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ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

Rational red blood cells administration – have we achieved a satisfactory level?

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SUMMARY

Introduction The important indicators of the quality of work in blood transfusion banks and health care facilities in general is the ratio of the cross-matched red blood cell (RBC) units, and the number of transfused RBC, known as cross-match to transfusion ratio (C:T).

The objective of this research was to provide an assessment of the quality of our work in a cross-sectional study, showing C:T ratios for certain areas of surgery or particular surgical indications.

Methods We analyzed the data related to the activities of the Department for Pre-Transfusion Testing and Blood Distribution at the Blood Transfusion Institute of Serbia during the September and November of 2017 period. In total, 341 patients were included in the study, for whom 1,067 RBC units were requested.

Results In pre-transfusion testing, 562 units were cross-matched and 249 units were transfused. The overall C:T ratio was 2.25. There are variations in C:T by departments. For the departments of abdominal surgery and reanimation, where uncrossmatched RBC units were requested, C:T was < 2. Other departments had C:T > 3 for almost all therapeutic areas.

Conclusion Our results show that the C:T ratio ranged 2.02–3.6, indicating the need to reevaluate the protocols based on which the blood is requested according to individual indications, to adequately prepare patients for surgery in order to reduce the risk of possible allogeneic transfusion, and to apply Patient Blood Management protocols, which include the use of alternatives to allogeneic blood transfusion.

Keywords: red blood cells administration; cross-match to transfusion ratio; Patient Blood Management

INTRODUCTION

Safe use of blood and blood components currently requires multidisciplinary collaboration among clinicians of different profiles such as surgeons, anesthesiologists, internists, and transfusion medicine specialist as the last instance that can affect the decision on administration of the particular blood component [1]. Although the use of transfusion remains an irreplaceable treatment modality for a large number of patients accompanied by a clear benefit through rapid correction of hemoglobin levels, and consequently of oxygenation, it is also associated with a range of risks of infectious and non-infectious nature [2]. Errors in transfusion medicine can be avoided in a large percentage and prevention is cost-effective, systematic, and applicable [3].

Hemoglobin binds 98% of oxygen; therefore, measurement of hemoglobin levels is to date the best and most commonly used test to estimate the necessity of RBC administration for the correction of anemia [4]. However, hemoglobin should not be the only parameter to be considered when deciding on potential RBC transfusion [5]. It should be noted that there are two approaches to the administration of RBC transfusion – a liberal one and a restrictive one. The liberal approach to transfusion is primarily based on hemoglobin levels, and it uses the hemoglobin level of 90 g/L as the threshold for RBC administration. In critically ill patients, as well as in bleeding patients, the restrictive approach uses hemoglobin threshold level below 70 g/L [6].

Managing the requirements for blood and blood components in relation to the needs of patients with Patient Blood Management (PBM) is an evidence-based multidisciplinary approach to treating patients with blood and blood components [7].

In order to establish a functional PBM system, close cooperation with doctors involved in the treatment of patients is particularly important, and the key moment is the training of health care staff. The aim of the above measures is to avoid any unnecessary transfusion [8]. Considering the experience of countries that have established the PBM system (Australia and New Zealand) and certain countries of the European Union, there is a clear benefit for both the patients and a country's health care system, which is reflected in the fact that PBM significantly affects the quality of the treatment of patients [9]. At this moment, there are no available data about PBM implementation in the surrounding states.

One of the important indicators of the quality of work of blood transfusion bank and health care facilities in general is the ratio of the number of requested RBC and the number of

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cross-matched RBC, known as C:T ratio (cross-match to transfusion ratio) [10]. This ratio should not exceed 2 [11]. Namely, the routine ordering of blood is usually carried out by the most junior clinical staff, who beside limited knowledge of the true nature or magnitude of the proposed surgery can cause at least three major problems. Firstly, in blood banks with a limited 'pool' of available blood, over-ordering actually leads to less blood being available for emergency transfusion. While in theory it is possible to recall blood that is out of circulation, this would inevitably lead to disruption of elective surgical lists. Secondly, if blood is cross-matched but not transfused, it is more likely to pass its expiry date and must be discarded. Third, cross-matching is costly. It would be easy to assume that the simple task of ordering the correct amount of blood for an elective surgical procedure is performed accurately in every hospital [12].

During 2012, according to the British Society of Hematology Guidelines, C:T ratio was listed as an important parameter for defining optimal administration of blood that implies the type of pre-transfusion analyses and the number of units for a particular type of surgical procedure [13].

