

Calculating the required transfusion volume in children

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BACKGROUND: The traditional method of calculating blood volume for pediatric transfusion in the UK is $\text{weight (kg)} \times \text{aimed increment in hemoglobin concentration (Hb; g/dL)} \times \text{the transfusion factor}$, usually quoted at 3 or 4. This equation is without evidence base. The aim was to assess how the volume of red cells (RBCs) affects the increase in serum Hb in children and to devise a formula that allows accurate volume calculation.

STUDY DESIGN AND METHODS: All pediatric intensive care charts for 2 years were examined retrospectively. The immediate pre- and posttransfusion Hb estimations and the precise volumes of RBC transfused were recorded. Fluid boluses and hemorrhagic loss during the transfusion were documented.

RESULTS: A total of 7679 patient charts were examined with a total of 564 transfusions. All patients who were bleeding, had drain losses, or had concurrent colloid infusions were excluded, giving 379 data points. The correlation gradient between mL per kg blood transfused and increase in Hb was 5.02. There was no significant association between effect and patient weight, age, starting Hb, transfusion time, or sex. No significant difference was found in Hb at 1 and 7 hours posttransfusion.

CONCLUSIONS: The following equation should be used to calculate transfusion volumes: $\text{weight (kg)} \times \text{increment in Hb (g/dL)} \times 3 / (\text{hematocrit [Hct] level of RBCs})$. This predicts that with a UK standard Hct of 0.6, 10 mL/kg gives an increment of 2 g/dL. Care must be taken not to risk hypervolemia, while minimizing donor exposure. Hb estimation 1 hour after transfusion is the same as 7 hours after transfusion.

In contrast to adults, children who need blood transfusions receive a calculated volume of blood depending on their weight, instead of a whole number of units. This makes the volume calculation formula crucial, because incorrect calculation risks circulatory overload or multiple transfusions with additional cost, resource use, and exposure implications. Blood transfusions have inherent risks that need to be minimized as far as possible. The aim must be to optimize the outcome of the transfusions whilst minimizing the number of donors each patient is exposed to.

The calculation of transfusion volumes in children has not previously been evidence-based. A search on Medline, on OVID, through textbooks, and of personal communication from oncologists and hematologists performed before starting this study revealed no studies on which practice could be based. In the UK, many pediatric unit protocols use a calculation of $(\text{weight of the patient in kg}) \times (\text{difference in hemoglobin [Hb] to be achieved in g/dL}) \times \text{a transfusion factor}$, usually either 3 or 4. Some individual pediatricians use 20 mL per kg for all patients. The British Committee for Standards in Haematology¹ guidelines advise a transfusion factor of 3 for children, and Forfar and Arneil's *Textbook of Paediatrics*² advises a factor of 4. There is even interdepartmental factor variation within individual hospitals. In a recent study giving written scenarios to 134 European pediatric intensive care

ABBREVIATION: PICU = pediatric intensive care unit.

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consultants, all transfusions requested were for between 10 and 20 mL per kg.³

Children on the pediatric intensive care unit (PICU) routinely need transfusions, occasionally due to active blood loss, but more commonly to optimize all possible parameters in a critically ill child. We noted on the PICU in Bristol, UK, that with use of our local formula of $\text{weight} \times \text{difference} \times 4$, we regularly did not achieve our desired increase in Hb. The intensive care setting requires frequent blood tests, including blood gases, enabling real-time tracking of the effect of giving a transfusion. We decided to analyze the increase in Hb that was achieved with each transfusion given and to investigate whether the conventional formula was accurate, and if not, whether we could devise a simple and more accurate calculation method.

MATERIALS AND METHODS

All observation charts on the PICU at the Bristol Royal Hospital for Children for all patients over a 24-month period from May 2002 onward were examined retrospectively. The intensive care records detail all fluid input and output by type and volume, as well as observations and blood gas measurements. We took volumes from the nursing charts that recorded the exact volumes given, rather than the prescriptions or the calculations on which they were based. The red blood cell (RBC) specification did not change during this period. They were resuspended in optimal additive solution (SAG-M) to a hematocrit (Hct) level of 0.6 (range, 0.55-0.65).

