POST-TRANSFUSION HEMOGLOBIN ESTIMATION IN FILIPINO CHILDREN AND ADOLESCENTS USING AN ALTERNATIVE RED CELL VOLUME TRANSFUSION FORMULA

MICHAEL C. CUARTERON, MD, CAROLINE T. HERNANDEZ, MD
AND MARIA BEATRIZ P. GEPTE, MD

ABSTRACT

BACKGROUND AND OBJECTIVE: Conventional red cell transfusion formulae used in clinical practice has shown underestimation of the actual post-transfusion hemoglobin level. To address this problem, we aimed to determine if there is an agreement between computed and actual post-transfusion hemoglobin levels using an alternative red cell transfusion formula.

METHODOLOGY: This was a prospective, cross-sectional study. Using Morris' formula, the red cell volume requirements of the participants were computed and post-transfusion hemoglobin levels were obtained for comparison.

RESULT: Majority of the 116participants belongs to age between 2 to 5 years (39.5%) and female (54.3%). Most common indication was hemoglobin level < 7 g/dL with manifestations of anemia (56%). The computed and actual post-transfusion hemoglobin were in agreement. The increase in hemoglobin had direct relationship to the volume of blood transfused and inverse relationship to the age and weight of the patients.

CONCLUSION: Using Morris' formula, the computed and actual post-transfusion hemoglobin values were in agreement. The volume of transfused red cells, age, and weight are predictors of the increase in post-transfusion hemoglobin. This formula can be adopted for Filipino pediatric patients and can obviate the need for hemoglobin determination after transfusion.

KEYWORDS: post-transfusion hemoglobin, red cell volume transfusion formula, blood transfusion formula, pediatrics, packed red blood cells

INTRODUCTION

Anemia may occur because of blood loss, hemolysis, or impaired production of red blood cells (RBC).Blood transfusion therapy is vital to supportive management of anemia. In the Philippines where there is high healthcare cost and limited medical resources, it is essential to evaluate existing clinical practice and determine guidelines to optimize the use of blood products.

Once a physician decides to transfuse packed RBC, a reliable formula is vital to compute for the volume of blood needed. Pediatric transfusion formulae take account of the child's weight, estimated circulating blood volume, and the hemoglobin (Hgb) concentration or hematocrit (Hct) of the blood to be transfused [1-5]. It has been shown that existing formulae used in clinical practice result in a lower than expected actual post-transfusion Hgb level [6]. Hence, the patient may need another transfusion resulting in exposure to further transfusion risks and additional costs. Moreover, since packed RBC transfusion in children requires only a fraction of a unit of blood and the remainder of the unit discarded, it is prudent to maximize the use of every blood units for resource-limited settings. Therefore, aside from the medical aspect of care, the caring physician should consider the impact of transfusion on the financial capacity of the patient's family and the utilization of limited blood products like packed RBC. Thus, the adoption of an alternative red cell transfusion formula that is valid to all pediatric age and diagnostic groups that will result in a close estimation of the actual post-transfusion Hgb level may provide substantial health and economic benefits in the local setting.

To date, there is no standard formula for calculation of RBC transfusion volumes in pediatrics. In our institution, the two commonly used formulae are: volume of packed RBC = [desired Hct (%) – actual Hct (%)] x weight (kg) x 1; and volume of packed RBC = [desired Hgb (g/dL) – actual Hgb (g/dL)] x weight (kg) x 3. Our experience with the above formulae showed that the actual post-transfusion Hgb values usually fall below the computed Hgb values. In 2014, our records showed that 95% of patients who were transfused with packed RBC had actual post-transfusion Hgb levels that were>1g/dL lower than the computed Hgb level. This means that the desired Hgb level is not attained.

Hence, to avoid the clinical consequences of having suboptimal Hgb level, the adoption of an alternative blood transfusion formula that will provide a higher level of actual post-transfusion Hgb than the conventional formulae are essential. The formula must be valid for all pediatric age groups and should give close estimation of the actual post-transfusion Hgb value.

