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ORIGINAL ARTICLE

Transfusions in the Emergency department: More than a blood transfusion ☆

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Abstract   Increasing haemoglobin and haematocrit levels with blood transfusions has been the gold standard for treating severe anaemia; however, the indication for transfusing concentrated red blood cells is based merely on a few laboratory markers, such as haemoglobin and haematocrit levels, rather than based on the symptoms according to clinical practice guidelines, the implementation of legal regulations and the consensus achieved by the hospitals' transfusion committees. The aim of this multicentre study was to reassess the suitability of the indication for transfusing concentrated red blood cells and the volumes transfused in emergency departments. We established an observational, multicentre, cross-sectional design with 2 participating centres: the La Paz University Hospital and the Hospital of Salamanca. In total, we obtained data from 381 patients, 220 (57.74%) of whom were men with an average age of 71.4 ± 14.0 years and 161 (42.26%) of whom were women with an average age of 75.3 ± 15.3 years (P < 0.001). The most prevalent underlying diseases in the patients who underwent transfusions were heart disease, which included haemorrhaging due to antiplatelet or anticoagulant therapy (57.7%), haematooncologic (15.3%) diseases and neurological disease. Only 54.9% (209/381) of the prescriptions for transfusion were considered appropriate, with significant differences according to the indication.
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Transfusión en Urgencias: algo más que una transfusión de sangre

Resumen La elevación del nivel de hemoglobina y de hematocrito con transfusiones sanguíneas ha sido el estándar de oro para el tratamiento de la anemia grave. Sin embargo, la indicación para la transfusión de concentrado de hematíes se basa meramente en unos marcadores analíticos, como el nivel de hemoglobina o hematocritos, en lugar de basarse en la clínica (según las guías de práctica clínica), en la implementación de regulaciones legales o en los consensos alcanzados por los comités de transfusión de los hospitales. El objetivo de este estudio multicéntrico es reevaluar la idoneidad de la indicación de transfusión de concentrado de hematíes y los volúmenes transfundidos en los servicios de urgencias. Se plantea un diseño observacional multicéntrico y transversal en 2 centros participantes: el Hospital Universitario de La Paz y el Hospital de Salamanca. En total se obtuvieron datos de 381 pacientes; 220 eran hombres (57,74%), con una edad promedio de 71,4 ± 14,0 años y 161 eran mujeres (42,26% con una edad promedio de 75,3 ± 15,3 años p < 0,001. Las enfermedades subyacentes más prevalentes en los pacientes que recibieron transfusión fueron las cardiológicas, que incluyeron hemorragia debido a la terapia antiagregante plaquetaria o anticoagulante 57.7%), las hematooncológicas (15.3%) y las neurológicas. Solo el 54.9% (209/381) de las prescripciones de transfusión se consideraron apropiadas, con diferencias significativas observadas según la indicación.

Background

For many years, correcting or increasing hemoglobin and hematocrit levels with blood transfusions has been the gold standard for treating moderate-severe or asymptomatic anemia. Packed red blood cell (PRBC) transfusion is indicated when faced with symptomatic anemia to rapidly increase the supply of oxygen to tissues, generally when the oxygen transport capacity[1] is reduced or the Hb concentration is low. PRBC transfusion is still an important therapeutic tool for increasing oxygen transport to increase its release and thereby ensure its consumption, correct tissue hypoxia or prevent it.

In standard clinical practice, the indication for PRBC transfusion is based merely on few laboratory markers, such as hemoglobin and hematocrit levels, rather than on symptoms (according to clinical practice guidelines). In recent years, the body of evidence[2] has recommended the administration of minimum clinically effective doses to correct symptoms and to recover hemoglobin levels to a safety margin (>7 or 8 g/dL).[3] In an international review of the appropriateness of PRBC transfusion in various scenarios, the International Consensus Conference on Transfusion Outcomes observed that 59% of transfusions were inappropriate, 29% were uncertain, and only 12% were appropriate.[4]

