Possible red blood cell damage due to iatrogenic transfusion filter-related mistakes during blood transfusion

Hirosi Fujita¹, Ryoko Sakuma² and Shigeko Nishimura¹

¹Correspondence: yuketsuka@bokutoh-hp.metro.tokyo.jp
²Department of Transfusion Medicine, Tokyo Metropolitan Bokutoh Hospital, Japan.
³Clinical Laboratory, Tokyo Metropolitan Bokutoh Hospital, Japan.

Abstract

Background: Red cell concentrates are usually transfused through a transfusion filter. Iatrogenic accidents can occur in which the red cell concentrate is transfused through the infusion filter by mistake. Therefore, we examined the extent of red blood cell damage in red cell concentrates transfused through transfusion and infusion filters ex vivo.

Methods: We evaluated red blood cell damage using lactate dehydrogenase, free hemoglobin, and erythrocyte membrane phosphatidylserine expression in red cell concentrates transfused through transfusion and infusion filters (transfusion rate: 100mL/h). In addition, we performed hemolytic experiments using a 50% glucose solution in red cell concentrates transfused through both filters.

Results: Red cell concentrates transfused through infusion filters revealed higher lactate dehydrogenase, free hemoglobin, and phosphatidylserine expression levels than those transfused through transfusion filters. The 50% glucose solution induced hemolysis of the red cell concentrates from the infusion filters more strongly than those from the transfusion filters.

Conclusion: An iatrogenic mistake from the transfusion filter to the infusion filter might induce red blood cell damage.

Keywords: Hemolysis, phosphatidylserine, lactate dehydrogenase, free hemoglobin, transfusion filters

Introduction

Transfusion-associated hemolysis is caused by either immune-mediated or non-immune hemolysis. Antibodies and/or complement proteins induce a hemolytic reaction during the acute (acute hemolytic transfusion reaction) [1] and delayed (delayed hemolytic transfusion reaction) phases [2]. Non-immune mediated causes of transfusion-associated hemolysis include thermal injury [3], osmotic injury [4], mechanical injury [5], infection [6], drugs [7] and others. In mechanical injuries, defective blood administration causes induced transfusion-associated hemolysis [8]. Blood components such as red cell concentrates (RCC), fresh frozen plasma, platelet concentrates, and others, are usually transfused through a transfusion filter with a pore size of 170–200µm to remove clots, aggregates, and other particles [9]. On the other hand, the therapeutic solution is usually infused intravenously through an infusion filter (intravenous fluid set) with a pore size of 15µm to remove small-sized crystals and glass. As transfusion incident reports are dependent on the practitioner’s knowledge of transfusion practice, new nurses sometimes mistakenly set the transfusion route from the transfusion filter to the infusion filter [10]. There are no recent reports regarding iatrogenic administration setting mistakes in transfused patients. Therefore, we examined the effects of infusion filters on red cell damage compared with a routinely used transfusion filter ex vivo. As a result, blood transfused through the infusion filter might be more fragile and easily lysed by the hyperosmolar solution. We concluded that adequate transfusion filters should be used in transfusion practice.

Materials and methods

Materials

Transfusion filters were purchased from Termo Co. Ltd. (Osaka, Japan). Infusion filters were purchased from Nipro Co. (Osaka, Japan). A 50% glucose solution (Otsuka Pharmaceutical, Tokyo, Japan) was used for the hemolytic experiments. The non-irradiated RCC (Japanese Red Cross Society, Tokyo, Japan) used in the experiments were out of date. The RCC is leukocyte-depleted before storage and must be transfused within 21 days after phlebotomy in Japan; we used RCC within 1 week after the expiration date for the experiments.

Evaluation of red blood cell damage in dynamic and static tests using blood passed through the transfusion and infusion filters

In the dynamic test, RCC was transfused through the transfusion or infusion filter at a flow rate of 100mL/hour. Lactate dehydrogenase (LD) and free hemoglobin (fHb) in the RCC plasma were used as hemolytic markers and measured by BML (Tokyo, Japan). In addition, we measured phosphatidylserine (PS) exposure on the erythrocyte membrane. In the static test, RCC from the transfusion and infusion filters were co-infused with the 50% glucose solution at a 1:1 ratio (final concentration: 25% glucose solution). Thirty minutes after mixing at room...
Table 1. Red blood cell damage in blood transfused through infusion filters.

|                      | Transfusion filter | Infusion filter |
|----------------------|--------------------|-----------------|
|                      | N=4                | N=4             |
| Lactate dehydrogenase (IU/L) | 50.5 (0.5)         | 58.3 (0.9)*     |
| Free hemoglobin (mg/dL)       | 15.2 (0.3)         | 18.5 (0.6)*     |
| % phosphatidylserine       | 0.39 (0.09)        | 1.04 (0.01)*    |

Data represent the means with standard errors in parentheses. The results are representative of 3 independent experiments. *p<0.05 vs. transfusion filter.

Results

Ex vivo dynamic red blood cell damage in blood transfused through infusion filters

Gross hemolysis was absent in the plasma transfused through the infusion and transfusion filters at a flow rate of 100mL/h. However, the LD and free Hb levels in the blood transfused through infusion filters were significantly higher than those transfused through transfusion filters, as shown in Table 1. In addition, erythrocyte membrane PS expression in the blood transfused through the infusion filters was significantly higher than that transfused through the transfusion filters.

