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Review article

Red blood cell alloimmunisation after platelet transfusion (excluding ABO blood group system)

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ABSTRACT

Red blood cell alloimmunisation after transfusion of red blood cell concentrates carries a risk for every recipient. This risk is particularly high for patients with conditions such as sickle cell disease. However, red blood cell alloimmunisation can also occur after platelet concentrate transfusion. All blood group systems other than ABO are affected, and there are several mechanisms responsible for this alloimmunisation. The practical implications of this are a need to match red blood cell concentrates in all alloimmunised patients and, in pregnant women, recongnition of the risk of developing haemolytic disease of the foetus and newborn. Several measures can be taken to prevent alloimmunisation: in the case of the D antigen, for example, anti-RhD immunoglobulins can be infused before transfusing platelet concentrates from an RhD-positive donor in a RhD-negative recipient.

1. Introduction

Red blood cell (RBC) alloimmunisation is a risk to recipients following the transfusion of cellular blood components. In 1996, Redman et al. [1] observed 38 (8.4%) primary RBC alloimmunisation cases with definite specificity out of 452 patients undergoing elective surgery and transfused with RBC units. Nevertheless, the rate of primary RBC alloimmunisation was linked to the alloimmunisation prevention policy implemented in different regions and the group of patients concerned. More recently, in 2018, Karafin et al. [2] detected 6597 patients (2.07%) with clinically significant RBC alloantibodies out of 319,177 patients screened for RBC antibodies. The rate of RBC alloimmunisation is higher in patients with sickle cell disease – between 30 and 50% – and these alloantibodies may cause severe complications like delayed haemolytic transfusion reactions [3,4]. Furthermore, in all recipients, it is estimated that only 30% of induced RBC antibodies are detected [4]. RBC alloantibodies may be acquired after transfusion of RBC concentrates and are a risk for all recipients. In alloimmunised patients, it is necessary to select matched RBC concentrates to avoid haemolytic reactions. In some cases, compatible RBC concentrates can be difficult to obtain. Furthermore, in RBC-alloimmunised pregnant women, haemolytic disease of the foetus and newborn (HDFN) can occur if these RBC alloantibodies are directed against RBC paternal antigens. More rarely, RBC alloantibodies can be detected after transfusion of platelet concentrates (PC), with the same consequences for patients (haemolysis reaction) and pregnant women (HDFN): however, the mechanisms of RBC alloimmunisation after PC transfusion are unique.

2. Blood group system antigens on the platelet membrane

The A and B antigens of the ABO blood group system are present on platelets [5] at a lower molecular density than on RBCs [6]. The presence of other blood group system antigens has also been investigated elsewhere. Ashhurst et al. [5] did not detect Rh (D, C, E and e) antigens on the platelet membrane using mixed erythrocyte platelet agglutination. With mixed packed leucocyte/platelet preparations and an indirect anti-globulin test, Marsh et al. [7] did not find Jk^a or Jk^b antigens on platelets. Similarly, antigens of the MNSs blood group system (M, N, S, s and U) were not observed on platelets by Marsh et al. [8]. Furthermore, using a more sensitive radioimmunoassay method, Dunstan et al. [9] did not detect Rh (D, C, E, c and e), Kell (K, k), Duffy (Fy^a, Fy^b), Kidd (Jk^a, Jk^b) or Lu^b antigens on human platelets.

For the vast majority of blood group systems that can induce anti-RBC alloimmunisation after RBC transfusions, the major specific antigens involved are not observed on the platelet membrane:

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RBC alloimmunisation acquired by the recipient after platelet transfusion cannot therefore be attributed to the platelets themselves.

3. Red blood cell alloimmunisation after platelet transfusion

3.1. D alloimmunisation

D alloimmunisation in RhD-negative patients receiving PCs from RhD-positive donors was not detected in several studies, and was found at varying rates in the others.