Blood transfusion is one of the medical practices with greatest overuse and highest number of ''Do Not Do'' recommendations, along with radiological tests, laboratory tests and antibiotic treatments.[5] Since 2013, the Spanish Society of Hematology and Hemotherapy (through the project Commitment to Quality by the Scientific Societies in Spain, coordinated by the Spanish Ministry of Health, Social Services and Equality) has recommended the following: Do not transfuse more packed red blood cells than is necessary to relieve the symptoms of anemia or to return a patient to a safe hemoglobin range (7 to 8 g/dL for cardiac unstable patients) and do not transfuse packed red blood cells in iron-deficiency anemia without hemodynamic instability.[2] The World Health Organization has warned of the transfusion risks and the risks of inappropriately using PRBC transfusions, urging health authorities, scientific authorities and healthcare practitioners to implement cross-sectional and multidisciplinary programs in patient blood management.[6] The implementation of these programs mainly for surgical patients has resulted in a reduction in the volume of transfusions for surgical and critically ill patients, while the use could have increased in oncohematology and emergency departments. In a recent Spanish multicenter study conducted in emergency departments, up to 58% of the PRBC transfusions were considered inappropriate.

A frequently observed problem is the poor therapeutic indication for transfusion when requesting these components. This decision carries the risk of adverse effects such as acute and delayed hemolytic transfusion reactions, anaphylaxis, alloimmunization, immunomodulation, allergic reactions, graft-versus-host disease and the transmission of infectious diseases. Moreover, blood components are scarce, and improving transfusion practices can considerably reduce costs, although studies on this subject are scarce.

Therefore, the aim of this multicenter study was to reassess the suitability of the indication for PRBC transfusion and the volumes transfused in emergency departments.

Patients and methods

Design

We conducted a multicenter, observational, cross-sectional, noninterventional study on the appropriateness of blood transfusions.

Inclusion criteria

- Adult patients (≥18 years) who underwent at least one PRBC transfusion episode.
- Admission to the emergency department of any of the participating centers.
- Admission during November 2017.

Exclusion criteria

- Critical hemorrhages or massive transfusions, defined as any life-threatening hemorrhage that requires the urgent and massive transfusion of blood products, considering the clinical parameters: obvious blood loss (class 3 and 4 of the American College of Surgeons classification), hypotension (systolic blood pressure <85 mm Hg), tachypnea (>30 breaths/min) and central nervous system disorders (low level of consciousness, confusion or lethargy), any significant blood loss that causes hemorrhagic shock and a score >2 on the Assessment of Blood Consumption scale. The definition also covers temporary parameters such as measurable blood loss ≥150 mL/min for 10 min or more, 50% loss of blood volume in 3 h or 4 units of PRBC in 1 h and still bleeding.
- Patients with plasma and platelet transfusions (did not reach 3% of the total transfusions).

Definitions

A *transfusion episode* is defined as the interval between the prescription of blood components transfusion and the completion of its administration. When administering several units of blood components to the same patient under the same condition, all units received are considered part of a single transfusion episode.

Participating centers

La Paz University Hospital (HULP) and Hospital of Salamanca (HoS)

Variables

The main study endpoint was the *appropriateness* of the prescription for PRBC transfusion and the volume transfused. To this end, we assessed the appropriateness of the transfusion according to the pretransfusion Hb levels and the patient's characteristics, according to the 5th edition of the 2015 guidelines on transfusing blood components and plasma derivatives of the Spanish Society of Blood Transfusion and Cell Therapy (Table 1).[7]

We also recorded the hospital where the transfusion was performed and the patients' demographic and clinical variables (age, sex, history, reason for admission and department they were admitted to, length of stay in the emergency department, reason for the transfusion, biochemical values, transfused component and quantity transfused).

To evaluate the *effectiveness* of the transfusion volume, we assessed the posttransfusion Hb value. According to the recommendations of the 2013 Forum of Seville, we defined

Table 1 Guideline Recommendations For the Transfusion of Blood Components and Plasma Derivatives of the Spanish Society of Blood Transfusion and Cell Therapy.

	Hemoglobin, g/dL	Clinical situation
Acute anemia	<7	Any clinical situation
	7–8.9	Hemodynamically unstable or associated risk factors: coronary artery disease, heart failure, cerebrovascular disease and myocardial infarction
	≥9	Distress controlling the hemorrhaging or signs and symptoms of anemia
Chronic anemia	<8	Signs and symptoms of anemia or associated risk factors
	<5	No signs or symptoms of anemia

"overtransfusion" when the Hb level after the transfusion was more than 2 g/dL above the Hb transfusion threshold for each particular indication (Table 1).

