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ORIGINAL RESEARCH

Chemical and Microbiological Changes of Expired Platelet Concentrate

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Background: Platelets are a commonly used blood component to prevent or treat bleeding in patients with thrombocytopenia or platelet dysfunction. They are stored at room temperature (22–24°C) for five days unless specific measures are taken to extend the shelf life to seven days or more. After five days, this study evaluated platelet units' biochemical changes and bacterial growth.

Study Design and Methods: Platelet concentrate was collected from 30 random donors: 8 females and 22 males. The collected samples were then placed on an agitator at room temperature and tested for their pH, protein content, and glucose levels using Roche Combur 100 Test® Strips. The Haemonetics eBDS™ System was used for bacterial detection. The measurements were taken on day five as the control and then repeated on days 7, 9, and 11 to observe any changes. On days 5 and 7, all parameters remained unchanged. However, glucose levels significantly changed (p=<0.0001) on days 9 and 11. Regarding pH, a significant change was observed on day 9 (p=0.033) and day 11 (p=0.0002).

Results: There were no significant changes in all parameters on days 5 and 7. However, glucose was substantially changed (p=<0.0001) on days 9 and 11. For pH, there was a significant change in pH on day 9 (p=0.033) and day 11 (p=0.0002).

Discussions: Our study found that platelet concentrate extension is possible for up to seven days. However, further studies are needed to evaluate platelet function during expiry time and to assess the stability of platelet morphology and function.

Keywords: platelet, thrombocytopenia, storage extension, bacterial detection

Introduction

Platelet transfusion is a crucial component of patient care as platelets are responsible for maintaining the integrity of the vascular system and mediating hemostasis. In some cases, platelets can be transfused prophylactically as platelet concentrates (PCs) to treat conditions such as thrombocytopenia or platelet dysfunction. Additionally, platelets can be transfused therapeutically to address active bleeding.[1–3]

Platelet concentrates (PCs) are made from whole blood or collected through apheresis. They can be stored for up to five days, but specific measures can be taken to extend their shelf life to seven days or more. Proper storage of PCs is crucial to maintaining their function and preventing platelet aggregation. While agitated, PCs should be stored in gas-permeable plastic bags at room temperature to achieve this. However, this method of storage can increase the risk of bacterial growth.[4]

Platelet availability and inventory are usually affected due to their limited lifespan. Consequently, extending platelets' shelf life and maintaining their function from 5 to 7 days without bacterial contamination is essential.[5] Screening for bacterial contamination and using pathogen reduction techniques can extend the shelf life of platelets by up to seven days in certain countries.[6]

Research suggests that to evaluate the effects of extending the shelf life of platelet concentrates, three essential quality standard parameters must be considered: platelet count, pH value, and lack of bacteria.[5]

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The United States Food and Drug Administration (US FDA) has created rules and guidelines to manage and prevent bacterial contamination of platelets. Blood establishments and transfusion services need to ensure that they use US FDA-approved or cleared devices or other acceptable and appropriate methods as determined by the FDA to control the risk of bacterial contamination of platelets adequately.[7]

Over time, both platelets and their storage medium undergo changes that lead to the accumulation of bio-reactive substances. Prolonged storage of platelets may result in decreased transfusion efficacy and increased adverse events in patients, such as transfusion-associated sepsis, inflammation, and immune-mediated events.[6]

Critically ill patients, including those who have undergone cardiac surgery, are the second largest group to receive platelets after hematology/oncology patients. These patients may be particularly susceptible to platelet adverse events due to their pre-transfusion inflammatory state.[8–10]

A platelet additive solution can be added to prevent contamination and optimize platelet functionality, which may help revise guidelines for the extended shelf life of platelet concentrates.[5]

Strategies to prevent sepsis caused by transfusing blood collected by apheresis machines involve disinfecting the donor's skin, diverting the first collected blood, and screening platelet components for bacterial contamination. Automated bacterial culture methods are commonly used for screening.

Blood operators routinely measure the pH value of platelet components at expiry to assess the so-called "storage lesion." This is because a decrease in pH level is a significant marker of platelet damage during storage. The pH level decreases due to lactic acid production from anaerobic glycolysis. The platelets become irreversibly damaged if the pH drops to 6.0 or below.[11–13]

This study aims to test the possibility of extending PC storage time for more than five days. We monitored the chemical and microbiological changes in outdated platelet concentrate.