In a study that analysed the clinical histories of 30 RhD-negative oncology patients treated by chemotherapy and transfused with 1350 platelet units, including 1066 units from RhD-positive donors, Lichtiger et al. [10] did not find any cases of D alloimmunisation, despite the absence of treatment with anti-RhD immunoglobulins. O'Brien et al. [11] retrospectively selected and analysed 130 RhD-negative patients out of 626 who received leukoreduced apheresis PCs from RhD-positive donors between 1st January 1997 and 31st December 2011 in a single hospital. These patients had no D alloimmunisation at the time of the PC transfusion, did not receive anti-RhD immunoglobulins and had one RBC antibody screen at least four weeks after the PCs from RhD-positive donors transfusion. Fifty-six (43.0%) were immunosuppressed. All 130 patients received 565 PCs from RhD-positive donors and 52.0% of them were transfused with more than one PC from RhD-positive donors. No D alloimmunisation was observed in these patients. In a prospective study, conducted between 16 October 2012 and 16 April 2014, 79 RhD-negative recipients transfused with at least one apheresis PC from RhD-positive donors were selected and analysed [12]. No anti-RhD immunoglobulins were given to these patients. They received a mean of 4.65 apheresis PCs from RhD-positive donors. D alloimmunisation was not detected in either in the 34 recipients in whom the last RBC antibody screening was performed less than 28 days after the first PC from RhD-positive donor transfusion or in the 45 recipients (57.0%) in whom RBC antibody screening was performed at a later date.

As regards paediatrics, Molnar et al. [13] studied 35 RhD-negative paediatric patients who had not received a bone marrow transplant and seven who had received a bone marrow transplant from January 1999 to June 2000 in a single hospital. All PCs were apheresis PCs and leukoreduced. No immune prophylaxis with anti-RhD immunoglobulins was performed. The first group received 490 RhD-incompatible PCs and the second received 255. All but one of the patients received RhD-incompatible PCs on more than one occasion. Exposure to RhD-incompatible PCs was high: 63% of patients were exposed six or more times. More than 60% of the non-transplanted patients were screened for RBC antibodies for more than 90 days: no D alloimmunisation was observed in these patients.

Baldwin et al. [14] studied 73 RhD-negative oncology patients who were treated with chemotherapy and received RhD-positive RBCs after platelet and white blood cell transfusions. Nine patients (12.3%) acquired D alloantibodies. Development of D alloimmunisation was observed between 16 and 390 days after contact with 2.6 – 481.2 mL of RhD-positive RBCs. In an earlier study, Goldfinger and McGinniss [15] observed that the rate of D alloimmunisation was 7.8% among 102 RhD-negative patients transfused with platelets from RhD-positive donors. In autologous bone marrow transplant recipients, McLeod et al. [16] detected three women (18.8%), out of 16 RhD-negative recipients, who developed D alloimmunisation at 13, 24 and 83 days after their first PC transfusion from an RhD-positive donor. Two of these three women had a history of pregnancy, and prior sensitisation due to pregnancy could not be ruled out.

