Letter to the Editor
Transfusion Medicine

Ann Lab Med 2020;40:190-192
https://doi.org/10.3343/alm.2020.40.2.190
ISSN 2234-3806 • eISSN 2234-3814

ANNALS OF LABORATORY MEDICINE

Extended Red Blood Cell Phenotype Matching Is Dependent on Ethnicity and Specificity of RBC Alloantibodies

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To the Editor,

We would like to thank Balbuena-Merle and colleagues [1] for their interest in our study of red blood cell (RBC) alloimmunization in Korean patients with myelodysplastic syndrome (MDS) and liver cirrhosis (LC) [2]. There is a high prevalence of sickle cell disease (SCD) in Africa, the Middle East, India, parts of the Mediterranean, and Puerto Rico, and high rates of RBC alloimmunization in SCD patients have been reported in these regions [3]. In contrast, SCD is extremely rare in Korea, and alloimmunization in SCD patients has never been documented. The frequencies of C, c, E, e, Fy^a, Jk^a, M, and K antigens differ across races. The K antigen is particularly important as it has high immunogenicity; however, the frequencies of the K antigen and the anti-K alloantibody are extremely low in the Korean and other South East Asian (i.e., Chinese and Japanese) populations, unlike in European and Caucasian populations [4, 5].

With respect to the transfusion policies, the study by Balbuena-Merle, *et al*. [1] from Puerto Rico was different from our study in Korea because of the differences in disease prevalence and alloantibody formation. While 91% of pediatric SCD patients SCD received RBCs matched for at least ABO, Rh, and K blood groups (limited RBC matching), none of the patients in our study received RBCs matched for groups other than ABO and RhD (Table 1). However, the overall alloimmunization rate (15.4% [8/52 patients] vs 6.3% [20/317 patients]) was much lower in our study despite the similar amount of transfused RBC units; this was considered to be due to the higher ethnic homogeneity of Koreans than that of Puerto Ricans. Although Balbuena-Merle, *et al*. [1] described Puerto Ricans as a genetically homogeneous group, their population comprises Caucasians (74.7%), people of African descent (15.3%), and other populations according to the 2013–2017 American Community Survey [6]. We additionally calculated the prevalence of alloantibody formation per transfusion events. After transfusion of 5,886 RBC units, the formation of 29 alloantibodies was recorded, and the prevalence of alloantibody formation per transfusion event was 0.49 alloantibodies per 100 units. Among the disease groups, the prevalence of alloantibody formation per transfusion event was the highest in the LC group (1.13 per 100 units), followed by the MDS group (0.22 per 100 units), and the prevalence among Puerto Rican patients was 3 per 100 units.

In our study, the most common alloantibody was that against

Received: September 26, 2019
Revision received: October 10, 2019
Accepted: October 14, 2019

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Table 1. Comparison of the studies by Kim, *et al*. [2] and Balbuena-Merle, *et al*. [1] for RBC antigen prevalence and alloimmunization rate

Study	Kim, *et al*. [2]	Balbuena-Merle, *et al*. [1]
Study Population	Adult LC and MDS patients	Pediatric SCD population
Ethnicity	Korean	Puerto Rican
RBC phenotype matching	ABO/D matched	ABO/D matched and other phenotype matched (limited- and/or extended matched)
RBC alloimmunization rate	6.3%	15.4%
Prevalence of alloantibody formation per transfusion events	0.49 per 100 units	3 per 100 units
Prevalence of RBC antigens*		
C	85%	67%
E	51%	25%
c	59%	86%
e	90%	98%
M	76%	69%
K	0%	6%
Fy^a	99%	46%
Jk^a	67%	88%
Identified RBC alloantibodies (N)		
Anti-E	13 (45%)	1 (11%)
Anti-c	5 (17%)	0
Anti-e	3 (10%)	0
Anti-C	2 (7%)	0
Anti-M	0	4 (44%)
Anti-Fy^a	0	2 (22%)
Anti-Fy^b	2 (7%)	0
Anti-Jk^a	2 (7%)	1 (11%)
Anti-K	0	1 (11%)

*Data on the prevalence of RBC antigens in Koreans were derived from references [5] and [10].
Abbreviations: LC, liver cirrhosis; MDS, myelodysplastic syndrome; SCD, sickle cell disease; RBC, red blood cell.

the Rh system, found in 80% of alloimmunized patients. However, Balbuena-Merle, *et al*. [1] reported only one patient with an Rh alloantibody (anti-E), and as expected, this must be the effect of limited or extended RBC phenotype matching. Several studies have reported reduced alloimmunization rates after limited RBC antigen (ABO, Rh, and Kell systems)-matched transfusion [7, 8].

Although RBC alloimmunization rates in Korea are low, these values are set to change in the near future owing to increased rates of immigration and interethnic marriages [9]. Both these factors could lead to changes in the RBC antigen expression profile and thereby the alloimmunization rate and alloantibody distribution of the population [5]. Therefore, continuous monitoring of RBC alloimmunization for various conditions is needed. When the specificity of RBC alloantibodies in Koreans changes significantly, the introduction of extended RBC antigen matching should be considered in Korea.

Conflicts of Interest

None declared.

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