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RED BLOOD CELLS TRANSFUSION IN GREECE: RESULTS OF A SURVEY OF RBC USE IN 2013

Serena Valsami, Elisavet Grouzi, Abraham Pouliakis, Leontini Fountoulaki-Paparisos, Elias Kyriakou, Maria Gavalaki, Elias Markopoulos, Ekaterini Kontopanou, Ioannis Tsolakis, Argyrios Tsantes, Alexandra Tsoka, Anastasia Livada, Vassiliki Rekari, Niki Vgontza, Dimitra Agoritsa, Marianna Politou, Stavros Nousis, Aspasia Argyrou, Ekaterini Manaka, Maria Baka, Maria Mouratidou, Stavroula Tsitlakidou, Konstantinos Malekas, Dimitrios Maltezos, Paraskevi Papadopoulou, Vassiliki Pournara, Ageliki Tirogala, Emmanouil Lysikatos, Sousanna Pefani, Konstantinos Stamoulis.

On behalf of the Working Committee of Transfusion Medicine & Apheresis of the Hellenic Society of Hematology

Corresponding Author:
Serena Valsami MD
Assistant Professor in Heamatology and Transfusion Medicine
National and Kapodistrian University of Athens Medical School
Blood Transfusion Department, Aretaieio Hospital
Athens Greece
Email serenavalsami@yahoo.com
Tel +306944602629
Tel/fax +302107230785

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RED BLOOD CELLS TRANSFUSION IN GREECE: RESULTS OF A SURVEY OF RBC USE IN 2013

Introduction

Greece is a member of the European Union, which has established guidelines for blood donation and inspection of blood establishments but so far no uniform rules, for treatment with blood and blood-products, have been adopted by the European Union. Accordingly, Greek authorities and blood donor associations adhere strictly to the principle of self-sufficiency, which has been laid out by the Council of Europe. The only source of blood in Greece is non remunerated blood donors. In a blood system based on voluntary donation the potential for blood shortage is an ongoing risk[1]. A number of emergency scenarios, including natural or man-made disasters, pandemic outbreak, extremes of weather, and seasonal variations of blood donations could contribute to extremely low blood inventory levels. It seems clear that the proportion of the population eligible to donate blood is likely to fall over the coming decades

while the proportion requiring these products is likely to rise. Further attention is therefore required both to manage the supply and influence the demand for existing blood and blood products.

Greece is ranked as the second highest consumer of blood components in Europe. Blood utilization in Greece exceeds 600,000 RBC units annually according to data provided by the national competent authority (Hellenic National Blood Transfusion Center). Adequate transfusion practice is essential in order to cover transfusion demands. Assessing data regarding RBC units transfused at medical institutions nationally could provide the data needed for developing plans to manage the demand and supply for blood units[2-4]. The aim of our study was to assess and evaluate the use of RBC-units in Greece in order to identify parameters that contribute to the proper RBC management, which can ensure blood sufficiency, taking into account the geographical particularities of our country, the large number of transfusion dependent thalassemia patients and the large number of car accident victims.

Material and methods

The study was conducted by the Working Committee of Transfusion Medicine&Apheresis of the Hellenic Society of Hematology. A preprinted data collection form was used and all Transfusion Services in Hospitals all over Greece were invited to participate in the study. The survey was conducted from January to December 2013. Data collection was prospective using preprinted forms that were filled monthly by the participating transfusionists. Monthly collected data included the number of RBC-units transfused, the ABO/D blood group and the patients' department who received the RBC-units. According to storage age (SA) on the day of transfusion RBC units were sorted in groups SA1:0-15 days (storage age on the day of transfusion), SA2:16-28 days and SA3:29-42 days[5,6]. Data regarding national RBC transfusion supplies were provided by the Hellenic National Blood Transfusion Center.

Data forms were manually entered onto an electronic database (Excel-2007, Microsoft/Corp, Redmond, WA) which was also used to perform part of the analysis. Additional Statistical analysis was performed using the SAS software (version 9.3 for Windows, SAS Institute Inc. NC, USA)[7,8].

