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ORIGINAL RESEARCH

To evaluate the effects of storage on platelets in platelet concentrate

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Abstract
Background: To evaluate the effects of storage on platelets in platelet concentrate.
Materials & methods: A total of 80 subjects were enrolled. Data regarding the age of the platelet concentrate were collected from the blood bank for the platelet transfusion administered at time of enrolment. The storage age was analyzed both as a categorical variable in three groups: 1–2 days, 3–4 days and 5–7 days of age, as well as a continuous variable. The results were analysed using SPSS software.
Results: There were differences in the source of platelets (apheresis versus whole-blood derived) ($p<0.001$) and volume reduction ($p<0.001$) between the storage age groups. There was no statistically significant association between storage age and incremental change in total platelet count ($p=0.2$).
Conclusion: Potential importance of storage age is considered. There can be seen increased transfusion reactions with fresher platelet concentrates.
Keywords: platelets, storage age, transfusion.

Introduction

Increasing platelet (PLT) demand coupled with their relatively short shelf-life may compromise PLT availability. One possible solution to address increasing demand and improve PLT availability is an extension of PLT storage duration. PLTs are stored at 22 °C to preserve function; however, this temperature facilitates growth of bacterial contaminants. As a result, PLT storage duration is commonly 5 days, although in some countries that screen for bacterial contamination or use pathogen reduction technologies, this duration is up to 7 days. [1,2] Over time, changes in both PLTs and their storage medium occur, with an accumulation of bioreactive substances. Extension of PLT storage duration may expose patients to potential decreases in PLT transfusion efficacy as well as possible increases in adverse events in addition to transfusion-associated sepsis, such as inflammation and/or immune-mediated events. [3-5] Critically ill patients, including post-cardiac surgery patients, are the second largest group to receive PLTs after haematology/oncology patients and may be particularly susceptible to PLT adverse events due to their pre-transfusion inflammatory state. [6,7] Nonetheless, the impact on clinical and transfusion outcomes of PLT storage changes is poorly described in this population. [7-11]

Traditionally, platelet concentrates are stored at 20–24°C for up to five to seven days. [12] Over time, as the stored platelets age, there are changes in their functional integrity, in their ability

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to aggregate, activate, and in their effect on immune and endothelial function and microvesiculation. [13,14] In addition, in vitro studies have shown that older platelet concentrates contain higher levels of inflammatory cytokines, such as IL-8. [15] Platelets of older storage age have been independently associated with adverse outcomes in certain adult cohorts including poorer response to platelet transfusions, increased transfusion reactions, and adverse inflammatory events. [16] Hence, this study was conducted to evaluate the effects of storage on platelets in platelet concentrate.

Materials & methods

A total of 80 subjects were enrolled. Data regarding the age of the platelet concentrate were collected from the blood bank for the platelet transfusion administered at time of enrolment. The storage age was analyzed both as a categorical variable in three groups: 1–2 days, 3–4 days and 5–7 days of age, as well as a continuous variable. Multivariable linear and logistic models were developed to assess the association between storage duration (as a continuous variable) and clinical outcomes. Outcomes (including platelet count increments and transfusion reactions) were evaluated by platelet storage age. Chi- squared test was done. The results were analysed using SPSS software.

Results

A total of 80 subjects were enrolled. There were differences in the source of platelets (apheresis versus whole-blood derived) ($p<0.001$) and volume reduction ($p<0.001$) between the storage age groups.

Table 1: Characteristics of the platelet concentrates grouped by storage age

Transfusion variable	1-2 days (20)	3-4 days of age (20)	5-7 days of age (40)	p-value
Source Apheresis	14 (70)	18 (90)	33 (82.5)	<0.001
Whole blood derived	6 (30)	2 (10)	7 (17.5)	
Volume reduced (washed)	4 (20)	1 (5)	4 (10)	<0.001

There was no statistically significant association between storage age and incremental change in total platelet count ($p=0.2$). However, there was a significant association between fresher storage age and febrile transfusion reactions ($p=0.002$)

Table 2: Multivariable model to evaluate associations between storage age of platelet concentrates and clinical outcomes

