



Pas III Added Donor Platelet Suspensions on Platelet Count Ph and Allergic Transfusion Reactions

**Mustafa Özgül^a, Irfan Kuku^a, Mehmet Ali Erkurt^{a*}, Ahmet Sarici^a,
Soykan Biçim^a, İlhami Berber^a, Emin Kaya^a, Emine Hidayet^a,
Ahmet Kaya^a and Ayşe Uysal^b**

^a Inonu University, Faculty of Medicine, Department of Haematology, Malatya, Turkey.
^b Fırat University, Faculty of Medicine, Department of Haematology, Elazığ, Turkey.

Author's contribution

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

Editor(s):

(1) Dr. Juan Carlos Troiano, University of Buenos Aires, Argentina.

Reviewers:

(1) Umarani.M.K., Rajiv Gandhi University of Health Sciences, India.

(2) Ali Doğan, Yuzuncu Yil University, Turkey.

Complete Peer review History, details of the editor(s), Reviewers and additional Reviewers are available here:
<https://www.sdiarticle5.com/review-history/77872>

Original Research Article

Received 14 September 2021

Accepted 28 November 2021

Published 03 December 2021

ABSTRACT

Aim: Platelet additive solutions (PAS) platelet collection methods, in which less donor plasma is used, are becoming more common in order to reduce the reactions occurring in patients. In our study, we aimed to evaluate the platelet quality in apheresis platelet suspensions (I) collected with PAS-III and to examine the frequencies of other transfusion reactions, especially allergic reactions related to platelet transfusion (II).

Materials and Methods: In our study, the results of routine use of apheresis platelet sets between July 2019 and March 2021 were evaluated retrospectively.

Results: All of the PAS-III added apheresis platelet concentrates collected in our center, whose quality control was performed in different time periods (100 platelet concentrates) were included. Platelet counts and pH values were examined on the 1st and 5th days of these apheresis platelet concentrates, which were stored in our blood bank at 20-24°C with agitation.

In our study, mean platelet counts measured on days 1 and 5 in 65% PAS-III/35% plasma apheresis platelet suspensions were found to be 3.44×10^{11} and 3.0×10^{11} , while pH values were determined as 6.83 and 6.62 on days 1 and 5, respectively. Also, no allergic or any other transfusion reaction was detected.

Conclusion: In conclusion, in our study, apheresis platelet concentrates suspended in 65% PAS-III/35% donor plasma were associated with (I) better donor comfort and (II) reduction in the frequency and/or severity of transfusion reactions originating from donor plasma.

Keywords: Apheresis platelet; platelet additive solution; allergic transfusion reaction.

1. INTRODUCTION

In current blood bank practice, apheresis platelet concentrates obtained from volunteer donors are suspended in the same donor's plasma. In each apheresis procedure, 200-300 ml of donor plasma taken from the donor both negatively affects the comfort of the donor (I) and prevents the recovery of plasma fractions (II). Therefore, it is important to reduce the plasma required for the suspension of apheresis platelets.

Although platelet transfusions are life-saving, they can sometimes cause serious reactions that can be life-threatening. The rate of transfusion reaction due to apheresis platelet suspensions is estimated to be 1-4%. The majority of these reactions are allergic transfusion reactions and febrile non-hemolytic transfusion reactions. However, various reactions such as infections, alloimmunization, transfusion-related acute lung injury, transfusion-related circulatory overload, transfusion-associated graft-versus host disease and post-transfusion purpura may also occur. For this reason, in order to reduce/prevent these reactions in the recipient, platelet collection methods with platelet additive solution, instead of which donor plasma is used less, gain importance. PAS-III (Intersol) is a platelet additive solution approved for use both in Europe and in the USA by the FDA. However, obtaining apheresis platelets with the addition of PAS-III is still not in routine use in our country. We aimed to share the results of our patients with apheresis platelet collection using PAS-III in our blood bank and therapeutic apheresis center within the body of İnönü University Turgut Özal Medical Center and contribute to the literature.

2. MATERIALS AND METHODS

In our study, eleven thousand (11,000) PAS-III added apheresis platelet concentrates collected from volunteer donors at İnönü University Turgut Özal Medical Center, blood bank and therapeutic apheresis center between July 2019 and March 2021 were evaluated retrospectively. All of the

11,000 apheresis platelet concentrates with PAS-III added in different time periods (100 platelet concentrates) were included in our study. The quality control evaluation can be summarized as, (I) taking 20 ml samples from these 100 platelet concentrates into a separate platelet storage bag (gas-permeable, 100 ml bags) under sterile conditions, (II) storing of these 20 ml platelet concentrate samples with agitation in our blood bank at 20-24 C⁰ for 5 days and (III) taking samples of concentrated platelet samples for required examinations on 1st and 5th days under sterile conditions.