Results

Transfusion Services in 23 Hospitals all over Greece accepted the invitation from the 94 Services initially invited, and were eligible and participated in the study. Twelve out of 23 Hospitals are located in Athens and the remaining 11 are General Hospitals located in cities outside Athens (Agrinio, Messologgi, Kavala, Zakynthos, Kefalonia, Livadia, Trikala, Larissa, Edessa, Xanthi, Florina) (Table1). Thirteen out of 23 hospitals (56.52%) provided data for 12 months, 9 (39.13%) for 5-8 months and one hospital (4.35%) for one month. The mean number of monthly reports from the participating Blood Banks was 9.2±3.5 and showed a declining trend during the year (20 reports were received in January 2013, while 15 reports were received in December 2013). It is worth noticing that participating hospitals were sending reports on a voluntary basis.

The total number of RBC-units evaluated was 103,702 out of 583,457 (103,702/583,457=17.77% ±0.10%, CI=95%) RBC-units transfused during the year 2013 in Greece. The number of units reported by the 12 hospitals in Athens was 76,068 (73.35%±0.29% CI=95%) while the units reported by the 11 hospitals outside Athens was 27,634 (26.65% ± 0.27% CI=95%).

More than 64% (66,293/103,702, ±0.29% CI=95%) of the total RBC units were transfused at five tertiary and general hospitals, four of which are located in Athens and account for the 55.72%±0.30% CI=95% (57,784/103,702) of the annual blood issue, and one outside Athens (University Hospital of Larissa), as shown on Table1.

The percentage of RBC units in each storage age group (SA1, SA2 and SA3) varied depending on the participating hospital (SA1: 4.94%-91.08%, SA2: 5.83%-76.01%, SA3: 0.74%-45.49%) as shown on Table2 and Figure1. The majority of RBCs were transfused in the first 15 days of storage: 64,799 (62.46%±0.29 CI=95%), 26,171 (25.24%±0.26 CI=95%) at 16 to 28 days and 12,732 (12.28%±0.20 CI=95%) at 29-42 days Table2 .

In order to investigate the different policies applied in large tertiary university hospitals located in urban centers and peripheral non university small (100-300 beds) hospitals, two groups were created: university urban hospitals (AH1, AH2 and AH4) and general peripheral hospitals (HOA2, HOA3, HOA4, HOA5, HOA6, HOA7 and HAO9). The number of units transfused in urban university hospitals group was 44,427 units and in peripheral hospitals 14,601. Interestingly university hospitals consume "fresher" blood compared to peripheral hospitals (SA1 group 78.9% vs 38.2%, $p<0.05$); and accordingly peripheral hospitals use "older" blood (SA3 group 15.8% vs 6.8%, $p<0.05$).

Regarding the total number of RBC-units transfused by hospital department the classification was as follows: Surgery-Departments: 30,421 (29.34%±0.28% CI=95%), Internal Medicine-Departments: 30,567 (29.48%±0.28% CI=95%), Oncology/Hematology-Departments: 14,159 (14.65%±0.22% CI=95%), Thalassemia-Departments: 9,195 (8.87%±0.17% CI=95%), ICU: 6,796 (6.55%±0.15% CI=95%), Nephrology-Departments: 1,850 (1.78%±0.08% CI=95%) Obstetrics/Gynaecology-Departments: 1,512 (1.46%±0.07% CI=95%), Neonatal&Pediatric-Departments: 319 (0.31%±0.03% CI=95%), Private Hospitals: 8,883 (8.57%±0.17% CI=95%) as depicted on Table2. It is worth mentioning that significant differences were observed regarding the number of RBC-units per department between participating hospitals (data not shown).

The proportion of RBCs-units transfused in Surgery Departments of urban university hospitals was greater than that of peripheral hospitals (32.7% vs 24.2%, $p<0.0001$). A similar pattern was observed in Oncology/Hematology Departments (17.6% vs 0.5%, $p<0.0001$), while in Internal Medicine Departments the percentages were 31.0% and 46.7% respectively ($p<0.0001$). Regarding thalassemia patients only 4.4% of RBCs units were transfused in urban university hospitals and 17.2% in peripheral general hospitals.