Calculation of RBC transfusion volumes varies among pediatricians and various institutions. Many pediatric unit protocols use a calculation of: weight of the patient (kg) x difference in Hgb(g/dL) x a transfusion factor [8]. Transfusion factors of 3 and 4 is recommended by The British Committee for Standards in Haematology guidelines [9], and by McIntosh et al.[10], respectively. As stated above, the formula used in our institution showed that the actual post-transfusion Hgb values were> 1g/dL lower than the computed Hgb level. Similarly, a study in 2005showedthat our conventional formulae performed poorly in achieving the desired post-transfusion Hgb level among pediatric patients in the United Kingdom (U.K.) [6]. Locally, no published studies exist that propose blood transfusion formula for children and adolescents.

The advantage of using the formula of Morris et al. [6] over the other red cell volume transfusion formulae like that proposed by Davies et al. [8]is the ability to compute the volume of red cell transfusion even without the Hct level of the packed RBC unit. Since the Hct level of the packed RBC unit is not readily available in actual clinical practice, it is more convenient to use the formula of Morris et al. in our setting.

We aimed to determine if there is an agreement between computed and actual post-transfusion Hgb levels using an alternative red cell volume transfusion formula in calculating for red cell transfusion requirement among Filipino children and adolescents who require RBC transfusion. We also aimed to establish the relationship between increase in Hgb count to the volume of RBC transfused, in terms of age, sex, and weight of the patients since it has not been clearly extrapolated among Filipino children.

METHODOLOGY

This was a prospective, cross-sectional study conducted from March 2015 to September 2015 wherein approximately 15-20 patients are transfused with packed RBC per day with an average of 450 packed RBC transfusions per month.

Patients more than 28 days old and less than 19 years old who required transfusion with packed RBC during admission or outpatient visit, and whose indication for transfusion was included in the institution's guideline. The following were excluded from the study: patients with (1) active bleeding; (2) autoimmune and alloimmune antibodies;(3) hypersplenism (defined as abnormally large spleen causing premature destruction of RBC and platelets); (4) plasma leakage; (5) disseminated intravascular coagulation;(6) acute leukemia with myelo suppression as a result of the disease and / or treatment;(7) severe anemia of $\leq$ 5 g/dL; (8) transfusion requirement of < 5 cc/kg/hour or > 10 cc/kg/hour;(9) prior transfusion of other blood products (e.g. platelet concentrates, fresh frozen plasma and cryoprecipitate), administration of colloid solutions (e.g. albumin) and plasma exchange that was administered 6 hours before or after packed RBC transfusion;(10) transfusion reaction to packed RBC; and (11) surgical procedure of any forms in the preceding 72 hours of packed RBC transfusion.

A minimum of 86 patients were required for this study based on an 80% power to detect a standardized mean difference of 0.4. Descriptive analysis was used to summarize the clinical profile of the patients who received packed RBC transfusion. To determine agreement between computed and actual post-transfusion Hgb levels, a Bland-Altman analysis was conducted. Multiple logistic regression was utilized to determine factors predictive of the increase in Hgb after transfusion. STATA 12 was used in data processing and analysis.

After eligible participants were identified and consents obtained, the RBC transfusion formula of Morris et al. was used to compute for the RBC transfusion requirement. After transfusion, the remaining RBC volume in the intravenous tubing was pushed with isotonic saline to deliver the complete volume of packed RBC to the recipient. Post-transfusion blood extraction was done via venipuncture after 6 hours. The Hgb level was determined using Unicel DHX 800 Beckman Coulter and Coulter HMX Hematology Analyzer at the hospital laboratory. Pertinent information was recorded using the Data Collection Sheet. Only one transfusion for each patient, even for those who had previous and subsequent transfusions, was recorded in the study.

