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Utilization patterns of group O red blood cell transfusion by ABO and D non-identical recipients in large academic hospital

Modèles d'utilisation de la transfusion de globules rouges du groupe O par des receveurs non identiques ABO et D dans un grand hôpital universitaire

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ABSTRACT

OBJECTIVES: Several studies have raised concerns that transfusion of O red blood cells (RBCs) to ABO and D non-identical recipients can intensify group O inventory shortages. The aim of this study was to retrospectively analyse particular clinical indications and polices responsible for O RBCs use by ABO and D non-identical recipients as well as to assess the impact of this practice on the overall utilisation of O RBCs.

MATERIAL AND METHODS: Data of all transfused RBCs from 2014 to 2018 were extracted from the comprehensive database of transfusion service. Extracted variables included date of transfusion, ABO and D group of the transfused RBCs and recipients, recipient's demographic, and specific characteristics regarding transfusion requirements.

RESULTS: Over 5-year period 124 220 RBCs were transfused: 38 962 (31.4%) group O D+ and 9109 (7.3%) group O D-. ABO and D non-identical recipient received 4842 (10.1%) of all administered O RBCs: 2880 (7.4%) of all transfused O D+ and 1962 (21.5%) of all transfused O D- RBCs. The common indications for this practice were: ABO and D mismatched hematopoietic stem cell transplantation (HSCT) (52.5%), infants under the age of 4 months (18.6%), shortage of ABO identical RBCs (9.0%), phenotype-matched RBCs (8,1%), and urgent transfusion (7.2%).

CONCLUSIONS: A significant proportion of O RBCs was transfused to ABO and D non-identical recipients, mainly due to transfusion of ABO and D mismatched HSCT recipients. However, the proportion of all transfused RBCs O D+ and especially O D- remained relatively low.

Key word: O RBCs, ABO non-identical, inventory, transfusion

Résumé

Objectif: Plusieurs études ont soulevé des inquiétudes quant au fait que la transfusion de globules rouges O (globules rouges) à des receveurs ABO et D non identiques peut intensifier les pénuries d'inventaire du groupe O. Le but de cette étude était d'analyser rétrospectivement les indications cliniques particulières et les politiques responsables de l'utilisation des globules rouges O par des receveurs non identiques ABO et D, ainsi que d'évaluer l'impact de cette pratique sur l'utilisation globale des globules rouges.

Méthodes: Les données de tous les globules rouges transfusés de 2014 à 2018 ont été extraites de la base de données complète des services de transfusion. Les variables extraites comprenaient la date de transfusion, le groupe ABO et D des globules rouges transfusés et des receveurs, la démographie du receveur et des caractéristiques spécifiques concernant les besoins transfusionnels.

Résultats: Sur une période de 5 ans, 124 220 globules rouges ont été transfusés: 38 962 (31.4%) groupe O D+ et 9 109 (7.3%) groupe O D-. Les receveurs ABO et D non identiques ont reçu 4 842 (10.1%) de tous les globules rouges O administrés: 2 880 (7.4%) de tous les O D + transfusés et 1 962 (21.5%) de tous les globules O D- transfusés. Les indications courantes de cette pratique étaient: la transplantation de cellules souches hématopoïétiques (GCSH) (52.5%) sans correspondance ABO et D, les nourrissons de moins de 4 mois (18.6%), la pénurie de globules rouges ABO identiques (9.0%), les globules rouges phénotypiques (8.1%) et les transfusions urgentes (7.2%).

Conclusion: Une proportion significative d'érythrocytes O a été transfusée à des receveurs ABO et D non identiques, principalement en raison de la transfusion de

receveurs de GCSH ABO et D non appariés. Cependant, la proportion de tous les O D+ et surtout les O D- globules rouges transfusés est restée relativement faible.

