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Impact of Agitation on Platelet Concentrate Quality: A Time-Series Analysis of Platelet Counts

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ABSTRACT

Storage procedures are the main factor that influences the quality of platelet concentrate. In vitro, platelet concentrate is stored in a platelet agitator at a temperature of 20ºC-24ºC for 5 days. This study aims to determine the difference in the number of platelets in platelet concentrate with and without the agitation process. This type of research is quasi-experimental using a time series design with an independent t-test. The research was conducted in April 2024. Samples of 16 bags of platelet concentrate with and without the agitation process which were stored on the 0th, 1st, 2nd, 3rd, 4th, and 5th days were checked for platelet counts. In the normality test of the platelet examination data, the p-value was <0.05, so it was stated that the data was not normally distributed so it had to be continued with the Mann-Whitney U test. The research results showed that the p-value on days 0, 1, 2, and 3 was >0.05, indicating no significant difference in the number of platelets between the groups with and without the agitation process. Meanwhile, on days 4 and 5, a p-value <0.05 was found, and there was a difference in the number of platelets with and without the agitation process. It can be concluded that agitation plays an important role in maintaining platelet stability after the third day of storage, indicating that the agitation process is necessary to preserve platelet quality during longer storage periods.

INTRODUCTION

Blood transfusion services are medical endeavors that utilize human blood as a vital resource for charitable objectives. Because blood services are crucial in various circumstances to save lives or aid in the healing process, high-quality blood products are required. Packed red blood cells, liquid plasma, fresh frozen plasma, platelet concentrate, cryoprecipitate anti-hemophilic factor (AHF), and whole blood can all be prepared and transfused (Kementerian Kesehatan Republik Indonesia, 2015). According to statistics from *Unit Transfusi Darah Rumah Sakit* (UTDRS) Dr. H. Abdul Moeloek, Lampung Province, in 2022 the demand and production of blood were as follows: whole blood components had a total demand of 2,393 bags and a total production of 947 bags; packed red cells had a total demand of 22,106 bags and a total output of 9,830 bags; fresh frozen plasma had a total demand of 1,287 bags and a total production of 926 bags; and platelet concentrate had a total demand of 7,543 bags and a total output of 6,495 bags (Unit Transfusi Darah Rumah Sakit, 2022). These data show that platelet concentrate is the secondutdrs most produced and in-demand blood component at UTDRS Dr. H. Abdul Moeloek, Lampung Province.

Platelet concentrate contains only platelets and no other blood cells (Safitri & Maulana, 2023). Patients with thrombocytopenia can benefit from platelet concentrate transfusion, a

supportive treatment that uses blood components to boost platelet counts (Rosyidah et al., 2022). The processing of platelet concentrate involves using aseptic techniques to separate donor blood into usable platelet components (Maharani & Noviar, 2018).

In general, various parameters related to collection, processing, storage, and external environmental conditions may affect the quality of platelet concentrate. The primary factor influencing the in vitro quality of platelet concentrate is storage protocols. The quality of platelet concentrate is expected to be affected by variations in several aspects related to storage time. After transfusion, thrombosis and other complications are more likely to occur when platelet concentration is low (Ariani et al., 2021). When conducting quality control on platelet concentrate, three parameters must be measured: pH >6.4 (from four bags per month), absence of bacterial contamination (from one percent of the total bags), and platelet count >60 x 10^9 (from one percent of the total bags) per final unit of blood (minimum 10 per month), as well as the presence of a swirl in the platelet concentrate (Kementerian Kesehatan Republik Indonesia, 2015).

Donor blood collection must be performed aseptically to prevent bacterial contamination of blood products. This is especially important for platelet concentrate, which should be stored between 20°C and 24°C. If the temperature is too high, bacteria can grow and lower the pH, leading to permanent oval platelet morphology, platelet enlargement, and a decrease in platelet resistance. The storage procedure has a major impact on the platelet count in platelet concentrate. Temperatures between 20°C and 24°C should be maintained with agitation to ensure optimal storage standards. During storage, agitation is essential because it inhibits platelet aggregation, maintains cell viability, promotes oxygen exchange through diffusion, and prevents lactic acid buildup, which can impair platelet function (Mentari et al, 2020).

A study conducted by Rosyidah et al. (2022) on the relationship between platelet count and storage duration of platelet concentrate revealed no significant relationship. Platelets were stored for 0, 1, 3, and 5 days in a platelet agitator at 20–24°C. In contrast, research by Ariani et al. (2021) found that platelet counts decreased with storage time. On day one of storage, the average platelet count per bag was 5527.74 ± 1741.22, but by day five it had decreased to 5388.71 ± 1786.38 per bag.