The storage age group (SA1, SA2 and SA3) of RBC-units transfused by hospital department classification was as shown on Table2 and Figure1. Neonates and thalassemia patients received "fresh" RBC-units of the SA1 group in a higher proportion than patients in the rest of the departments, specifically 84.95% and 87.31% of cases in neonates and thalassemia patients respectively received SA1 RBC-units while the percentage of the total studied population that received SA1 RBC-units was 62.49%. This difference was statistically significant both for neonates (difference:22.46%, 95%CI:17.623%-26.516%, $x^2=57.18$ $p<0.0001$), and for thalassemia patients (difference:24.82%, 95%CI:23.984%-25.632%, $x^2=1938.95$, $p<0.0001$).

The distribution of RBC-units transfused according to ABO and RhD blood group was: A: 40,461 (39.02%±0.30 CI=95%), B: 12,868 (12.41%±0.20 CI=95%), AB: 5,355 (5.16%±0.13 CI=95%), O: 45,018 (43.41%±0.30 CI=95%), D(+): 91,248

(87.99%±0.20 CI=95%), D(-): 12,454 (12.01%±0.20 CI=95%), reflecting the ABO/D distribution in the Greek population[9,10].

RBC-units per ABO/D blood group and storage age group distribution is depicted on Table3. The distribution between SA1, SA2 and SA3 storage age groups was similar for all ABO/D blood groups. In particular the transfusion practice applied to O RhD negative blood units was identical to other blood groups, as 63.2% of O RhD negative units were transfused in the first two weeks while the percentage of RBC-units of SA1 group for the rest of the RBC types was 62.4% (difference=0.76%, p=0.26).

The mean number of RBC-units transfused per month in all hospitals was 8,642 ± 604 (CI=95%). Monthly distribution of transfusions and storage age data, as depicted on Table 4, show that older blood (SA3) was issued during summer months (May, June and July), specifically 4,615 SA3 RBC-units were issued during these three months (mean=1,538.3, SD=349.3) while 8,117 SA3 RBC-units during the rest of the months (mean=901.9, SD=295.6), ($p< 0.0001$). Additionally, in terms of consumption months May, June and July presented increased requirements for transfusions (mean units/month=9,213) while for the rest of the year a mean of 8,451 units/month were used, reflecting an increment by about 9% ($p< 0.0001$).

Discussion

Effective blood management is affected not only by donor deficit but also by the complexity of managing inventories of blood products and availability within hospitals and health systems. Overuse or inappropriate use of blood products is a less-recognized problem that presents significant patient safety issues[11,12]. Assessing the RBC transfusion trends in various clinical settings especially at National level has evolved into a major tool for promotion and development of best practices for hemotherapy[2]. In this setting we conducted a benchmark study for RBC use across Greece.

The legal and regulatory framework governing the organization and functioning of Greek blood services reflects the transposition of EU dedicated directives. Attention of the decision making level focused mainly on strengthening vigilance and safety of blood supplies[13]. Blood transfusion services in Greece continue to be decentralized, are located in almost every hospital and are responsible for the whole blood transfusion chain. Blood supplies come from voluntary non-remunerated donors (51%) and replacement donors (49%). Greece has 32 blood donors/1000 inhabitants, which is close to the median range of EU average[1,14]. The total blood collection figure for 2013 was of 590,000 units and proved insufficient to cover consumption at national level, according to data provided by the Hellenic National Blood Transfusion Center. Blood insufficiency in our Country is related not only to increased demands but also to poor implementation of patients' blood management programs, and to the fact that a central inventory management (ie on line system) across the country has not been applied yet.

In our study, data from 23 blood transfusions services regarding 103,702 RBC-units transfused during the year 2013 were evaluated. The sample size was considered representative and thus the analysis lead to safe conclusions (with 95% confidence interval, margin of error=0.28%).