Mots clés: O globules rouges, ABO non identiques, inventaire, transfusion

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1. INTRODUCTION

Blood services worldwide have been experiencing a decline in the demand of red blood cells (RBCs), primarily due to the growing implementation of patient blood management (PBM). On the contrary, demand for O RBCs, particularly O D-, as a proportion of the overall RBCs demand has been increasing [1-3]. The reason for this disproportionate increase in group O RBCs demand is using of O RBCs as universal RBCs, since they can be transfused to all other ABO groups [4]. Depending on the size, location and complexity of hospitals, there are different predominant reasons for utilization of O RBCs by ABO and D non-identical recipients. Rural and/or smaller hospitals stock only group A and O D- RBCs to simplify inventory and decrease wastage, as these units are compatible with the majority of patient blood types. As well, using this practice, shortages during bleeding emergency could be avoided. On the other side large hospitals, commonly located in urban areas, often require sizable inventories of group O RBCs to accommodate complex patient populations, including: neonates; hematopoietic stem cell transplant (HSCT) recipients; and patients requiring antigen-negative blood and trauma patient requiring emergent transfusion prior to blood group determination [5].

The practice of using O RBCs by ABO and D non-identical recipients can additionally intensify group O inventory shortages, especially D- RBCs that are often in short supply. In order to protect O D- RBC supply indications for use of group O RBCs for ABO and D non-identical individuals should be monitored, in order to explore areas where policy changes could help to alleviate inventory shortages [6]. Consequently, this ensures availability of O D- RBCs for the most vulnerable patients to harmful consequences of developing D alloantibodies, such as women of

childbearing age and those requiring chronic or recurrent transfusions throughout their lifetime [7].

Knowing the importance of maintaining sufficient inventory of O RBCs the aim of this study was to retrospectively analyse particular clinical indications and policies responsible for O RBCs use by ABO and D non-identical recipients as well as to assess the impact of this practice on overall utilisation of O RBCs.

2. MATERIALS AND METHODS

University Hospital Centre Zagreb (UHC Zagreb) is a large academic hospital of maximum medical care (approximate capacity of 1800 beds) with the obstetrics, orthopaedic and thoracic surgery clinics in three remote locations. The study was approved by the Hospital Ethics Committee. A retrospective analysis of all transfused RBCs in UHC Zagreb from 1 January 2014 to 31 December 2018 was conducted. Data were extracted from the comprehensive database of transfusion service.

Variables extracted included the following: date of transfusion; ABO and D group of the transfused RBCs and recipients; most responsible diagnosis; indication for transfusion; date of birth; sex; and specific characteristics (presence of red cell alloantibodies, special requirements regarding ABO and D group, and phenotype-matched RBCs, HSC or organ transplantation). Data were analysed with computer software SPSS Statistics 26 (IBM Corp). Descriptive statistics, including numbers (percentages), medians (ranges) are used to present the data. Comparison between D+ and D- O RBCs transfused in 2014. and 2018. has been made using chi-square test. All analyses were performed using SPSS 26.0 for Windows (IBM Corp., New York, USA).

2.1. Definition of ABO and D non-identical transfusion

The following RBCs transfusions were considered ABO and D non-identical: group O RBCs transfused to A, B, AB recipients and recipients with indeterminate or unknown ABO group; O D- RBCs transfused to D+ recipients or to recipients with indeterminate or unknown D type; and O D+ RBCs transfused to D- recipients or to recipients with indeterminate or unknown D type.

2.2. Indication for ABO and D non-identical RBC transfusions

The indications for ABO and D non-identical RBC transfusions were hierarchically categorized and defined for the study as follows:

- (1) ABO and D allogeneic mismatched HSCT: ABO and D mismatched patients with requirement to receive O RBCs.
- (2) Infants under the age of four months: infants up to 4 months old at the time of transfusion, transfused with O RBCs due to low gestation age/weight and ABO haemolytic disease of the fetus and newborn (HDFN).
- (3) Shortage of ABO identical RBCs: this was the default category if none of the other conditions were met as it was presumed that the non-identical RBC transfusion was due to an inventory shortage of ABO-identical RBCs.
- (4) Phenotype-matched RBCs: patients with the presence of RBCs alloantibodies and requirement for phenotype-matched RBCs, if there was not available phenotype-matched RBCs in identical ABO and D group.
- (5) Urgent transfusion: massively haemorrhaged patients of unknown ABO and D group.
- (6) Indeterminate ABO or D group: patients with ABO and D blood group discrepancies.
- (7) D variant: patients with serologic weak reaction with anti-D reagents.