During a ten-year follow-up study, Cid et al. [17] analysed 1014 RhD-negative patients who were transfused with 5128 PCs from RhD-positive donors. These PCs were collected from apheresis or from whole blood and eighty-nine percent were pooled PCs. No prevention of D alloimmunisation using anti-RhD immunoglobulins in RhD-negative recipients of PCs from RhD-positive donors was performed. A blood sample to test RBC antibodies was available after the transfusion of the first PC from RhD-positive donor for 867 of the recipients. Blood samples of 315 patients taken four or more weeks after the first PC transfusion from RhD-positive donor (median follow-up of 29 weeks), were also analysed. D antibodies were detected in 12 (3.8%) of these patients. Ten patients were immunosuppressed and two were immunocompetent. In the ADAPT study, a multi-centre study conducted over three years (2010–2012), Cid et al. [18] confirmed these data by observing a low rate of D alloimmunisation. Primary D alloimmunisation, beyond 28 days was detected in just seven (1.44%) of 485 RhD-negative recipients transfused with PCs from RhD-positive donors. In the French haemovigilance system, RBC alloimmunisation is classed as an adverse transfusion reaction. A retrospective study revealed that 48 cases of RBC alloimmunisation were reported after PC transfusion, between 1st January 2007 and 31st December 2011 [19]. Fifteen cases of D alloimmunisation alone were reported, one of which was associated with E antibodies. A recent study by Villalba et al. [20] conducted in RhD-negative women under 55 years of age with acute leukaemia observed few cases of D alloimmunisation after transfusion of PCs from RhD-positive donors. Over an 18-year period (January 1998–October 2016), 56 out of 382 women under 55 years of age with acute leukaemia were RhD-negative 48 of whom (85.7%) received transfusions of PCs from RhD-positive donors. Two cases of D alloimmunisation were detected. The first case was observed in a 36-year-old patient with M3 acute promyelocytic leukaemia who became D alloimmunised two months later after transfusion of 9 PCs from RhD-positive donors. The second case was reported in a 52-year-old patient with secondary acute myeloblastic leukaemia who had previously received 25 PCs from RhD-positive donors and was D alloimmunised less than 7 days after the last PC from an RhD-positive donor was transfused.

Several discrepancies can be observed between the studies in the literature in terms of the development of D alloimmunisation after transfusion of PCs from RhD-positive donors in RhD-negative recipients. Firstly, D alloimmunisation was not systematically acquired by RhD-negative patients after receiving PCs from RhD-positive donors, including those who were not administred with anti-RhD immunoglobulins to prevent D alloimmunisation. Secondly, the rate of D alloimmunisation was higher in the older studies than in the most recent studies: 7.8% [15], 12.3% [14] and 18.8% [16] pre-1991 versus 3.8% [17], 1.44% [18] and 4.2% [20] post-2010 (Table 1). In the older studies, the numbers of patients included were lower and the studies were limited to a single patient group (oncology). In two studies [17,18], the numbers of patients included were higher but the pathologies were mixed (i.e. not just oncology) (Table 1). One study [19] was based on the reporting of the post-transfusion RBC alloimmunisation and this was a limitation of this study. Thirdly, in RhD-negative immunosuppressed patients treated with chemotherapy and transfused with platelets from RhD-positive donors, D alloimmunisation was both present [14] and absent [10]. Several hypotheses could explain these discrepancies including presence of a secondary immune response in patients when RBC antibodies were detected shortly after the incompatible PC transfusion (immunisation due to prior transfusions or pregnancies), exposure to numerous incompatible PCs and individual factors like responders and non-responders. In their study, Baldwin et al. [14] did not find a correlation between D alloimmunisation and HLA immunisation in 73 RhD-negative oncology patients transfused with RhD-positive blood components.

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Table 1
D alloimmunisation in RhD-negative recipients transfused with platelet concentrates from RhD-positive donors.

Study (Year)	Number of patients	Pathology	Percentage of D alloimmunisation
Godfinger and Mc Guinniss (1971)	102	Immunosuppressive treatment (except one patient)	7.8
Baldwin et al. (1988)	73	Oncology chemotherapy	12.3
Mc Leod et al. (1990)	16	Malignant disease treatment prior transplantation	18.8
Cid et al. (2011)	315[a]	Mixed immunosuppressed or immunocompetent	3.8
Cid et al. (2015)	485[b]	Mixed haematological oncological other diseases	1.4
Villalba et al. (2018)	48	Acute leukemia	4.2

[a] 315 recipients out of 1014 with a blood sample for RBC antibodies testing four or more weeks after transfusion of the first platelet concentrate from an RhD-positive donor (primary immune response).
[b] Range of the serological follow-up: 28–2111 days (a primary anti-D response was based on the detection of D alloimmunisation 28 days or more after transfusion of the first platelet concentrate from an RhD-positive donor).

Fourthly, there was variation across the studies in length of monitoring after the RhD-incompatible PCs, number and frequency of RBC antibody screening tests and study population.

