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SCIENTIFIC ARTICLE

Transfusional profile in different types of intensive care units☆

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Abstract
Background and objectives: anemia is a common clinical finding in intensive care units. The red blood cell transfusion is the main form of treatment, despite the associated risks. Thus, we proposed to evaluate the profile of transfusional patients in different intensive care units.
Methods: prospective analysis of patients admitted in the intensive care units of a tertiary university hospital with an indication for transfusion of packed red blood cells. Demographic profile and transfusional profile were collected, a univariate analysis was done, and the results were considered significant at $p \leq 0.05$.
Results: 408 transfusions were analyzed in 71 patients. The mean hemoglobin concentration on admission was 9.7 ± 2.3 g/dL and the pre-transfusional concentration was 6.9 ± 1.1 g/dL. The main indications for transfusion were hemoglobin concentration (49%) and active bleeding (32%). The median number of units transfused per episode was 2 (1–2) and the median storage time was 14 (7–21) days. The number of patients transfused with hemoglobin levels greater than 7 g/dL and the number of bags transfused per episode were significantly different among intensive care units. Patients who received three or more transfusions had longer mechanical ventilation time and intensive care unit stay and higher mortality after 60 days. There was an association of mortality with disease severity but not with transfusional characteristics.
Conclusions: the practice of blood products transfusion was partially in agreement with the guidelines recommended, although there are differences in behavior between the different profiles of intensive care units. Transfused patients evolved with unfavorable outcomes. Despite the scarcity of blood in blood banks, the mean storage time of the bags was high.

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Introduction

Anemia is a frequent clinical finding in intensive care units (ICU). It has been shown that up to 77% of critically ill patients have anemia during their hospital stay and more than a third of them receive blood transfusions.[1,2] Factors associated with the development of anemia in the ICU include blood loss from obvious bleeding, as the ''iatrogenic anemia'' caused by the serial blood collection for laboratory tests; invasive procedures; nutritional deficiencies (iron, folic acid and vitamin B12); hemolysis; occult blood loss; and decreased erythropoiesis by reduced release of erythropoietin, mainly by the action of inflammatory cytokines.[3–6]

The red blood cell transfusion is still the main form of treatment for anemia, despite the risks of complications associated with it. Possible complications include transmission of infectious agents, febrile reactions, alloimmunization, acute lung injury, pulmonary edema fluid overload, citrate toxicity, and immunosuppression, with consequent increase in nosocomial infections.[7–11] Thus, blood transfusion became a constant topic of discussion in ICUs, and there is controversy regarding the possible benefits and risks of maintaining lower levels of hemoglobin.[12,13] From the late 1990s, studies with restrictive transfusional strategies in the ICU began to be published. In this sense, Hébert et al. showed no benefit in maintaining hemoglobin (Hb) >10 g/dL, when compared to a group with hemoglobin levels between 7 and 9 g/dL, in patients admitted to intensive care units, with the possible exception of those with acute coronary syndromes.[13] Since its publication, this study guided the transfusional therapy, and the current recommendation is the transfusion of packed red blood cells (pRBC) in critically ill patients with Hb less than 7 g/dL.

Therefore, there is great interest in the understanding of transfusional therapy in intensive care and the impact of anemia on the progression and prognosis of these patients. Nevertheless, in Brazilian hospitals, there are few the studies evaluating transfusional practice, clinical characteristics and outcome of these patients.[14–16] Thus, the aim of this study was to evaluate the transfusional profile of different ICUs within a tertiary university hospital with analysis of indications and criteria for transfusion. We also sought to determine the number of pRBC units received, its mean storage time and possible correlations with morbidity and mortality.

Methods

In this study, patients older than 18 years and with indication for transfusion of pRBC units by the attending physician, being hospitalized in five ICUs (general-SUS, general-supplementary health, internal medicine, cardiology and pneumology) of a tertiary university hospital between October 1 and November 30, 2005 were included. No exclusion criteria were used. The study was approved by the Ethics in Research Committee under number 1534/04 without the need to collecting informed consent, for this paper deals with data registry without intervention.