- (8) Solid organ transplantation: ABO mismatched transplant patients with requirement to receive O RBCs.
- (9) Close to outdating: RBCs were classified as close to outdating if the transfused product had been stored for ≥ 32 days, since RBCs have shelf life of 35 days.

3. RESULTS

Over the 5-year study period 124 220 RBCs were transfused: 38 278 (30.8%) group A D+, 8646 (7.0%) group A D-, 17 129 (13.8%) group B D+, 34 817 (3.1%) group B D-, 6971 (5.6%) group AB D+, 1308 (1.1%) group AB D-, 38 962 (31.4%) group O D+, 9109 (7.3%) group O D-. The proportion of transfused O D+ RBCs increased from 29.6% in 2014 to 32.5% in 2018 (an increase of 2.9%) and proportion of transfused O D- decreases from 8.4% in 2014 to 6.5% in 2018 (a decrease of 1.9%).

Out of 48 071 analysed group O RBCs in total, 43 229 (89.9%) were transfused to ABO and D identical and 4842 (10.1%) were transfused to ABO and D non-identical recipients. Out of the all administered O D+ RBCs, 92.6% (36 082/38 962) were transfused to ABO and D identical and 7.4% (2880/38 962) were transfused to ABO and D non-identical recipients. Out of the all administered O D- RBCs, 78.5% (7147/9109) were transfused to ABO and D identical and 21.5% (1962/9109) were transfused to ABO and D non-identical recipients (Table 1.).

Only 0.7% (279/38 962) O D+ RBCs were transfused to D- recipients and 9.4% (859/9109) O D- RBCs were transfused to D + recipients (Table 1.).

Total of 2880 O D+ RBCs were transfused to 335 ABO and D non-identical recipients. The median of three O D+ RBC units were transfused per ABO and D non-identical recipients (range, 1 - 144 units). As shown in the Table 2. ABO and D mismatched HSCT (57.1%) was the most frequent indication for transfusion of O D+

RBCs to ABO and D non-identical recipients, followed by the transfusion to infants under the age of 4 months (25.8%) and shortage of ABO identical RBCs (10.8%).

Total of 1962 O D- RBCs were transfused to 330 ABO and D non-identical recipients. The median of two O D- RBC units were transfused per ABO and D non-identical recipients (range, 1-103 units). As shown in Table 2. ABO and D mismatched HSCT (45.9%) was the most frequent indication for transfusion of O D- RBCs to ABO and D non-identical recipients, followed by the urgent transfusion (16.8%) and phenotype-matched RBSs (15.8%).

Over the study period, the number of transfused O RBCs to ABO and D non-identical recipients was reduced, from 1029 units in 2014 to 742 units in 2018 (Figure 1.). The decrease in number of transfused D- O RBCs from 462 (44,9%) units in 2014 to 266 (35,8%) units in 2018 was statistically significant ($\chi^2=14.58$, $p<0.01$) (Figure 1.). As shown in Figure 2., the number of O RBCs transfused to ABO and D non-identical recipients slightly decreased for the following indications: phenotype-matched RBCs, indeterminate ABO or D, and D variant.

4. DISCUSSION

Rational utilisation of O RBCs is essential to maintain adequate inventory of this “universal” RBCs not only for the recipients of O blood group, but also for recipients of other blood groups who in certain occasions also should receive O RBCs.

This study demonstrates that almost 39% of all transfused RBCs were group O RBCs and 10.1% of all transfused O RBCs were administered to ABO and D non-identical recipients, slightly higher than reported in the studies performed in academic and large hospitals [4,6]. Importantly, the proportion of transfused O D- RBCs were 7.3%, lower than reported by recent studies [1-3,8], even with a decreasing tendency over

the study period reaching 6.5% at the end of the study period. In this study only 9.4% group O D- RBCs were transfused to D+ recipients, which is much lower than reported in the studies performed in Canada and Australia [6,9]. Furthermore, 21.5% of O D- RBCs were transfused to non-O D- recipients, much lower than in the recent studies ranging 43.2% to even 67% [4,8-10]. All those data regarding transfusion of O D- RBCs shows how carefully and reasonable this lifesaving resources are used in UHC Zagreb.