Since variations in platelet count may also be affected by the volume of CPDA-1 anticoagulant in the blood bag, storage must be carefully matched with donor blood and platelet concentrate in the agitator at 20–24°C (Rosyidah et al., 2022). An initial survey conducted by the author at hospitals with blood banks revealed that some blood banks lack platelet agitators. As a result, platelet storage is still performed at 20–24°C without agitation.

To ensure smooth blood transfusion services, the blood transfusion unit at Dr. H. Abdul Moeloek Hospital is equipped with a platelet agitator for storing platelet concentrate. However, due to occasional technical problems, such as equipment damage, the agitator cannot always be used. In such cases, platelet storage must be carried out at 20–24°C without agitation, limiting the storage period to three days (Maharani & Noviar, 2018). Therefore, this study aims to evaluate the effect of storage without agitation on the quality of platelet concentrate at Dr. H. Abdul Moeloek Hospital.

METHOD

This study employed a quasi-experimental design, specifically a time-series approach. On day 0, a pretest was conducted on platelet concentrate, followed by examinations on days 1–5 of platelet concentrate stored under two different conditions: (1) on a platelet agitator at 20–24°C and (2) at 20–24°C without agitation. Platelet counts were measured prior to storage and subsequently on each observation day. The independent variable in this study was the storage method of the platelet concentrate (with agitation vs. without agitation), while the dependent variable was the platelet count.

The observation period of 1–5 days was selected because platelet concentrates are generally stored for a maximum of five days according to international and national blood bank standards (PMK No. 91/2015; AABB, 2021). Storage beyond this period is not recommended due to an increased risk of bacterial contamination and reduced platelet viability. This research has

passed an ethical review and received an ethical clearance from the Health Research Ethics Commission of the Poltekkes Kemenkes Tanjung Karang with number 172/KEPK-TJK/11/2024.

A total of six platelet concentrate bags were used in this study. The sample size was limited due to restricted availability of platelet concentrate at the blood bank and ethical considerations, as each unit of platelet concentrate is a valuable product intended for patient transfusion. However, the use of a time-series design with repeated measures on each bag allowed for the observation of changes over time, thereby enhancing the reliability of the findings despite the small sample size.

RESULTS

In this study, the platelet counts of sixteen platelet concentrate bags (stored with and without agitation) were examined on days 0, 1, 2, 3, 4, and 5. A univariate analysis was conducted to assess the frequency distribution of platelet counts on each day for platelet concentrates stored with agitation. The collected data are presented in the following table:

Table 1. Frequency distribution of platelet count examination results on days 0, 1, 2, 3, 4, and 5 for platelet concentrate using the agitation process

	Mean	Platelet Decrease (%)	Max	Min	SD
Day 0	681.125	0	911.000	401.000	166.073,510
Day 1	612.000	10	843.000	362.000	163.731,827
Day 2	587.375	14	816.000	346.000	167.731,024
Day 3	550.625	19	789.000	340.000	160.090,097
Day 4	493.500	28	690.000	329.000	127.760,937
Day 5	437.500	36	662.000	318.000	118.619,440

Table 2. Frequency distribution of platelet count examination results on days 0, 1, 2, 3, 4, and 5 for platelet concentrate without agitation process

	Mean	Platelet Decrease (%)	Max	Min	SD
Day 0	612.125	0	989.000	337.000	263.831,893
Day 1	541.875	11	808.000	328.000	191.624,959
Day 2	489.500	20	771.000	306.000	172.014,950
Day 3	430.250	30	646.000	259.000	152.791,875
Day 4	356.750	42	585.000	238.000	107.382,827
Day 5	293.250	52	481.000	214.000	84.149,102

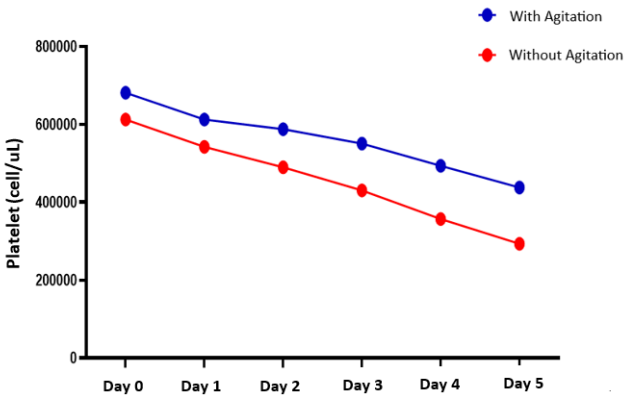

Figure 1. Platelet counts decreased progressively during storage in both conditions, but samples with agitation consistently maintained higher platelet levels compared to those without agitation

To determine the relationship between the dependent and independent variables, a bivariate analysis was performed. Prior to this, a Shapiro-Wilk test was used to assess data normality. Since the p-value was <0.05, indicating that the data were not normally distributed, the

analysis was continued using the Mann-Whitney U test. In the normality test of platelet count results, the p-value was 0.0332 for samples stored with agitation and 0.0003 for samples stored without agitation.

