Red Cell Transfusion Decreases Hemoglobin A\textsubscript{1c} in Patients with Diabetes

To the Editor:

Hemoglobin A\textsubscript{1c} (Hb A\textsubscript{1c})\textsuperscript{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 A\textsubscript{1c} represents the integrated glucose concentration in RBCs over their life span.

RBC transfusion can complicate the interpretation of Hb A\textsubscript{1c} 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 A\textsubscript{1c} 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 A\textsubscript{1c} values to increase over time, which would predict that Hb A\textsubscript{1c} 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 A\textsubscript{1c} 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 A\textsubscript{1c} values in diabetic patients. Indeed, the majority of blood donors are not diabetic, and donor RBCs would dilute the increased Hb A\textsubscript{1c} value (>6.5%) in a diabetic patient. To our knowledge, no study has used contemporary Hb A\textsubscript{1c} methods to examine the effect of RBC storage conditions on Hb A\textsubscript{1c} or the overall effect of RBC transfusion on Hb A\textsubscript{1c} in patients.

To investigate these questions, we used an immunoassay (Siemens Dimension RxL) to measure Hb A\textsubscript{1c} 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 A\textsubscript{1c} 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 A\textsubscript{1c} 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 A\textsubscript{1c} in patients, we retrospectively queried an institutional review board–approved database of deidentified patient data from our hospital for patients who received RBC transfusions and had Hb A\textsubscript{1c} 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 A\textsubscript{1c} measurements was 49 days. Fig. 1 shows the change in Hb A\textsubscript{1c} after transfusion for 45 patients who met the inclusion criteria. The Hb A\textsubscript{1c} decreased in 31 (69%) of the patients overall and in all 21 patients whose pretransfusion Hb A\textsubscript{1c} measurement was ≥7%. Of the 14 patients whose Hb A\textsubscript{1c} value increased or remained unchanged, 12 had a pretransfusion Hb A\textsubscript{1c} value of <6.5%; thus, one would not expect the transfusion of RBCs with a typical Hb A\textsubscript{1c} value to have a large effect. The mean decrease in Hb A\textsubscript{1c} 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 A\textsubscript{1c}.

These results suggest that RBC transfusion will reduce the Hb A\textsubscript{1c} 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 A\textsubscript{1c} values after transfusion to be most pronounced in patients who receive large transfusion volumes and/or who have a high pretransfusion Hb A\textsubscript{1c} because of dilution with RBCs containing typical amounts of Hb A\textsubscript{1c}. Indeed, patients with the highest pretransfusion Hb A\textsubscript{1c} values showed the largest decreases after transfusion (Fig. 1). This effect is worth noting because we are likely to see expanded application of Hb A\textsubscript{1c} testing, given new guidelines that make Hb A\textsubscript{1c} measurement suffi-

\textsuperscript{1} Nonstandard abbreviations: Hb A\textsubscript{1c}, hemoglobin A\textsubscript{1c}; RBC, red blood cell.
cient for diabetes screening and because of the recent American Diabetes Association recommendation to measure Hb A1c in all hospitalized diabetics 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.

**Author Contributions:** All authors confirmed they have contributed to the intellectual content of this paper and have met the following 3 requirements: (a) significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (b) drafting or revising the article for intellectual content; and (c) final approval of the published article.

**Authors’ Disclosures of Potential Conflicts of Interest:** Upon manuscript submission, all authors completed the Disclosures of Potential Conflict of Interest form. Potential conflicts of interest:

**Employment or Leadership:** M.G. Scott, past president, Academy of Clinical Laboratory Physicians and Scientists.

**Consultant or Advisory Role:** M.G. Scott, scientific advisory board, Becton Dickinson.

**Stock Ownership:** None declared.

**Honoraria:** None declared.

**Research Funding:** M.G. Scott, Siemens Healthcare Diagnostics.

**Expert Testimony:** None declared.

**Role of Sponsor:** The funding organizations played no role in the design of study, choice of enrolled patients, review and interpretation of data, or preparation or approval of manuscript.

### References


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**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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Previously published online at
DOI: 10.1373/clinchem.2010.157321