Group O RBCs were the most commonly transfused to patients transplanted with ABO and D mismatched HSC, due to expanding HSCT program using mostly unrelated donors. In this study, 57.1% of O D+ and 46.3% of O D- RBCs were given to recipients with ABO and D mismatched allogeneic HSCT. Until the day of transplantation patients receive RBCs of their ABO and D type. After infusion of ABO and D mismatched HSCT, patients always receive RBCs that are compatible with both, recipient and donor blood groups, until complete engraftment and the change to the donor blood group is established. Our policy is to confirm the change to the donor blood group when the donor blood group is determined at two consecutive samples and after being independent of RBC transfusion for 3 months. Different policies are used to determine the establishment of donor type blood group after ABO mismatched transplantations, and our policy is among the stricter ones [11]. However, we consider such policy to be reasonable since The Handbook of European Society for Blood and Marrow Transplantation from 2018, recommends that exposure of HSCT recipients to isoagglutinins should be avoided [12]. ABO blood group antigens are expressed in many non-hematopoietic tissues which continue to express the recipients' ABO antigens also after engraftment and ABO antigens can be secreted into body fluids. Thus, ABO compatible RBCs with both

HSC donor and recipient are mandatory not only after transplantation until complete engraftment but also after complete engraftment [12].

The second most common indication for transfusion of O RBCs to ABO and D recipients is transfusion to infants up to 4 months of age, particularly for O D+ RBCs. According to international investigation on O RBCs administration performed by Zeller et al., 56% of hospitals are exclusively transfusing O RBC to neonates. According to Zeller et al., those hospitals had a higher transfusion rate of transfusing group O RBCs to non-O recipients [4]. On the other hand, this practice has many advantages: provide RBCs that are compatible with both mother and baby; limit wastage of RBCs by using aliquots of the same RBC unit for transfusion of multiple neonates; and reduces the risk of transfusing the wrong blood. The UHC Zagreb policy is to transfuse ABO and D specific RBCs to neonates and infants. However, O RBCs are transfused in circumstances like: low gestational age and weight and ABO HDFN.

In our study, shortage of ABO identical RBCs is responsible for 9.0% of O RBCs transfused to ABO and D non-identical recipients. Due to increased demand for RBCs as well as seasonal fluctuation in the blood supply, there have been recurrent shortages of RBCs, particularly D- RBCs. Although the shortage of ABO identical RBCs is sometimes unavoidable situation, there are a lot of data showing that transfusion of ABO non-identical products may lead to adverse clinical outcomes. Recent study even reported significantly increased risk of in-hospital death in a group of A patients upon receiving O RBCs without knowing the mechanism [13].

A substantial percentage of O RBCs, particularly O D- RBCs, were given to match specific phenotype in alloimmunized patients. This proportion was notably reduced over the study period, since our blood supplier Croatian Institute of

Transfusion Medicine (CITM) increased the number of available extended phenotype RBCs (Rh, Kell, Kidd, MNS) across all ABO groups.

In UHC Zagreb, the use of O RBCs in emergency situations when blood group is unknown, was found to be far less common than expected. However, urgent transfusions were the second leading indication for transfusion of O D- RBCs to ABO and D non-identical recipients. That is related with our hospital policy to issue two O D- RBCs during urgent massive transfusion if ABO and D blood group of recipients is unknown. Meanwhile, pretransfusion sample should be sent to transfusion service as soon as possible with the intention to quickly switch the patient to type-specific RBCs. On the other hand, growing practice worldwide is to initially supply adult male patients and women > 50 years of age with O D+ RBCs if ABO and D blood group is unknown, especially in trauma patients considering the low risk of adverse reactions in those patients [14,15]. In our study, 215 (64.6%) of all urgent ABO and D non-identical RBCs were transfused to adult male and female > 50 years of age and 143 (42.8%) were transfused at UHC Zagreb remote locations.