Data collection

We created an electronic case report form for the data for the transfusions. The form was then downloaded in Excel format for subsequent analysis. These calculation sheets contained the data provided by the transfusion department of each hospital, especially the transfusion episodes of the emergency department during the study period. Additional data on the patients who underwent PRBC transfusion in the emergency department during the study period were obtained from the hospitals' computer systems and added to complete the database. Subsequently, the databases from each of the hospitals was merged and imported into STATA/SE 14.0® for statistical analysis.

Statistical analysis

The qualitative variables are listed using frequency distributions. For the quantitative variables, we calculated the mean values and standard deviations (±SD) or medians and interquartile ranges. We employed the Shapiro-Wilk test to compare the normal distribution of the quantitative variables; For the qualitative variables, we employed the chi-squared test. For the continuous variables, we employed Student's t-test or the Mann–Whitney U test to compare whether the transfusion was appropriate, depending on the normality of the data. We considered a type 1 error <0.05 (p < 0.05) statistically significant for all analyses.

Results

In total, we obtained data from 381 patients admitted to the emergency department during the study period; 220 were
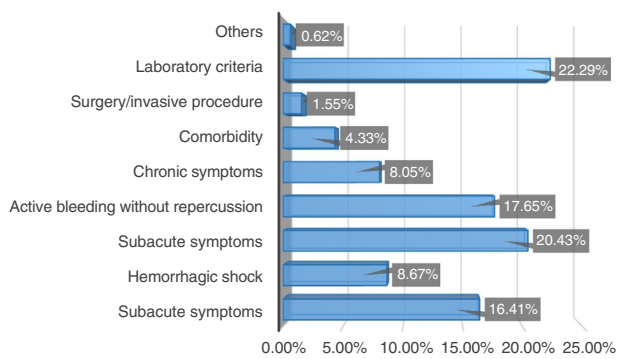
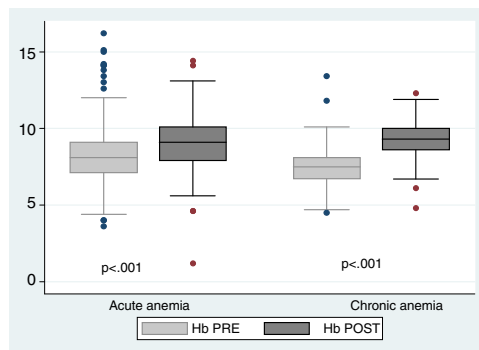**Figure 1**   Reason for transfusing red blood cells.

Figure 2   Differences between values before and after hemoglobin transfusion, according to the type of anemia.

Figure 3   Appropriateness of the indication for red blood cell transfusion in the emergency department. a) According to pretransfusion hemoglobin level. b) According to posttransfusion hemoglobin level.

men (57.74%), with an average age of 71.4 ± 14.0 years, and 161 women (42.26%), with an average age of 75.3 ± 15.3 years (p < 0.001). Some 93.19% of the patients were directly admitted to the emergency department due to medical causes, while the rest were referred from other departments (4.02% after surgery, generally due to loss of blood during the procedure; 1.86% from the gynecology department; and 0.93% from the trauma department). Also, 69.35% of these patients were discharged from the emergency department the same day they were admitted, while 28.79% were discharged the following day. Of the 381 study patients, 323 were from HULP (84.78%) and 58 were from HoS (15.22%).

The transfused patients received a median of 2 units of PRBCs (range, 1–7).

The most prevalent underlying diseases in the patients who underwent transfusions were heart disease, which included hemorrhaging due to antiplatelet or anticoagulant therapy (57.7%), hemato-oncologic (15.3%) diseases and neurological disease (4.2%). The most common reason for the transfusion was based on laboratory criteria (22.29% of the sample, a rate very similar to that of subacute symptoms, which reached 20.43%) (Fig. 1).

The mean pretransfusion hemoglobin level was 7.8 ± 1.8 g/dL (7.22 ± 1.49 in HoS and 7.91 ± 1.83 in HULP), while the mean post-transfusion hemoglobin level was 9.2 ± 1.7 g/dL (8.77 ± 1.13 in HoS and 9.31 ± 1.79 in HULP). In all cases, there were statistically significant differences between the two values (p < 0.001) (Fig. 2).

