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Title: CRITICAL IMPORTANCE OF DILUTING PACKED RBC FOR TRANSFUSION

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Introduction: Faced with the enormous demand yet scarce resources of blood, component therapy has evolved as a paramount conservation effort by hospital blood banks. Anesthesiologists are faced with the resultant problem: How should packed red blood cells (PRBC) be transfused to minimize RBC damage (hemolysis) while maximizing rate of blood administration (flowrate)? Currently, no data exist to guide optimum administration of PRBC transfusions (Tf). The purpose of this prospective, randomized study was to measure both the independent and interactional effects of dilution, pressure, and apparatus on RBC hemolysis and flowrate to guide Tf therapy.

Methods: Twelve units (bags) of PRBC's were obtained from the local blood bank. Three levels of dilution (none, with 100 ml normal saline (NS), and with 200 ml NS), 2 levels of external bag pressure (150 torr, 300 torr), and 2 types of apparatus (abbreviated or complete) were randomly allocated to the 12 units. Composition of each unit of blood was described according to the following variables: age, blood type, dextrose concentration, PaO_2, $PaCO_2$, pH, and hematocrit. After the 12 units were set up, 72 paired aliquots of blood were sampled (6 pairs from each unit) in a random fashion. For each pair, one sample was drawn at the bag (inlet), and the other was drawn after blood flow through the administration apparatus (outlet). Free hemoglobin was measured in each of the paired samples. The hematocrit of the sample drawn at the end of the apparatus was measured. Other measurements taken for each of the six paired observations were flow volume and flow time. Flow rate was calculated by dividing flow time into flow volume. Three-way analysis of variance was used to assess the effects of dilution, pressure, and apparatus plus their interactions on hemolysis [the difference in free hemoglobin concentration (outlet—inlet)] and flowrate. One-way analysis of variance and the Student t-test for grouped data were used for univariate comparisons. Following a significant one-way analysis of variance, Scheffe's method was employed to detect difference in means. Linear regression was used to examine the association of extraneous variables with flowrate and hemolysis. Significance was defined at $p < 0.05$.

Results: Of the twelve PRBC units studied, descriptors were as follows: age (days)--19d (n = 3), 21d (n = 3), 24d (n = 6); blood type (A, AB, O)--A (n = 3), AB (n = 2), O (n = 7); dextrose concentration (mg/dl)--25 mg/dl (n = 3), 45 mg/dl (n = 8), 90 mg/dl (n = 1); PaO_2 (mean ± SEM)--162.3 ± 1.6; $PaCO_2$--27.6 ± 0.8 torr; pH--6.47 ± .01; hematocrit--81.5 ± 1.4%.

Degree of dilution was the only independent variable which significantly affected hemolysis as measured by increase in free hemoglobin concentrations. However, a three-way interaction effect of dilution, pressure, and apparatus was noted ($p = 0.024$). Undiluted PRBC resulted in a significantly greater increase in free hemoglobin concentration than did dilution with either 100 ml or 200 ml of NS ($p < 0.05$, see Table). Hemolysis was not significantly correlated with age of the blood, dextrose concenration, $PaCO_2$, pH, or hematocrit. However, type AB blood was associated with a significantly greater increase in free hemoglobin concentration than was type A or type O blood ($p < 0.05$). Also, change in free hemoglobin was significantly correlated with the PaO_2 of the unit ($r = -0.38$, $p = 0.001$).

Flowrate was a significant function of all three independent variables [dilution, pressure, and apparatus ($p < 0.001$)].and was also a function of a two-way interaction between dilution and apparatus ($p < 0.001$). Flowrate was significantly less with no dilution, at lower pressure, and with the complete apparatus ($p < 0.05$). No correlation was observed between flowrate and $PaCO_2$, pH, or dextrose concentration. However, the blood that was 21 days old had a significantly higher flowrate than did either the 19-day-old or 24-day-old blood ($p < 0.05$); also, type AB blood had a significantly lower flowrate than did type A or type O blood ($p < 0.05$). Flowrate was significantly correlated with PaO_2 ($r = 0.61$, $p < 0.001$) and hematocrit ($r = -0.62$, $p < 0.001$), but was not correlated with change in free hemoglobin concentration.

Dilution (ml NS)	Increase in Free Hemoglobin (mg/dl)	Flow Rate (ml/sec)
0	2.07 ± 0.92*	0.31 ± 0.04*
100	-0.23 ± 0.15	1.33 ± 0.16
200	0.02 ± 0.05	1.74 ± 0.17

*$p < 0.05$ among three dilution groups

Discussion/Conclusions: Regardless of the external bag pressure applied or the Tf apparatus used, PRBC should be diluted to minimize hemolysis and maximize flowrate. Administration of undiluted PRBC will maximize mechanical damage to the RBC by known rheologic factors (shear stress). That damage will result in an increase in free hemoglobin concentration. Although PRBC flowrate is determined by dilution, pressure, and apparatus, no significant correlation was found between flowrate and hemolysis. Finally, steps directed at increased PaO_2 of the PRBC unit would seem advantageous both to minimize hemolysis and optimize flowrate.