**Letters to the Editor**

Red Cell Transfusion Decreases Hemoglobin A1c in Patients with Diabetes

To the Editor:

Hemoglobin A1c (Hb A1c),\(^1\) is a mainstay of diabetes diagnosis and management that allows clinicians to estimate the recent mean blood glucose concentration of a patient. Glycation of hemoglobin is an irreversible, nonenzymatic process that depends on the glucose concentration in red blood cells (RBCs), and Hb A1c represents the integrated glucose concentration in RBCs over their life span.

RBC transfusion can complicate the interpretation of Hb A1c values in diabetic patients because it introduces hemoglobin molecules exposed to glucose concentrations that may have been different from the glucose concentrations in the diabetic transfusion recipient. The potential effect of transfusion on Hb A1c has been recognized for some time, but opinions on the direction of the effect are contradictory. Data from the older literature (1–3) suggest that the high concentration of glucose in RBC storage medium promotes glycation and causes Hb A1c values to increase over time, which would predict that Hb A1c might increase in transfused patients. This concept has been stated in a recent review article (4) and on consumer Web sites, such as Lab Tests Online (http://labtestsonline.org/understanding/analytes/a1c/test.html); however, a recent case in which a pathology resident was contacted to explain a patient’s Hb A1c value decreasing from 7.4% to 5.4% in 3 days after the patient received 3 units of RBCs suggested that transfusion may lower Hb A1c values in diabetic patients. Indeed, the majority of blood donors are not diabetic, and donor RBCs would dilute the increased Hb A1c value (>6.5%) in a diabetic patient. To our knowledge, no study has used contemporary Hb A1c methods to examine the effect of RBC storage conditions on Hb A1c or the overall effect of RBC transfusion on Hb A1c in patients.

To investigate these questions, we used an immunoassay (Siemens Dimension RxL) to measure Hb A1c in 2 unused RBC units stored in additive storage medium (AS-1) under standard blood bank conditions. These 2 units were unacceptable for transfusion because they had been out of the control of the blood bank for >30 min. The Hb A1c values for samples obtained from the units on their expiration date (42 days after collection) were 5.4% (B Rh-positive) and 5.7% (O Rh-positive), which are within our reference interval (<6.0%). The glucose concentrations in the blood units at this time were 36.9 mmol/L (665 mg/dL) and 32.5 mmol/L (586 mg/dL), confirming the supraphysiological glucose content of the RBC storage medium. We observed minimal increases in Hb A1c values in the units after additional incubation at room temperature for 9 days (5.7% and 5.9%) and at 37 °C for another 14 days (6.0% and 6.0%). This finding strongly suggests that glycation of hemoglobin in stored RBC units is negligible despite the high glucose concentrations in stored RBC units.

To determine if RBC transfusion has a measurable effect on Hb A1c in patients, we retrospectively queried an institutional review board–approved database of de-identified patient data from our hospital for patients who received RBC transfusions and had Hb A1c measurements performed within 28 days before and 14 days after they received at least 1 RBC transfusion. We allowed a maximum of 7 days between the first and last transfusions for patients who received multiple transfusions; therefore, the maximum time between the pre- and posttransfusion Hb A1c measurements was 49 days. Fig. 1 shows the change in Hb A1c after transfusion for 45 patients who met the inclusion criteria. The Hb A1c decreased in 31 (69%) of the patients overall and in all 21 patients whose pretransfusion Hb A1c measurement was ≥7%. Of the 14 patients whose Hb A1c value increased or remained unchanged, 12 had a pretransfusion Hb A1c value of <6.5%; thus, one would not expect the transfusion of RBCs with a typical Hb A1c value to have a large effect. The mean decrease in Hb A1c across all patients was 0.829%, which is statistically significant (P = 0.00124, 2-sided paired t-test). The mean decrease for the 21 patients with pretransfusion values ≥7% was 1.97% Hb A1c.

These results suggest that RBC transfusion will reduce the Hb A1c concentration in diabetic patients. We did not design this study to fully characterize this phenomenon, but it does show that appreciable glycation does not occur during typical blood bank storage. Thus, we would expect decreased Hb A1c values after transfusion to be most pronounced in patients who receive large transfusion volumes and/or who have a high pretransfusion Hb A1c, because of dilution with RBCs containing typical amounts of Hb A1c. Indeed, pa-

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1 Nonstandard abbreviations: Hb A1c, hemoglobin A1c; RBC, red blood cell.

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Patients with the highest pretransfusion Hb A1c values showed the largest decreases after transfusion (Fig. 1). This effect is worth noting because we are likely to see expanded application of Hb A1c testing, given new guidelines that make Hb A1c measurement sufficient for diabetes screening and because of the recent American Diabetes Association recommendation to measure Hb A1c in all hospitalized diabetic patients who have not had an Hb A1c measurement taken within the previous 60 days (5). The Joint Commission has adopted this recommendation as a standard for inpatient diabetes care.

**Fig. 1. Change in Hb A1c after RBC transfusion.**
Each line represents a patient with Hb A1c measurements taken ≤28 days before and ≤14 days after receiving an RBC transfusion. The left and right ends indicate the dates (x axis) and values (y axis) of the pretransfusion and posttransfusion Hb A1c measurements, respectively. The dates are relative to the day of transfusion (day 0, vertical dashed line).

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