The initial screening was done by the request of transfusion records of the hospital blood bank. All patients admitted to the ICUs for whom pRBC units were administered during this period were included. Two physicians responsible for the study recorded the following demographic data: age, gender, diagnosis of ICU stay, and presence of comorbidities. For assessment of the severity, Physiology and Acute Chronic Health Evaluation II (APACHE II)[17] index for ICU admission and the Sequential Organ Failure Assessment (SOFA)[18] were used on the day of transfusion and seven days later. Regarding data directly related to transfusions, we registered the indication for transfusion, ICU admission and pre-transfusional hemoglobin, storage time of each bag, presence of transfusional reactions and number of pRBC units transfused in the same transfusional episode, as well as the total number of bags received by the patient.

The group of transfused patients was followed prospectively with regard to morbidity and mortality until hospital discharge, or 60 days after the first transfusion. Occurrence of infectious (as documented or suspected infection, severe sepsis, septic shock), respiratory (acute respiratory distress syndrome) and renal (acute renal failure) complications were recorded, as well as the duration of mechanical ventilation and of vasopressor use, time of ICU stay, and survival after 28 and 60 days of transfusion. As part of the analysis of morbidity, Δ SOFA was calculated, corresponding to SOFA of 7th day minus SOFA of day zero. This finding was categorized according to the variation occurred in terms of worsening or no change ($\Delta \geq 0$) and improvement ($\Delta < 0$).

Data were presented descriptively. Continuous variables were expressed as mean and standard deviation, or median and percentile 25–75%, according to normalcy; the categorical variables were expressed as a percentage. The normalcy of continuous variables was assessed using the Kolmogorov–Smirnov test. Demographic findings and transfusional characteristics of different ICUs, as well as the relationship with the number of bags, storage time and the risk factors for mortality were analyzed using the chi-square test (for categorical variables), Student's t test/ANOVA (for parametric continuous variables) or Mann–Whitney/Kruskal–Wallis test (for nonparametric continuous variables). The correlations among quantitative variables were tested by Spearman correlation. The variable ''total number of transfused bags'' was categorized using, as a cutoff point, the value obtained in the receiver operator characteristics (ROC) curve for mortality after 60 days. To analyze the storage time, we used the median value found in the sample. The analysis was performed using SPSS (Statistical Package for Social Sciences) program and the results were considered significant at $p \leq 0.05$.

Results

Seventy-one patients were included in the five ICUs participating in the study, totaling 241 episodes of transfusion and 408 pRBC units. Table 1 shows the global demographics of the patients and their division by ICUs. The median age of patients was 63 (43–73) years and 53% were female. Most patients (84%) had comorbidities at ICU admission and in 14% of these, prior diagnosis of chronic coronary insufficiency was present.

Table 2 describes the general data and the data of each unit relating to transfusional characteristics. The median hemoglobin value that triggered the transfusion was 6.8

Table 1 Global and specific demographic data for each ICU.