It was determined that platelet count (CBC) on the 1st and 5th days and pH measurements on the 1st and 5th days were made from these PAS-III apheresis platelet samples, which were stored with agitation in the blood bank, for quality control purposes.

PAS-III apheresis platelet suspensions were automatically collected from donors in Fresenius (AmiCORE) model apheresis devices.

Fresenius brand R6R8884 model single arm platelet apheresis set was used in the procedures performed on the device. The set has a cassette system, gamma sterile and connection section with a 0.2 µ filter for PAS connection. The procedures were performed using the "Intelligent Flow Control" feature of the apheresis device. In this way, the appropriate flow value according to the donor's vascular access was determined by the device, real-time pressure control and numerical follow-up of the flow rate were performed.

At the end of the procedure, the separated platelet and plasma were transferred to a gas permeable bag where the platelet could be stored for 5 days. When it is desired to store the product with 65%PAS-III/35% plasma, 65% of the product volume is sent to the automatic product bag by the PAS-III device and the platelet product is suspended in this way.

Day 1 and day 5 pH values were measured with a Radiometer brand ABL800 Basic model blood gas analyzer, as described above, from platelet concentrates stored in the blood bank with 65%PAS-III/35% plasma.

Complete blood count (CBC) was measured with XN-1000-Sysmex model analyzer for day 1 and day 5 platelet values from platelet concentrates stored in blood bank with 65%PAS-III/35% plasma as described above.

After sampling for quality control, these apheresis platelet concentrates (100 pieces) were given to the relevant patients within the indication. The files and/or automation records of these 100 patients were retrospectively investigated in terms of allergic reactions and other possible transfusion reactions.

2.1 Statistical Analysis

SPSS T-test was used for statistical analysis.

3. RESULTS

Of these 100 samples analyzed, 64 (64%) were male and 36 (36%) female donors. The lowest platelet value was found to be 201.000/mm³ and

the highest 341.000/mm³ in the donors in the study. The mean platelet value was found to be 276,150 ±26.67/mm³. The lowest hematocrit value was 39.2%, the highest 49.9%, and the mean hematocrit value was 44.72± 3.05%. The demographic characteristics of the patients included in our study are in Table 1.

In the procedures performed in our center, a platelet yield of 3.0x10¹¹ - 7.5x10¹¹ is targeted. The platelet recovery of the platelet product collected in PAS III platelet concentrates was 87.34% on the 5th day.

The mean time for platelet collection from donors was 76.97±6.6 minutes (60-85 minutes). The product volume collected from the donors was found to be 230±22.38 ml (200 - 250 ml) on average. In PAS III platelet concentrates, the mean platelet count was 3.44 x 10¹¹ (2.75 - 9.66 x 10¹¹) on the 1st day, and 3.0 ± 1.09 x 10¹¹ (2.22 - 4.12 x 10¹¹) on the 5th day. While the mean pH_{22°C} value was 6.83± 0.22 (7.22 - 6.40) on the 1st day in PAS III platelet concentrates, the pH_{22°C} value was 6.62 ± 0.23 (7.21 - 6.40) on the 5th day. These parameters are given in Table 2.

There was no information about the development of any transfusion reaction in the patients included in the study.

Table 1. Demographic characteristics of the study group

| % 35 Plasma % 65 PAS III | | | |
|-------------------------------|-------------------------------|---------|--------------------|
| Donor Information | n= 100 (64 males, 36 females) | | |
| Parameters | Minimum-Maximum | Average | Standard Deviation |
| Weight (kg) | 58 - 96 | 73.19 | ± 8.72 |
| Height (m) | 1.55 - 1.92 | 1.69 | ± 0.06 |
| Donor Hct (%) | 39.2 - 49.9 | 44.72 | ± 3.05 |
| Donor PLT (/mm ³) | 201.000 - 341.000 | 276.150 | ± 26.67 |

