Appropriate use of red blood cell transfusion in emergency departments: a study in five emergency departments

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Background. Transfusion of blood components continues to be an important therapeutic resource into the 21st century. Between 5 and 58% of transfusions carried out are estimated to be unnecessary. According to several studies, at least 20% of packed red blood cell transfusions (RBCT) are administered in hospital emergency departments (ED), but few data are available about the appropriateness of RBCT in this setting. This multicentre, cross-sectional observational study aims to assess the appropriateness of RBCT indications and transfused volumes in patients who attend ED.

Materials and methods. The study cohort is made up of consecutive consenting adult patients (≥18 years old) who received RBCT in ED over a 3-month period and for whom relevant clinical data were collected and analysed.

Results. Data from 908 RBCT episodes (2±1 units per transfused patient) were analysed. RBCT was considered appropriate in 21.4% (n=195), with significant differences according to RBCT indication ($p<0.001$), hospital level ($p<0.001$) and prescribing physician ($p=0.002$). Pre-transfusion haemoglobin level (Hb) negatively correlated with RBCT appropriateness ($r=-0.616$; $p<0.01$). Only 72.4% of appropriate RBCT had a post-transfusion Hb assessment (n=516). Of these, 45% were considered to be over-transfused (n=232), with significant differences according to RBCT indication ($p=0.012$) and prescribing physician ($p=0.047$). Overall, 584/1,433 (41%) of evaluable RBC units were unnecessarily transfused.

Discussion. The appropriateness of RBCT in ED is similar to other hospital departments, but the rate of over-transfusion was high. These data support the need for a reassessment after transfusion of each RBC unit before further units are prescribed. In view of these results, we recommend that physicians should be made more aware of the need to prescribe RBCT appropriately in order to reduce over-transfusion.

Keywords: red blood cell transfusion, emergency department, appropriateness, over-transfusion.

Introduction

Transfusion of blood components (TBC) continues to be an important therapeutic resource into the 21st century. Thanks to advances in science and the implementation of legal regulations, in recent years, TBC has achieved reasonably high levels of safety[1-5]. Such progress has meant that Transfusion Medicine is now an established area of medical specialisation made up of a multidisciplinary team of health-care professionals[6]. The establishment of Hospital Transfusion Committees has also led to improvements in the quality of clinical care through promoting audits, educational programs, the development of guidelines, and the implementation of cost-saving strategies[7].

However, despite such advances, there are still significant potential risks involved in TBC. The safety of the transfusion lies not only in the correct selection, preparation and administration of blood products, but also in the ability to correctly interpret when such intervention is appropriate. It is estimated that between 5 and 58% of transfusions are unnecessary[6-10]. Administration should always be performed by medical prescription, and, whenever possible, a signed informed consent should be obtained from the patient. An indication for TBC is generally based on clinical practice guidelines or consensus recommendations from expert panels, but is rarely supported by clinical trials[11-13]. In this context, TBC is a complex intervention which must be based on clinical evidence and adjusted

according to cardiovascular risk factors and laboratory test results. It is essential to rationalise and optimise TBC prescription since blood is a limited therapeutic resource, which depends exclusively on the altruism of individual donors[2].

Over 50% of all TBCs are given to surgical or critically ill patients. Red blood cell transfusion (RBCT) is the most frequently used and anaesthesiologists are responsible for about 50% of these[6,14,15]. In recent years, there has been an increase in the use of TBC in Emergency Departments (ED) when compared to other hospital areas. In Spain, several studies have assessed the epidemiology and adequacy of the indication of TBC in different hospital areas, but the incidence of inadequate TBC indications in the ED is still unknown[16-20]. However, it is expected to be higher than in other departments because decisions related to treatment must be taken much quicker in ED than in other hospital areas, and this could contribute to some laxity in the application of established TBC criteria.

This multicentre study was aimed at assessing the appropriateness of RBCT prescriptions and transfused volumes in ED. Secondary study variables were the appropriateness of RBCT according to indication, hospital and level of expertise of the prescribing physician.

Materials and methods

Study design

This was a multicentre, cross-sectional observational study. The study cohort was made up of consecutive consenting adult patients (≥18 years old) who received RBCT in ED of any of 5 participating centres (Hospitals A to E) over a 3-month period. A transfusion episode was defined as the interval between the prescription of an RBCT and completion of its administration. When several RBC units were administered to the same patient under the same condition (e.g. acute haemorrhage), all the units received are considered to be part of a single transfusion episode.