The number of units reported by the 12 hospitals in Athens was 2.75 times greater than the units reported by the 11 hospitals outside Athens (73.35% vs 26.65%). Interestingly, the majority of RBCs were transfused in the first 15 days of storage (62.49±0.29). In this case the use of fresh blood possibly illustrates and highiligts the problem of blood sufficiency in our country, which leads to the direct use of fresh

blood. Transfusion of blood in the first 15 days of storage (SA1) was as phenomenon more pronounced in hospitals with the highest blood consumption mainly urban university hospitals (Figure 1). These Hospitals have extended surgical departments also treating multitrauma patients as reference centers. However, according to the last census results on 2011, Athens gathers the 35% of the population of Greece[15]. This reverse percentage in relation to the population is indicative to the fact that health care services focus on the country capital. Accordingly increase consumption of "older" blood (SA3) takes place mainly in small hospitals, including countryside ones, with limited inventory, that mostly treat chronic patients. These small hospitals often use RBC-units close to expiry date, supplied from other hospitals in order to decrease in time expiry losses, according to data provided by the Hellenic National Blood Transfusion Center.

Regarding the total number of RBC-units transfused by hospital department and despite intercenter variability, reflecting the existing variability in transfusion practice in our country, the vast majority of RBC-units i.e. 75,138 units (73.47%±0.27% CI=95%) were transfused at patients in Surgery and Internal Medicine-Departments including Hematology/Oncology ones. The lack of strong evidence supporting specific transfusion practices could explain the overuse of blood products in specific patient populations[16,17]. Neonates and thalassemia patients received RBC of younger storage age group in a statistically significant higher proportion ($p<0.001$), which has been considered as good transfusion practice by several studies for both patient populations [3,18,19]. Blood consumption in multitrauma patients could not be assessed due to the establishment plan of public hospitals in Greece that does not include an independent accident and emergency (A&E) department.

The similar distribution of ABO/D blood groups between RBC units of the three storage age groups (Table 3), highlights the lack of an established policy for appropriate use of group O RhD negative RBC-units as in other developed countries. An additional explanation could also be that there has not been established yet a centralized targeted recruitment of O RhD negative universal donors. Provision of O RhD negative RBCs can be a challenge for blood services especially at times of short supply or increased demand [2,20].

According to Table4, depicting monthly distribution of transfusions and storage age data, older blood is issued during summer. May, June, July and August are the months of summer holidays in Greece, with an impact on RBC stocks due to the decline in blood donation. Consequently, the system reacts by providing stocked RBCs of higher storage age group (SA2 and SA3). In addition during summer many tourists visit Greece. The population increase along with car accidents victims resulting in higher blood transfusion demands. Thus, implementing more intensive voluntary blood donations campaigns could attribute more intensively to cover increased demands during these months, as in other developed countries[2].

Conclusions

In conclusion according to our study, and despite a high intercenter variability in RBC transfusions, surgical and internal medicine patients continue to be the most common group of patients transfused with an increasing rate for internal medicine patients. Additionally it was revealed that the majority of RBC-units were transfused within the first 15 days of storage. The applied blood transfusion trend in our country seems to follow the European practice regarding the transfusion of fresh blood in certain specific patients' populations such as neonates and multi-transfused thalassemia

patients. However the increased use of fresh blood possibly represents and reveals at the same time the problem of blood sufficiency which leads to the direct use of fresh blood due to increased demand. The conduction of a larger survey that incorporates the determinants of patient blood management the geographical particularities related to blood transport difficulties, the hospital capacity variation, the data regarding RBC-wastage and blood units supplied from other hospitals could provide more data and conclusions needed for developing and implementing integrated evidence based transfusion strategy and structure.

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Table 1: Number of RBC units transfused, percentages and confidence intervals for the participating hospitals, in declining order according to blood consumption.