The Mann-Whitney U test produced a p-value of 0.0006. As this value was less than 0.05, H_0 was rejected, indicating a significant difference between platelet counts in concentrates stored with agitation and those stored without agitation. The results of the Mann-Whitney U test comparing platelet counts under both storage conditions are shown in Figure 2.

Additionally, an independent t-test with a 5% significance level was conducted to compare daily platelet counts in greater detail. Before performing this analysis, a Shapiro-Wilk test was again used to determine whether the daily platelet count data followed a normal distribution.

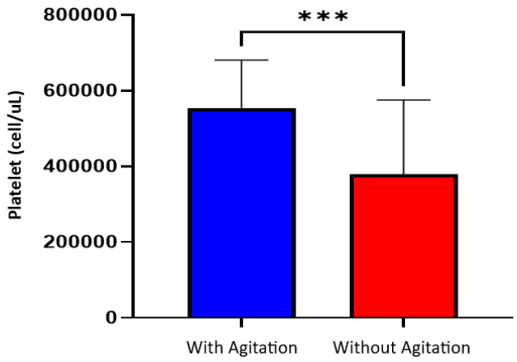

Figure 2. Overall platelet counts were significantly higher in samples stored with agitation compared to without agitation (p<0.001)**

The normality test for platelet count results on days 0 through 4 produced p-values greater than 0.05, indicating that the data followed a normal distribution and were suitable for analysis using an independent t-test. When a p-value of less than 0.05 was found on day 5, the data was declared to be abnormally distributed, and the Mann-Whitney U test was used to continue the test. The following is a graph that represents the daily analysis's findings.

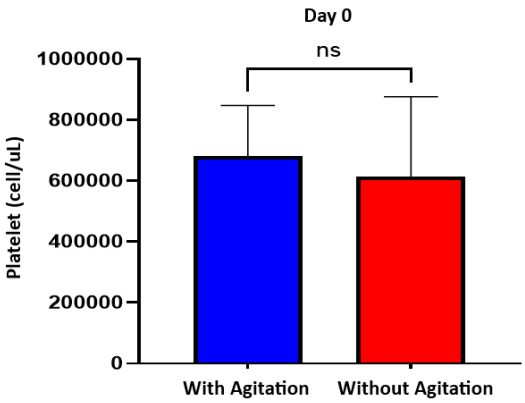

Figure 3. Platelet counts on day 0 showed no significant difference between storage with and without agitation (p>0.05)

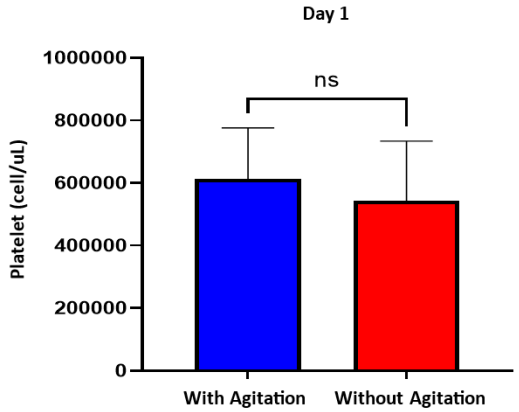

Figure 4. Platelet counts on day-1 were not significantly different between storage with and without agitation (p>0.05)

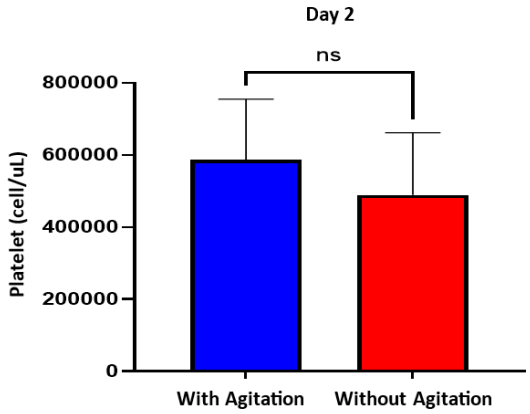

Figure 5. Platelet counts on day-2 showed no significant difference between storage conditions (p>0.05)