Table 2 shows the rest of the pretransfusion and post-transfusion values, both for the laboratory results and the case history. There were significant differences in all mea-
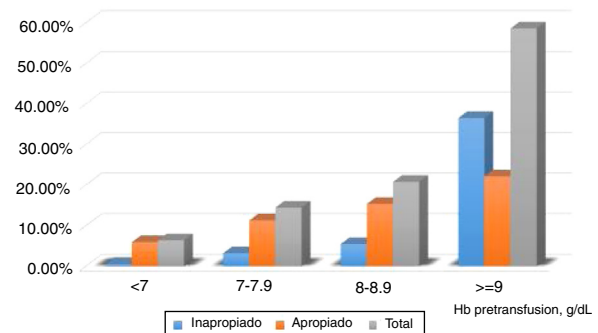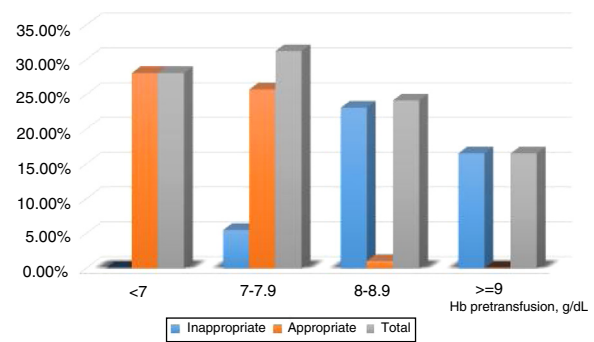
sures, except body temperature (p = 0.438) and diastolic blood pressure (p = 0.211). It is worth noting that posttransfusion values were recorded in only 54.79% of the patients.

Appropriateness

As shown in Fig. 3, only 54.9% (209/381) of the prescriptions for transfusion were considered *appropriate*, with significant differences according to the indication (p < 0.001).

Of the 209 patients with an appropriate prescription, 143 (68.4%) received an improper volume of blood components (overtransfusion).
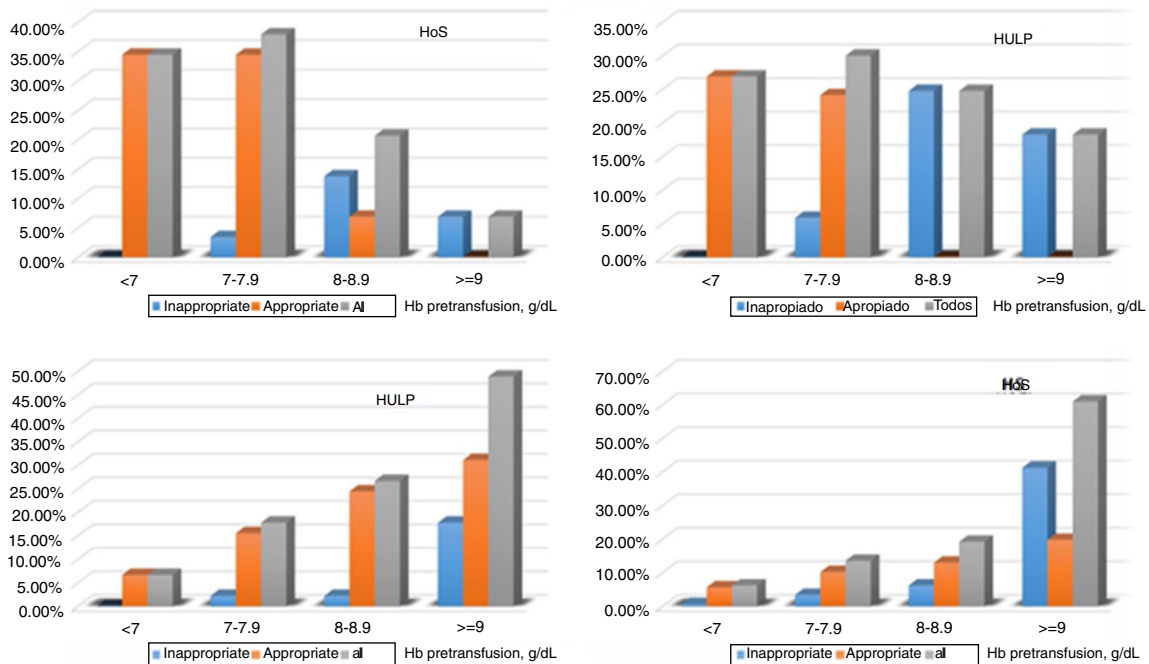
Appropriateness analysis

In terms of the potential differences between hospital type, we found that 75.86% of the transfusions performed by HoS were appropriate, while only 51.08% of those performed by HULP were appropriate, a difference that was statistically significant (p < 0.001).