The aim of our study was to provide an assessment of the quality of our work in a cross-section study by showing the C:T ratio for certain areas of surgery, i.e. particular surgical indications. Considering that PBM system has not been established in our country, this study represents one of the first of its kind in our country. However, we must note that the General Hospital in Pančevo has introduced its own protocols for the application of RBC, which has led to a significant reduction in blood consumption [14].

METHODS

In this retrospective study, the data related to the activities of the Department for Pre-Transfusion Testing and Distribution of Blood, Blood Components and Hemovigilance at the Blood Transfusion Institute of Serbia for the period of two months (September and November of 2017) were analyzed. During this period, 341 patients were monitored, for whom a total of 1,067 RBC units were requested.

The analyzed data refer to RBC administration at the Emergency Center of the Clinical Center of Serbia, including requests from the Department of General Surgery, Orthopedics, Neurosurgery and Reanimation. The data were collected based on requests for blood and blood components coming from those departments that were subsequently entered into the protocol, while one portion of the data was taken from the electronic database of the Department for pre-transfusion testing. The data collected included the departments where the patients were treated, the leading diagnosis at the time of blood request, requisition date, and the purpose of requisition (surgery or treatment). Patient data included first and last name, year of birth, hemoglobin level, blood type, number of requested RBC, number of cross-matched RBC units as well as the number of transfused RBC units. Since the data on hemoglobin levels were available in a small proportion of patients [only 29 (7.9%)], they were not taken into account during the statistical analysis performed to determine the C:T ratio.

The data collected were used to monitor the relationship between the number of requested and processed RBC units, depending on the therapeutic area, as well as to determine the C:T ratio. Institutional approval for the study was granted by the local research ethics committee in accordance with internationally accepted ethical standards.

Statistical analysis included methods of descriptive and analytical statistics using IBM SPSS Statistics, Version 21.0 (IBM Corp., Armonk, NY, USA). The significance of the difference for continuous variables with normal distribution was estimated using analysis of variance (ANOVA).

The value of $p < 0.001$ was considered to be statistically significant.

RESULTS

Table 1 shows an overview of the requested, cross-matched, and transfused RBC units per department. A total of 1,067 RBC units were requested for 341 patients. During pre-transfusion testing, 562 units were cross-matched and 249 were transfused. The overall C:T ratio was 2.25, which corresponds to the consumption of 44.36% of used RBC (Table 2).

Table 1. Number of issued *vs*. requested and processed red blood cells by departments

Emergency Center department	Number of patients	Requested	Cross-matched	Transfused
Surgery	223	654	255	126
Orthopedics	38	118	95	27
Neurosurgery	10	23	18	5
Reanimation	52	218	144	44
Reanimation without interaction	18	54	50	47
Total	341	1,067	562	249

Table 2. Cross-match to transfusion (C:T) ratio with regard to the departments

Emergency Center department	C:T
Surgery	2.02
Orthopedics	3.51
Neurosurgery	3.60
Reanimation	3.27
Reanimation without interaction	1.06
Total	2.25

ANOVA, $p < 0.001$

The largest number of RBC requests (654) were obtained from the Department of Surgery, where the highest number of patients (223) were treated. In this group, a corresponding C:T of 2.02 was obtained. The minimum number of RBC requests (23) was obtained from the

Table 3. Number of requisitions showing hemoglobin levels compared to the total number of patients and the purpose of blood requisition

Department	Number of requisitions with hemoglobin level n/N (%)	For treatment purposes	As part of surgical program	Hemoglobin level range
Surgery	23/223 (10.3)	19	4	53–91
Reanimation	0/52 (0)	0	0	0
Reanimation without interaction	0/18 (0)	0	0	0
Neurosurgery	0/10 (0)	0	0	0
Orthopedics	6/38 (15.79)	6	0	76–86
Total	29/341 (8.5)	25	4	53–91

Only two patients had hemoglobin level < 70

Table 4. Number of issued vs. requested and processed red blood cells with regard to the surgical procedure

Surgical procedure	Number of patients	Requested	Cross-matched	Transfused
Polytrauma	22	87	61	14
Subarachnoid hemorrhage, intracranial hemorrhage	7	25	10	2
Gastric ulcer, hernia, gallbladder and choledochal surgery, acute appendicitis, abdominal pain of unknown etiology, idiopathic jaundice	95	230	33	11
"Status post op"	34	103	33	8
Femoral fracture	18	63	53	17
Hip surgery	3	9	9	3
Total	179	517	199	55

Department of Neurosurgery, where the highest C:T was calculated to be 3.6 (Tables 1 and 2), $p < 0.001$; $p < 0.001$ is considered a statistically significant difference.