3.2. Other forms of RBC alloimmunisation

Recipients transfused with PCs can acquire RBC antibodies against RBC antigens other than D in both the Rh and other blood group systems. In their study of 1014 recipients, Cid et al. [17] detected 78 patients (7.7%) with new RBC antibodies, including 49 (4.8%) with anti-D alloimmunisation and 29 (2.9%) who acquired non-RhD antibodies. In the ADAPT study, 21 recipients acquired RBC antibodies [18]. Eleven patients (52.4%) developed an anti-D alloimmunisation and ten (47.6%) patients had RBC antibodies other than anti-D: four anti-Jk^a, two anti-E, one anti-K, one anti-Fy^a and two warm autoantibodies. Reckhaus et al. [21] identified 13 acquired Rh antibodies in 11 recipients, including four anti-E, two anti-c and one anti-f after transfusion of incompatible PCs. Nevertheless, D antibodies remained the most frequent, with 6 cases (54.5%). Lastly, out of 45 RBC alloimmunisation cases in recipients following PC transfusion where only one specificity was reported in a regional haemovigilance area, non-RhD alloimmunisation was notified in 30 cases (66.7%) and anti-D alloimmunisation in only 15 cases. Anti-E was frequently observed (20 cases) [19]. Other specificities were reported, including anti-C (one case), anti-c (two cases), anti-e (one case) anti-K (two cases) and anti-Fy^a (two cases).

RBC antibodies with non-RhD specificities are detected in recipients after PC transfusion, but at highly variable frequencies, with non-RhD alloimmunisation seemingly less frequent than anti-D alloimmunisation. Nevertheless, studies with larger cohorts are needed in order to determine more precisely the prevalence of non-RhD alloimmunisation in recipients of PCs. In these studies, the number of screenings and the delay between RhD-incompatible PC transfusion and the first RBC antibody screening are important factors in detecting RBC antibodies. Cid et al. [17] observed that out of 49 recipients who developed anti-D antibodies, these antibodies were acquired within 0–3 weeks after the first PCs from RhD-positive donors were transfused in 37 recipients, and within four or more weeks in a further 12 recipients. D alloimmunisation was a primary immune response in these 12 recipients.

4. Mechanisms of RBC alloimmunisation

Several mechanisms may be involved in RBC alloimmunisation after PC transfusion, including residual RBCs in PCs and microvesicles or microparticles. This RBC alloimmunisation can be a primary form of alloimmunisation. However, secondary alloimmunisation can also be observed in a recipient with a history of RBC alloimmunisation due to transfusion or pregnancy.

4.1. Residual RBCs in PCs

During the manufacturing process, residual RBCs remain in the PCs and the estimated number or volume of these RBCs varies. In fact, the studies highlight differences between apheresis PCs and pooled PCs.

Residual RBCs were higher in volume and number in pooled PCs than in apheresis PCs. Cid et al. [17] observed that the mean volume of residual RBCs was 0.036 mL in pooled PCs versus 0.00043 mL in apheresis PCs. In 20 apheresis PCs, Molnar et al. [13] obtained a mean of 1.7×10^6 RBCs per unit, corresponding to approximately 0.00017 mL of RBCs per unit. With flow cytometry, Santana et al. [22] observed a median of 17.4×10^3 residual RBC/L in apheresis PCs. More recently, Reckhaus et al. [21] observed a higher number of residual RBCs in pooled PCs (0.304×10^9 RBC/L) than in apheresis PCs (0.014×10^9 RBC/L).

Pooled PCs contain more residual RBCs than apheresis PCs. In 35 RhD-negative paediatric patients transfused with D-incompatible apheresis PCs, no D alloimmunisation was detected [13]. The same result was obtained by O'Brien et al. [11]. Nevertheless, RBC alloimmunisation after apheresis PC transfusion has been reported [19].

