ABO and RhD matching in platelet transfusions: Real-world data

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Abstract. ABO and Rhesus D (RhD) matching in platelet transfusions varies widely worldwide, since it does not preclude good clinical responses. However, it has been shown that ABO and RhD matching selection for platelet transfusions raises efficacy and safety concerns. The present study aimed to assess and evaluate ABO and RhD matching in platelet transfusions. The present study was part of a national survey that evaluated the platelet units, and ABO and RhD blood group of patients, along with the number of platelet units produced and transfused from May to June, 2015. A total of 13,250 [12,061 random donor platelets (RDPs) and 1,189 single donor platelets (SDPs)] were evaluated. ABO identical platelets were transfused in 58.99±0.88% RDPs and 45.75±2.87% SDPs. ABO major incompatible platelets (with antigen incompatibility) were transfused in 15.92±0.66% RDPs and 24.05±2.47% SDPs. ABO minor incompatible platelets (with plasma incompatibility) were transfused in 19.70±0.71% and 22.96±2.43% RDPs and SDPs, respectively, while a combination of ABO major and minor incompatible platelets (combination of plasma and antigen incompatibility) in 5.38±0.41% and 7.23±1.51%, RDPs and SDPs respectively. A total of 6.69 and 12.29% of RhD-positive RDPs and SDPs were transfused in RhD-negative patients (both P<0.001). On the whole, the analysis of real-world data indicates variations in platelet ABO and RhD matching. Further studies are required to elucidate the real impact in the management of patients, while the upcoming centralization of blood services may also be a decisive step in this direction.

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Introduction

Platelet transfusions are currently performed worldwide mainly for the treatment of hypoproliferative thrombocytopenia. Since the early years of platelet transfusions, it has been shown that platelet ABO and Rhesus D (RhD) incompatibility does not preclude good clinical responses. However, platelet transfusions non-identical to ABO and RhD have been found to be associated with lower platelet counts increments following transfusion, as well as with adverse reactions such as hemolytic transfusion reactions and alloimmunization. Hence, despite the long-term application of platelet transfusions, there is still a lack of consensus guidelines, as well as a lack of specific recommendations on ABO and RhD matching (1-4).

A key factor, which also affects platelet transfusion practice regarding ABO and RhD matching, is their short self-life which is up to 5 days, and the resulting limited stock of this blood product, particularly in the absence of central inventory management. The need to ensure adequate platelet supply, along with the lack of strict transfusion guidelines as mentioned above, explains the wide variability in practices associated with the transfusion of ABO and RhD mismatched platelets by transfusion centers worldwide (2,5).

The present study was conducted to assess, elucidate and evaluate ABO and RhD matching in platelet transfusions in Greece, given the upcoming centralization of blood services.

Materials and methods

Data collection. The present study was carried out from May to June, 2015 by the Working Committee of Transfusion Medicine and Apheresis of the Hellenic Society of Hematology, as part of a national survey. An electronic data collection form (Excel 2016, Microsoft/Corp, WA, USA) was used, and all transfusion services in Greece were invited to participate in the study. Data collection was conducted using the aforementioned data forms that were filled by the participating centers (6). The study was approved by the Medical Ethics Committee of Aretaieion Hospital, National and Kapodistrian University of Athens (Athens, Greece). Informed consent was obtained from all patients prior to ef8nrolment.

Table I. Platelet transfusion according to Rhesus D (RhD) type.

	Patient's RhD type				
Platelet donor (unit)	RDPs			SDPs	
RhD type	RhD (-) (%)	RhD (+) (%)	Total (%)	RhD (-) (%)	RhD (+) (%)
RhD (-)	158 (13.52)	1,011 (86.48)	1,169 (100)	30 (26.09)	85 (73.91)
RhD (+)	729 (6.69)	10,163 (93.31)	10,892 (100)	132 (12.29)	942 (87.71)
Total	887 (7.35)	11,174 (92.65)	12,061 (100)	162 (87.71)	1,027 (86.38)

RhD incompatibility occurs in cases of different RhD type between the platelet donor (platelet unit) and the patient (platelet recipient). Only transfusion cases of platelets from RhD-positive donors to RhD-negative patients pose the risk of RhD alloimmunization in the recipient. The percentage of RhD-negative patients receiving RhD-positive platelets at least once was 82.19% (729/887) for RDPs and 81.48% (132/162) for SDPs. RDPs: random donor platelets; SDPs, single donor platelets.