Fig. 4 lists the rates of transfusion appropriateness in HoS and HULP, showing differences in the distribution of PRBC transfusion appropriateness in the various criteria.

When considering the diagnoses of acute and chronic anemia (Fig. 5), there are differences only in the rates of appropriate transfusions in acute anemia, where 69.23% of the transfusions were appropriate in HoS and 31.29% of the transfusions were appropriate in HULP (p < 0.001). For chronic anemia, the difference was not significant (p = 0.123), despite the higher appropriateness rate for PRBC transfusion in HoS.

Table 2 Patients' Biochemical and Exploratory Values Before and After the Transfusion.

Other values	Mean	SD	Median	25th percentile	75th percentile
[0,1-6]*Pretransfusion values*					
Hematocrit	24.35	6.44	23.75	21.00	26.20
Mean corpuscular volume	87.24	11.96	89.00	79.85	95.05
Mean corpuscular hemoglobin	38.55	177.46	29.50	26.00	32.00
Prothrombin time	69.73	26.99	78.00	53.00	92.00
International Normalized Ratio (INR)	2.59	13.53	1.18	1.05	1.59
Platelets	239.03	154.27	224.00	132.00	314.00
Creatinine	1.88	7.97	1.15	0.80	1.67
Total bilirubin	1.05	2.09	0.50	0.30	0.85
Temperature	36.38	0.57	36.40	36.00	36.70
Systolic blood pressure	126.18	31.59	129.00	105.00	145.00
Diastolic blood pressure	65.34	14.09	64.00	57.00	73.00
[0,1-6]					
[0,1-6]*Posttransfusion values*					
Hematocrit	28.13	4.99	28.20	25.20	31.00
Mean corpuscular volume	88.16	9.20	90.00	82.70	94.00
Mean corpuscular hemoglobin	29.33	3.64	30.40	27.00	32.00
Prothrombin time	73.68	18.74	78.00	61.00	89.00
International Normalized Ratio (INR)	1.31	0.43	1.17	1.09	1.41
Platelets	197.75	126.07	165.00	108.00	270.00
Creatinine	1.38	1.11	1.10	0.71	1.59
Total bilirubin	0.84	1.03	0.50	0.40	0.90
Temperature	36.56	0.67	36.50	36.00	36.70
Systolic blood pressure	120.52	22.90	119.50	108.00	130.00
Diastolic blood pressure	62.02	10.31	60.00	55.00	70.00

Figure 4 Appropriateness of the indication for red blood cell transfusion in the emergency department, for each hospital in the sample.

Discussion

Evidence from 10 years ago showed that more than 50% of all PRBC transfusions in Spain were administered to surgical patients and those in critical condition. The transfusion of red blood cells was the most widely used, and anesthesiologists were responsible for approximately 50% of transfusions. In recent years, however, the use of transfu-
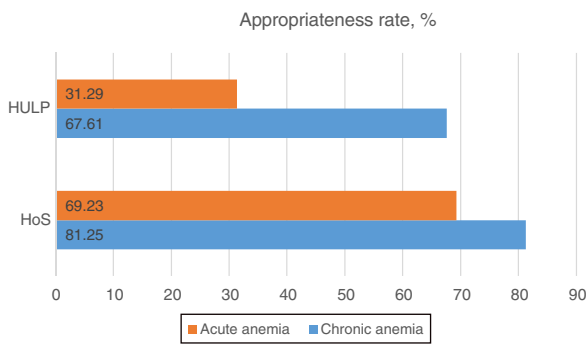
Appropriateness rate, %

Figure 5   Appropriateness of the indication for red blood cell transfusion in the emergency department, according to the type of anemia.

sions has decreased in surgical areas, and currently the 2 departments that employ most employ transfusions are the oncohematology and emergency departments.[4]

Although PRBC transfusions have been employed for many years and can save many patients with acute or chronic anemia, the results of this study conducted in emergency departments show that there is a high rate of unnecessary transfusions in both diseases. In HoS, which has a commitment to train practitioners on the appropriateness of PRBC transfusion,[8–10] we observed that the management of blood products had greater appropriateness. A recent survey by the American Association of Blood Banks showed that only 38% of public hospitals had an established program for managing blood products and patient transfusions. This program should be extended to all hospitals because it has been shown that local transfusion programs and committees promote patient safety, improve the quality of medical care and reduce unnecessary expenses.