Patient demographics included age, weight, and sex. Variables documented for each transfusion episode included volume of RBCs given, number of hours over which the transfusion was given, and the immediate pretransfusion, posttransfusion, and 6-hour posttransfusion blood gas estimations of serum Hb. Blood gas sampling from an arterial line requires the collection of only 0.5 mL of blood by syringe, discarding blood and saline in the line. All colloid infusions and drain losses for the transfusion period, the 5 hours after, and the whole day involved were documented.

We excluded from analysis all patients for whom there were confounding variables associated with accelerated RBC destruction, RBC loss, or changes in blood volume that would be expected to affect the post transfusion Hb. Criteria for exclusion were

1. Patients who received any colloid infusions (4.5% human albumin solution), platelets, fresh-frozen plasma, or cryoprecipitate) or plasma exchange during the transfusion period.
2. Patients with active bleeding.
3. All patients on renal replacement therapy or extracorporeal membrane oxygenation.

4. All patients with a diagnosis of active hemolysis.
5. Patients in whom there had been any drain losses. This included chest drains and postoperative drains; for the purposes of the study these could not be guaranteed to be blood-free losses and were therefore excluded. Crystalloid fluid boluses are not given on our unit. Enteral feeds and intravenous maintenance fluids were not corrected for in the analysis, because all patients require and receive some form of hydration maintenance. Urine output was also not analyzed.

Hb measurements were performed on a blood gas machine (ABL 700, Radiometer A/S, Brønshøj, Denmark), from which clinicians on the Bristol PICU routinely base patient transfusion requirements. Hb measurements from the blood gas machine have a daily in-house calibration and a monthly external calibration. The calibrations for the study period were found to be always within the laboratory limits. Local research ethics committee approval and in-house research and development committee approval were granted. Data were inputted to computer spreadsheet software (Microsoft Excel 2003, Microsoft Corp., Redmond, WA) and analyzed with computer software (STATA, Version 7, StataCorp LP).

Statistical analysis

Associations between variables were calculated with Pearson's correlation coefficient and examined with scatter plots. To quantify the association between volume of RBC transfused and incremental increase in Hb, a linear regression model was used in which the increment was modeled as the dependent variable, and volume of transfusion divided by patient weight was used as the independent variable. The constant term was excluded from the regression model to allow for no change to be predicted from no transfusion.

Some patients had repeated blood transfusions within this cohort. To include all the data, but at the same time deal with the assumption that separate data points for the same individual might not be independent, robust standard errors were calculated with STATA Version 7.

RESULTS

A total of 7679 charts were examined from 1494 admissions, on which 564 blood transfusions were identified (transfusion rate, 37.8%). A total of 185 transfusions were excluded due to the above exclusion criteria (Fig. 1). A total of 94,476 mL of blood was transfused (mean, 167 mL). Demographic data for the patients receiving analyzed transfusion episodes are shown in Table 1.

For each of the 379 valid data sets the transfusion factor was calculated by dividing the mL per kg of blood

transfused by the increment achieved in the individual patient. Increment and mL per kg were strongly associated with each other with a Pearson correlation coefficient of 0.64. A scatter plot was drawn and a regression line fitted. The gradient of the regression model was 0.1991 with $p < 0.001$ and robust standard error 0.0054, which equates to a transfusion factor of 5.02 (95% confidence interval, 4.77-5.30; Fig. 2).

