

Assessment of the prescription of red blood cell concentrates in the pediatric age group

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SUMMARY

Objective: To verify the adequacy of red blood cell (RBC) prescription to pediatric patients in different sectors of a pediatric hospital.

Method: A retrospective study was conducted including 837/990 RBC transfusion requisition forms for children and adolescents (0 to 13 years old) filed in between January 2007 and April 2015 by the pediatricians of the emergency room (ER), infirmary ward and intensive care unit (pICU). Transfusion requisition forms belonging to patients with chronic anemia or acute hemorrhage, as well as incompletes requisition forms, were excluded.

Results: Trigger, prescribed volume and subtype of RBC concentrates were adequate in 532 (65.3%), 460 (58.8%) and 805 (96.2%) of the transfusions, respectively. When the clinical picture was considered, prescription adequacy was higher compared to the use of the hemoglobin level alone (70.9% vs. 41%). The pICU had the highest correct trigger percentage (343 [71.6%]; $p < 0.001$) while the ER showed more often adequate prescribed volumes (119 [66.1%]; $p = 0.020$). The most common inadequacy regarding volume was that of prescriptions above the recommendation > 15 mL/kg found in 309 cases (36.9%). Thirty-two (32) RBC subtypes were requested and none were consistent with current recommendations.

Conclusion: The results obtained in our study showed that RBC transfusion occurred more appropriately when the clinical picture was taken into account at request. There was a tendency to prescribe higher volumes and RBC subtypes without the justification of current protocols. Hemotherapeutic teachings at undergraduate level and medical residency must be improved.

Keywords: Transfusion Medicine. Erythrocyte Transfusion. Child. Prescriptions.

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INTRODUCTION

Performed since the 17th century, blood transfusion entered its scientific era in 1901 with the discovery of the ABO blood system by Karl Landsteiner.¹ Initially, the goal of transfusions was to maintain a hemoglobin (Hb) level greater than or equal to 10 g/dL.² Later, especially in the last two decades, publications have shown safety and superior results with lower triggers. Normovolemic patients were shown to tolerate Hb concentrations between 5 and 6 g/dL.³ Regardless of the cause of anemia (decreased production of red blood cells, hemolysis or bleeding),⁴ the goal of transfusion is to normalize the transport of oxygen² and, therefore, the transfusion trigger has

different values in different situations, ranging from Hb 7 g/dL in clinically stable children,⁵⁻⁸ with acute bleeding⁹ and sepsis but no shock;¹⁰ to 7-8 g/dL in the post-surgical period,¹¹⁻¹⁴ and 10 g/dL in case of severe sepsis or septic shock.^{15,16}

Despite this knowledge, several services still adopt different transfusion protocols even for patients in similar clinical contexts, so that higher triggers relate to a greater frequency of transfusion reactions.^{3,7,8,17,18}

Transfusion is a mortality risk factor in critically ill children¹⁹ and may cause immune and non immune-mediated reactions including, more frequently: febrile non-hemolytic transfusion reaction, hemolytic reaction, allergies,

volume overload and infections.^{1,2,5,20} Microcirculatory changes can also occur,^{5,21} as well as increased incidence of cancers.²² Reactions may occur in 0.95%²³ to 3.8% of cases.²⁴

Calculation of the correct volume is also important, since low volume results in less than ideal yield and high volume is associated with risk of circulatory overload. This is one of the most common transfusion reactions, with a mortality rate of 12%.²⁰ In children with acute anemia and normovolemia, a volume of transfused red blood cells (RBC) concentrates between 10²⁵⁻²⁷ and 15²⁵ mL/kg is indicated.