Materials and Methods

Experimental Design

Our research is an experiment to monitor platelet concentrates' chemical and microbiological changes after the expiry date. Quantitative results were collected during the investigation using a urine dipstick with chemical parameters for glucose(mg/dl), pH, and protein. Bacterial contamination was measured using a particular machine (Haemonetics eBDS™). A total of 30 volunteer donors (8 females and 22 Males) contributed to the research using a consent form describing all the information regarding our experiment without exclusion criteria. We aimed to measure different analytes at different time points (on days 5, 7, 9, and 11).

Sample Collection

Our samples were whole blood (WB) bags collected at the blood donation department at King Abdulaziz University Hospital, with the approval of the bioethics unit and research committee of KAUH (IRB registration no.H-02-J-008). Volunteers' information was recorded in a particular form, including their names, ages, weights, heights, and vital signs. Accepting volunteers for donation was based on the department's policies that follow the Association for the Advancement of Blood & Biotherapies (AABB) regulation regarding rejecting/ accepting blood donors. Hb level and vital signs had to be within normal ranges. A quadruple blood bag without a leukoreduction filter (TERUFLEX® blood bags system Terumo BCT) was used for blood collection.

Sample Processing

Blood bags were further processed at the blood components department in the blood transfusion services. Centrifugation of the blood bags was carried out using the SIGMA ks8 machine with a specific program for PC separation. Centrifugation started with light spin (2000 rpm at 20°C for 11 min) and gave PRBC and PRP products. Next, PRP is transferred into empty bags for a second heavy spin (3500 rpm at 20°C for 11 min), giving PC and fresh frozen plasma (FFP). PC is stored at room temperature (20–24°C) with continuous agitation (Figure 1).

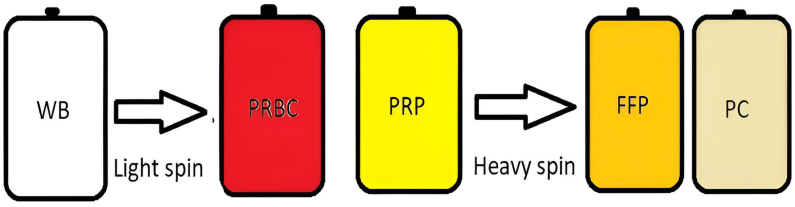

Figure 1 Preparation of Platelet Concentrate using plasma-rich platelet-platelet concentrate (PRP-PC): PRP-PC preparation starts with whole blood centrifugation at light spin (1500 rpm for 5 min at 22°C), removes PRP into a storage bag, then takes the PRP bag and centrifuge it a heavy spin (5000 rpm at four °C). After that, fresh frozen plasma (FFP) is removed into different bags and resuspended to prepare the platelet concentrate for storage.

Data Analysis

On the 5th day of collection, we used a decontaminated tube sealer and a connecting device (TSCD) machine that allowed PC bags' attachment with any container under sterilized conditions and permitted small segments to be used later for analysis. Pouches were used for bacterial detection using the Haemonetics eBDS™, which measures oxygen levels within the pouch. If bacterial growth occurs during incubation (24 hours), the oxygen will drop due to bacterial metabolism. Chemical parameters, including pH, glucose, proteins, and nitrite, were analyzed in our research, as these parameters are strongly affected by bacterial presence and cell biological reaction, using computer 10 test urine analysis. The previous steps were repeated on days 7, 9, and 11. We collected all data in Excel sheets and then ran the statistical analysis using the Prism 9 program to analyze all data using a one-way ANOVA statistical test with a significant p-*value* < *0.05*.

Results

Personal Data

We recorded the donor's vital signs, including Hemoglobin (mean=14.9 g/dl) and weight (mean=82.27 kg). The blood pressure was around the normal range (120/80 mmHg). Furthermore, the donor's average age was 25 years.

Microbiological Results

There was no sign of bacterial detection from day five to day eleven using the Haemonetics eBDS™ machine. All samples were passed after the incubation period, as displayed in (Table 1).

Chemical Results

Glucose Value

Glucose results showed no changes regarding the mean value on day five (Control, mean=300); hence, no change in the value occurred, and a slight shift in the mean happened on day seven (mean=292.3). However, there was a significant difference in mean values on days five and eleven, as seen in (Figure 2) compared with day five. This affected the p-value on days nine and eleven (p= <0.0001).

3.3.2 pH Value

There was a slight change in mean results for pH on day five (mean=7.167) compared to day seven (mean=7.133). Nonetheless, there was a clear difference in mean results on days nine and eleven, as shown in (Figure 3). There was no significant difference in p-value on day seven. However, there was a significant difference on day nine (p=0.033) and eleven (p=0.0002).