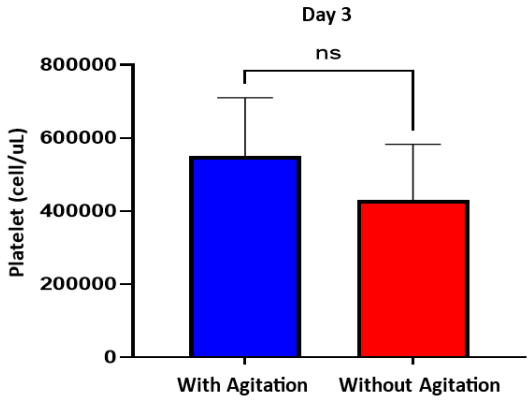

Figure 6. Platelet counts on day-3 were not significantly different between agitation and non-agitation storage (p>0.05)

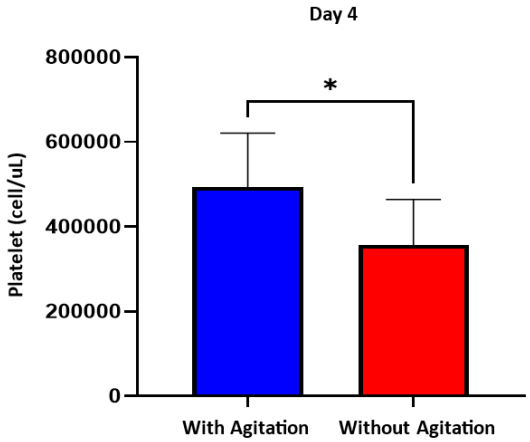

Figure 7. Platelet counts on day-4 were significantly higher with agitation compared to without agitation (p=0.0361)

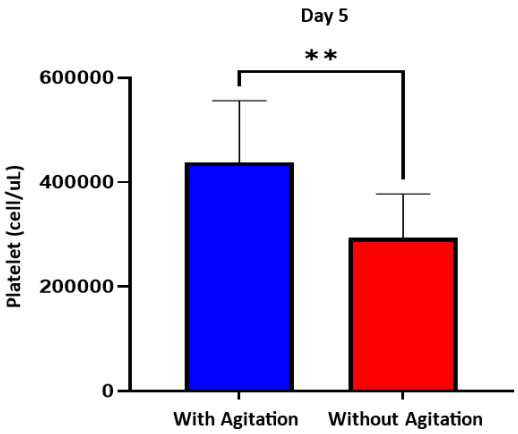

Figure 8. Platelet counts on day-5 were significantly higher with agitation compared to without agitation (p=0.0070)

According to the graphical visualization, there was no significant difference in platelet counts between samples stored with and without agitation on days 0, 1, 2, and 3. However, on days 4 and 5, a significant difference was observed, with p-values <0.05.

DISCUSSION

The results of examining the platelet counts in platelet concentrate bags, with or without agitation, showed a progressive decrease from day to day. This decline occurs because platelet cells have a shorter lifespan compared to other blood cells. During the storage period, platelets become activated, undergo metabolic activity, and eventually lyse. The absence of agitation further accelerates platelet lysis. In the bloodstream, platelets have a lifespan of 7–10 days. In vitro, platelet concentrate can be stored at a temperature of 20ºC–24ºC for up to 3 days without agitation and 5 days with agitation (Maharani & Noviar, 2018; Trochanowska-Pauk et al., 2024).

The results also demonstrated significant differences between the groups stored with and without agitation. Platelets stored with agitation maintained a more stable condition, were less likely to be activated, and therefore did not undergo substantial changes in metabolic activity, cell morphology, or platelet count (Hermawan & Dede, 2023). Agitation keeps platelets oxygenated, allowing sufficient oxygen to enter the concentrate bag while removing excess carbon dioxide. In contrast, storage without agitation, combined with prolonged duration, leads to platelet activation, causing morphological changes from smooth disks to round, spiny forms, which promote aggregation. The key adhesion molecule in this process is the glycoprotein IIb/IIIa complex, which binds plasma fibrinogen (Rumbaut & Thiagarajan, 2010). These findings are

consistent with recent work showing that metabolic deterioration and hemostatic imbalance are strongly influenced by storage medium and conditions (Petrou et al., 2024).