Anemia is characterized by an insufficient quantity of healthy red blood cells, which are responsible for oxygenating the tissues and organs of the body and whose deficiency can therefore cause severe damage in these vital organs. In general, anemia is considered hemoglobin values <12 g/dL and <14 g/dL and hematocrit levels <36% and <41% for women and men, respectively. This disease is often underdiagnosed and undertreated and has a very high rate of comorbidity. Detection and appropriate treatment help reduce the need for transfusions, given that transfusions, although effective against anemia, are associated with numerous risks and complications. It is therefore essential to implement patient blood management programs, as urged by the World Health Organization in the 63rd Assembly of June 2010 and promoted the same year by the Council of Europe in the so-called ''optimal use of blood''.[11]

Depending on the mechanism of red blood cell destruction, the treatment for anemia should focus on its origin and not prioritize increasing hemoglobin levels. Blood transfusion is currently one of the most widely used treatments in Spanish emergency departments to treat anemia. Although this disease is generally accompanied by a reduction in erythrocyte mass, a reduction in the number of red blood cells does not have to occur. Therefore, a PRBC transfusion is perhaps not the best treatment option in these cases. Our study showed that only 54.86% of the PRBC transfusions were performed appropriately following the clinical guidelines criteria based on the patients' hemoglobin levels and

previous diseases; however, there was a considerable difference between the two diagnoses, with 69.71% of the cases of chronic anemia having appropriate PRBC transfusions versus 36.99% in the case of acute anemia.

For this reason and because PRBC transfusions are an expensive and scarce resource associated with known complications and adverse effects to be considered when prescribing them to patients, other better alternatives for the treatment of anemia should be considered, based on the disease's etiology, symptom severity and associated comorbidity. In these cases, a detailed medical history and anamnesis are essential when administering the best treatment for the patient. Logically, treating anemia will depend on its cause and severity. On many occasions, however, the prescription of iron, vitamin B12 and folic acid supplements, erythropoietin and medications that inhibit the immune system can be good alternatives to blood component transfusion. In fact, in countries such as the US and the UK, treatment based on PRBC transfusion fell 30–50% within a few years,[12,13] with a priority on therapeutic alternatives. Morbidity and mortality, hospital stays and readmissions also fell.

Article 40 of the Spanish Royal Decree 1088/2005[14] governs the existence and functions of hospital and independent transfusion centers and committees. Within their delegated powers, the autonomous communities of Spain have established that all centers with transfusion practices require a transfusion committee for the correct use of blood and blood components. The committee's functions, as a minimum, are the following: a) Determine the standards and procedures for the transfusion practice adapted to the clinical activities performed in each hospital center; b) Periodically analyze and evaluate the transfusion practice; c) Analyze and assess the adverse reactions associated with transfusions; d) Develop educational programs that promote the optimal use of blood components; e) Develop and implement preventive and/or corrective safety measures; and f) Any other functions they consider would help promote the optimal use of blood, components and derivatives and in reducing their consumption.

Other options studied in the context of the politics of managing patients' blood include multifactorial strategies. Langlais et al.[15] adopted a series of strategies aimed at improving the transfusion practices in surgery departments through seminars, classes, periodic consultations and the creation of information points. Through these measures, the authors improved transfusion appropriateness from 37.7% to 64.5%. In other studies, the rate of appropriateness was only 8.3% for patients with trauma, 11.5% for patients who underwent surgery and 12.8% for transfusions ordered by a specialist.[4] The introduction of policies that help improve these figures would therefore be a short-term objective that can help increase the appropriateness of PRBC transfusions.

In our study, we observed high overtransfusion rates, which were also found in other studies.[16] As a result and as proposed by a number of these studies, we emphasize the concept of reassessing the patient's state after each unit of transfused PRBC and before prescribing additional units. A zero-tolerance policy can be effectively implemented only with exhaustive work with local physicians, including repeated rounds of information, updates on current trans-

fusion practices and the knowledge of established regimens over time.[17–19]

The limitations of our study include the heterogeneity between the 2 hospitals, given the fact that the transfusion policy employed by each hospital is different. The appropriateness results therefore differ between them. Further studies are warranted to analyze the shortcomings in these types of policies, as well as to create a commitment to improve the transfusion policies for all public hospitals in Spain to determine the effects on patient health and on the healthcare cost of these policies.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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