Table 1 Bacterial Detection from Day Five Up to Day Eleven Using the Haemonetics eBDS™ Machine

Days	5th day	7th day	9th day	11th day
eBDS	Pass	Pass	Pass	Pass

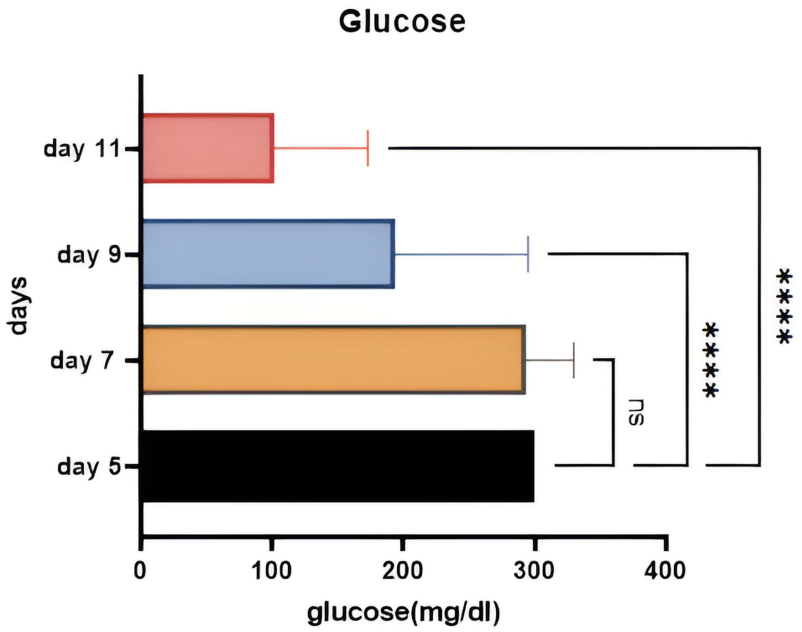

Figure 2 A statistical analysis of glucose results demonstrates the changes during the days of the experiment; days 5 and 7 show no significant change and are almost typical, while days 9 and 11 present a significant variation in results. ns= no significant, ****: p <0.0001.

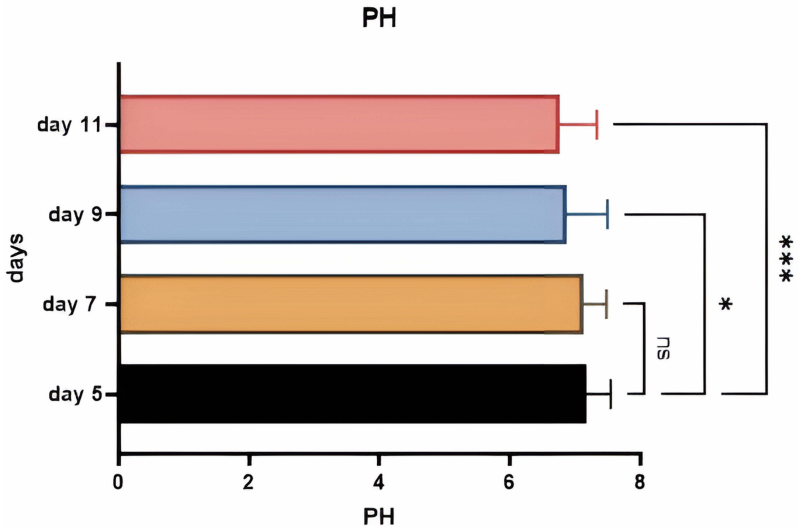

Figure 3 pH results illustrate no significant changes on days 5 and 7; however, the changes were significant on days 9 and 11. ns= no significant difference, (* = 0.033, *** = 0.0002).

Protein Values

Protein results did not change during our experiment and remained at 500 mg/dl on all measured days. Furthermore, nitrite results were null, indicating no presence of nitrite from day five to day eleven.

Discussion

Platelet transfusion is necessary for patients in oncology, hematology, and certain infections. However, platelet transfusions are only feasible in some cases due to limited availability. Maintaining a sufficient daily inventory of platelets is a significant challenge for most blood banks.[14]

Platelets' survival depends on maintaining a delicate biochemical balance between various substances, including glucose and hydrogen ions. The quality of platelets during storage is influenced by several factors, such as the preparation method, composition of the storage bag, additive solutions, temperature, and the requirement for adequate oxygen to maintain aerobic metabolism. Platelets are stored while continuously agitated to enhance the transport of gases such as oxygen and carbon dioxide through the storage container.[5]

We conducted a study to investigate the influence of prolonged storage on platelet metabolism and the chances of bacterial proliferation in randomly donated platelets stored at room temperature. Our main objective was to assess the possibility of extending the life span of platelet concentrates (PC) as this would serve more patients. However, during platelet storage, Platelet Storage Lesions (PSL) may occur due to energy consumption, pH drop, and platelet activation or apoptosis, leading to chemical and microbial changes.