The primary outcome is the statistical agreement between the computed and actual post-transfusion Hgb levels after using the RBC transfusion formula of Morris et al. Secondary outcome measure is the assessment of the relationship between the increases in Hgb count to the volume of packed RBC transfused with consideration of predictive factors such as age, sex, and weight of the patient.

This study was conducted in accordance to the ethical principles based on the Declaration of Helsinki and the National Guidelines for Biomedical Research of the National Ethics Committee of the Philippines and approved by the Institutional Review Board – Ethics Committee. All observations were preceded by a written documentation of informed consent / assent. Participation in the study was purely voluntary and without financial compensation. The interventions and data were recorded only in writing, and were not recorded via video or audio. An alphanumeric code was assigned for each subject to maintain confidentiality of patient information and results.

RESULTS

A total of 116 patients referred for packed RBC transfusion were included in the study [Table 1]with a median age of 4 years (5 months to 18 years old) and majority are females (54.3%).By etiology[Table 2], anemia secondary to a chronic illness / infection accounts for half the cases with the following breakdown: anemia of chronic illness (47%), iron deficiency anemia (36%), anemia secondary to infection (10%), and anemia due to multifactorial etiology (7%). The rest belongs to anemia due to a primary hematologic disease (49.1%) that was composedof: acute lymphoblastic leukemia (65%), acute myeloid leukemia (21%), and thalassemia (14%). There was a single case (0.9%) of 5-month old male who presented with Hgb level of 8 g/dL and had packed RBC transfusion prior to excision of a choledochal cyst. The most common indication for transfusion was Hgb < 7 g/dL innormovolemic patients with clinical manifestations of anemia(56.9%). The second most common indication (40.5%) were cases of patients who had Hgb level of >7 g/dL with clinical manifestations of anemia; or asymptomatic patients with concomitant illness / condition (e.g. leukemia)that warranted supportive transfusion. The average pre-transfusion Hgb was 7.025 (± 0.93) g/dL, with an overall mean packed RBC volume of 274.5 (± 183.95) mL transfused and a mean actual post-transfusion Hgb of 10.75 (± 1.4) g/dL.

Table 1. General characteristics of study participants (n = 116)

	Frequency (%); Mean ± SD
Age	
Below 2 years old	22 (19.0)
Two to below 5 years old	46 (39.7)
5 to 12 years old	35 (30.2)
Above 12 years old	13 (11.2)
Gender	
Male	53 (45.7)
Female	63 (54.3)
Weight	
≤ 15 Kg	58 (50)
>15 kg	58 (50)
Diagnostic category	
Primary hematologic disorder	57 (49.1)
Anemia secondary to a chronic illness / infection	58 (50)
Others	1 (0.9)
Indication for packed RBC transfusion	
Hemoglobin level less than 7 g/dL in normovolemic patients with clinical manifestations of anemia	65 (56.0)
Hypertransfusion for chronic hemolytic anemias (e.g. thalassemia)	2 (1.7)
Candidates for major surgery and hematocrit less than 30%	1 (0.9)
Hypovolemia from acute blood loss with signs of shock or anticipated blood loss of >10%	0
Hemoglobin less than 13 mg/dL / hematocrit less than 40% in patients with severe pulmonary disease, with assisted ventilation, cyanotic heart disease	0
Standby for operation use	0
Others	47 (40.5)
Transfusion variables	
Pre-transfusion hemoglobin (g/dL)	7.025 ± 0.93
Actual post-transfusion hemoglobin (g/dL)	10.75 ± 1.4
Volume of transfused packed RBC (mL)	274.5 ± 183.95