Spanish public health hospitals are classified according to a cluster analysis of the National Health System, as follows[21].

- Group V: very large hospitals covering many square metres that offer a wide range of care for a large number of patients, in a large structure with extensive care services; over 1,000 beds; more than 500 doctors, and an average 300 resident physicians in 36 different specialties (minimum 17). Technologically very advanced, with a broad portfolio of complex services (≥5 complex services), these hospitals receive more than 200,000 emergency cases per year.
- Group IV: includes large hospitals, with 500-1,000 beds, and 200-900 staff physicians. With an average of 4 complex services, they are characterised by having at least 25 accredited residency programmes (mean 30) and over 100 resident physicians. These hospitals receive approximately 150,000 emergency cases per year.
- Group III: medium-sized hospitals, with around 500 beds (although there is considerable variability), around 100-500 staff physicians, and 160 resident physicians.
- Group II: have fewer than 500 beds, reduced teaching capacity (although some have up to 8 different specialties; 2 complex services at most) and deal with less than 100,000 emergency cases per year.
- Group I: small community hospitals with on average less than 150 beds, with little provision of high-tech equipment or facilities, few doctors, that do not treat more complex cases.

Among participating hospitals, A and B belong to Group V, C was assigned to Group IV, and D and E belong to Group II.

Data collection

A Microsoft Office Excel® (Redmond, WA, USA) database was set-up for each centre using data provided by Blood Banks (Transfusion Services) for transfusion episodes that occurred during the study period. Additional data from patients receiving RBCT at the ED during the study period were collected from hospital information systems (electronic medical records, laboratories, electronic prescription systems) and were up-loaded to complete the database. Subsequently, databases of all the hospitals were merged and exported to SPSS 22.0® (IBM SPSS Statistics v.22.0, Chicago, IL, USA) for further analysis.

End-point variables

The primary end point was the "appropriateness" of the RBCT prescription and transfused volume. Appropriateness of RCBT was evaluated according to pre-transfusion haemoglobin (Hb) levels and patients' characteristics, according to the Spanish Society of Blood Transfusion Guidelines 2010 (Table I)[1]. Two members of the research team (a Clinical Pharmacologist and a Pharmacist) defined appropriateness. Any discrepancies were then discussed with a third member of the research team (a Haematologist) until a consensus was reached.

To evaluate the "appropriateness" of RCBT volume, as estimated by post-transfusion Hb according to the Seville Consensus Document Update 2013[11], we defined over-transfusion as occurring when the post-transfusion Hb level was more than 2 g/dL above the relevant Hb transfusion threshold for each particular RBCT indication (Table I). The RBCT index is the median (interquartile range) number of RBC units per transfused patient. The number of RBC units over-transfused was estimated as the sum of the differences between actual post-transfusion Hb and the target post-transfusion Hb for each transfusion episode, assuming that one RBC unit increased Hb level by 1 g/dL[22].

Table I - Recommendations of the guide to the transfusion of blood components and plasma derivatives of the Spanish Society of Blood Transfusion and Cell Therapy.

	Hb (g/dL)	Clinical situation
Acute anaemia	**<7**	Any clinical situation.
	7-8.9	Haemodynamically unstable or associated risk factors: coronary heart disease, heart failure, cerebrovascular disease, myocardial infarction.
	≥9	Difficult to control haemorrhage/signs and symptoms of anaemia.
Chronic anaemia	<8	Signs and symptoms of anaemia and/or associated risk factors.

The "appropriateness" of the RBCT prescription and transfused volume, according to indication, hospital level and prescribing physician, were secondary study variables. Indications for RBCT were divided into acute anaemia, chronic anaemia, low Hb level, and reason for transfusion not registered. Physicians prescribing RBCT at the ED were classified as follows: ED consultant (EDC), resident physicians of any specialty who work shifts at ED (MDR), consultant not belonging to the ED (NEDC) who request transfusion at ED, or "unknown" physician.

Statistical analyses

Qualitative variables were summarised by their frequency distribution as well as quantitative variables by their mean and standard deviation (±SD) or median (interquartile range). The Kolmogorov-Smirnov test was used to prove Gaussian distribution. In case of qualitative variables, comparison was evaluated by the χ^2 test. For continuous normally distributed variables, the Student's *t*-test was used to compare two groups. The Mann-Whitney U test was used for continuous not normally distributed variables. Correlations were assessed with the Pearson's r coefficient. Null hypothesis was rejected by a type I error less than 0.05 ($p<0.05$).

