Deformability of transfused red blood cells is a potent effector of transfusion-induced hemoglobin increment: A study with β-thalassemia major patients

To the Editor:

In the current routine, blood donations are subjected to testing of blood type and pathogenic gents on day of donation, and the supply of packed red blood cells (PRBC) units for transfusion is conducted primarily according to storage duration, namely by the first-in-first-out (FIFO) criterion. However, the actual functionality of the transfused PRBC, namely their capacity to effect the expected transfusion outcome is ignored. This is especially pertinent to patients with chronic anemia, like β-thalassemia major (TM), who are treated with lifelong frequent transfusions (of one or two units) every 2–4 weeks. The transfused RBC are aimed at raising the hemoglobin (Hb) level in the recipients’ blood. However, RBC have unique mechanical properties, deformability in particular, which play a major role in blood circulation and in the RBC survival. In a recent study1 with TM patients, we have shown, for the first time in humans, that the transfusion-induced change in the recipients’ skin blood flow strongly correlated with the deformability of the transfused PRBC.

In the present study, we examined the effect of transfused RBC deformability on the immediate transfusion outcome, as expressed by the increase in the recipients’ Hb (ΔHb), as well as the time interval between consecutive transfusions (TIBT). Employing TM patients for this study has specific advantages; TM patients are treated with lifelong frequent transfusions (every 2–4 weeks). Therefore, testing the effect of repeated, consecutive transfusions in the same patient, having about the same baseline throughout the study, provides solid grounds for attributing the observed effect to the properties of the transfused PRBC units. In addition, TM patients at the Hadassah Hospital Thalassemia Clinic are routinely given PRBC units stored for up to about 10 days, when the potential storage-lesion is insignificant. Twenty-four TM patients were employed; their characteristics are summarized in Supporting Information Table S1. The transfusion-induced changes in the recipients’ hemoglobin (ΔHb) and hematocrit (ΔHct) were determined 10 minutes after the transfusion completion. The results clearly showed that:

1. ΔHb exhibited a highly significant positive correlation with RBC deformability: The transfusion outcome was analyzed vs. various parameters derived from deformability distribution of the PRBC. It was found that ΔHb, shown in Figure 1, as well as ΔHct (Supporting Information Table S2), were best correlated with the percent of low deformable cells (LDFC), with highly significant inverse dependence on this parameter.

2. In addition to the immediate increase in the recipients’ hemoglobin, an important criterion of the transfusion efficacy in TM patients is the time interval between consecutive transfusions (TIBT). As noted above, TM patients are treated with frequent (every 2–4 weeks) transfusions, and the longer is the TIBT, the better is the transfusion outcome. In the present study we have found that PRBC with low level of rigid RBC yields a longer interval between two consecutive transfusions (> 21 days), suggesting that RBC with good deformability would endure longer in the circulation and enable less frequent consecutive transfusions (Supporting Information Figure S2).

References


SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article.

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3. While the transfusion of one PRBC unit is normally expected to induce ΔHb of 1 g/dL in the recipient’s blood, in the TM patients, ΔHb, determined 10 minutes after transfusion, was 0.84 ± 0.40 g/dL following a one-unit transfusion, and 0.71 ± 0.29 g/dL (average) following a two-unit transfusion (Supporting Information Table S3). It thus seems that even in splenectomized TM patients, as employed in this study, the clearance of transfused PRBC is accelerated. Notably, dependence of ΔHb and ΔHct, determined upon completion of the transfusion, on the % LDFC, suggests that the relatively rigid cells in the transfused PRBC are cleared rapidly, practically during the transfusion procedure. This is in accord with previous reports that the clearance of transfused PRBC starts immediately with the administration of the PRBC into the blood stream. In splenectomized TM patients, as employed in the present study, the clearance of transfused RBC is expected to be slower. However, the opposite was observed here, as the transfusion-induced ΔHb was considerably lower than normally expected.

Rigid and fragile RBC are prone to facilitated removal from the blood circulation within the first hours after transfusion, mainly due to the shear forces in the blood stream, in addition to splenic removal. In line with that, Nagababu et al. observed the elevation of plasma-free Hb immediately after PRBC transfusion. In addition, RBCs phagocytosis, in the spleen or liver, has been proposed to be the result of a balance between clearance enhancing (“eat me”) signals, including phosphatidylycerine (PS) on membrane surface and membrane band-3 clustering, and clearance-attenuating (“don’t eat me”) signals, such as CD44. In accord with that, we have shown that the rigid RBC are especially susceptible to mechanical stress, such as that applied by flow-induced shear stress, and are enriched with cell surface PS. These non-splenic routes may account for the accelerated clearance of transfused RBC in splenectomized TM patients, observed in the present study.

As noted above, the supply of PRBC units for transfusion is conducted primarily according to the FIFO criterion, while the actual functionality of the transfused PRBC is ignored. In a preceding study with TM patients, we have shown that the transfusion-induced change in the recipients’ skin blood flow was strongly correlated to the deformability of the transfused PRBC. In the present study we show, for the first time in humans, that the deformability of the transfused PRBC, in particular the % LDFC, is a major determinant of the transfusion-induced increase in the recipient’s hemoglobin, the definitive goal of blood transfusion. Taken together, these studies strongly support the need for considering the hemodynamic functionality of transfused blood units in blood banking, which can be a powerful tool for reducing transfusion-related risks, especially for patients with chronic anemia, who are treated with frequent, long-life blood transfusions. The additional testing of the PRBC hemodynamic functionality will introduce a new concept into blood banking which will make a considerable contribution to improving transfusion therapy.

CONFLICT OF INTEREST
The authors have no conflict of interest to disclose.

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