There was a significant association between the age in days of the patient and the transfusion factor ($p = 0.049$);

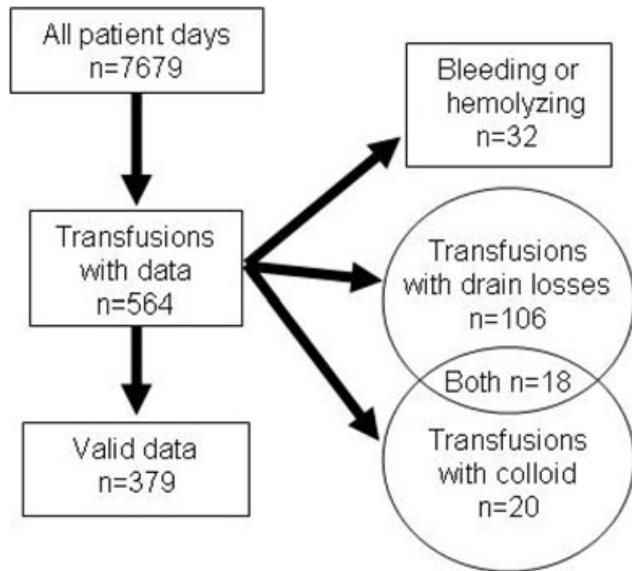


Fig. 1. Data flowchart.

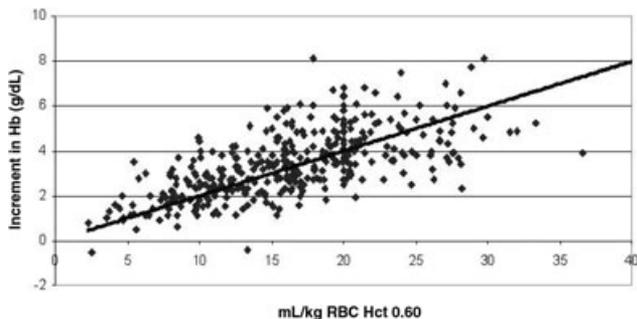


Fig. 2. Scatter plot of transfusion volume (mL/kg) versus increment increase in Hb (g/dL).

TABLE 1. Demographic data of individuals receiving analyzed transfusions

Variable	Number or range
Included transfusions	379
Transfusions to males	216 (57.9%)
Number of individuals	223 (mean, 1.7 per patient)
Age	1 day to 17 years 7 months (median, 6 months 15 days)
Weight	2.1-77.3 kg (median, 5.4 kg)
Volume per kg given	2.3-47.3 mL/kg (median, 16.1 mL/kg)

however, this has a slope of 1.2×10^{-4} (transfusion factor = $5.252 - (\text{age in days} \times 1.2 \times 10^{-4})$). This implies a change in transfusion factor of -0.04 per year, which is not clinically significant. This is demonstrated in Fig. 3.

There was no association between the transfusion factor and other external variables, including weight, length of transfusion, and starting Hb. There was no difference between the effect of transfusions given to male or to female patients. Analysis of increase in Hb measured as a percentage of the starting Hb found a correlation coefficient of 0.63 (SE, 17.6% of starting Hb), which was a less accurate correlation than by simple increment in g per dL Hb.

Analysis by type of patient showed no significant difference in transfusion factor by patient category. Cardiac patients (mostly postoperative; $n = 185$; mean factor, 4.93), sepsis patients ($n = 60$; mean, 5.35), and other patients ($n = 134$; mean, 5.04) had no significant difference.

Transfusions were given over a mean duration of 3.4 hours (median, 3 hr) with a standard deviation (SD) of 1.5 hours. Patients who had multiple transfusions had a mean intertransfusion time of 8.9 days (median, 3 days), and statistical analysis showed that each transfusion episode was independent.

We had data of Hb estimation a mean of 2 hours 22 minutes (median, 2 hr) before each transfusion, and 1 hour 23 minutes (median, 1 hr) after transfusion. Analysis of Hb concentrations taken a mean of 7 hours 47 minutes (median, 6 hr) after the end of the transfusion was no different from those 1 hour after (difference in g/dL, mean 0.2, median 0.1, SD 0.7; Fig. 4).

DISCUSSION

In this consecutive, single-center study we have described how transfusions affect Hb concentration in children, across a broad age and size range. This should help pediatricians and hematologists to practice evidence-based medicine in this important and common field of clinical care.