Results

Overall, data from 1,098 RBCT episodes at the ED were collected. Those transfusion episodes performed for any surgical or gynaecological reason, involving no RBCT or without a pre-transfusion Hb level, were excluded; this left 908 transfusion episodes that went forward for analysis (Figure 1). Transfused patients (55.6% men; mean age 72.6±15.7 years) received 2 (interquartile range 1-2) packed RBC units. Underlying pathologies in patients receiving RBCT were haemato-oncological diseases (24%), bleeding due to antiplatelet (20%) or anticoagulation (20%) therapy, chronic kidney disease (15%), chronic heart failure (13%), and chronic liver disease (8%). Mean pre-transfusion Hb was 7.7±1.8 g/dL, and mean post-transfusion Hb 9.5±1.6 g/dL. Patients remained at the ED an average of 1.1±2.6 days.

Patients were divided into four groups according to the RBCT indication: acute anaemia (63.9%), chronic anaemia (10.7%), low Hb level (16.8%), and reason for transfusion not registered (8.6%). Prescription of RBCT was found inappropriate in 21.4% of all the episodes. Distribution of RBCT episodes according to pre-transfusion Hb is shown in Figure 2. Appropriateness of RBTC for patients with pre-transfusion Hb less than 7 g/dL was 100%, 95% for pre-transfusion Hb 7-7.9 g/dL, 71% for pre-transfusion Hb 8.0-8.9 g/dL, and only 21% for RBCT with pre-transfusion Hb 9 g/dL or more, a cut-off point at which clinical characteristics should be carefully evaluated before making a decision about RBCT (Figure 2). Pre-transfusion Hb negatively correlated with RBCT appropriateness ($p<0.001$). As shown in Figure 3, 78.6% (713/908) of RBCT prescriptions were considered appropriate, with significant differences observed according to RBCT indication ($p<0.001$), hospital level ($p<0.001$), and prescribing physician ($p=0.002$). RBCT index was 2 (1-2) (1,388 RBC units) and 2 (1-2) (366 RBC units), for appropriate and inappropriate RBCT, respectively ($p=0.436$).

We then evaluated the appropriateness of RBCT volume, as estimated by post-transfusion Hb level, for those episodes that had adequate transfusion indication. Only 72.4% (516/713) of appropriate RBCT episodes (1,067 RBC units) have a post-transfusion Hb control (Figure 1). Of these, 45% (232/516) received an inappropriate RBCT volume (over-transfusion), with differences according to indication ($p=0.012$) or prescribing physician ($p=0.047$) (Figure 4). In addition, all RBCT episodes without an appropriate indication (197/908, 21.5%) (Figure 1) were also considered to be an over-transfusion. Thus, over-transfusion was estimated to occur in 60% of RBCT episodes analysed for this variable (n=711), resulting in 584 RBC units unnecessarily transfused (584/1,433, 41%).

Discussion

Blood components are a scarce resource and their use should, therefore, be limited to specific indications. Several scientific associations have developed clinical practice guidelines, issuing recommendations to reduce unnecessary transfusions and optimise the use of donated units[1,11,13]. Although in recent years these clinical guidelines have been made widely available, this does not necessarily mean that their recommendations are followed. Nevertheless, a progressive improvement in the appropriateness of TBC indication has been seen over the years.