4.2. Microvesicles or microparticles

RBC membrane lesions have been known to appear during storage, with the production of extracellular vesicles, also known as microparticles [23]. Several factors are involved in this phenomenon, including blood-component preparation methods, storage solutions and inter-donor variation [24]. The presence of both D antigen and other antigens from several blood group systems on microvesicles has been established [25,26].

Kitazawa et al. [27] analysed residual RBCs and RBC-derived microparticles in apheresis PCs prepared with devices from two different manufacturers. With the first device, means of 7.5×10^6 residual RBCs per unit and 210.7×10^6 RBC-derived microparticles per unit were obtained in apheresis PCs. Means of 5.2×10^6 residual RBCs per unit and 232.3×10^6 RBC-derived microparticles per unit were obtained with the second device. In spite of the lower volume of an RBC-derived microparticle, the number of microparticles detected in the apheresis PCs was higher than the number

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of residual RBCs. For apheresis PCs, the mean volume of residual RBCs was estimated at 0.4–0.8 μL and the mean volume of RBC-derived microparticles 0.8–1 μL. RBC-derived microparticles may be more immunogenic than residual RBCs because they are more easily phagocytosed. The volume of residual RBCs was less than the volume that induced RhD-alloimmunisation (30–50 μL). Nevertheless, the involvement of RBC-derived microparticles in alloimmunisation against other RBC antigens could not be totally ruled out.

Thibault et al. [28] had studied RhD determinants on residual RBCs in apheresis and pooled PCs. Using flow cytometry, they had confirmed that the residual RBC count was higher in pooled PCs (121×10^6 per unit) than in apheresis PCs (29×10^6 per unit). They also analysed RBC-derived particles and observed that the total burden of these particles was similar in both products. Nevertheless, the average size of the RBC-derived particles is smaller in apheresis PCs (1.7 μm versus 3.1 μm in pooled PCs). Expression of RhD antigen was different between the residual RBCs and RBC-derived particles in each type of PCs and between the two types of PCs. On residual RBCs, the level of RhD antigen per cell was higher in apheresis PCs than in pooled PCs (15,319 versus 3721) as did the density of this antigen ($125/\mu m^2$ versus $34/\mu m^2$). On RBC-derived particles, the level and density of RhD antigen were also higher in apheresis PCs. In pooled and apheresis PCs, RBC-derived particles contributed to 66% and 75% of the total RhD antigenic load respectively.

Both the presence of residual RBCs and RBC-derived microparticles in PCs and their impact on both D alloimmunisation in RhD-negative recipients transfused with PCs from RhD-positive donors without infusion of RhD immunoglobulins and non-RhD alloimmunisation warrant further investigation. In practice, simultaneous analysis of residual RBCs and RBC-derived micropaticles can be performed in PCs as demontrated by Thibault et al. [28]. These two parameters could also be introduced as quality control steps.

4.3. Other factors

4.3.1. Immunosuppression

Results for D alloimmunisation vary across number of studies. In a study with immunosuppressed patients [10], no D alloimmunisation was detected after transfusion of platelets from RhD-positive donors. In a separate study, however, D alloimmunisation was observed after transfusion of PC from RhD-positive donors in RhD-negative oncology patients treated with chemotherapy [14]. Overall, the presence of immunosuppression in a patient did not protect against D alloimmunisation.

4.3.2. Inflammation

The production of new RBC alloantibodies after transfusion can be enhanced by inflammation present in the recipient. Several studies have established that patients with inflammatory diseases are at risk of RBC alloimmunisation. In patients with sickle cell disease, RBC alloimmunisation was higher than in the general population [3], and pro-inflammatory events such as acute chest syndrome and vaso-occlusive crisis increased the risk of RBC alloimmunisation [29]. Chronic inflammatory autoimmune disorders are also a risk factor for RBC alloimmunisation, as reported by Ryder et al. [30]. Transfusion during a severe bacterial infection with tissue invasion or a disseminated viral infection has been shown to increase the risk of RBC alloimmunisation [31]. In these studies, alloimmunisation was observed after transfusion of RBC concentrates. The role of the inflammation in RBC alloimmunisation after PC transfusion was not established, but cannot be totally ruled out. Nevertheless, there appear to be several obstacles that should be addressed in future studies: first, the rate of RBC alloimmunisation after PC transfusion is lower than after RBC concentrates; second, the involvement of PCs in RBC alloimmunisation is in some cases difficult to establish because patients were often transfused with both PCs and RBC concentrates; finally, studies with very large populations need to be conducted.