An appropriate choice of RBC subtype (filtered, irradiated, washed and phenotyped) influences the transfusion yield and causes fewer transfusion reactions in specific contexts.^{2,25} Filtered RBC has 99% of its neutrophils removed and is indicated mainly to avoid febrile non-hemolytic reaction in polytransfusion and the transmission of cytomegalovirus in immunosuppressed patients.²⁵ RBC concentrates irradiated at 25 gray prevents clonal proliferation of donor lymphocytes in the immunodepressed recipient, thereby avoiding transfusional graft versus host disease.²⁵ Washed RBCs have the highest possible amount of their plasma replaced with 0.9% saline solution in order to remove plasma proteins that may cause anaphylactic reaction in individuals with congenital deficiency of some serum protein (immunoglobulin A, haptoglobin and ferritin) or who already presented a severe allergic reaction to the previous transfusion.²⁵ Phenotyped RBC is transfused to patients that required extended compatibility research between donor and recipient, in addition to ABO and Rh blood groups (kell, Duffy, Kidd and MNS). In pediatrics, this phenotyping procedure is carried out mainly in the poly-transfused to avoid erythrocyte alloimmunization.²⁵

There are few studies evaluating the adequacy of RBC prescription in pediatrics^{7,9,14}, and those available in the literature evaluated the trigger, but not the volume and subtype indicated.

The objective of our study was to evaluate the transfusional trigger, the prescribed volume and the choice of red blood cell subtypes in children admitted into a public hospital and compare with current recommendations in the literature.

METHOD

A retrospective study carried out at Hospital e Pronto-Socorro Central de São Bernardo do Campo, in the Greater São Paulo area, Brazil. We reviewed the transfusion requisition forms for children and adolescents from 0 to 13 years of age, filled out by pediatricians from three sectors: Emergency room (ER), the infirmary ward and the

pediatric intensive care unit (pICU) from January 2007 to April 2015.

During the study period, the pediatrics consisted of four beds in the emergency room, five in the observation room, 40 in the infirmary ward, and five pICU beds. The hospital did not include an obstetrical center, a nursery, a surgical center or oncology/hematology service. It did have a transfusion agency that stored some blood components and performed simple tests such as ABO and Rh blood typing, and direct and reverse cross-tests. Whenever a subtype of blood component was requested and the transfusion agency did not have it, the request was sent to the head office in the city of São Paulo. The supplied RBC preservative solution was CPDA-1 (citrate, phosphate, dextrose and adenine).

Of the 990 RBC transfusions performed during the study period, 837 were included in the series. In all, 94 and 59 transfusion requests were excluded because they were made for patients with chronic anemia (81-sickle cell disease, 11-bone marrow aplasia, 1-hemoglobinopathy C and 1-spherocytosis) and acute hemorrhage, respectively, on account of trigger variability in these two conditions and the absence of information in the form, which are essential for assessing adequacy. Later, we excluded 23 other requests from the transfusion trigger analysis and 55 from the prescribed volume analysis, as Hb value and the patient's weight, respectively, were not recorded.

In order to assess the adequacy of the transfusional trigger, prescribed volume and choice of RBC subtypes, we used the 2015 recommendations of the Brazilian Ministry of Health.²⁵ However, these guidelines do not discuss some of the situations found in our study. Therefore, to analyze the transfusion trigger in children older than 4 months, with acute normovolemic anemia but otherwise stable, we used the 2012 recommendations of the American Association of Blood Banks (7 g/dL).⁶ To analyze the trigger in cases of septic shock, we used the recommendations of the American Heart Association – Pediatric Advanced Life Support (10 g/dL).²⁷

Data collected from the transfusion requisition forms:

- General: age (months), gender, presence of underlying conditions and origin of the transfusion request form (ER, infirmary ward or pICU).
- Transfusion characteristics:
 - Trigger (reason and justification for transfusion): evaluated whether it was based solely on Hb value or clinical-laboratory correlation. All transfusions performed in patients with Hb levels below 7 g/dL were considered adequate. Requests for patients with Hb greater than or equal

to 7 g/dL were evaluated individually, taking into account the clinical reason, the presence of underlying disease and if there was hemodynamic decompensation.

- Volume prescribed: Volumes between 10 and 15 mL/kg were considered adequate.
- RBC subtype: the request for filtered, irradiated, washed or phenotyped components was evaluated, considering the presence of underlying disease and the patient's history.