Variable	Global	UTI general	UTI supplementary health	UTI internal medicine	UTI pneumology	UTI cardiology	*p* value
Patients (n)	71	28	12	13	12	6	–
Age (years)	63 (43–73)	52 (36–72)	62 (47–70)	54 (38–74)	68 (42–73)	70 (63–77)	0.45
Male gender	33 (46)	15 (52)	6 (50)	5 (39)	4 (33)	3 (50)	0.76
Admission type							0.001
Clinical	35 (49)	6 (21)	4 (33)	11 (85)	9 (75)	5 (83)	
Surgical, elective	21 (27)	10 (36)	5 (41)	2 (15)	3 (25)	1 (17)	
Surgical, urgency	15 (21)	12 (43)	3 (25)	0 (0)	0 (0)	0 (0)	
Syndromic diagnoses							0.20
Sepsis	10 (14)	5 (18)	0 (0)	4 (31)	0 (0)	1 (17)	
Severe sepsis	16 (22)	7 (25)	1 (8)	4 (31)	4 (33)	0 (0)	
Septic shock	15 (21)	5 (18)	2 (17)	2 (15)	3 (25)	3 (50)	
ARDS	9 (12)	1 (4)	0 (0)	0 (0)	1 (8)	1 (17)	
Acute COI	3 (4)	5 (18)	2 (17)	1 (8)	1 (8)	0 (0)	
Other diagnoses	18 (25)	5 (18)	7 (58)	2 (15)	3 (25)	1 (17)	
Chronic COI	10 (14)	5 (18)	1 (8)	1 (8)	0 (0)	3 (50)	0.05
APACHE II	17.7 ± 5.3	17.3 ± 5.1	14.5 ± 5.5	17.6 ± 3.7	20.2 ± 7.1	20.5 ± 3.2	0.10
SOFA of day initial transfusion	5 (4.7)	6 (4.7)	5 (3.10)	4 (3.7)	4 (2.6)	5 (3.7)	0.66
Hb at ICU admission (g/dL)	9.7 ± 2.3	9.9 ± 2.4	10.2 ± 2.6	8.8 ± 2.2	9.6 ± 2.1	9.6 ± 1.1	0.58
Vasoprssors	47 (66)	18 (64)	5 (41)	11 (85)	7 (58)	6 (100)	0.15
Inotropes	31 (43)	19 (68)	3 (25)	3 (23)	1 (8)	5 (83)	0.001
VM use	63 (89)	27 (96)	7 (58)	12 (92)	12 (100)	5 (83)	0.08
ICU hospitalization time (days)	23 (11–38)	27 (15–41)	12 (2–20)	16 (10–38)	34 (9–40)	28 (14–68)	0.06
Mortality at 28 days	33 (46)	10 (36)	6 (50)	7 (54)	5 (42)	5 (83)	0.26
Mortality at 60 days	38 (54)	12 (43)	7 (58)	9 (69)	7 (58)	5 (83)	0.35

ARDS, acute respiratory distress syndrome; COI, coronary insufficiency; APACHE, Acute Physiologic and Chronic Health Evaluation; SOFA, Sequential Organ Failure Assessment; ICU, intensive care unit, Hb, hemoglobin.
Results are expressed as mean ± standard deviation, median (p25, p75) or number (percentage).
Kruskal–Wallis, ANOVA or chi-square tests.

(6.35–7.4) g/dL, and hemoglobin concentration was the main indication for transfusion (49.8%). A significant percentage of patients (39.8%) received a blood transfusion with pre-transfusion Hb values >7 g/dL. The median number of pRBC units transfused in each transfusional episode was 2 (1–2), with a median storage time for bags of 14 (7–21) days. In addition, 46.3% of pRBC units had more than 14 days of storage and at a certain point 57.7% of patients received bags with this characteristic. Significant differences among the units in relation to the median number of bags in each transfusional episode were noted, with one of the ICUs with a median of one unit per transfusion and all other with two units. No significant transfusional reaction was observed.

Table 3 shows the relationship between the presence of respiratory, renal or infectious complications and evolution of SOFA with the total number of transfused bags and the mean storage time of pRBC units. These variables did not correlate significantly with the occurrence of infectious, respiratory, or renal complications. In categorical analysis, patients who received three or more pRBC units had longer ICU stay, longer duration of mechanical ventilation and increased mortality at 60 days. The storage time of pRBC units does not correlate with any of these outcomes (Table 4). Even in the comparison among patients who received at some point bags with more than 14 days *versus* those who only received bags with less storage time, there was no significant difference in any outcome (data not shown). Significant correlations, although weak, were only found between the total number of transfused bags and length of stay in the ICU ($r = 0.417$, $p < 0.001$) and duration of mechanical ventilation ($r = 0.363$, $p = 0.002$).