Table 3 shows the number of requisitions that listed the hemoglobin levels. The analysis showed that only 29/341 (8.5%) requisitions listed the hemoglobin level – 23/223 from the Surgery Department and 6/36 from the Orthopedics Department. For 25 patients, blood was requested to correct anemia, and for four patients as part of the surgical program (Table 3).

Tables 4 and 5 provide an overview of requested, cross-matched, and transfused RBC units by the most common surgical procedures. The highest number of RBC requests were obtained for abdominal surgery and for the treatment of hip surgery. In both types of surgery, C:T of 3.0 was recorded, while the highest C:T of 5.0 was obtained for cases of bleeding into the central nervous system that required surgical intervention – $p < 0.001$.

Table 5. Cross-match to transfusion (C:T) ratio calculated for departments with regard to the surgical procedure

Surgical procedure	C:T
Polytrauma	4.35
Subarachnoid hemorrhage, intracranial hemorrhage	50
Gastric ulcer, hernia, gallbladder and choledochal surgery, acute appendicitis, abdominal pain of unknown etiology, idiopathic jaundice	30
"Status post op"	4.12
Femoral fracture	3.11
Hip surgery	3.00
Total	3.61

ANOVA, $p < 0.001$

Although the International Classification of Diseases lists the diagnosis code "status post op," this term is quite broad, and it is used frequently at emergency center surgical departments as an indication for blood requisitions. During the examined period, there were 34 such requisitions. A total of 103 RBC units were requested, 33 were cross-matched, and eight were transfused; C:T ratio was 4.12.

DISCUSSION

This study has shown that there is a substantial variation in the estimated C:T values between the departments requesting the blood, and according to the type of surgical procedure.

The analysis of the pooled data for the studied time period related to the requisition and issuing of RBC blood components showed that the overall ratio of processed and transfused RBC resulted in C:T of 2.25 – very close to the recommended value of < 2. However, when analyzed structurally, there are differences in C:T between the departments. Thus, the department of abdominal surgery and reanimation had C:T < 2. The reanimation department also had C:T < 2 in cases where uncrossmatched RBC units were requested, but it should be noted that such circumstances mainly included massive transfusions accompanied by risk of a number of adverse reactions. By contrast, all other departments for almost all therapeutic areas had C:T > 3. This indicates a high degree of uneconomical blood administration and a subsequent risk of blood shortage for all patients in need due to irrational blood processing and consumption.

Among the first countries in the world that recognized the importance of PBM are Australia and New Zealand. By introducing PBM, these countries reduced the consumption of RBC units in patient treatment, subsequently reducing the cost of treatment and the transfusion risk, but also allowing more appropriate RBC distribution. In

accordance with their recommendations, the C:T ratio should not exceed 1.8. If it does, for patients for whom requisition was made, it is sufficient to determine the patient's blood type and antibody screening [7]. It should be noted that such a policy implies that a health care facility carrying out surgical procedures has its permanently available transfusion service.

In order to reduce the number of unnecessary cross-matched RBC units and to provide an adequate amount of RBC units, a recommendation was made in India to introduce the Maximum Surgical Blood Ordering Schedule (MSBOS) according to the C:T parameter. Research was conducted in a tertiary facility and it monitored patients planned for elective abdominal and neurosurgery. According to this recommendation, C:T should ideally be 1:1, but all values that are < 2.5 with the aim of lowering the index towards 2 are acceptable for the efficient RBC use [15]. In India, analyses were performed in orthopedic surgery, and C:T indexes were monitored, which indicated the benefits of lowering the C:T ratio to values < 2. Based on this, protocols were designed that suggest the optimal number of RBC components which should be prepared for various surgical procedures [16].

Given these circumstances, it is necessary to apply multidisciplinary approach to determine the criteria for blood administration according to therapeutic areas. Based on the data collected, therapeutic areas can be divided into two large groups: (1) those that need to be recorded and that require determination of blood type, and for which blood is almost never requested, and (2) those for which blood is requested and cross-matched, but is almost never used or is used very rarely, as well as those for which larger amount of blood loss is expected with certainty, which needs to be substituted by allogeneic transfusion. Currently, patients from the first group are tested for blood type according to the ABO and Rh system. For patients in the second group, blood type is determined without exception, as well as the indirect antiglobulin antibody screen [17].