Table 2. Characteristics of donor PAS III platelet concentrates

| % 35 Plasma % 65 PAS III | | | |
|--|-----------------|---------|--------------------|
| Product Information | Minimum-Maximum | Average | Standard Deviation |
| Process time (min) | 60 - 85 | 76.97 | ± 6.6 |
| Product Volume (ml) | 200 - 250 | 230 | ± 22.38 |
| Platelet count in the product on day 1 (x 10 ¹¹) | 2.75 - 9.66 | 3.44 | ± 1.23 |
| Platelet count in the product on day 5 (x 10 ¹¹) | 2.22-8.23 | 3.0 | ± 1.09 |
| 5th day platelet product recovery | % 87.34 | | |
| Day 1 pH _{22°C} | 7.22 - 6.40 | 6.83 | ± 0.22 |
| Day 5 pH _{22°C} | 7.21- 6.40 | 6.62 | ± 0.23 |

4. DISCUSSION

It has been reported in studies that the use of whey in platelet production extends the shelf life of platelets by protecting their hemostatic functions [1,2] In our study, we aimed to investigate the effect of platelet additive solution (PAS-III) on apheresis platelet quality as the first aim in line with this information.

We evaluated the platelet quality by measuring the platelet counts on days 1 and 5 and pH values on days 1 and 5 in 65% PAS-III/35% plasma platelet concentrates. Similarly, in some studies, the pH value of the product is used as a parameter in the quality evaluation of platelet concentrates [3]. In this study reported from Malaysia, it is reported that pH >6.5 is required to ensure platelet concentrate quality. In the same study, in the comparison of 19 PAS and 19 100% plasma suspended platelets, Mokhtar et al. found the median pH values in PAS platelet concentrates; They reported it as 7.21 on the 1st day, 7.00 on the 5th day and 6.60 on the 8th day [3]. Unlike our study, in this study, the number of donors was less and PAS-D (Composol PS) was used instead of PAS-III (PAS-C).

In the European Union blood safety and quality regulations in 2016, it is stated that the pH value at the end of the storage period in >95% of platelet products should be in the range of 6.4 - 7.4 [4]. Studies have demonstrated that pH values above 7.4 do not have a negative effect on thrombocyte functions, and the upper limit value of thrombocyte pH in its criterion has been removed [4]. In our study, pH values of 65% PAS-III/35% plasma platelet concentrates were found to be 6.83 (7.22-6.40) on day 1 and 6.62 (7.21-6.40) on day 5, consistent with the literature.

The quality of 70 apheresis platelet suspensions collected by Ralph et al. Amicus apheresis device and stored with 65% PAS-III/35% plasma were evaluated and it was determined that the median value of pH_{22°C} on the 5th day was 7.2. The 5th day gain in products was 80.5% for apheresis platelets containing 65% PAS-III/35% plasma and 72.1% for apheresis platelets with autologous plasma. In conclusion, in this study, it was shown that apheresis platelets collected in the Amicus device with reduced leukocytes and 65% PAS-III/35% plasma ratio were pH ≥6.9 after 5 days of storage [5]. In our study, we also found a higher platelet gain as 87.34%.

Our second aim in our study was to investigate the effect of platelet concentrates stored with 65% PAS-III/35% donor plasma on allergic transfusion reactions. Apart from allergic transfusion reactions, the incidence of other transfusion reactions such as infections, alloimmunization, transfusion-related acute lung injury, transfusion-related circulatory overload, anaphylactic reaction, febrile non-hemolytic transfusion reaction, transfusion-associated graft-versus host disease, and post-transfusion purpura were investigated. In our study, allergic and/or other transfusion reactions could not be detected in any of our 100 patients due to apheresis platelet transfusion suspended in 65% PAS-III/35% plasma. We think that the fact that we could not detect any reaction related to apheresis platelet transfusions in our patients may be related to (I) the small number of our study group and (II) the retrospective nature of the study. However, in the literature, the rate of transfusion reaction related to apheresis platelet suspensions is estimated to be 1-4% [6-9]. Larry et al. reported that platelets stored in platelet additive solution (PAS) may reduce transfusion reactions, including allergic reaction from plasma and lung injury due to transfusion [10]. In another study, Kacker et al. reported that allergic transfusion reactions were the most common among transfusion complications, and allergic reactions were reduced with the use of apheresis platelets stored in whey solution [11].

Tobian et al. reported the allergic transfusion reaction rate as 1.85% (72/3884 transfusions) in standard (collected with plasma) platelet transfusions and 1.01% (12/1194 transfusions) in apheresis platelet transfusions stored with PAS (statistically significant, p=0.04). they reported (12). [12] In the same study, they reported that although febrile non-hemolytic transfusion reactions were lower (0.59% vs. 0.70%) in apheresis platelet transfusions stored with PAS, it was not significant. In a study investigating the French Hemovigilans data between 2008 and 2014, it was reported that 232 of every 100,000 platelet concentrates transfused had transfusion-related hypersensitivity reactions [13]. It has been stated that this rate is higher in apheresis platelet transfusions with only plasma (337/100.000) than in platelet concentrates prepared with PAS (94/100.000).