Table 5 lists the analysis of demographic and transfusional variables with mortality at 60 days. There was an association between mortality at 60 days and SOFA of the day of enrollment in the study and the use of vasopressors during the ICU stay. Transfusional variables did not correlate with mortality, both at 28 and at 60 days (Table 5).

Discussion

This study characterized the transfusional profile of patients treated in ICUs of a university hospital undergoing pRBC transfusions during hospitalization. Our results identify differences in hemoglobin concentration that served as

Table 2 Global and specific transfusional characteristics of each intensive care unit.

Variable	Global	UTI general	UTI supplementary health	UTI internal medicine	UTI pneumology	UTI cardiology	*p* value
Transfusion episodes (n)	241	109	25	58	27	23	–
Hb at transfusion indication (g/dL)	6.8 (6.35–7.4)	6.7 (6.4–7.05)	7.2 (6.25–7.85)	6.4 (5.67–6.92)	7.4 (6.85–7.8)	7.5 (7.1–8.6)	<0.001
Transfusions with Hb > 7g/dL	96 (39.8)	31 (28.4)	14 (56.0)	14 (24.1)	19 (73.1)	18 (78.3)	<0.001
Indication of transfusion							<0.001
Low hemoglobin	116 (49.8)	60 (58.8)	6 (25.0)	30 (50.8)	10 (40.0)	10 (43.5)	–
Active bleeding	74 (31.8)	27 (26.5)	3 (12.5)	27 (45.8)	4 (16.0)	13 (56.5)	–
Acute COI	14 (6.0)	6 (5.9)	5 (20.8)	0 (0)	3 (12.0)	0 (0)	–
Heart failure	6 (2.6)	0 (0)	6 (25.0)	0 (0)	0 (0)	0 (0)	–
Surgical procedure	3 (1.3)	0 (0)	0 (0)	2 (3.4)	1 (4)	0 (0)	–
Other	20 (8.6)	9 (8.8)	4 (16.7)	0 (0)	7 (28.0)	0 (0)	–
Bags/transfusional episode (n)	2 (1.2)	1 (1.2)	2 (1.2)	2 (2.2)	2 (1.2)	2 (2.2)	<0.001
Storage time for bags (days)[a]	14 (7–21)	15 (10–23)	11 (6–19)	11 (6–20)	11 (6–19.5)	16 (14–21)	0.002

ICU, intensive care unit; Hb, hemoglobin; COI, coronary insufficiency.
Data expressed as median (p25, p75) or number (percentage).
Kruskal–Wallis, ANOVA or chi-square tests.
[a] $n = 408$.

Table 3 Relationship between total transfused bags and storage time with the presence of complications during the intensive care unit stay.

Complications	Total of transfunded bags (*n*)	*p* value	Storage time (days)	*p* value
Respiratory				
Yes ($n = 16$)	5 (2–12.2)	0.48	15.3 (8.6–19.9)	0.38
No ($n = 55$)	4 (2–7)		11.6 (6.6–20.3)	
Renal				
Yes ($n = 28$)	4 (2–6.5)	0.57	15 (10.4–20.3)	0.30
No ($n = 43$)	4 (2–12)		115 (6–18.6)	
Infectious				
Yes ($n = 62$)	4 (2–8.5)	0.15	15 (7.3–26.5)	0.41
No ($n = 9$)	3 (1–4)		12.7 (7–18.6)	
Progression of SOFA $\Delta 0 - \Delta 7$[a]				
Worsening/no change ($n = 26$)	5 (3–13.5)	0.35	15 (7.9–22.2)	0.36
Improvement ($n = 21$)	5 (2–8)		11.5 (7–16.1)	

SOFA, Sequential Organ Failure Assessment.
Results expressed as median (p25, p75).
Mann–Whitney test.
[a] Only surviving patients.

Table 4 Analysis of total transfused bags and of storage time in relation to outcomes.

