

In response to Joubeh and Singh: Allergic reactions to platelets; to B or not to B?

We read the recent letter by Joubeh and Singh discussing allergic reactions to psoralen-treated platelets (PI-Platelets) and found their data intriguing.¹ These authors describe two cases of O+ male patients developing allergic reactions after psoralen-treated platelet transfusions, and they wonder whether PI-Platelets may cause allergic transfusion reactions. However, as they noted, the allergic reactions in these patients were exclusively to AB or B platelets, raising the possibility that the ABO compatibility may provide a better explanation for their results than the PI-Platelets. In fact, we recently examined transfusion reaction rates in platelets and found that A or B antigen incompatible platelets (analyzed in aggregate) had higher rates of allergic reactions compared to ABO compatible transfusions.²

To examine specifically whether Type B platelets may cause allergic reactions in some patients, platelet transfusion records from October 2015 to April 2022 were analyzed. As previously described,² these records were merged with patient and product ABO type as well as with a transfusion reaction data set that included all reported reactions to platelet transfusions during that time. Allergic reaction rates for type O patients to O, A, B, and AB were calculated and demonstrated that AB/B platelets were significantly more likely to cause allergic reaction in type O patients than O or A platelets (Table 1). Analysis of these data using the Fisher's Exact test showed that these differences were highly significant (OR = 2.53, $p = 0.0072$). Reaction rate in type A patients found the allergic reaction rate for AB/B platelets was 0.41% which was not significantly ($p = 0.59$) different than the rate for A/O platelets (0.31%).

The data were also analyzed to determine if allergic reaction rates for psoralen-treated (PT) platelets were higher than the rate found for non-psoralen-treated platelets. The rate of allergic reaction to PT platelets was (1 in 214 PT and 0 of 177 PT-PAS- 0.26% overall) not statistically different ($p > 0.99$) than for conventional platelets (112 in 31,645–0.36%) ($p > 0.99$). While likely under-powered, this

does not support the possibility that psoralen treated platelets increase allergic reaction rates as suggested previously.¹

In our data set there were 10 type O patients and 4 type A patients who had allergic reactions to B or AB platelets. A summary of the platelet transfusions and allergic reactions for these 14 patients is shown in Table 2. Of these patients, two were particularly noteworthy, as they received more than 20 transfusions and allergic reactions were noted only when B platelets were transfused. Patient 1 was a male in his 70s who received 22 transfusions and he had three allergic reactions to all three B platelets (7th, 13th, and 16th transfusion) he received. Patient 2, also a male in his 70s, received 23 transfusions and had allergic reactions to both B platelets he received (1st and 8th transfusion). Of note, neither patient 1 or 2 was noted to have environmental allergies. Five other Type O patients (Table 2 #3–7) were found that had allergic reactions to all B antigen positive units they received but these patients received fewer platelet transfusions, and all had just a single allergic reaction making the possibility that this occurred by chance much higher. Two of these patients had a reaction on the first platelet transfusion they received. Of the four type A patients, only one (#11) had a reaction to all the B antigen positive platelets they received but this patient only received three platelet transfusions in total, so it is unknown if this is related to the B antigen. It is noteworthy that 11 of the 14 patients described here (included patient 1 and 2) and both of the subjects described by Joubeh et al.¹ were male. It is unclear if this occurred by chance or not.

In our view, these data coupled with the previous report by Joubeh et al.¹ can best be explained by a small fraction of patients who have allergic reactions to the B antigen expressed on platelets or secreted in plasma. In our study, there were 890 type O patients transfused with 1798 units of B or AB products and an allergic reaction was reported in only 10 (1.1%) of these patients. We estimate that this is the upper limit for allergic reaction to the B antigen as it is very unlikely that all of these were due to the B antigen.

TABLE 1 Allergic reaction rates in type O patients reaction rate calculated by taking ("Allergic Rx"/["No Rx + "Allergic Rx"]) $\times 100$

Patients	Product transfused	No Rx	Allergic Rx	Rx rate
2275	O	9648	24	0.25%
1324	A	4152	16	0.38%
460	AB	683	2	0.29%
637	B	1087	11	1.00%

TABLE 2 A/O patients with at least one allergic reaction to a B or AB platelet

Patient	Sex	Age	Pt ABO	Transfused Prod ABO				Total	ABO Allergic Reaction (Trans #)
				A	AB	B	O		
1	M	70s	O	3		3	16	22	B (7), B (13), B (16)
2	M	70s	O	4		2	17	23	B (1), B (8)
3	M	20s	O	6		1	5	12	B (2)
4	M	60s	O			1		1	B (1)
5	M	under 10	O		1		7	8	AB (1), O (2)
6	M	80s	O	5	1		11	17	AB (9)
7	M	70s	O			1		1	B (1)
8	F	60s	O	1	1	1		3	B (3)
9	F	60s	O	18	1	4	31	54	B (6)
10	M	60s	O	8	2	4	14	28	B (2)
11	F	70s	A	2		1		3	B (1)
12	M	teens	A	4	1	1	1	7	B (7)
13	M	60s	A	34	4	5	13	56	AB (14), B (17)
14	M	teens	A	15	2	2	12	31	AB (8), A (18)

Allergic reactions to carbohydrate antigens have been previously described.³ Recent studies have demonstrated that people who are allergic to red meat have been found to have antibodies to galactose- α -1,3-galactose (alpha-gal), which is the terminal carbohydrate that forms the B antigen in the ABO blood group system.⁴ Of note, patients who are blood group B or AB have been reported to have a reduced incidence of red meat allergies.⁵ It would be of interest to determine if this association could be reproduced in larger data sets and if patients suspected of being allergic to Type B platelets have a history of allergies to meat or are positive for either IgE or IgG alpha-gal antibodies.

CONFLICT OF INTEREST

The authors have disclosed no conflict of interest.

Siera Rossi¹

Linder Wendt²

Zuhair Ballas³

C. Michael Knudson¹ 

¹Department of Pathology, University of Iowa, Iowa City, Iowa, USA

²ICTS, University of Iowa, Iowa City, Iowa, USA

³Department of Internal Medicine, University of Iowa, Iowa City, Iowa, USA

Correspondence

C Michael Knudson, Department of Pathology,
University of Iowa, Iowa City, IA, USA.

Email: c-knudson@uiowa.edu

DOI 10.1111/trf.17161

ORCID

C. Michael Knudson  <https://orcid.org/0000-0003-3964-5466>

REFERENCES

1. Joubeh S, Lima JLO, Wooten M, Marques MB, Singh N. Allergic reaction to psoralen-treated platelets: real or coincidence? *Transfusion*. 2022;62:716–7.
2. Malvik N, Leon J, Schlueter AJ, Wu C, Knudson CM. ABO-incompatible platelets are associated with increased transfusion reaction rates. *Transfusion*. 2020;60:285–93.
3. Cabezas-Cruz A, Hodžić A, Román-Carrasco P, Mateos-Hernández L, Duscher GG, Sinha DK, et al. Environmental and molecular drivers of the α -Gal syndrome. *Front Immunol*. 2019; 10:1210.
4. Apostolovic D, Rodrigues R, Thomas P, Starkhammar M, Hamsten C, van Hage M. Immunoprofile of α -Gal- and B-antigen-specific responses differentiates red meat-allergic patients from healthy individuals. *Allergy*. 2018;73:1525–31.
5. Cabezas-Cruz A, Mateos-Hernández L, Alberdi P, Villar M, Riveau G, Hermann E, et al. Effect of blood type on anti- α -Gal immunity and the incidence of infectious diseases. *Exp Mol Med*. 2017;49:e301.