Monitoring the changes to the outdated PC in our study revealed an evident shift in glucose and pH on days 9 and 11. Glucose results showed a significant difference on day nine and day 11 compared with day 5 (the control).

In addition, lactic acid decreases pH levels as it builds up, which supports the fall down of pH levels in our study on days nine and 11. A survey backing these findings by Hans Gulliksson stated that as the higher glycolysis rate increased, more lactic acids were produced, thus further reducing pH in PC.[15]

Protein results were unchanged in our study; levels were 500 mg/dl from the 5th to the 11th day. This constant level may be due to platelets' ability to maintain more than 97% of their cytoplasmic proteins unchanged, as stated in a study by Thomas Thiele.[16]

There was no sign of bacterial detection during our experiment, as Haemonetics eBDS™ results were passed on all days. Many policies have been developed to reduce the risk of bacterial transfusion in blood components, including proper donor selection, effective skin disinfection, and discarding the first volume from blood donation.[17] Many bacteria can multiply to massive and clinically dangerous levels during PC storage.[18]

Any finding of bacterial growth is considered significant. S. Ribault et al mentioned that the most common bacteria isolated from a platelet concentrate include *Staphylococcus epidermidis* and *Propionibacterium* acnes. Most of the bacterial presence is due to insufficient skin disinfection during donation.[19,20]

According to a study conducted by Tulika Chandra, platelets can be stored in plasma for up to seven days at 18°C without compromising their functions. This can be achieved with the help of an additive solution that keeps the platelets' tasks in check on the seventh day with minimal deviation from the control value.[5]

According to a study conducted by Ramirez-Arcos, there is no significant difference in the rate of confirmed positive results during bacterial screening of 5-day and 7-day platelet concentrates (PCs) when considering only facultative anaerobes. The study concluded that the risk of bacterial contamination in PCs can be effectively reduced using pathogen reduction technologies, which have already been implemented in several countries.[4]

A systematic review by Aubron et al investigated the effect of platelet storage duration on clinical and transfusion outcomes. The review revealed that prolonged storage time of platelets is associated with a decrease in the Platelet Count Increment (CI) and Corrected Count Increment (CCI) compared to fresher platelets less than three days old. However, no evidence suggests that platelets stored for up to 7 days are less effective on CCI than those stored for five days.[6]

A recent study by Ning et al found that platelet transfusions after 7-day storage were non-inferior to transfusions in the 5-day policy period, and there was no increase in adverse clinical outcomes.[21]

According to available literature in both hematology and critically ill patients, platelet (PLT) storage time of up to 5 days does not affect the ability to prevent bleeding, indicating that transfusion of older platelets is safe in large cohorts.

Limitations of the study

One limitation of our research is the sample size; only 30 were studied. Another area for improvement is the preparation of the PC; we followed the PRP-PC method and could not try the BC-PC due to regulations and policies in Saudi Arabia. The third limitation is the need for more platelet morphology and functionality testing.

Conclusions

Platelet concentrate, among other blood components, is considered an inventory management challenge due to its short shelf life. This study showed that extending platelet concentrate storage is possible for up to seven days without any

chemical or microbial changes. Extending storage time for platelet concentrate will save money, increase availability, and save more patients. Further studies are required to evaluate platelet function during expiry time and to assess the stability of platelet morphology and function.

It is recommended that platelet concentrate storage time be extended to day seven after obtaining approval from the medical director in case of shortages or high demands. However, further studies must confirm these findings and determine the most effective strategies for improving platelet concentrate quality. Additionally, it would be ideal to investigate the clinical implications of these findings.

Ethical Approval

IRB number H-02-J-008 has been granted by the bioethics unit and research committee of King Abdulaziz University Hospital (KAUH). This study complies with the Declaration of Helsinki.

Informed Consent Statement

Written informed consent has been obtained from the participants to publish this paper.

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The authors declare that the abstract for this paper was presented at ISBT conference, Cape Town, 2023

Author Contributions

All of the authors have made a significant contribution to the work being reported. This includes the conception of the study design, execution, acquisition of data, analysis, interpretation, or any combination of these areas. Every author has also participated in drafting, revising, or critically reviewing the article. They have given final approval for the version to be published and have agreed on the journal to which the article has been submitted. Furthermore, all authors agree to be accountable for every aspect of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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