Variable	Total of transfunded bags			Mean time of storage		
	<3 transfusions	≥3 transfusions	*p* value	<14 days	>14 days	*p* value
ICU time (days)	12 (4.5–24.0)	28.5 (16.2–41.5)	0.002	23 (6.5–47.7)	27 (15.5–38.5)	0.38
MV time (days)	11 (2.5–16.0)	23 (7.2–35.7)	0.008	15 (3–35)	15 (7–30)	0.93
Vasopressor time (days)	1 (0–4.0)	3 (0.2–8.0)	0.09	3 (1–8.5)	3 (0–6)	0.30
Mortality 28 days	7 (33.3)	26 (53.1)	0.13	18 (50)	15 (44.1)	0.62
Mortality 60 days	8 (38.1)	30 (63.8)	0.05	21 (58.3)	17 (53.1)	0.66

ICU, intensive care unit, MV, mechanical ventilation.
Results expressed as median (p25, p75) or number (percentage).
Mann–Whitney or chi-square test.

Table 5 Analysis of risk factors associated with mortality after 60 days.

Variable	Survivors ($n = 30$)	Not survivors ($n = 38$)	OR (IC 95%)	*p* value
Age (years)	62 (33.7–70)	66.5 (45.7–73.2)	1.015 (0.988–1.043)	0.27
Male	13 (43)	19 (50)	0.765 (0.292–2.002)	0.58
APACHE II	16.9 ± 5.1	18.5 ± 5.5	1.061 (0.963–1.169)	0.23
Admission SOFA (points)	5 (2.5–6.5)	6 (4–8.7).	1.228 (1.022–1.477)	0.02
Admission Hb (g/dl)	9.7 ± 2.0	9.7 ± 2.4	0.984 (0.790–1.225)	0.88
Pre-transfusion Hb (g/dl)	7.1 ± 1.1	6.9 ± 1.3	0.875 (0.594–1.228)	0.49
Storage time for bags (days)	14.2 (8.3–22.3)	11.2 (6.3–16.4)	0.949 (0.887–1.014)	0.12
Total transfused bags (*n*)	3 (2–5.2)	5 (3–9.2)	1.072 (0.964–1.193)	0.19
Presence of active bleeding	10 (30)	15 (40)	1.067 (0.326–3.945)	0.91
ICU time (days)	26 (12.5–40.2)	22 (10.2–37)	0.990 (0.973–1.008)	0.27
MV time (days)	15 (1.7–31)	16 (6.7–35)	0.997 (0.975–1.019)	0.78
Use of MV	25 (83)	37 (97)	7.400 (0.815–7.199)	0.04
Vasopressors	13 (43)	34 (90)	11.115 (3.144–39.299)	<0.001

APACHE, Acute Physiologic and Chronic Health Evaluation; SOFA, Sequential Organ Failure Assessment; Hb, hemoglobin; ICU, intensive care therapy; MV, mechanical ventilation.
Results are expressed as mean ± standard deviation, median (25.75) or number (percentage).
Mann–Whitney, Student's *t* or chi-square tests.

indication for transfusion among different ICUs with different patient profiles. Furthermore, it was shown that the storage time of pRBC units is relatively long. Additionally, the transfusion of three or more units of pRBC was associated with worse outcome in terms of length of stay in ICU, duration of mechanical ventilation and mortality at 60 days.