There were substantial proportion of RBCs used for ABO and D non-identical recipients because of indeterminate ABO or D at the time of transfusion, as well as because of D variant. This proportion was reduced during the study, since ABO and D genotype testing was speed up and now the results are available within 24 hours. The most prominent reason for indeterminate ABO or D was emergency situation when patients received compatible, but not identical RBCs in another hospital, before transportation to UHC Zagreb.

There were only two O D- RBC units and none of O D+ was given in order to prevent the waste. This is the result of high turnover and low RBCs inventory, since we are located only 1.5 miles away from our blood supplier and have regular delivery

few times a day and as well on urgent demand. As well, there are only 7.2% O D- RBCs out of all RBCs on stock, in order to avoid outdating. In refrigerators at remote locations, stock of O D- RBCs for emergency situations is limited to two units and once a week they are replenished with fresh ones.

This study was limited by the sample size and by the retrospective study design. However, to our knowledge this is the first large academic hospital study to separately analyse in detail indications for group O D- and O D+ RBCs transfused to ABO and D non-identical recipients.

5. CONCLUSION

These results illustrated that even a large academic hospital with a significant proportion of O RBCs transfused to ABO and D non-identical individuals can maintain acceptable proportions of transfused D+ and especially D- O RBCs. However, it is important to emphasise that transfusion service should ensure that identical ABO and D RBCs are almost always transfused. Indications for O RBCs transfusion to ABO and D non-identical individuals should be well regulated, as well as regularly reviewed and revised, since appropriate utilization of O RBC and especially O D- RBCs is important to maintain an optimal inventory of this lifesaving blood product.

Disclosure of interest:

The authors declare that they have no competing interest.

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Table 1. Distribution of transfused D+ and D- O RBCs by recipients ABO and D group

Recipients	Group O RBCs				
		D + N	%	D - N	%
Group A	D+	810	2,1	196	2,2
	D-	0	0,0	266	2,9
	D‡	0	0,0	0	0,0
Group B	D+	401	1,0	44	0,5
	D-	0	0,0	173	1,9
	D ^a	0	0,0	2	0,0
Group AB	D+	160	0,4	11	0,1
	D-	0	0,0	31	0,3
	D‡	0	0,0	11	0,1
Group O	D+	36 082	92,6	549	6,0
	D-	279	0,7	7147	78,5
	D‡	16	0,0	10	0,1
Group †	D+	1198	3,1	59	0,6
	D-	0	0,0	339	3,7
	D‡	16	0,0	271	3,0
Total		38 962	100,0	9109	100,0

† unknown ABO group, indeterminate results of ABO testing, low gestation age/weight, ABO mismatched HSCT

‡ unknown D, indeterminate results of D testing, low gestation age/weight, D mismatched HSCT

Table 2. Indications for transfusion of D+ and D - O RBCs to ABO and D non-identical recipients

Indications	Group O RBCs				Total	
	D + N	%	D - N	%		%
ABO and D mismatched allogenic HSCT	1645	57.1	909	45.9	2554	52.5
Infant (under 4 months) transfusion	743	25.8	162	8.2	905	18.6
Shortage of ABO identical RBCs	311	10.8	125	6.3	436	9.0
Phenotype-matched RBCs	79	2.7	313	15.8	392	8.1
Urgent transfusion	15	0.5	333	16.8	348	7.2
Indeterminate ABO and D group	87	3.0	59	3.0	146	3.0
D variant	0	0.0	74	3.7	74	1.5
Solid organs transplantation	0	0.0	5	0.3	5	0.1
Close to outdating RBCs	0	0.0	2	0.1	2	0.0
Total	2880	100.0	1982	100.0	4862	100.0

Figure 1. Distribution of D- and D+ O RBCs to ABO and D non-identical recipients

Figure 2. Distribution of transfused O RBCs to ABO and D non-identical recipients by different indications

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