The study was approved by the Research Ethics Committee of Faculdade de Medicina do ABC (Opinion no. 1.402.884).

The data were typed and consolidated into an Excel (Microsoft) worksheet and analyzed using SPSS 24.0 statistical program. Qualitative variables were described in the form of absolute numbers and percentages. Continuous variables were analyzed for their distribution and presented as mean \pm standard deviation. To compare the qualitative data we used the Chi-square test. The confidence level was 5%.

RESULTS

In our sample, the male gender predominated (471 [56.3%]), the mean age was 23.3 ± 8 months and the median was 8 months; 504 (60.2%) of the transfusions were performed in children less than 12 months old and the most common clinical contexts were hemodynamic and respiratory changes (Table 1). Regarding the origin of the transfusion request, 201 (24%) were made in the ER, 148 (17.7%) in the infirmary ward and 488 (58.3%) in the pICU (Table 1). A greater percentage of transfusions in patients older than 12 months were performed in the pICU compared to the ER and the infirmary ward (329 [65.2%] vs. 75 [14.9%] vs. 100 [19.8%], $p < 0.001$). There was no difference between the places of origin of the transfusion request in relation to gender ($p = 0.441$) and presence of underlying diseases ($p = 0.061$).

The most common inadequacy, in relation to volume, was prescription above the recommendation (> 15 mL/kg; 309 [36.9%]) (Table 1). Mean Hb and mean prescribed volume were 8.3 ± 1.5 g/dL (range: 2.6 to 16.1 g/dL) and 15.2 ± 4.3 mL/kg (range: 4.9 to 57.1 mL/kg), respectively.

The clinical status was considered in 682 (81.5%) of transfusions (Table 1). There were 663 transfusions with a description of the clinical context that caused it (Table 1).

Trigger, prescribed volume and subtype of red cell concentrate were adequate in 532 (65.3%); 460 (58.8%) and 805 (96.2%) of transfusions, respectively (Table 2).

TABLE 1 General characteristics for the transfusions performed.

Variable		N	%
Gender	Male	471	56.3
	Female	366	43.7
Age	< 1 year	504	60.2
	1 to 2 years	123	14.7
	2 to 5 years	108	12.9
	5 to 10 years	74	8.8
	> 10 years	28	3.3
Clinical status	Septic shock	287	34.3
	Acute respiratory failure	124	14.8
	Pneumonia	117	14
	Hemodynamic decompensation	55	6.6
	Mechanical ventilation	32	3.8
	Other	48	5.7
	Not described	174	20.8
Underlying disease	Congenital heart disease	38	4.5
	NPCE	18	2.2
	Nephrotic syndrome	10	1.2
	Other	29	3.5
	No underlying disease	742	88.6
Origin	ER	201	24.0
	Infirmary	148	17.7
	pICU	488	58.3
Reason	Clinical	14	1.7
	Laboratorial	155	18.5
	Both	668	79.8
Pre-transfusion Hb	< 7 g/dL	125	14.9
	7 to 10 g/dL	582	69.5
	> 10 g/dL	107	12.8
	Lack of Hb record	23	2.7
Volume	< 10 mL/kg/day	13	1.5
	10 to 15 mL/kg/day	460	55
	> 15 mL/kg/day	309	36.9
	Lack of weight record	55	6.6
Subtype	Plain RBC	805	96.2
	RBC with subtype(s)*	32	3.8
	Filtered	24	2.9
	Irradiated	17	2.0
	Washed	10	1.2
	Phenotyped	0	0

*In some RBC concentrates there was a request for more than one subtype, so the sum of filtered, irradiated and washed is greater than the number of RBC packs with subtypes. ER: emergency room; NPCE: non-progressive chronic encephalopathy; Hb: hemoglobin; pICU: pediatric intensive care unit; RBC: red blood cells.