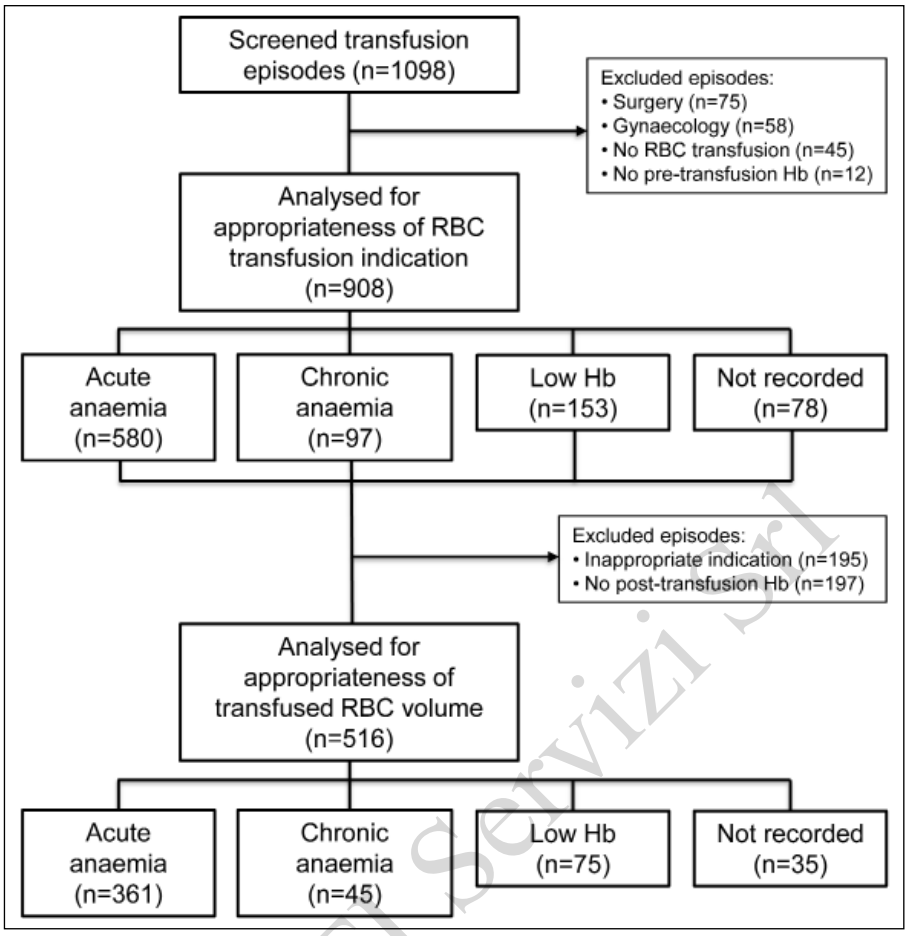

Figure 1 - Transfusion episodes in the Emergency Department.
RBC: red blood cell; Hb: haemoglobin.

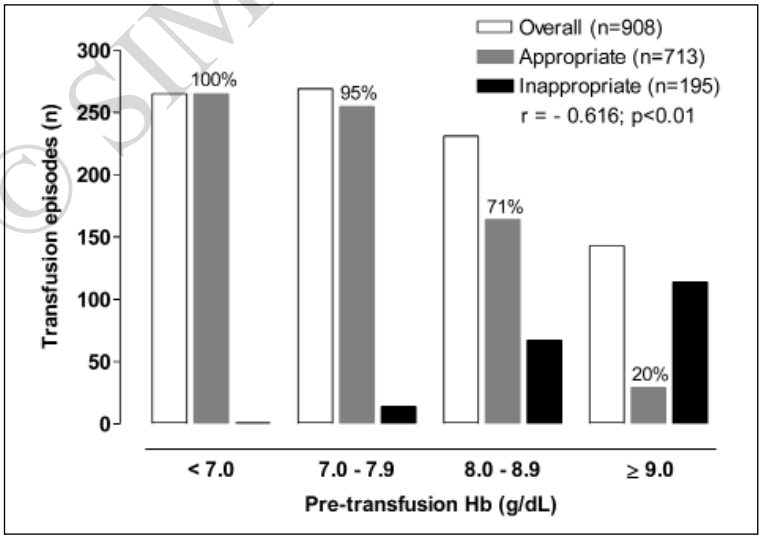

Figure 2 - Distribution of transfusion episodes in the Emergency Department, according to pre-transfusion haemoglobin levels (g/dL).
Appropriateness of the transfusion indication was assessed according to the transfusion criteria shown in Table I. (%): percentage of appropriate transfusion for each pre-transfusion haemoglobin level; Hb: haemoglobin; r: Pearson's correlation coefficient.