Published data on which to assess the relative risks of undertransfusion versus those of overtransfusion are lacking. We would, however, wish to avoid both scenarios and therefore would hope for good correlation between prediction and outcome. Our results show a correlation coefficient of 0.64 with an R^2 value of 0.35. As far as is possible, we have attempted to reduce all confounding factors by eliminating all data with drain losses and colloid infusions from the analysis. Within the PICU, boluses of crystalloid fluids are not given, while the effects of urine output and normal maintenance fluid

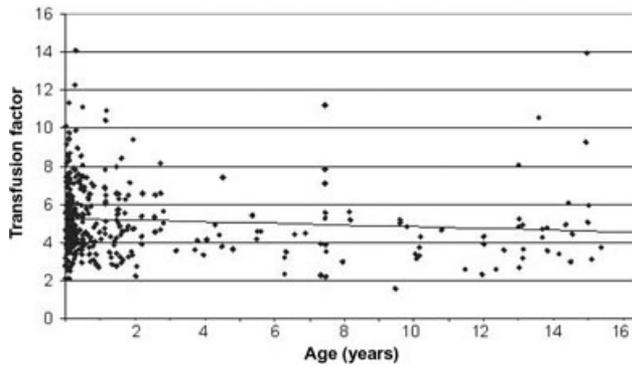


Fig. 3. Transfusion factor and age.

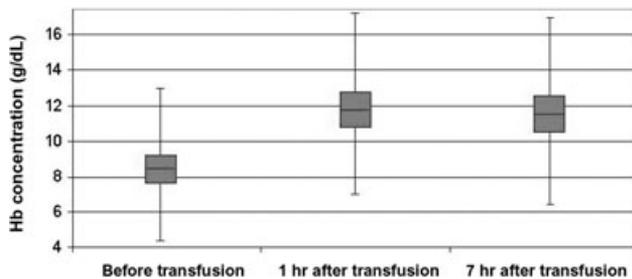


Fig. 4. Hb level before and 1 and 7 hours after transfusion.

Box = interquartile range; bars = absolute range; line = median.

input or feeds were not analyzed as these were felt to be normal physiologic factors.

Our derived transfusion factor of 5 has confidence intervals within 0.28 of the estimate, which implies a small potential difference in predicted and achieved Hb in individual patients. The higher the aimed increase in Hb concentration, the wider the potential for error between the aimed and actual end Hb. Caution must be advised if the need for large increments arises, which may be better given in two smaller amounts with a check Hb value performed in between.

The weak association found between increasing age and decreasing transfusion factor may be explained by the differences in circulating blood volumes with age. It has been suggested that neonates have a greater blood volume per kilogram of body weight compared to older children, but supporting data are limited and contradictory.⁴⁻⁷

The effect we describe is very small and would not be clinically apparent. We support the advice of Morris and coworkers⁸ to use of a consistent factor (we would suggest 5) for all patients whatever their age.

A questionnaire study of intensivists in Canada and Europe showed a high variation in transfusion volume being given to children, with most transfusions at between 10 and 20 mL per kg.⁹ The threshold for transfusion ranged from 7 to 13 g per dL. Studies from adults indicate that a

more restrictive strategy (maintaining an Hb between 7 and 9) may be more beneficial, especially in the younger than 55 years group.¹⁰ This has major implications for the amount of blood transfused into each patient. A recent Canadian study has suggested a transfusion rate in children admitted to PICU of just 14 percent, although there were certain exclusions.¹¹ Our transfusion rate of 37.8 percent was more in keeping with that reported in a small US study.¹²

We studied exclusively PICU patients and this is a population that may have different attributes to general patients on the wards. Most of our cardiac patients are postoperative, and there may be small amounts of occult blood loss. We have excluded any patients who had overt blood loss, however, or who had enough to cause hemodynamic compromise. The PICU population also allows close and frequent monitoring, leading to well-documented, robust data sets. Although it would be ideal to repeat the study in all categories of patients, this is unlikely to be ethical because it would need many episodes of venipuncture in a large number of children. There is scope for further study especially in premature babies, a population that has not been covered by our study. A recent study assessed RBC survival in premature babies with a different model of RBC recovery and found that the measured values were modestly lower than those predicted, older transfused blood being associated with poorer recovery.¹³

