donors (P<0.001), a significant decrease in blood count values.
Sachdeva et al. [13]	171 plateletpheresis donors on amicus automated blood collection system.	Hb and HCT (P<0.001) statistically significant increase.
Mahmood et al. [14]	76 plateletpheresis donors on Hemonetics MCS+ and Trima Accel (Gambro BCT, Lakewood, CO, USA) cell separators	A significant decrease from ((p<0.001) with mean difference between pre-donation and post-donation values for Hb (0.2±0.5), Hct (0.6±1.3), PLT (70.5±21.9), MPV (0.3±0.3), and PDW (0.6±0.5), but in contrast, they found a significant increase in mean difference for WBC (−0.4±0.6) (P<0.001)
Nomani et al. [15]	60 plateletpheresis donations by Fenwal CS3000 plus (Baxter, Deerfield, IL, USA)	A significant decrease from the pre-donation values for Hb (7.82%), PLT (31.85%), HCT (9.96) %, and WBC (7.15%) (P<0.001)

Lazarus et al. documented a transient but significant decrease in blood cell counts in donors undergoing platelet apheresis. However, clinically significant thrombocytopenia is rare. After each intervention, our data were Hb, Hct, PLT, MPV, and PDW significantly reduced in donors (p<0.001) [12].

Study by Mahmood et al. found that Significant reduction in pre- and post-delivery hemoglobin (Pre-delivery:14.9g/dl after donation:14.7g/dL), hematocrit (before donation:44.6%, Subsequent Donations:44.1%), platelet count (previous donation: $264.0x10^9$/L, after donation:$193.4x10^9$/L), average platelet count (before donation:10.0fL, after donation:9.7fL) and platelet distribution range (before donation:12.3fL, after donation:11.8fL). After each treatment, the donor's Hb, Hct, PLT, MPV, and PDW values decreased significantly (p<0.001). A significant increase in total white blood cell count was also observed (pre-delivery:$7.1x10^9$ /L, after donation:$7.5x10^9$/l) [14].

Nomani et al. found that all hematological parameters post-donation showed significant decreases compared with pre-donation values (p < 0.001). Post-donation hemoglobin <12 g (defined as anemia by WHO) occurred in 25% (n = 15) of blood donors, regardless of gender. Post-donation platelet counts were <100 × 109/L in 16.6% (n = 10) of treatments[15].

In a study by Sachdeva et al. using the Amicus automated blood collection system, they reported results that contradicted previous studies, namely an increase in Hb and Hct levels; there was a statistically significant increase in post-donation Hb (1.7%) (P<0.001). This can happen because the concentrated red blood cells are transported back to the donor, and the plasma is retained at the end of the procedure, while the same explanation was given for the increase in Hct [13].

We have summarized several studies about the effect of plateletpheresis on hematological parameters. From table 1, it can be seen that there are different effects. Some studies reveal that plateletpheresis can decrease hematological parameters (HB, HCT, PLT, PDW), and some can cause an increase in hematological parameters (HB, HCT). Variable cell separator technologies can cause these different effects, residual blood volume lost during apheresis, mechanical hemolysis of blood in tubes by machine pumps, and hemodilution due to citrate infusion may all contribute to the variation in the hematological change values following the apheresis operation [14]. It could also occur due to the procedures used to collect blood samples, the varied cell counts and reagents utilized, the interval between the procedure's conclusion and the sample's collection, or physiological changes in the donor [12]. When examining the impact of plateletpheresis on the donor platelet, numerous additional factors, including the period between donations and the quantity of units given during a single treatment, should be considered [16].

Several studies revealed that the decrease in hematological parameters (HB, HCT, PLT, PDW) could be due to the use of older or first-generation apheresis devices that lost more red blood cells during plateletpheresis than more modern models. Several reasons were responsible for these blood losses. The first factor relates to blood loss in the apheresis kit's void volume after the procedure. The second factor is mechanical hemolysis, which can happen when a device's pumps squeeze the blood tubes. The third consideration is anemia, which may be brought on by hemodilution brought on by the infusion of saline and citrate solutions during the apheresis operation [17].

The mean platelet volume and PDW in the post-plateletpheresis donors were not found to have a significant decrease in Das et al. study's conducted in India ($p>0.5$) [18]. In contrast, Suresh et al. and Mahmud et al. discovered a considerable reduction in PDW of plateletpheresis donors. Although the cause of this discrepancy is not fully understood, it is expected that younger, reticulated platelets with larger sizes will enter the system as platelets regenerate after being lost from the body. This will lead to platelet anisocytosis and the rise of PDW. Future research may be able to determine these results [11,14].

The majority of studies have demonstrated that the amount of platelets within a short period after apheresis is significantly decreased, but the platelets stored in the spleen will be immediately released to the peripheral blood through compensatory mechanisms of the body, stimulating more bone marrow hematopoietic stem cells to be quickly differentiated and transformed into mature megakaryocytes, which are detached and enter the blood circulation. Therefore, about 4-6 days following platelet apheresis, the number of platelets can usually be restored to precollection levels [12].

There was a considerable reduction in platelet count among platelet-pheresis donors, which may have been caused by platelet adherence to the centrifuge bowl or tubing in addition to platelet collection [19]. Single plateletpheresis may result in a loss of 25–50% of circulating platelets, but the spleen usually restores this. Therefore donors who have undergone plateletpheresis are not typically found to have significant thrombocytopenia [20]. As a result, thrombocytopenia's clinical findings are rare. It has been demonstrated that plateletpheresis decreases platelet count, which activates thrombopoiesis to produce new platelets for peripheral circulation. Following platelet collection, the activation of the thrombopoiesis will result in a brief elevation in the serum thrombopoietin level [21].