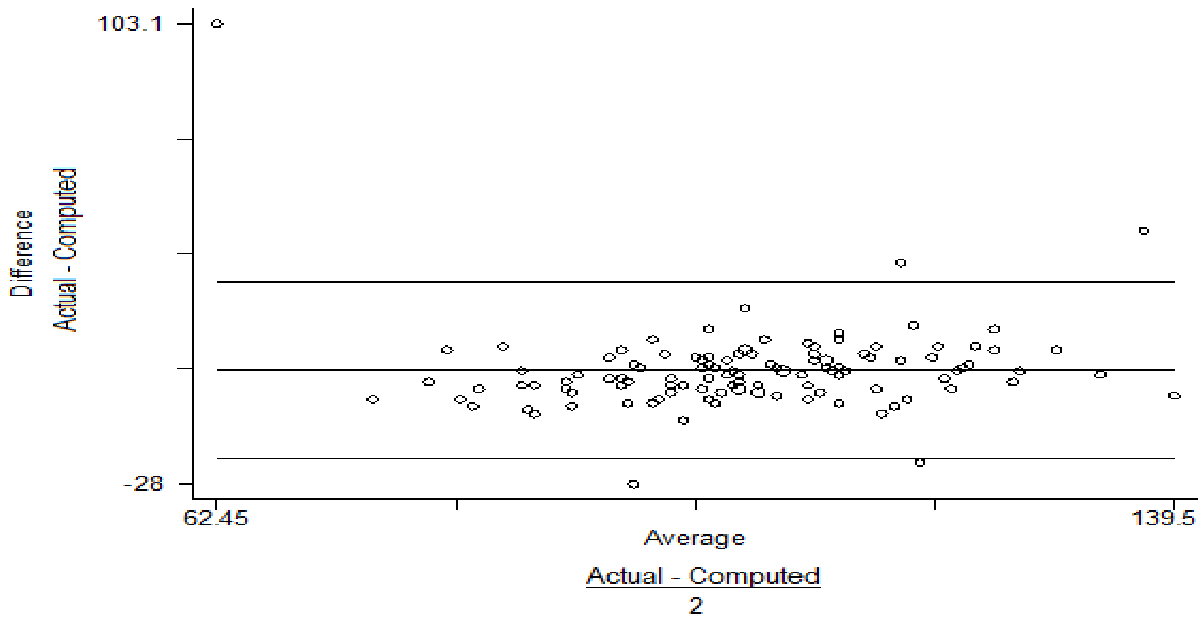
Table 2. Breakdown of cases in terms of diagnostic category (n = 116)

Diagnostic category	**Frequency (%)**
Anemia secondary to a chronic illness / infection	58 (50)
Anemia of chronic illness	27 (47)
Iron deficiency anemia	21 (36)
Anemia secondary to infection	6 (10)
Anemia due to multifactorial etiology	4 (7)
Primary hematologic disease	57 (49.1)
Acute lymphoblastic leukemia	37 (65)
Thalassemia	12 (21)
Acute myeloid leukemia	8 (14)
Others	1 (0.9)
Choledochal cyst *	1 (100)

* *transfused prior to excision*

Our results showed that the computed and actual post-transfusion Hgb were in agreement, with values falling within a 95% confidence interval (CI -20.8 to +29.8). The mean difference between computed and actual Hgb was at 4.441 g/dL (95% CI 2.12 to 6.76). These parameters of agreement are applicable for actual post-transfusion Hgb values from 6.245 g/dL to 13.95 g/dL. Furthermore, there was no significant difference between computed and actual post-transfusion Hgb values. The figure shows the Bland-Altman plot illustrating the agreement between the computed and actual Hgb values.

Figure 1. Bland-Altman plot depicting agreement between computed and actual post-transfusion Hgb using the transfusion formula provided by Morris et al.



For every unit increase in transfused packed RBC, Hgb increased by approximately 0.085 g/dL provided that other factors were constant. Age and weight on the other hand showed an inverse relationship, wherein for every unit increase in age (years) and weight (kg), the difference in pre- and post- transfusion Hgb decreased by 1.04 and 0.778 g/dL, respectively. Multiple logistic regression analysis conducted revealed the following factors to be significant in the model: volume of transfused RBC, age, and weight. The model had an R-square of 52.81%, which means that these factors explain 52.81% of the variation of the difference between pre-transfusion and actual post-transfusion Hgb.