Among the clinical contexts that led to the indication of transfusion, there was a high adequacy in critically-ill children (94.5%, hemodynamic decompensation; 92.7%, acute respiratory failure; 87.5%, mechanical ventilation;

83.6%, septic shock). However, the adequacy was lower in children with non-severe conditions at the time of transfusion, such as pneumonia without respiratory failure or mechanical ventilation, with only 12% (Table 2).

pICU had the highest correct trigger percentage (343 [71.6%]; $p < 0.001$), whereas ER had the prescribed volume right more often (119 [66.1%]; $p = 0.020$) (Table 3) compared to the other groups.

There were 32 RBCs with subtype (3.8% of the total), 15 RBCs with only one subtype of red cells and 17 combining 2 or 3 subtypes. There was no difference between the sites of origin in relation to the subtype of red blood cells requested (Table 3).

DISCUSSION

Our study identified that, among red blood cell transfusions performed, 1 in 3 and 41% were not in accordance with the current recommendations for indication and volume calculation, respectively. It should be emphasized that in none of the cases the use of specific subtypes of RBC would be indicated.

TABLE 2 Adequacy of red blood cell transfusion.

Variable	N	%	
	(adequate)	(adequate)	
Clinical context (n=663)	Septic shock	240	83.6
	Acute respiratory failure	115	92.7
	Pneumonia	14	12
	Hemodynamic decompensation	52	94.5
	Mechanical ventilation	28	87.5
	Other	21	43.7
Trigger (n=814)	Adequate	532	65.3
Reason (n=814) was considered	Clinical picture	470	70.9
	Hb only	62	41
	Pre-transfusion Hb		
(n=814)	< 7 g/dL	125	100
	7 to 10 g/dL	391	67.2
	> 10 g/dL	16	15
Volume adequacy (n=782)	Adequate	460	58.8
Subtype (n=837)	Plain RBC	805	100
	RBC with subtype(s)	0	0
	Filtered	0	0
	Irradiated	0	0
	Washed	0	0

Hb: hemoglobin; RBC: red blood cells.

TABLE 3 Comparison of the trigger, volume and subtype adequacy in relation to the site where red blood cell transfusion was performed.

	ER	Infirmarary	pICU	p-value
Adequate trigger	121/188 (64.4%)	68/147 (46.3%)	343/479 (71.6%)*	<0.001
Adequate volume	119/180 (66.1%)*	66/131 (50.4%)	275/471 (58.4%)	0.020
Adequate subtype	191/201 (95.0%)	140/148 (94.6%)	474/488 (97.1%)	0.230

*Chi-square test significance level.

ER: emergency room; pICU: pediatric intensive care unit.

There was no difference between the male and female gender regarding the adequacy of the trigger, volume and subtype of the red blood cell concentrate. More than half of the transfusions occurred in children less than 1 year of age, data similar to those observed in a publication that included a similar population.²⁸

In the trigger analysis, there was inadequacy mainly in transfusions based only on Hb values, without considering the clinical picture, with pre transfusion Hb ≥ 10 g/dL, performed in the infirmary ward and in patients with respiratory disease without respiratory failure or mechanical ventilation. The largest study ever published with a pediatric population has shown that the prescription of red blood cells based on current recommendations decreases the number of transfused RBCs by 44%.⁷ However, the study included exclusively children hospitalized in the pICU and thus in a clinical scenario different from ours with more stable children.

With respect to the prescribed volume, attention was drawn to the request for volumes above the recommended level, which increases the risk of transfusion-related circulatory overload. This transfusion reaction is one of the most frequent, with a growing incidence in the past years and mortality of 12%.²⁰

The prescription of a specific subtype of RBCs leads to a longer waiting time for RBC concentrates, which may influence the prognosis of an unstable patient. After analyzing the requisitions, no clear justification for prescribing these components was found.