Furthermore, it is necessary to clearly indicate on the requisition forms the diagnosis under which the blood is requested. The current principle which uses working diagnoses that are, although listed in the International Classification of Diseases, often unclear (e.g. "Status post op"), and very often without accompanying hemoglobin level, as shown by our research, does not provide enough data, seems confusing and often leads to wrong decisions on whether or not to prepare blood for such patients.

RBC transfusion in patients with anemia in whom compensatory mechanisms for adequate tissue oxygenation are reduced increases the capacity for oxygen transport [18]. A well-compensated anemia resulting from iron deficiency is the most common form of anemia and is not an indication for RBC administration itself, but as such requires the administration of iron via oral or intravenous route, with or without erythropoietin and with an assessment of the risk of adverse reactions [19]. Allogeneic transfusion has long been used to correct perioperative anemia. However, for the purpose of safety of blood transfusion itself, as well as due to limited resources and limited blood supply, modern transfusion tends to avoid this type of treatment for anemia [20]. It has been found that 30.4% (in some populations up to 75%) of patients had anemia of various grade in the preoperative period, that the risk of postoperative complications in these patients was 35% higher (most often infections), and that the 30-day risk for fatal outcome was increased by as much as 42% [21].

A restrictive transfusion strategy compared to a liberal strategy implies lower number of patients undergoing transfusion, as well as fewer RBC units used, while mortality, morbidity, and the number of myocardial infarction events remained unchanged. On the other hand, the liberal transfusion strategy did not show any benefit to patients [22].

Although our study has its limitations based on the facts that the study was retrospective and that the analysis covered a relatively short time interval, as well the obtained results were related to requested, cross-matched, and transfused RBC units but not using needed/not needed RBC, the estimated C:T ratios indicate the need to introduce and observe the procedures which would allow a more rational use of blood. Therefore, this study may be characterized as a pilot study, and results will be confirmed in a prospective study that will include an analysis of RBC administration over a longer period.

CONCLUSION

The results of our study examining the requested, cross-matched, and transfused RBC units indicate the need to introduce procedures that would allow rational use of blood. Considering the overall C:T ratio, it could be concluded that we performed close to the recommended value; however, data analysis by the department or by the type of surgical intervention shows that the C:T value varies 2.02–3.60, indicating that it is necessary to reevaluate protocols used for blood requisitions according to individual indications, to adequately prepare patients for surgery whenever possible to reduce the risk of possible use of allogeneic transfusion, and to establish PBM protocols that include the possibility of using alternatives to allogeneic blood transfusion.

Conflict of interest: None declared.

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Рационална примена еритроцита – да ли смо постигли задовољавајући ниво?

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САЖЕТАК

Увод Један од битних индикатора квалитета рада трансфузиолошке банке крви и здравствене установе у целини је однос броја обрађених јединица еритроцита којима је урађена интеракција и броја трансфундованих јединица еритроцита, однос *C : T*.

Циљ нашег истраживања је био да у студији пресека дамо процену квалитета нашег рада приказујући однос *C : T* за одређене хируршке гране, односно одређене индикације у хирургији.

Методе У ретроспективној студији извршена је анализа података која се односила на двомесечну активност Одељења за претрансфузиона испитивања и дистрибуцију крви, компонената крви и хемовигиланцу Института за трансфузију крви Србије (септембар и новембар) 2017. године. У наведеном периоду праћен је 341 болесник, за које је укупно требовано 1067 јединица еритроцита.

Резултати У претрансфузионом тестирању је обрађено 562, а издато 249 јединица еритроцита. Свеобухватни однос *C : T* је био 2,25, што одговара потрошњи од 44,36% искоришћених еритроцита. У односу на одељења постоје разлике у односу *C : T*. За одељења абдоминалне хирургије и реанимације, када је крв тражена без интеракције, утврђен је *C : T* < 2. Друга одељења су за готово све терапијске области имала *C : T* > 3.

Закључак Анализа података у односу на одељења или тип хируршке интервенције показује да вредност *C : T* варира од 2,02 до 3,6, што указује да је неопходно преиспитати протоколе по којима се крв требује према појединим индикацијама, адекватно припремити болеснике за операцију, како би се смањио ризик за евентуалну примену алогене трансфузије и применити протоколе управљања крвљу болесника, који подразумевају могућност примене алтернативних средстава алогеној трансфузији крви.

Кључне речи: примена еритроцита; однос броја еритроцита са урађеном интерреакцијом и броја трансфундованих еритроцита; управљање крвљу болесника