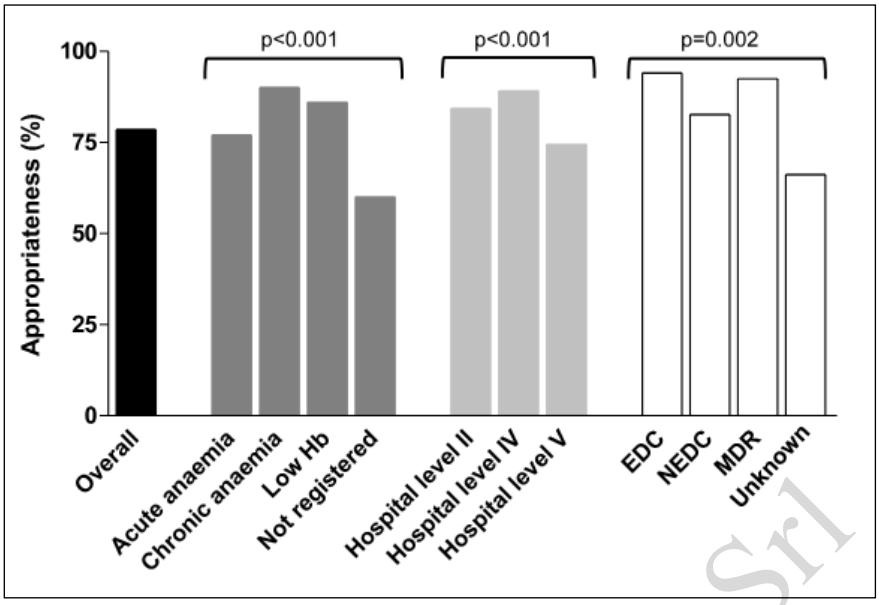

Figure 3 - Appropriateness of RBC transfusion indication at the Emergency Department, according to criteria depicted in Table I, according to underlying cause, hospital level and prescribing physician (n=908).
EDC: Emergency Department consultant; MDR: resident physicians of any specialty who perform shifts at Emergency Department; NEDC: consultant not belonging to the ED; Unknown: unknown physician.

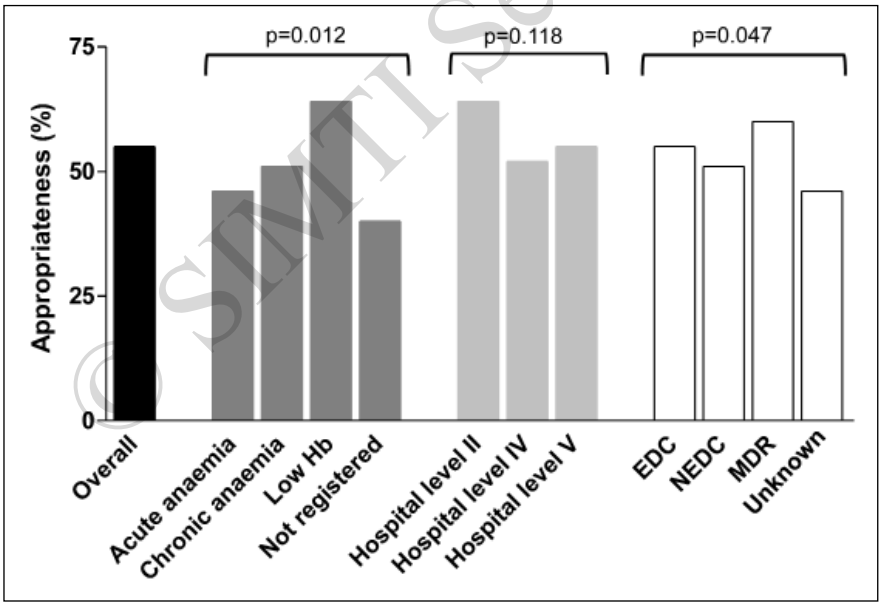

Figure 4 - Appropriateness of RBC transfusion volume at the Emergency Department, as reflected by post-transfusion haemoglobin in patients with a correct indication for transfusion, according to criteria depicted in Table I, according to underlying cause, hospital level and prescribing physician (n=516).
EDC: Emergency Department consultant; MDR: resident physician of any specialty who perform shifts at Emergency Department; NEDC: consultant not belonging to the ED; Unknown: unknown physician.

A 1997 study evaluated the appropriateness of RBCT in the ED of a Spanish hospital, and found that 44% were appropriate and 40% inappropriate, whereas appropriateness could not be established in 16% transfusion episodes[23]. Compared to these results, our analysis showed a significant improvement in the appropriateness of RBCT, which might reflect the gradual influence of clinical transfusion guidelines on physician's decision-making, as well as the concerns of hospital managers regarding the consequences of an inappropriate use of RBCT[24].

In this context, a study evaluating the appropriateness of transfusion practice at a hospital in Northern Ireland during 2005 observed that 23% of RBCT transfusions were considered inappropriate[22], whereas a French study provided evidence that only 7% of RBCT were not in accordance with recommendations of national protocols for transfusion[25]. A study investigating the impact of three national blood transfusion indicators (specifically designed for critical care) on appropriate blood transfusion indications found 13% of RBCT were given off protocol, whereas appropriateness of platelet concentrate transfusion (36-52%) and fresh-frozen plasma administration (26%) was much lower[20]. Interestingly, in the Northern Ireland study, it was also observed that 19% of patients were over-transfused[22].