In this study, the mean values of pre-transfusion hemoglobin was very close to the limits recommended by the literature and by current clinical practice, suggesting that pRBC transfusions in stable patients be done only if the Hb concentration are < 7 g/dL.[19] However, a high percentage (46%) of the patients were transfused with Hb values greater than 7 g/dL, and in this aspect, a significant difference between the various ICUs was perceived. There is considerable controversy in the literature regarding transfusion thresholds adopted by ICUs in different parts of the world. Studies of Israel and the United Kingdom have shown that the transfusional thresholds were respectively 7.9 and 7.8 g/dL.[20,21] The transfusional thresholds obtained in this study are similar to another Brazilian study in ICU patients, in which the transfusional threshold was 6.6 g/dL.[16] However, in three other Brazilian studies on transfusion in critically ill patients, [22,23] one of them multicentric, [23] the transfusional thresholds remained always greater than 7 g/dL. In one of these studies, the mean pre-transfusion Hb was 8.1 g/dL.[24] It is possible that aspects such as availability of blood products have influenced these results. Another possible difference between ours and previous studies concerns the inclusion of patients from the ICU-Cardiology. As we know, one of the subgroups of patients in whom the transfusional threshold is most discussed is that with cardiovascular diseases, especially coronary insufficiency. In fact, studies on this subgroup now demonstrate sometimes beneficial, sometimes harmful, effects of more liberal transfusional strategies.[25] Thus, eventually higher transfusion thresholds in patients with underlying heart disease are justified. Another interesting finding is the highest value found in the supplemental health unit. This ICU exhibits a mixed, semi-open support profile, *i.e.*, assistant physicians sometimes dictate the procedures. In this sense, a possible explanation would be that the intensivist, more accustomed to unfavorable evidence for transfusion, has a more restrictive profile, while other medical specialties are more liberal.

In this study, we identified that in each transfusional episode most of the ICUs infused a median of two pRBC units. These data are consistent with national and international[16,20,22,24,26] literature, reporting that most patients received two units of pRBC per transfusional episode. However, increasingly the dogma ''Who needs a single transfusion needs no transfusion'' is being challenged, because studies show that the policies restricting transfusion, with release of a pRBC unit at a time, are associated with lower use of blood products, without losses in terms of morbidity and mortality.[27,28] Studies showing benefit with the infusion of two pRBC units, compared to a single bag, are older and were based on surgical and obstetric patients. In the light of our current knowledge, patients in whom only one bag was transfused exhibited transfusion thresholds that would not indicate the administration of these components.[28] However, none of these studies was done in ICU patients.

Another interesting finding was the median storage time of pRBC units, 14 (7–21) days, with 46.3% of pRBC units with more than 14 days old. This result differs from that previously reported in a Brazilian study that included 211 transfusions in one private hospital, where the mean storage time was six days, with only 20% of the bags with more than 15 days.[29] The storage time found in our study is close to that reported in the United States and Europe, 16–21 days.[1,2] In this study we could not demonstrate a correlation between transfusion of pRBC units with more than 14 days and mortality, complications or organ dysfunction. It is possible that the number of patients enrolled was insufficient. However, it should be considered that, despite the pathophysiological basis of transfusional harm with the use of pRBC units with a prolonged storage time, the literature is controversial on this respect. In the CRIT study, for instance, the storage time of the bags also did not correlate with morbidity or mortality.[2]

Our study has identified a significant association between greater number of pRBC units transfused and unfavorable outcomes, such as length of ICU stay, duration of mechanical ventilation and mortality at 60 days. This finding reinforces data already well established in the literature: a greater need for transfusion is a marker of morbidity and mortality,[19,25] even in national[22] studies, and there is not necessarily a causal relationship between the two events, but only an association.

The strong points of our study are the analysis of the transfusional characteristics of various ICUs in the same hospital and the prospective data collection with clear definition of inclusion criteria. On the other hand, it has some limitations, for instance, a small case series from a single center and the short period for collecting the sample. Accordingly, data were collected in 2005. However, as the current guidelines are older, we believe that the transfusional practices should not have changed significantly since then. Moreover, given the observational nature of the study, it was not possible to test causal relationships.

Therefore, the blood component transfusion practice in a university hospital partially agreed with current guidelines, although there are some differences in behavior among the different profiles of ICUs. Transfused patients evolved with unfavorable outcomes. Despite the shortage in blood banks, the bags had a high mean storage time. We must emphasize the need for further Brazilian studies on this subject, in order to determine the actual role of blood component transfusions in critically ill patients and their implications on morbidity and mortality.

Conflicts of interest

The authors declare no conflicts of interest.

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