In vitro hemolytic effects of a 50% glucose solution on blood transfused through an infusion filter

Gross hemolysis was present in the plasma transfused through the infusion and transfusion filters, at 30 min after mixing the co-infused blood and 50% glucose solution at room temperature (20°C). The LD and free Hb levels of co-infused blood transfused through the infusion filters with the 50% glucose solution were significantly higher than those transfused through the transfusion filters, as shown in Table 2. In addition, PS expression on the erythrocyte membrane from the co-infused blood transfused through the infusion filter with the 50% glucose solution was significantly higher than that transfused through the transfusion filter.

Discussion

Blood transfused through an infusion filter with a pore size of 15μm was more fragile than that through a routinely used transfusion filter, as shown in Table 1. Although no strong hemolysis was observed, these data suggested the possibility that blood transfused through an infusion filter might be lysed in transfused patients. The erythrocyte membrane PS expression in the blood transfused through the infusion filters was significantly higher than that transfused through the transfusion filters (infusion filter: 1.04±0.01%, transfusion filter: 0.39±0.09%). Since erythrocyte membrane PS expression is a marker of aging erythrocytes [13], macrophages present in the liver and spleen may easily phagocytose erythrocytes with high PS expression [14]. Therefore, erythrocytes transfused through an infusion filter might have shortened intravascular life compared with those transfused through a transfusion filter. High-percentage glucose solutions have been shown to induce hemolysis and enhance the expression of PS on erythrocyte membranes [15]. The high-percentage glucose solution (50% glucose) induced hemolysis in the co-infused blood transfused through the infusion filters to a greater extent than that transfused through the routinely used transfusion filters. These data suggested that the erythrocytes from the blood transfused through the infusion filters were more sensitive to the infusion process.
damaged. Erythrocyte membrane PS expression also increases in hemolytic anemia [16].

These data suggested that iatrogenic mistakes from the transfusion filter to the infusion filter could induce transfusion-associated hemolysis. Therefore, adequate education regarding administration settings is critical for nurses who perform blood transfusion.

Conclusions
An iatrogenic mistake from the transfusion filter to the infusion filter might induce red blood cell damage.

Competing interests
The authors declare that they have no competing interests.

Authors’ contributions
HF designed and planned the experiments, performed the research, and wrote the manuscript. RS performed the PS expression experiments. SN performed the experiments and analyzed the data.

Acknowledgement and funding
This study was supported by a grant from the Tokyo Metropolitan Government.

Publication history
EIC: Robert A. Lodder, University of Kentucky, USA.
Received: 11-Apr-2013 Revised: 20-Jun-2013 Accepted: 27-Jun-2013 Published: 28-Jun-2013

References
1. Sazama K: Reports of 355 transfusion-associated deaths: 1976 through 1985. Transfusion 1990, 30:583-90. | Article | PubMed
2. Schorn TF and Knospe WH: Fatal delayed hemolytic transfusion reaction without previous blood transfusion. Ann Intern Med 1989, 110:241-2. | Article | PubMed
3. Utoh J and Harasaki H: Damage to erythrocytes from long-term heat stress. Clin Sci (Lond) 1992, 82:9-11. | Article | PubMed
4. Mulligan J, Parfrey P, Phillips ME, Brown EA and Curtis JR: Acute haemolysis due to concentrated dialysis fluid. Br Med J (Clin Res Ed) 1982, 284:1151-2. | Article | PubMed Abstract | PubMed Full Text
5. Mair DC, Eastlund T, Rosen G, Covin R, Harmon JV, Menser M, Carr R and Shrwany S: Hemolysis during percutaneous mechanical thrombectomy can mimic a hemolytic transfusion reaction. Transfusion 2005, 45:1291-4. | Article | PubMed
6. Kleinman S, Chan P and Robillard P: Risks associated with transfusion of cellular blood components in Canada. Transfus Med Rev 2003, 17:120-62. | Article | PubMed
7. Fujita H, Sakuma R, Fujimoto S, Hazama Y, Ohtake C, Moriyama A, Kuhara K and Nishimura S: Nafamostat mesilate, a noncalcium compound, as an anticoagulant, induces calcium-dependent haemolysis when infused with packed erythrocytes. Transfus Med 2012, 22:186-91. | Article | PubMed
8. Dubey A, Verma A, Sonker A, Sachan D and Chaudhary R: Transfusion medicine illustrated. Sudden increased incidence of transfusion reactions reported from a ward: root cause analysis. Transfusion 2009, 49:409-10. | Article | PubMed
9. The administration of blood and blood components and the management of transfused patients. British Committee for Standards in Haematology, Blood Transfusion Task Force. Royal College of Nursing and the Royal College of Surgeons of England. Transfus Med 1999, 9:227-38. | Article | PubMed
10. Hijji BM, Owais AE and Dabbours RS: Measuring knowledge of blood transfusion: a survey of Jordanian nurses. Am Int J Contemp Res 2012,