When assessing whether or not RBCT has been used appropriately, consideration should be given not only to the "patient's need for transfusion", but also to "how many units" were transfused. Besides being a waste of resources, the Serious Hazards of Transfusion (SHOT) reports have indicated that over-transfusion is dangerous; e.g. a single unit of RBCT is strongly recommended in some populations of haemodynamically stable, non-bleeding patients to avoid "transfusion-associated cardiac overload"[26]. Compared with a liberal transfusion strategy, a restrictive strategy significantly reduced the number of RBCT (1.5±2.3 *vs* 3.7±3.8 units/patient) and improved outcomes in patients with acute upper gastrointestinal bleeding[27]. In critical and surgical patients, it has been recently shown that transfusion of a single unit of RBCT increased the multivariate risk of mortality, wound problems, pulmonary complications, post-operative renal dysfunction, systemic sepsis, composite morbidity, and length of hospital stay compared to propensity-matched patients who did not receive RBCT[28,29]. There was also a dose-dependent increase in the risk of a poorer outcome[29].

However, a few studies have examined this aspect of RBCT, reporting over-transfusion rates between 19 and 75%[22,30,31]. The need, therefore, for a post-transfusion Hb target has been recognised[11]. Consistent with other research[22], our study found that post-transfusion Hb remained around 9.5 g/dL, regardless of pre-transfusion Hb, resulting in high rates of over-transfusion. In daily practice, rates of adherence to the traditional goal of post-transfusion Hb of 10 g/dL, which is mostly based on the physician's routine approach and not according to patient need, might still be behind those of over-transfusion events[32].

Although not the focus of this research, we can speculate that the inappropriate requests for RBCT could be due to: a) lack of adherence of physicians to transfusion protocols; b) a lack of the strict supervision required by the Transfusion Service (Blood Bank) staff to limit the number of RBC units requested; c) incomplete RBC request forms; and d) a lack of awareness of the risks and unnecessary costs of the indiscriminate use of blood products. In Spain, most physicians have very low awareness of the real socio-economic cost burden of TBC. In this regard, at the Pennine Acute Trust (UK), it has been estimated that if anaemic patients with ID were stabilised with one RBC unit and then backed with IV iron infusion, there would be a 4.5% reduction in the number of RBC units transfused each year, with a potential total cost saving of about 60,000 Euro/year[33]. Data from a recently published study support the feasibility of a clinical protocol for management of sub-acute anaemia at the ED, and the efficacy, safety and tolerability of IV iron in this setting[34].

Several studies have suggested the need for greater control over the use of blood products, of underlining the importance of the Transfusion Service's staff reviewing the indications for TBC, and of establishing hospital transfusion committees[35,36]. Adherence to transfusion indicators has been shown to play a key role in reducing the variability in transfusion practice (especially for RBCT), the percentage of patients transfused, the volume of transfused components, and transfusion-associated complications (e.g. nosocomial infection)[20,37,38].

Our study may have been limited by its observational design, e.g. data collection was not uniform across all the participating hospitals. Some medical records did not provide full information about the reasons for transfusion and/or information about the transfusion procedure itself, which limits data collection and analysis. However, this circumstance is not unique to our study but is a common characteristic in multicentre observational studies. Audet *et al.* found significant limitations in a retrospective analysis of the appropriateness of RBCT due to insufficient documentation of transfusion episodes[39]. A national survey conducted in Brazil mentioned that Hb values were not recorded before RBCT[40] and, again in Brazil, de Sousa *et al.* found that 14% of RBCT had an adequate indication, and 8.9% were inappropriate; but the most relevant finding was that appropriateness was classified as inconclusive in 74.6% of RBCT because of the lack of information about the transfusion requests[41]. Likewise, after reviewing medical records, Friedman *et al.* observed a positive correlation

between inadequate physician documentation of RBCT and inappropriateness of RBCT, as measured by disagreement with the hospital transfusion protocol[42].

Conclusions

In conclusion, our data suggest that appropriateness of RBCT in ED is similar to that in other hospital departments, and reinforce the need to reassess the patient after transfusion of each RBCT unit before prescribing additional ones. In view of these results, we recommend the implementation of educational interventions aimed at the staff responsible for prescribing RBCT in order to increase the number of appropriate indications and to reduce the rate of over-transfusion in the ED.

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Authorship contributions

All those who met authorship criteria are listed as Authors, and all Authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the concept, design, analysis, writing, or revision of the manuscript. Furthermore, each Author certifies that this material or similar material has not been and will not be submitted to or published in any other publication before its appearance in Blood Transfusion.

The Authors declare no conflicts of interest.

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