The ER did not document the value of Hb in 6.5% of the transfusion requests, a fact that can be partly explained by the greater instability of the patients. The infirmary ward failed to record the weight in 1 out of 10 request forms. This fact may increase the risk of inadequacy of the prescribed volume. Failure to record the weight and/or type of Hb makes it impossible for the transfusion agency to detect if there is any indication or calculation error and thus act to improve the transfusion practice of the service.

Some hypotheses may be considered to justify the results obtained in our study. First, non-frequent updating of non-hematologic health professionals about proposed transfusion guidelines; second, the limited time available to address this issue in the medical undergraduate course and pediatric residency; and finally, the shortage of institutional continuing education programs on transfusion of blood components for the pediatric population.

Standardization of transfusion procedures according to current literature can reduce the cost of hospitalization, avoid waste of blood components and, especially, reduce the number of transfusion reactions.²⁹

The implementation of continuing education in transfusion medicine should be emphasized at all levels (undergraduate, medical residency and professional) minimizing potential harm to the pediatric patient and the health care system. Emphasis should be given to the teaching of transfusion medicine in medical school and medical residency settings by both professor and preceptor, in addition to the updating of professionals by facilitating the provision of continuing education materials and courses, which could be done by hospital transfusion committees.

The results were reported to the hospital transfusion committee. Informative and up-to-date material on transfusional adequacy was prepared and is intended to be delivered to the pediatricians of the service, also available on the hospital's computers for consultation. Training for pediatricians who make RBC prescriptions at our institution was also proposed.

The strengths of this study include the number of transfusions analyzed, the analysis of requests made by pediatricians alone, a small percentage of loss (6.5%) and the availability of an official guide that has been continually updated to compare the results obtained.

Regarding the limitations, the retrospective design, a lack of more detailed data on the clinical characteristics of the patients and the absence of a control between prescribed vs. infused volume can be cited.

CONCLUSION

The results obtained in our study show that transfusion of RBC concentrates was more adequate when clinical status was taken into account. Also, there was a tendency to prescribe high volumes and subtypes of erythrocytes that cannot be justified according to current protocols.

Improving teaching of hemotherapy at medical undergraduate and residency levels as well as the implementation of a continuing education project for pediatricians who work with critically ill children are crucial.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

RESUMO

Avaliação da prescrição de concentrados de hemácias na faixa etária pediátrica

Objetivo: Verificar a adequação na prescrição de concentrado de hemácias (CH) por pediatras em diferentes setores de um hospital pediátrico.

Método: Realizou-se estudo retrospectivo onde avaliamos 837/990 fichas de requisição de CH para crianças e adolescentes (0 a 13 anos), preenchidas entre janeiro de 2007 e abril de 2015 pelos médicos pediatras do pronto-socorro (PS), da enfermaria e da unidade de terapia intensiva (UTI). Excluíram-se as transfusões realizadas em portadores de anemia crônica, crianças com hemorragia aguda e requisições incompletas.

Resultados: Gatilho, volume prescrito e subtipo de concentrado de hemácias foram adequados em 532 (65,3%), 460 (58,8%) e 805 (96,2%) das transfusões, respectivamente. Quando foi considerado o quadro clínico, a adequação foi maior em comparação à prescrição pelo valor isolado da hemoglobina (70,9% vs. 41%). A UTI teve o maior percentual de acerto no gatilho (343 [71,6%]; $p < 0,001$) e o PS, no volume prescrito (119 [66,1%]; $p = 0,020$). A inadequação mais comum, em relação ao volume, foi a prescrição acima da recomendação (> 15 mL/kg, 309 [36,9%]). Foram solicitados 32 subtipos de CH e nenhum estava de acordo com as indicações atuais.

Conclusão: Os resultados obtidos mostram que a transfusão de CH aconteceu de forma mais adequada quando a situação clínica era levada em conta na solicitação. Houve uma tendência à prescrição de volumes elevados e de subtipos de hemácias não justificados segundo os protocolos atuais. É necessário melhorar o ensino de hemoterapia na graduação e residência médica.

Palavras-chave: Medicina Transfusional. Transfusão de Eritrócitos. Criança. Prescrições.

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