Participating Hospital	RBC units transfused (N)	%	Number of beds
AH1	20,133	19.4 ± 0.2	947
AH2	14,152	13.6 ± 0.2	562
AH3	13,357	12.9 ± 0.2	615
AH4	10,142	9.8 ± 0.2	596
HOA1	8,509	8.2 ± 0.2	566
AH5	4,440	4.3 ± 0.1	346
HOA2	4,045	3.9 ± 0.1	256
AH6	3,983	3.8 ± 0.1	279
HOA3	3,682	3.6 ± 0.1	303
AH7	3,194	3.1 ± 0.1	380
AH8	3,136	3.0 ± 0.1	150
HOA4	2,268	2.2 ± 0.1	161
AH9	2,255	2.2 ± 0.1	268
AH10	2,242	2.2 ± 0.1	736
AH11	2,228	2.1 ± 0.1	106

HOA5	2,139	2.1 ± 0.1	394
HOA6	1,163	1.1 ± 0.1	136
HOA7	895	0.9 ± 0.1	155
HOA8	837	0.8 ± 0.1	98
HOA9	409	0.4 ± 0.0	120
HOA10	271	0.3 ± 0.0	89
HOA11	135	0.1 ± 0.0	85
HOA12	87	0.1 ± 0.0	102
Total	**103,702**	**100%**	**7450**

AH: Athens Hospital, HOA: Hospital Outside Athens, AH1: Evangelismos Hospital, AH2: Laikon Hospital, AH3: General Hospital "Saint Panteleimon", AH4: General Hospital "ATTIKON", HOA1: Larissa University Hospital, AH5: St. Savvas Oncology Hospital, HOA2: General Hospital of Xanthi, AH6: General Hospital Nea Ionia "Agia Olga", HOA3: General Hospital of Trikala, AH7:Thriasio Hospital, AH8: Aretaieio University Hospital, HOA4: General Hospital Edessa, AH9:"Amalia Fleming" Hospital, AH10:"Sotiria" Hospital, AH11:"Saints Anargyroi" Hospital, HOA5: General Hospital of Kavala, HOA6: General Hospital of Agrinio, HOA7: General Hospital of Messologgi, HOA8: General Hospital of Livadia, HOA9: General Hospital of Florina, HOA10: General Hospital of Zakynthos, HOA11: General Hospital of Kalymnos, HOA12: General Hospital of Kefalonia.

Table 2: Percentages, totals and confidence intervals for RBCs consumption for the different hospital departments

Hospital Department	SA1(0-15 ds)	SA2 (16-28 ds)	SA3 (29-42 ds)	N	%
Thalassemia Departments	87.3% ± 0.7	9.0% ± 0.6	3.7% ± 0.4	9,195	8.9 ± 0.2
Pediatrics- Neonates	84.5% ± 3.9	14.1% ± 3.8	0.9% ± 1.0	319	0.3 ± 0.0
Oncology / Hematology	66.9% ± 0.8	20.8% ± 0.7	12.4% ± 0.5	14,159	13.7 ± 0.2
Nephrology	62.2% ± 1.2	26.0% ± 2.0	11.8% ± 1.5	1,850	1.8 ± 0.1
Surgery	61.7% ± 0.6	26.9% ± 0.5	11.4% ± 0.4	30,421	29.3 ± 0.3
Private Hospitals	59.4% ± 1.0	20.3% ± 0.8	20.2% ± 0.8	8,883	8.6 ± 0.2
Intensive Care Unit	58.2% ± 1.2	27.3% ± 1.1	14.5% ± 0.8	6,796	6.6 ± 0.2
Internal Medicine	56.1% ± 0.6	31.1% ± 0.5	12.8% ± 0.4	30,567	29.5 ± 0.3
Gynecology / Obstetrics	47.7% ± 2.5	36.4% ± 2.4	15.9% ± 1.8	1,512	1.5 ± 0.1
TOTAL	62.5% ± 0.3	25.2% ± 0.3	12.3% ± 0.2	103,702	100.00

Table 3: Number of RBC units, percentages and confidence intervals according to ABO and RhD blood group for the three storage age groups (SA1, SA2 and SA3).