The data collected comprised the number of platelet units produced, transfused and the platelet units and ABO/D blood group of the patients. Platelet units consisted of random donor platelets (RDPs), each of which was derived from a single whole blood donation prepared from platelet-rich plasma and of single-donor platelets (SDPs), that were prepared by apheresis.

Statistical analysis. Statistical analysis was performed using the Excel electronic spreadsheet data forms and using SAS software version 9.3 for Windows (SAS Institute Inc.). For descriptive statistics arithmetic data are presented as the mean value and standard deviation (SD), while the categorical data are presented the frequency of occurrence and the relevant percentage. The confidence interval of the various calculated proportions was based on normal approximation and the χ^2 test statistical test was applied for the comparisons of the percentages between groups. All tests were two-sided. A P-value <0.05 was considered to indicate a statistically significant difference.

Results

From the 97 transfusion services located all over Greece that had been invited to join the study, 21 (21.6%) participated in the study. The total number of platelet units evaluated was 13,250; 12,061 RDPs and 1,189 SDPs.

Platelet transfusions by platelet product ABO blood group and patient ABO group are shown in (Fig. 1) ABO identical platelet transfusion was recorded in 58.99±0.88% of the cases for RDPs and in 45.75±2.87% for SDPs. Transfusion of platelets with major ABO incompatibility was recorded in 15.92±0.66% of the cases for RDPs and in 24.05±2.47% for SDPs. The transfusion of platelets with minor ABO incompatibility was reported in 19.70±0.71% of the cases for RDPs and in 22.96±2.43% for SDPs. However, a combination of major and minor ABO incompatibility occurred in 5.38±0.41% and 7.23±1.51% of the cases for RDPs and SDPs, respectively (Fig. 1).

As regards RhD, as shown in Table I, 729/10,892 (6.69%) RhD-positive RDPs were transfused in RhD-negative patients and accordingly, 132/1,074 (12.29%) RhD-positive SDPs were transfused in RhD-negative patients (both P<0.001). The percentage of RhD-negative patients receiving at least one RhD-positive platelet transfusion was 82.19% (729/887) for RDPs and 81.48% (132/162) for SDPs.

Discussion

The transfusion of platelets with major ABO incompatibility in the present study was 16% for RDPs and 24% for SDPs, which is lower than the 32.4% and the 21% previously reported for SDPs (5,7). The transfusion of platelets with minor ABO incompatibility (incompatible plasma) was 20 and 23% for RDPs and SDPs, respectively, in the present study, which is consistent with the percentage estimated in the USA (10-40%), but higher than the 12.6% reported by Dunbar *et al* (5) and the 15% reported by Adamidou *et al* (7). No acute hemolytic transfusion reactions related to platelet transfusion was recorded by the Greek Hemovigilance Scheme in 2015 (8). However, the fact that hemolytic transfusion reactions due to plasma incompatible platelet transfusions are under-reported, cannot be overlooked (9,10). A s

The rather high rate of ABO non-identical platelet transfusion recorded in the present study mas be attributed to the lack of central inventory management. The geographical particularities of Greece may hinder adequate platelet supply in some cases. In addition, a number of transfusion services issue platelets for transfusion mainly, according to the first in/first out strategy to conserve resources and reduce wastage (1,11).

In the present study, ABO non-identical platelet transfusion was more prominent in apheresis platelets and this may also be attributed to the fact that SDPs are mainly provided from non-remunerated replacement donors recruited from the family and social environment of each patient. It is evident that it is not always feasible to exchange or replace such donations according to ABO in the absence of central inventory management (1,5,6).

