## Red blood cell alloimmunisation in 18 to 50-year old transfused women: a 3-year study

Pierre Moncharmont, Gregory Barday, Francis Meyer

Rhône-Alpes French Blood Establishment, Lyon Gerland Site, Haemovigilance Department, Lyon, France

Dear Sir,

Red blood cell (RBC) alloimmunisation is a delayed adverse transfusion reaction whose rate has been evaluated in women in comparison to men in various studies. In their review, Verduin et al.1 showed that women with sickle cell disease were at a higher relative risk (27.0%) of developing RBC alloimmunisation compared to men with the same disease. In the other groups of patients, the risk of RBC alloimmunisation appeared to be similar among men and women. However, Verduin et al. observed that RBC antibodies were slightly more present in women. Among 55,350 recipients, Spielmann and Seidl<sup>2</sup> detected 322 RBC antibodies in 29,580 females (1.09%) and 121 in 25,770 males (0.47%). Saverimuttu et al.3 evaluated 27,968 RBC antibodies screens from 15,966 patients: they found 457 patients with RBC alloimmunisation (2.9%) and among them 304 (1.9%) had clinically significant RBC antibodies. According to their observations the prevalence of RBC antibodies increased with age and was higher in females.

The 3 studies confirm a higher rate of RBC alloimmunisation in women. As the risk of alloimmunisation for women is more important (through transfusion and pregnancy), a strict transfusion policy is essential in order to facilitate uneventful pregnancies and to prevent haemolytic disease of the foetus and newborn. To this end, according to French transfusion regulations, matching of RBC concentrates for the Rhesus and Kell systems (antigens C, E, c, e and K) is the rule for female patients from birth to 50 years of age.

In France, each adverse transfusion reaction is notified in a report which is included in the national haemovigilance database. In order to evaluate the incidence of delayed RBC alloimmunisation in the population of 18 to 50-year old transfused women, all adverse transfusion reaction reports from all hospitals of the Rhone-Alpes area collected during a period of 3 years were studied. The specificity of the RBC antibodies, the blood product involved and the imputability were considered.

From January 1st 2010 to December 31st 2012, 8,953 women (age range 18 to 50) were transfused. Thirty-one delayed RBC alloimmunisation reports were notified in 30 female patients. Of the 30 women, three (10.0%)

had sickle cell disease and two (6.7%) had thalassaemia. Sixteen women (53.3%) had had at least one prior gestation, 18 (60.0%) had been transfused previously and six (20.0%) were RBC alloimmunised at the time of their transfusion. The blood components involved were RBC concentrates in 28 cases (90.3%), apheresis platelet concentrate in one case and pooled platelet concentrates in two cases. In 30 cases, the newly acquired RBC antibodies had one specificity and in one case it had two. Of the 30 new RBC alloimmunisations with only one specificity, anti-S was observed in seven cases, anti-Kp<sup>a</sup> in seven, anti-Fy<sup>a</sup> in four and anti-Jk<sup>a</sup> in four. In the RBC alloimmunisation with two specificities, anti-K and anti-Jkb were observed. It appears that despite matching between RBC concentrates and recipients, alloimmunisation was detected after transfusion in two patients (anti-c in one case and anti-K in the other case). The anti-c alloimmunised woman was transfused with c-positive RBC concentrates because of a lifethreatening condition (severe anaemia due to bleeding in an ectopic pregnancy). The anti-K alloimmunised woman had thalassemia and was transfused with three "K-negative" RBC concentrates. Only 2 out of the 3 donors were tested again and were confirmed to be K-negative. Lastly, the woman with a combination of RBC antibodies (K and Jkb) had received 2 K-negative and Jkb-positive RBC concentrates because of post-partum anaemia (haemoglobin level 67 g/L). The K- antibodies detected after transfusion were probably due to pregnancy. The imputability of the blood component was certain in 13 cases (42.0%), probable in 17 cases (54.8%) and possible in one case (3.2%).

In our study, focused on a regional area, the matching of RBC concentrates for the Rhesus and Kell systems has proven to be efficient; only 2 female recipients acquired new RBC antibodies (anti-c and anti-K) after transfusion. In the other cases of alloimmunisation, the antibodies were not caused by antigens of the Rhesus or Kell systems (antigens C, E, c, e and K); the most common antibodies were anti-S and anti-Kpa which occurred in 7 cases each. Matching of RBC concentrates for groups other than the Rhesus and Kell systems (Duffy, Kidd, ...) is not currently performed in patients without RBC allo-antibodies.

Three cases of RBC alloimmunisation were detected after transfusion of platelet concentrates: anti-Jk<sup>a</sup> (one case), anti-DAU5 (one case) with two pooled platelet concentrates and anti-E (one case) with one apheresis platelet concentrate. In a previous study<sup>4</sup> performed over a 5-year period, RBC alloimmunisation was detected after transfusion of both apheresis platelet concentrates (24 cases) and pooled platelet concentrates (24 cases). In our study several cases of RBC alloimmunisation developed after transfusion of RBC concentrates, including seven cases of anti-S.

As the female patients of our study belonged to the 18 to 50-year old age group, they benefited from Rhesus and Kell matching of RBC. The national regulatory specifications set up for the protection of women of child-bearing age were respected; however, there were still 3 cases of RBC alloimmunisation subsequent to platelet transfusion and some women developed an anti-S (a potential cause of haemolytic disease of the foetus and newborn).

Among the adverse transfusion reaction reports indicating delayed RBC alloimmunisation in our study over a period of 3 years, only 5 (16.7%) notified an haemoglobinopathy. Anti-S and anti-Kp<sup>a</sup> specificities were the most common in patients with such conditions and RBC concentrates were the blood component most frequently involved.

The Authors declare no conflicts of interest.

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