Although our study is retrospective, we have included all charts from all patient days over 2 years, with the aim of eradicating selection bias. We also have confidence in the accuracy of the nursing documentation. Furthermore, our findings are corroborated by a recently published small-scale study, which also suggested that existing formulae underestimate the volume of RBCs required to achieve a target Hb value and had trialled a derived factor of 4.8 in 50 critically ill children, with greater success.⁸

Previous anecdotal teaching that analysis of Hb just after a transfusion would not give a reliable reading is shown to be untrue. Hb level 7 hours after was only 0.2 g per dL lower. This simplifies the management of patients who need posttransfusion Hb checks and is in keeping with the results of a recent small scale study in neonates, which has also suggested that there is no need to wait more than 15 minutes after a transfusion before checking for its effect on the Hct.¹⁴ This is important as it may allow for further administration of blood from the same unit, before its time expiry, therefore limiting potential additional donor exposure to the child.

The blood transfused in this study was RBCs resuspended in additive solution containing saline, adenine, glucose, and mannitol (SAG-M). A mean Hct level of close to 0.60 has been adopted in the UK and by many transfusion centers internationally, but this may differ in various parts of the world. Nonresuspended RBCs, which were

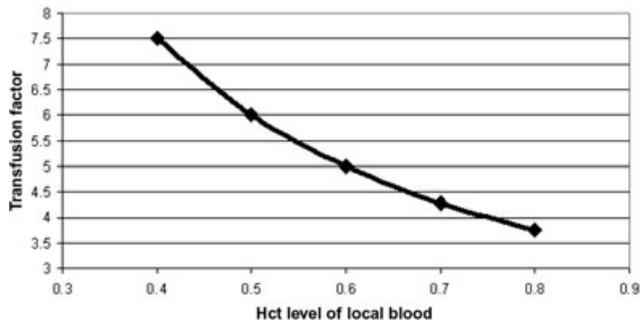


Fig. 5. Transfusion factor by local Hct level.

commonly transfused in the past, have an Hct level approaching 0.8. It is possible that the current transfusion factor of 4 was calculated from blood with an Hct of 0.80 several decades ago. To correct for this difference in Hct (and therefore in the amount of RBCs being transfused), any local transfusion factor should be in the format transfusion constant/Hct, a lower volume of blood to be transfused if it has a higher Hct.

Extrapolation of our data suggests a possible transfusion constant which would be applicable to all Hct levels as follows:

$$\text{Transfusion factor} = 3/\text{Hct of transfused blood.}$$

This can be demonstrated by Fig. 5.

With the UK transfused blood Hct level of 0.60 this calculates to a transfusion factor of 5 (this would be predicted to lead to an increment of 2 g/dL when 10 mL/kg RBCs of this Hct are transfused). Whole blood (Hct, 0.40) would have a factor of 7.5, and blood with an Hct level of 0.80 would have a factor of 3.75. This is at present an extrapolation and we encourage further study in units that use differing transfusion blood Hct levels.

We present evidence-based transfusion volume calculations for children receiving RBCs with an Hct level of 0.6. Based on our results we suggest the following formula for calculating volume of transfusion:

$$\text{Volume of RBCs} = \text{Weight (kg)} \times \text{Increment desired (g/dL Hb)} \times 3/\text{Hct.}$$

We advise caution in large relative volume transfusions, but confidence in transfusing up to an aimed concentration with our formula. Posttransfusion checks can be done 1 hour after transfusion instead of the current 4 to 6 hours. In our unit we have changed practice in line with the above formula. There is a need for a large prospective trial in children outside of PICU to precisely delineate the predictive power of the factor of 3/Hct as a transfusion factor.

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