The ABO and RhD distribution of platelets units transfused depicted in Fig. 1, reflects the ABO and RhD distribution in the Greek population (12). Additionally, it reveals the lack of an established policy to encourage A group apheresis platelet

Platelet donor (unit) ABO blood group	RDPs					SDP apheresis				
	Patient ABO blood group									
	O	A	B	AB	Total	O	A	B	AB	Total
O	3,343 (65.25%)	1,351 (26.37%)	270 (5.27%)	159 (21.66%)	5,123 (42.47%)	280 (54.90%)	152 (29.8%)	52 (10.20%)	26 (5.10%)	510 (42.89%)
A	1,074 (22.08%)	3,147 (69.69%)	209 (4.29%)	435 (25.24%)	4,865 (40.34%)	160 (34.26%)	223 (47.75%)	52 (11.13%)	32 (6.85%)	467 (39.28%)
B	383 (26.12%)	440 (29.99%)	483 (32.92%)	161 (26.11%)	1,467 (12.17%)	64 (45.39%)	34 (24.11%)	32 (22.7%)	11 (7.80%)	141 (11.86%)
AB	157 (25.91%)	213 (35.15%)	94 (15.51%)	142 (65.25%)	606 (5.02%)	28 (39.44%)	21 (29.58%)	13 (18.31%)	9 (12.68%)	71 (5.97%)

Figure 1. Transfusion of platelets according to the ABO blood group may be ABO-identical (green boxes), major ABO-incompatible-antigen incompatible (orange boxes), minor ABO-incompatible-plasma incompatible (blue boxes), or both major and minor incompatible (yellow boxes). In major ABO-incompatibility, donor ABO antigens are incompatible with recipient ABO antibodies (e.g., transfusion of group A platelets to a group O recipient). In minor ABO-incompatibility, donor ABO antibodies are incompatible with recipient ABO antigens. (e.g., transfusion of group O platelets to a group A recipient). In combined major and minor ABO-incompatibility, both donor ABO antigens are incompatible with recipient ABO antibodies and donor ABO antibodies are incompatible with recipient ABO antigens (e.g., transfusion of group A platelets to a group B recipient). RDPs, random donor platelets; SDPs, single donor platelets.