5. Prevention of RBC alloimmunisation in recipients

5.1. D alloimmunisation

In practice, PCs from RhD-positive donors are transfused to RhD-negative recipients because RhD-negative PCs are not always available in blood banks. In this context, it may be necessary to prevent D alloimmunisation in a RhD-negative recipients transfused with platelets from RhD-positive donors, particularly in women of childbearing potential. This can be achieved with anti-RhD immunoglobulins.

In 1968, using experimental animal models (rabbits), Pollack et al. [32] studied the mechanisms of action of antibody-mediated immune suppression. They also analysed the dose of anti-RhD immunoglobulins needed to prevent D alloimmunisation in male human volunteers. In 1970, using O R_2R_2 (DDccEE) RBCs injected intravenously to male volunteers at two different doses (0.5 mL and 5.0 mL), Gunson et al. [33] established that a dose of 0.5 mL of RBC is effective to obtain D alloimmunisation (4 males immunised out of 5 tested). In 1971, Pollack et al. [34] found that a dose of 20 μg of human anti-RhD immunoglobulins per 1 mL of RBC was effective in suppressing an immune response to D antigen. A dose of 300 μg can prevent immunisation with 15 mL of RBC.

In one study, 37 RhD-negative oncology patients transfused with PCs from RhD-positive donors received 200 μg of intravenous anti-RhD immunoglobulins immediately before the transfusion [35]. Repeat anti-RhD immunoglobulins administrations were performed in the multi-transfused patients. No RhD-negative patients developed D antibodies. Nevertheless, despite the context of immunosuppression, several patients still acquired new RBC antibodies with other specificities than anti-D.

Zeiler et al. [36] studied 20 RhD-negative oncology patients transfused with PCs from RhD-positive donors and evaluated the efficacy of D alloimmunisation prevention with a lower dose of anti-RhD immunoglobulins. In this study, 20 μg of anti-RhD immunoglobulins was added directly to the PC or intravenously infused to the recipient before the transfusion. The maximal residual RBC volume in PCs was 0.75 mL. No D alloimmunisation was observed despite of the reduction in the anti-RhD immunoglobulins dose. Furthermore, the authors noted that this dose was efficient with apheresis PCs manufactured using second-generation separators and good monitoring of RBC contamination.

In October 2015, the French National Authority for Health (HAS) established guidelines for preventing D alloimmunisation when RhD-incompatible PCs are transfused to a RhD-negative recipients [37]. A dose of 100 μg of anti-RhD immunoglobulins must be infused in non-immunosuppressed female recipients of childbearing potential within 72 hours of a platelet transfusion from RhD-positive donor. The dose of 100 μg of anti-RhD immunoglobulins is enough to protect the recipient for at least transfusions of 10 apheresis PCs. Over three weeks, the efficiency of this protection must be assessed by residual anti-D testing.

D alloimmunisation in RhD-negative patients can be prevented through three measures: the use of D-matched concentrates, where possible (delivery of PCs from RhD-negative donor to RhD-negative patients); reducing the residual RBC contamination and the number of RBC-derived microvesicles in PCs by improving the efficiency and quality of PC manufacturing; and infusion of RhD immunoglobulins

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in selected RhD-negative patients transfused with PCs from RhD-positive donors.