Clinical outcome	Adjusted or beta coefficient	p- value
Incremental Change in Total Platelet Count	Beta= - 3.206	0.2
Febrile Transfusion Reactions	OR= 0.45	0.002

Reported as Adjusted Odds Ratio (OR) for categorical outcomes or Beta regression coefficient for continuous outcomes

Discussion

Many biochemical and functional changes occur in platelet concentrates over time. Because of the interactions between platelets and their storage containers and conditions, platelet lysis and activation occur with subsequent elevation in lactate dehydrogenase, von Willebrand factor and serotonin. [17] Glucose is depleted, lactate accumulates and acidification occurs within the platelet concentrate media over time. [18] In addition, the surface proteins expressed

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on stored platelets change over time affecting their thrombin sensitivity and they become more sensitized to nitric oxide which impairs their ability to aggregate. [19,20] Counter to the reduced aggregation with increased storage time, the accumulation of platelet microparticles amplifies thrombin formation. [21] Hence, this study was conducted to evaluate the effects of storage on platelets in platelet concentrate.

In the present study, a total of 80 subjects were enrolled. There were differences in the source of platelets (apheresis versus whole-blood derived) ($p<0.001$) and volume reduction ($p<0.001$between the storage age groups. Our results were in concordance with the results obtained by previous authors who also reported similar findings. A study by Singh H et al, studied morphological changes in platelets were monitored by automated haematological cell counter for platelet count and mean platelet volume (MPV). Samples were incubated with K2EDTA for 1 h and platelet indices were repeated on the EDTA incubated samples. There was no significant change in the indices without EDTA during storage, however, after EDTA incubation, significant changes were noted in dPLT and dMPV. The mean dPLT on day 0 was 75.15 x 10(3)/microl decreasing to 44.4 x 10(3)/microl on day 7, while dMPV from 0.76 fl on day 0 increased to 1.34 fl on day 7 ($P < 0.05$). Metabolic parameters showed a significant decrease in pH and pCO2 concurrent with increasing pO2 during storage ($P < 0.05$). Average ATP level on day 0 was 21.09 micromol/dl falling to 10.59 micromol/dl on day 7. [22]

In the present study, there was no statistically significant association between storage age and incremental change in total platelet count ($p=0.2$). However, there was a significant association between fresher storage age and febrile transfusion reactions ($p=0.002$). Another study by Winkler AM et al, studied 77 LR-ADP underwent metabolic (n=67) or metabolic and aggregation (n=10) studies. All products maintained a pH > 6.89 throughout storage. Lactate and pCO2 increased proportionally with longer storage time. Regardless of acceptable metabolism during storage, aggregation in 10-20 ml aliquots was impaired by day 4 and aliquots less than 40 ml demonstrated the most dramatic decrease in aggregation from baseline. Despite maintenance of acceptable metabolic conditions, residual volumes of LR-ADP develop impaired aggregation in vitro that may adversely affect platelet survival and function in vivo. At volumes below 40 ml, LR-ADP revealed reduced aggregation. As a result, it is recommended to monitor and record volumes of LR-ADP used for pediatric transfusion. Moreover, once LR-ADP attain a volume of 50 ml or less on day 4 or 5 of storage, consider discarding these products until their in vivo efficacy can be studied. [23] The consequences of storage duration on PLT transfusion efficacy can be assessed using transfusion outcomes such as post-transfusion absolute platelet count increment (CI), the corrected count increment (CCI; absolute platelet count increase normalised to body surface area and platelet dose) and the time to next PLT transfusion. More importantly, efficacy can also be assessed using clinical outcomes, including prevention or treatment of bleeding, volume of red blood cells (RBCs) required and mortality. The safety of stored PLTs can be assessed from adverse events following PLT transfusion, such as febrile non-haemolytic transfusion reactions, transfusion-transmitted infection and overall morbidity and mortality. Difficulties in determining whether stored PLTs are as safe and as effective as fresher PLTs in critically ill patients are related to the fact that most of these outcomes are affected by other factors, including population characteristics, severity of underlying illness, cause of thrombocytopenia, concomitant bleeding, administration of other blood products and other co-morbidities impacting on these endpoints. [24]

Conclusion

Potential importance of storage age is considered. There can be seen increased transfusion reactions with fresher platelet concentrates.

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