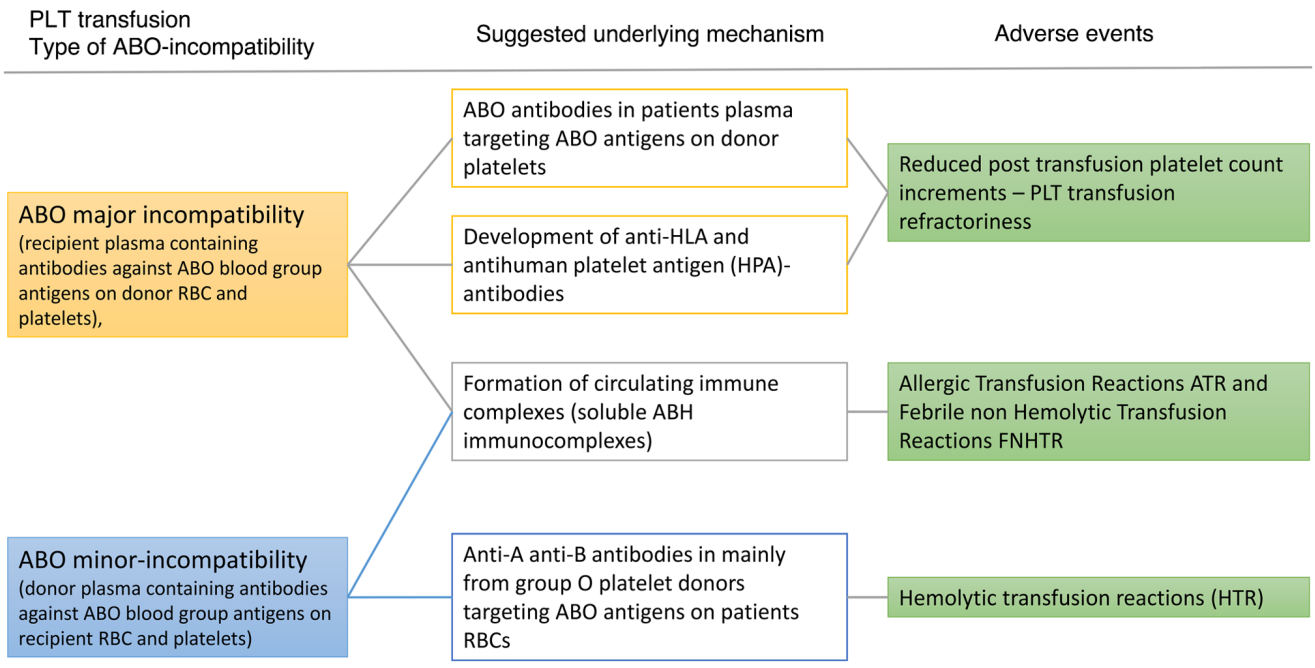

Figure 2. Platelet transfusions, proposed mechanisms of ABO incompatibility, adverse events and suggested underlying mechanisms. PLT, platelet; RBC, red blood cell.

donors, ideally A2, that have a weaker A antigen expression on platelets and lower anti-B titers, instead of O group donors, as in other developed countries (5,11,13).

As regards RhD in the present study, 86.48 and 73.91% of RhD-negative patients received at least one unit of RhD-positive RDP or SDP, respectively, which is similar to the 83% reported by Dunbar *et al* (5), but slightly higher than the 60.6% recently reported by Gottschall *et al* (14). High immunogenic RhD antigen, although it is not expressed on platelets, RhD group status is labeled on platelet bags, as residual RBCs and microparticles can cause alloimmunization in RhD-negative patients after being exposed to as little as 0.5 ml of RhD-positive RBCs contaminating platelets (15,16). Whole blood derived RDPs (a dose) and pooled platelets have up to 0.3 ml of contaminating RBCs, while SDPs apheresis platelets have <0.001 ml (17). Thus, the risk of alloimmunization appears to be higher for whole blood derived RDPs than for SDPs produced by apheresis (18). In cancer patients however, older studies have indicated a rate of anti-D alloimmunization greater than 7% (19-21), although current studies suggest a much lower alloimmunization rate of ~1% (10,15,22). Nevertheless, anti-D alloimmunization is still particularly important for RhD-negative girls or women of child-bearing potential, due to the risk of hemolytic disease of the fetus and newborn. Immunoprophylaxis with RhIG should be given in the case of an inevitable RhD-positive platelet transfusion in this population. A standard 300 μg dose provides prophylaxis for multiple transfusions of RhD-positive platelets over a 2-4-week period in RhD-negative individuals (23,24).

The present study represents a national survey regarding ABO and RhD matching in platelet transfusion that assessed 13,250 platelet units transfused. A limitation concerns the lack of pre-transfusion and post-transfusion platelet count to assess the impact of ABO major incompatibility, and the lack of the rate of anti-D alloimmunization due to platelet transfusion of RhD-positive platelet products to RhD-negative patients. A summary of the proposed mechanisms of ABO incompatibility, adverse events and suggested underlying mechanisms is illustrated in Fig. 2.

In conclusion according to the real-world data presented herein, ABO and RhD matching in platelet transfusion practice varies in Greece, as also demonstrated by other researchers (14,25), highlighting the necessity for further studies to clarify the real impact of platelet ABO compatibility in the management and outcomes of patients. Thus, the implementation of specific strategies, such as screening group O platelet donors for high titer ABO antibodies, and new initiatives may further improve the platelet transfusion practice.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

SV conceived, designed and supervised the study, and wrote the manuscript. AA performed the data entry and evaluation, and wrote the manuscript. GD analyzed the data, was involved in the conception of the study and wrote a draft of the manuscript, MG and EG contributed to study design and analyzed the data in the study. AP performed the whole statistical analysis. SV and EG confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by the Medical Ethics Committee of Aretaieion Hospital, National and Kapodistrian University of Athens (Athens, Greece). All procedures were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the1964 Declaration of Helsinki, and later versions. Informed consent was obtained from all patients.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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