Delivering of PCs from RhD-negative donors to RhD-negative recipients, particularly to women of childbearing potential, is not always possible due to the availability of these PCs in blood banks. As demonstrated by Dunbar et al. [38], delivery of both ABO identical and D-negative matched PCs to D-negative recipients represented a great challenge to the blood banks. Over a 51-months period, the transfusions of 10,154 leukoreduced and irradiated apheresis PCs were studied retrospectively. Of the 9671 PCs transfused to 2294 recipients of known ABO type, 5281 (54.6%) were ABO-identical: 4180 (55.5%) in RhD-positive patients and 1101 (51.4%) in RhD-negative patients. The RhD-negative recipients received ABO non-identical PCs more frequently, and this difference was statistically significant. Furthermore, out of 361 RhD-negative patients, 298 (83%) received at least one PC from an RhD-positive donor. In practice, today, delivery of RhD-negative PC to RhD-negative recipients cannot always be guaranteed. Similar difficulties have been observed for the ABO blood group compatibility. Delivery of PCs must be adapted to each individual patient and their clinical status (with infusion of RhD immunoglobulins to prevent D alloimmunisation if necessary).

There is no mandatory requirement in France to measure the parameter "number of residual RBCs" in PC [39] as it does for "number of RBC-derived microparticles" in PC manufacturing [39]. Because residual RBCs and RBC-derived microparticles in PCs could induce RBC alloimmunisation in the recipients, further studies and improvement in quality control are necessary, and introducing "the number of residual RBCs" as a parameter in PC specifications should be discussed. Consequently, standardised methods should be established in order to obtain the maximum value of this new parameter in different types of PCs and to obtain reliable results for this measurement. Lastly, RBC antibody screening should be performed one to three months after the last PC transfusion in order to determine the incidence of RBC alloimmunisation, as is the case after the final RBC concentrate transfusion.

Reducing the number of residual RBCs in PCs is an objective of blood collection and manufacturing process of blood products. In the study conducted by Kitazawa et al. [27], the number of residual RBCs differed between two apheresis systems analysed in platelets products (7.5×10^6 and 5.2×10^6) and plasmas (4.3×10^6 and 1.7×10^6). Improvements in blood cell separation of blood cells could decrease the number of residual RBCs in PCs but without negatively affecting platelet count and or functions. Reducing RBC storage lesions which are a source of RBC-derived microparticles is also important [40]. Donor factors, blood collection, manufacturing processes, additive solutions are all involved in RBC storage lesions [40]. Despite the storage conditions for PCs which are different to those for RBC concentrates, the risk of RBC lesions still remains. Improvements at each step of the blood component production with the aim of reducing RBC storage lesions are likely to decrease RBC-derived microparticles generation and increase the safety of blood products transfused to the patients.

5.2. Other forms of alloimmunisation

Preventing of other forms of alloimmunisation, particularly from Rh antigens (C, E, c and e) and Kell antigen, remains difficult. As reported by Rekhaus et al. [21], changes to national guidelines in Switzerland are set to be discussed. For apheresis PCs, Rh and Kell compatibility should be respected in women of childbearing potential and in chronically transfused recipients with haemoglobinopathies.

While introducing this measure is possible, two major hurdles need to be overcome for it to be practicable: ensuring the delivery of apheresis PCs only and guaranteeing the availability of compatible PCs in blood banks.

6. Conclusion

RBC alloimmunisation after PC transfusion is observed in blood group systems other than the ABO system. This alloimmunisation may be a primary or secondary form of immunisation and appears in both immunocompromised and non-immunocompromised patients. The mechanisms underlying this alloimmunisation involve residual RBCs and RBC-derived microvesicles. Consequently, matched RBC concentrates should be provided to patients and the risk of developing HDFN in pregnant women should be recognised. D alloimmunisation can be prevented by delivering PCs from RhD-negative donors to RhD-negative recipients or, where this is not possible, by infusing anti-RhD immunoglobulins before transfusion of PCs from RhD positive donors. Finally, improvements in PC processes will reduce residual RBCs and RBC-derived microparticles content and the risk of RBC alloimmunisation.

Contribution

P.M. drafted the paper.

Disclosure of interest

The author declares that he has no competing interest.

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