Plateletpheresis is a safe procedure with few risks, but donors may occasionally experience discomfort due to symptoms related to citrate poisoning and other unfavorable occurrences. A previous study reported that 40 donors (1.33%) had adverse events, including citrate poisoning, hematomas, and vasovagal responses. Citrate toxicity was found in 20 out of the 40 affected donors in the current study [23, 24], despite giving prophylactic oral calcium (1000 mg), as suggested by previous authors. It was found that 20% of procedures involving prophylactic calcium were connected with symptoms, most of which were mild [25]. To promote donor retention, it is critical to identify and stop the occurrence of plateletpheresis-related adverse events as soon as possible [22].

Platelets are essential for forming primary hemostatic plugs and maintaining hemostasis. Platelet acts by two important functions, (1) Get adhered to exposed subendothelium with subsequent formation of aggregates at the site of vessel injury. (2) Facilitate thrombin and fibrin formation to strengthen these aggregates. Platelet transfusions are needed, either prophylactic or therapeutic. Adverse events in a study reported an overall incidence of 1.06% of adverse reactions. Several complications may occur. Anticoagulant (ACD) intoxication, which can cause hypocalcemia, may occur. Signs and symptoms of hypocalcemia include perioral numbness, paresthesia of the extremities, tremors, dizziness, chills, and uncoordinated involuntary movements. The vasovagal reaction is characterized by pallor, sweating, nausea, hypotension, fainting, and loss of consciousness [26, 27]. Plateletpheresis is also useful and essential in a wide variety of clinical situations, such as dengue fever, gestational thrombocytopenia-elective caesarean, DIC, acute ITP with bleeding, malaria-induced severe thrombocytopenia, chronic ITP in pregnancy-for elective LSCS, for surgical intervention, aplastic anemia, Fanconi anemia, coagulopathy of massive hemorrhage, Bernard Soulier syndrome, fracture of the wrist, and hematological malignancies [27].

Donor health, including coagulation function, may be impacted by several plateletpheresis contributions. Regular blood coagulation testing in the plateletpheresis donations in the earlier studies typically only involved measuring the activity of a single coagulation factor or evaluation of prothrombin time (PT), activated partial thromboplastin time (APTT), and activated clotting time [28, 29,30]. According to Beyan et al., there was no risk of bleeding despite a slight lengthening of PT time in blood donors following apheresis. Previous research has shown that 30 minutes after procedures, the coagulation profile begins to change. Therefore, it may be concluded that even if there is a modest decrease in coagulation function immediately after the following apheresis, this change is slight and transitory and is unlikely to result in serious changes to bleeding and also unlikely to produce a long-term adverse effect on the coagulation function [30].

Yilmaz et al. observed the clotting factors in donors undergoing dual platelet apheresis and discovered that while factor V, VIII, and IX levels declined following collection, fibrinogen levels remained within the normal range of PT, and APTT levels did not significantly drop. In the current study, following platelet apheresis, the K time was delayed, and the a-angle value was reduced, but they remained within the normal range. Furthermore, the K and a-angle values in various platelet apheresis frequency groups were also within the normal ranges. They did not demonstrate significant differences, suggesting a slight effect on thrombin formation and fibrinogen function in these donors after platelet apheresis [31].

After plateletpheresis, the prothrombin time (PT) and activated partial thromboplastin time (APTT) were significantly prolonged, but they were still within the normal range. After the apheresis operation, there was a prolonged PT/APTT, likely caused by the citrate in the ACD-A solution. However, because of its brief in vivo half-life, it does not result in systemic anticoagulation. In plateletpheresis donors, Beyan et al. investigated the impact of cell separators on coagulation. They

contrasted the previously obtained data and discovered prolonged PT and APTT [32]. However, some research indicated that PT was significantly prolonged following plasmapheresis, whereas APTT was unchanged [30].

A prior study comparing coagulation markers before and after apheresis found no difference that might have caused thrombosis [33]. The mechanism of thrombosis following plateletpheresis is unknown. However, some authors have hypothesized that modifications are brought on by a decrease in anti-thrombin, protein C, and protein S, an induction of coagulation activation, platelet activation, aggregation, and microparticle formation, and a hypercoagulable state after automated apheresis [34, 35, 36, 37]. Extracorporeal circulation is another potential method for increasing the hypercoagulable state. Hypercoagulable conditions can also result from the adsorption of clotting factors, platelet adhesion, aggregation, and adherence of white blood cells and red blood cells to the surfaces of the blood circulation tubes in the blood cell separator [36, 38].

Conclusion

Some studies reveal that plateletpheresis can lead to a decrease in hematological parameters (HB, HCT, PLT, PDW), and some can cause an increase in hematological parameters (HB, HCT). Clotting factors in donors undergoing dual platelet apheresis discovered that while factor V, VIII, and IX levels declined following collection, fibrinogen levels remained within the normal range and that PT and APTT levels did not significantly drop. After the apheresis operation, there was a prolonged PT/APTT, likely caused by the citrate in the ACD-A solution.

Plateletpheresis is a safe procedure with few risks, but donors may occasionally experience discomfort due to symptoms related to citrate poisoning and other unfavorable occurrences. To promote donor retention, it is critical to identify and stop the occurrence of plateletpheresis-related adverse events as soon as possible.

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