As is known, apheresis platelet concentrates prepared with 100% plasma contain 200-300 ml of donor plasma, while the amount of donor plasma is 70-105 ml in apheresis platelet

concentrates containing 65% PAS-III/35% plasma. As a result, it is easy to understand that suspending the collected platelet concentrates (with PAS-III added) with less plasma will have a positive effect on transfusion reactions. In cases where 2 or 3 doses of platelets are collected from the same donor, donor plasma loss can increase to 600-900 ml. This amount of plasma loss also leads to some undesirable reactions such as nausea, vomiting and fatigue in donors. However, since the plasma loss will be 210-315 ml in 2 or 3 doses of platelet collection with PAS-III, it can be tolerated much more easily by this donor. As a result of these, it is seen that apheresis platelet collection with PAS-III added from donors is important both in reducing transfusion reactions and in terms of donor comfort.

5. CONCLUSION

In conclusion, our study is one of the first studies performed with PAS-III in apheresis platelet donation in our country and our results were found to be compatible with the literature. However, both the retrospective nature of our study and the small number of patients limit the value of our study. Therefore, prospective and comprehensive studies are needed to strengthen our findings.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

For this retrospective study, approval was obtained from the ethics committee of İnönü University with the number of 2020/28-10.

COMPETING INTERESTS

Author has declared that no competing interests exist.

REFERENCES

1. Ringwald J, Zimmermann R and Eckstein R The new generation of platelet additive solution for storage at 22 degrees C: development and current experience. *Transfus Med Rev.* 2006;20: 158-64.

2. Cardigan R, Sutherland J, Garwood M, et al. In vitro function of buffy coat-derived platelet concentrates stored for 9 days in CompoSol, PASII or 100% plasma in three different storage bags. *Vox Sang.* 2008;94:103-12.
3. Mokhtar MB, Hashim HB, Joshi SR. Assessment of quality of platelets preserved in plasma and platelet additive solution: A Malaysian experience. *Asian J Transfus Sci.* 2016;10:84-7.
4. De Kort W, Mayr W, Jungbauer C, et al. Blood donor selection in European Union directives: room for improvement. *Blood Transfus.* 2016;14:101-8.
5. Vassallo RR, Adamson JW, Gottschall JL, et al. *In vitro* and *in vivo* evaluation of apheresis platelets stored for 5 days in 65% platelet additive solution/35% plasma. *Transfusion.* 2010;50: 2376-85.
6. Domen RE, Hoeltge GA. Allergic transfusion reactions: An evaluation of 273 consecutive reactions. *Archives of Pathology & Laboratory Medicine.* 2003; 127:316-320.
7. Enright H, Davis K, Gernsheimer T, et al. Factors influencing moderate to severe reactions to PLT transfusions: experience of the TRAP multicenter clinical trial. *Transfusion.* 2003;43:1545-1552.
8. Tormey CA, Sweeney JD, Champion MH, et al. Analysis of transfusion reactions associated with prestorage-pooled platelet components. *Transfusion.* 2009;49:1242-1247.
9. Mazzei C, Popovsky M, Kopko P, Fung M, Grossman B, Hillyer C. Technical manual. Maryland: American Association of Blood Banks; 2008.
10. Dumont LJ, Cancelas JA, Graminske S, et al. *In vitro* and *in vivo* quality of leukoreduced apheresis platelets stored in a new platelet additive solution. *Transfusion.* 2013;53:972-80.
11. Kacker S, Ness PM, Savage WJ, et al. Cost-effectiveness of prospective red blood cell antigen matching to prevent alloimmunization among sickle cell patients. *Transfusion.* 2014;54:86-97.
12. Tobian AA, Fuller AK, Ugluk K, et al. The impact of platelet additive solution apheresis platelets on allergic transfusion reactions and corrected count increment (CME). *Transfusion.* 2014;54: 1523-9; quiz 1522.

13. Mertes PM, Tacquard C, Andreu G, et al. analysis of the French hemovigilance network. *Transfusion.* 2020;60:507-512.
Hypersensitivity transfusion reactions to platelet concentrate: A retrospective

© 2021 Özgül et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:
The peer review history for this paper can be accessed here:
<https://www.sdiarticle5.com/review-history/77872>