ABO/D	SA1 (0-15 ds)		SA2 (16-28 ds)		SA3 (29-42 ds)		Total	
	N	%	N	%	N	%	N	% (±CI)
A+	23,452	65.3 ± 0.5	8,757	24.4 ± 0.4	3,718	10.3±0.3	35,927	34.6 ± 0.3
A-	2,234	49.3 ± 1.5	1,323	29.2 ± 1.3	977	21.5±1.2	4,534	4.4 ± 0.1
B+	6,444	55.7 ± 0.9	3,257	28.2 ± 0.8	1,867	16.1±0.7	11,568	11.2 ± 0.2
B-	584	44.9 ± 2.7	368	28.3 ± 2.5	348	26.8±2.4	1,300	1.3 ± 0.1
AB+	2,411	55.2 ± 1.5	1,070	24.5 ± 1.3	883	20.2±1.2	4,364	4.2 ± 0.1
AB-	662	66.8 ± 2.9	221	22.3 ± 2.6	108	10.9±1.9	991	1.0 ± 0.1
O+	25,454	64.6 ± 0.5	9,901	25.1 ± 0.4	4,034	10.2±0.3	39,389	38.0 ± 0.3
O-	3,558	63.2 ± 1.3	1,274	22.6 ± 1.1	797	14.2±0.9	5,629	5.4 ± 0.1
Total	**64,799**	**62.5 ± 0.3**	**26,171**	**25.2 ± 0.3**	**12,732**	**12.3±0.2**	**103,702**	**100.0**

Table 4: RBC units transfused, percentages and confidence intervals for each month during the study and the storage age groups (SA1, SA2 and SA3).

Month	**SA1** (0-15 ds)	**SA2** (16-28 ds)	**SA3** (29-42 ds)	N	%
January	68.9% ± 0.1	19.9% ± 0.7	11.2% ± 0.7	8,224	7.9% ± 0.2
February	73.6% ± 1.0	20.9% ± 0.9	5.5% ± 0.5	8,317	8.0% ± 0.2
March	62.0% ± 1.0	25.5% ± 0.9	12.6% ± 0.7	8,499	8.2% ± 0.2
April	58.5% ± 1.1	26.9% ± 1.0	14.6% ± 0.8	8,108	7.8% ± 0.2
May	54.2% ± 1.0	27.7% ± 0.9	18.1% ± 0.8	9,011	8.7% ± 0.2
June	58.2% ± 1.0	29.9% ± 0.9	12.0% ± 0.7	9,618	9.3% ± 0.2
July	44.3% ± 1.0	35.4% ± 1.0	20.3% ± 0.8	9,011	8.7% ± 0.2
August	61.7% ± 1.1	26.1% ± 1.0	12.2% ± 0.7	7,874	7.6% ± 0.2
September	78.7% ± 0.9	15.7% ± 0.8	5.6% ± 0.5	7,847	7.6% ± 0.2
October	71.2% ± 0.9	21.0% ± 0.8	7.8% ± 0.5	9,610	9.3% ± 0.2
November	64.1% ± 1.0	23.7% ± 0.9	12.2% ± 0.7	8,807	8.5% ± 0.2
December	57.1% ± 1.0	28.6% ± 0.0	14.3% ± 0.7	8,776	8.5% ± 0.1

Total	62.5% ± 0.29	25.2% ± 0.3	12.3% ± 0.2	103,702	100%

Percentages of RBCs consumption for the three storage age groups (SA1: 0-15 days, SA2: 16-28
days and SA3: 29-42 days) for the participating hospitals
Abbreviations: AH: Athens Hospital, HOA: Hospital Outside Athens, AH1: Evangelismos Hospital, AH2:
Laikon Hospital, AH3:General Hospital "Saint Panteleimon", AH4: General Hospital "ATTIKON", HOA1:
Larissa University Hospital, AH5: St. Savvas Oncology Hospital, HOA2: General Hospital of Xanthi, AH6:
General Hospital Nea Ionia "Agia Olga", HOA3: General Hospital of Trikala, AH7: Thriasio Hospital, AH8:
Aretaeio University Hospital, HOA4: General Hospital Edessa, AH9: "Amalia Fleming" Hospital,
AH10:"Sotiria" Hospital, AH11:"Saints Anargyroi" Hospital, HOA5: General Hospital of Kavala, HOA6:
General Hospital of Agrinio, HOA7: General Hospital of Messologgi, HOA8: General Hospital of Livadia,
HOA9: General Hospital of Florina, HOA10: General Hospital of Zakynthos, HOA11: General Hospital of
Kalymnos, HOA12: General Hospital of Kefalonia.