



Revista Brasileira de Hematologia e Hemoterapia Brazilian Journal of Hematology and Hemotherapy

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Scientific Comment

ABO isohemagglutinin titration or hemolysin test: what should we do to reduce the risk of passive hemolysis?☆



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ARTICLE INFO

Article history:

Received 14 April 2015

Accepted 14 April 2015

Available online 18 May 2015

Platelet concentrates from ABO-identical donors are the components of choice for transfusions. Since platelet inventories are generally insufficient and because there is usually a higher frequency of group O donors, perfect matches are not always possible and therefore ABO-incompatible platelet transfusions are an accepted practice when ABO-identical platelets are unavailable.¹ However, an acute hemolytic transfusion reaction (HTR) can be a severe complication after this type of transfusion due to the passive transfusion of antibodies from donors possessing unusually high-titers of anti-A and/or anti-B antibodies.²

Reducing the risk of HTRs due to plasma-incompatible platelet transfusions has been generating interest and discussions. Strategies to reduce the risk of platelet-associated HTRs include volume reduction of platelets and screening donor plasma for high titers of antibodies by performing anti-A and/or anti-B titration or assays for *in vitro* hemolysis.¹

Methods currently employed to identify high titers of anti-A and/or anti-B antibodies include titration by the saline agglutination test, with and without incubation, gel test,

solid-phase test, flow cytometry, automated technologies and a qualitative hemolysin test. Many countries have adopted universal screening where a critical IgM titer is between 64 and 100 in tube or gel tests, and a critical IgG titer is between 200 and 512.^{3,4} However, non-standardized methods of IgM or IgG isohemagglutinin titration and the lack of agreement of a 'critical titer' that will predict *in vivo* hemolysis have made the determination of ABO antibody titers difficult and limited to a few blood banks.⁵ Additionally, documentation that titer methods prevent HTRs is not clear. Based on this, it remains unclear whether titration is the best or most cost-effective approach. Currently, the use of the hemolysin test for the identification of hemolytic anti-A and anti-B antibodies has emerged as a useful screening test to identify high levels of anti-A and/or anti-B antibodies and has recently been suggested by the Brazilian legislation as prophylaxis for acute HTRs.

Regulatory agencies require that blood banks have a policy to prevent HTRs due to plasma-incompatible platelet transfusions but the choice of the best approach to predict HTRs

DOI of original article: <http://dx.doi.org/10.1016/j.bjhh.2015.05.001>.

☆ See paper by Landim et al. on pages 217–22.

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<http://dx.doi.org/10.1016/j.bjhh.2015.04.002>

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is still a big challenge as little is known about the correlation between isohemagglutinin titration and the hemolysin test, and the impact of each test on the prevention of hemolysis and on platelet inventory management.

In this issue, there is an important study on the correlation between isohemagglutinin titration and the qualitative hemolysin test as prophylactic tests to prevent HTRs.⁶ The authors evaluated the impact of each prophylaxis on platelet inventory management and the ability of the hemolysin test to avoid red blood cell (RBC) sensitization after the transfusion of incompatible units.⁶ In this study, they demonstrate that the results of isohemagglutinin titration are not related to the results of the hemolysin qualitative test and the absence of hemolysis does not prevent RBC sensitization. They also conclude that the implementation of the hemolysin test as the prophylaxis of choice for hemolysis significantly affects the platelet inventory management. Therefore, according to the authors, isohemagglutinin titration using a well-standardized method determining a cut-off for labeling a product as high-titer is still the best approach.

This paper represents an additional contribution for designing and implementing policies to improve the safety of ABO-incompatible platelet transfusions. The results of the studies by Landim et al.⁶ also show that no standard strategy exists to mitigate *in vivo* hemolysis and serve to stimulate a review of Brazilian practices and policies for the advancement of platelet transfusion safety.

The finding that none of the methods (isohemagglutinin titration and the hemolysin test) is guaranteed to eliminate the risk of passive hemolysis supports the concept that there are combinations of factors influencing hemolysis due to plasma-incompatible platelets.³

Although HTR after ABO-incompatible platelet transfusions is a rare event we will have to look to future studies to better understand other risk factors in addition to the best cut-off for ABO plasma-incompatible titers.

Conflicts of interest

The author declares no conflicts of interest.

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