Increased metabolism also occurs in activated platelets through glycolysis, one of the main pathways for synthesizing adenosine triphosphate (ATP), the primary energy source for platelets. Glycolysis produces 2 ATP molecules, ADP, and CO_2. The accumulation of dissolved CO_2 increases acidity within the bag, resulting in a pH decline (Mentari et al, 2020). Glycolysis is also reflected in decreased glucose levels during prolonged storage of platelet concentrate, reducing the glucose supply available to platelets. The reduction in glucose ultimately causes platelet death and a significant decline in platelet count (Rafika, 2021). Newer studies also indicate that biochemical parameters such as LDH, glucose, and calcium levels are critical markers of platelet quality during storage (Arastehnazar et al., 2025).

Glucose is oxidized to generate ATP with the help of the cytoplasmic enzyme lactate dehydrogenase (LDH). Between days 1 and 5, LDH levels increased, indicating a loss of platelet membrane integrity and subsequent cell damage. Due to their short lifespan, platelet lysis occurs naturally during storage, but this process is accelerated without agitation. Prolonged storage time also affects pH, leading to changes in platelet morphology. According to the Indonesian Ministry of Health Regulation No. 91 of 2015 concerning blood service standards, platelet concentrate can be stored at 20ºC–24ºC with a pH above 6.4. A pH value below 6.0 leads to platelet abnormalities and poor viability (Mentari et al, 2020). This standard is in line with international recommendations such as the WHO guidelines on good manufacturing practices for blood establishments (World Health Organization, 2011).

The longer platelet concentrate is stored, the more calcium levels decrease. This occurs because the blood bag contains the anticoagulant Citrate Phosphate Dextrose Adenine-1 (CPDA-1). The citrate binds to calcium ions to form calcium citrate, reducing calcium levels throughout storage. Calcium plays an essential role in the blood coagulation process. In the intrinsic pathway, calcium works with factor IXa, factor VIII, and PF3 to activate factor X.

A decline in platelet concentrate quality before transfusion reduces treatment effectiveness because the number of viable platelets decreases due to lysis. Lysed platelets release granules containing components such as adenosine diphosphate (ADP), von Willebrand factor (vWF), and calcium ions. ADP initiates platelet aggregation by promoting adhesion to injured subendothelial tissue (a reversible primary aggregation). Activated platelets then release more ADP, which triggers secondary aggregation, an irreversible process (Mentari et al, 2020).

Examination results from day 0 to day 3 revealed a decline in platelet counts for both storage conditions, but the difference between the agitation and non-agitation groups was not statistically significant. This is because storage temperature influences platelet viability, and platelets stored at 20ºC–24ºC generally remain viable for up to 3 days (Maharani & Noviar, 2018). However, on days 4 and 5, significant differences were observed between the two groups. This is due to the metabolic activity of stored platelets, which affects glucose consumption, lactate accumulation, and pH reduction. Recent comparative studies also showed that platelets stored at lower temperatures (4ºC) retain functional advantages over those stored at 22 ºC, further highlighting the role of optimized storage conditions in maintaining platelet viability (Yang et al., 2018).

These findings are consistent with a study by Ariani et al. (2021), which reported significant differences in platelet counts on days 1 and 5. Conversely, a study by Rosyidah et al. (2022) found no significant effect of storage duration on platelet counts from days 1 to 5.

Based on the findings of this study, storing platelet concentrate with agitation and under controlled temperature conditions is crucial to maintain platelet viability and function. Agitation prevents platelet clumping and ensures continuous oxygenation, allowing sufficient oxygen to diffuse into the bag while removing carbon dioxide. Because of the significant decline in platelet counts on days 4 and 5, particularly in the non-agitation group, platelet concentrate should ideally be transfused as soon as possible and no later than the 3rd day of storage. This is consistent with previous reports that emphasize the importance of limiting storage time to preserve platelet stability (Trochanowska-Pauk et al., 2024; World Health Organization, 2011).

CONCLUSION

There is a significant difference in platelet counts between platelet concentrate stored with agitation and without agitation. No significant difference was found during the first three days of storage, but by days 4 and 5, the difference became significant. To ensure the viability and function of platelet cells, platelet concentrate should always be stored with agitation and under controlled temperature conditions. Therefore, all blood banks and transfusion services must be equipped with platelet agitators. Moreover, platelet concentrate should be transfused promptly and should not exceed 3 days of storage, especially if stored without agitation.

AUTHOR'S DECLARATION

Authors' contributions and responsibilities

WWD: Supervision (lead), validation, writing original draft, visualization, conceptualization; **KK:** Writing original draft (supporting), funding acquisition; laboratory work; **AZA:** Supervision (supporting), review and editing.

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Availability of data and materials

All data are available from the authors.

Competing interests

The authors declare no competing interest.

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