DISCUSSION

Our study showed the agreement between the computed and actual post-transfusion Hgb values using the formula of Morris et al. The noted predictors of increase in the Hgb level include volume of transfused packed RBC, age, and weight of the recipient.

The most common indication of packed RBC transfusion for these patients was a hemoglobin level less than 7 g/dL in normovolemic patients with clinical manifestations of anemia. Although no standard optimal Hgb threshold for RBC transfusion is established in pediatrics, most of the practicing physicians in our institution follow the guideline set by the BTC. In 2007, a trial was conducted among stable, critically ill children to find out the optimal Hgb threshold for RBC transfusions. Their conclusion was that Hgb threshold of 7 g/dL for RBC transfusion could decrease the requirement for transfusion without increasing adverse outcomes [11].

The formula proposed by Morris et al. was shown to be valid among all pediatric age groups in U.K. [6]. Locally, we wanted to test whether this formula was applicable to the Filipino child's hematologic profile. To further elucidate the hematologic variation between different races, Dallman et al. studied the hemoglobin concentration among children of black, white and Oriental ancestry [12]. They found that the median Hgb concentration values were consistently lower in black children. Additionally, the median values are almost identical among whites and Orientals. Thus, the formula of Morris et al. appears reliable and applicable to be used among Filipino children provided that they have the same clinical conditions as those included in this study.

Clinically, this agreement between the computed and actual post-transfusion Hgb values may imply that a post-transfusion CBC may be obviated. For some institution such as ours, wherein most physicians request post-transfusion CBC, the economic implication of this finding is remarkable. The cost of additional laboratory like CBC adds burden to financially-challenged patients. Another advantage of obviating post-transfusion CBC is minimizing the exposure of patients to painful blood extraction procedure. Several studies have stated that many hospitalized children are experiencing acute procedural pain related to procedures that may potentially cause immediate and long-term consequences [13-14]. Furthermore, our results revealed that there was insufficient evidence to demonstrate a significant difference between computed and actual post-transfusion Hgb levels, hence the probability of under and over transfusion becomes very minimal.

Our results showed that the increase in Hgb had a direct relationship with the volume of packed RBC, and an inverse relationship to age and weight. This means that an increase in Hgb is more attainable with a higher volume of transfused packed RBC, younger age of the patient, and lower weight of the recipient. In contrast, the study of Davies et al. found no association between the transfusion factor and the other external variables such as weight, starting Hgb level, and length of transfusion [8]. However, similar to their study, we also found no relationship between the increase in Hgb and the gender of the patient.

The technical aspect of packed RBC preparation and transfusion is also vital to achieve the optimum rise in Hgb. RBC viability drops progressively once taken out of the body leading to a decline in survival [15]. The post-transfusion RBC survival index fall to<70% if transfusion is done longer than the shelf life of the blood unit[16]. In our study, all packed RBC units were transfused within its shelf life with Hct levels ranging from 0.65 to 0.75. Another important aspect is the transfusion of the exact volume of blood. This was carried out in the study by pushing intravenously the remaining RBC in the tubing to the recipient using isotonic saline solution.

The scope of the limits of agreement that we demonstrated is appropriate only to a certain range of Hgb level (6.245 g/dL to 13.95 g/dL)that was included in this study. We cannot conclude for Hgb values outside of this range, i.e. those who are severely anemic and polycythemic patients.

CONCLUSION / RECOMMENDATION

Using the red cell transfusion formula of Morris et al., the computed and actual post-transfusion Hgb values were in agreement. The volume of transfused packed RBC, age, and weight were predictors of the increase in Hgb after transfusion. The use of the above formula in calculating the red cell transfusion volume provided a more accurate estimation of actual post-transfusion Hgb level. It is applicable among Filipino children and adolescents. Therefore, the practice of performing post-transfusion CBC to check the Hgb level may be obviated.

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