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Prevention in Transfusion Medicine

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Blood transfusion is a life-saving therapeutic option but is also associated with significant risks or hazard. For this reason it is necessary to stress the importance of prevention of reaction of ABO major-incompatibility, adverse transfusion reactions and transmission of infective diseases by blood components.

Recently many developed countries have promoted safe transfusion practices through hemovigilance programs by reporting of transfusion reactions. These programs aim to detect and analyze untoward effects of blood transfusion in order to correct the causes and prevent their recurrence. Actually, the immunological risk of red blood cell transfusions seems higher than viral risk. According to French studies, severe accidents due to blood incompatibility occur with a frequency estimated at 1/6000 to 1/29000,[1] American studies also report an error rate equal to 1/19000 units transfused;[2-3] despite technical progress, the risk does not significantly diminish. The majority of accidents do not originate from laboratory or production stages, but from defects in the application of clinical procedures. Preventive measures are based on the elaboration of clinical guidelines with the compliance to strict rules in carrying out bedsides ABO check. The implementation of quality assurance system and of the epidemiological surveillance system, which define the basis of a prevention policy, leads to the expectation of an improvement of transfusion safety.

Transfusion of ABO major-incompatible red blood cells may result in severe hemolysis leading to major morbidity or death. The hemolysis is caused by the isoemoagglutinins, antibodies directed against the ABO antigens that are not expressed on the cells of the transfused individual. They can activate the complement system and can cause severe and even lethal acute hemolytic reactions. The activation of the complement system with formation of C3a, C5a and consequently of MAC (membrane attack complex) and the release of hemoglobin from the lysed RBCs are thought to mediate clinical signs like fever, hypotension, pain and acute renal failure. Currently, several studies have been done to explain this problem on transfusional error. A monoclonal antibody has been developed, Eculizumab, that blocks the cleavage of C5 and therefore inhibits formation of the MAC. However treatment with Eculizumab may have adverse effect as headache, dizziness, nausea, vomiting, joint aches, upper respiratory tract infections and it is associated with an increased risk for meningococcal infections. Even then this monoclonal antibody might be a suitable intervention to limit sequelae of ABO-incompatible RBC transfusion, our effort in the first place must focus on avoiding such events.[4-5]

In Italy, after the fatal transfusion error occurred in August 2013, the Regional Health Council of Tuscany imposed to draft guidelines for the utilization of Eculizimab in case of transfusion error, as well as other security safeguards, such as the identification bracelet for the patient.[6] Several studies point out that, among the causes of most ABO-incompatible transfusion events and near-misses, there are patient misidentification not detected by bedside control, and/or wristband check, incomplete or incorrect labeling, but there are also identification errors involving namesake, i.e. name similarity issues, and impersonation, i.e., fraudulent identity documents. It is therefore necessary to identify the correct methods of labeling and draw up guidelines which indicate the exact process of identification of the patient undergoing transfusion.[7-8-9-10]

Actually in Italy, on 28th December 2015, a new Decree Law, on Annex 7, makes mandatory to use an identification bracelet for patients undergoing transfusion therapy. An important chapter on prevention in transfusion medicine is certainly the one regarding the transmission of infectious diseases. Improvements in donor screening and testing have significantly reduced the risk of transfusion-transmitted infections. Also, evidence-based transfusion guidelines as well as patient blood management programs aiming at the optimal use of blood components, contribute to blood safety by limiting the exposure of patient to potentially infectious blood. However, a relevant risk of transmission of viruses, bacteria, protozoa and prions to recipients remains. The relatively high incidence of pathogens not detected by conventional blood screening methods, viruses missed due to low titles (window period) and newly emerging transfusion-transmitted agents such as Ebola, Zica virus, WNV, American Trypanosomiasis, Chikungunya virus, continue to threaten the safety of the blood supply.[11]

Pathogen Reduction Technologies (PRTs) have the potential to close or, at least, to reduce this safety gap. Most of them have already been evaluated in plasma and platelets, and their potential use in red blood cells is being explored. Whereas early PRTs, such as solvent/detergent, is only suitable for plasma, newer methods can treat cellular blood components with the use of ultraviolet (UV) light and photosensitizers or photoreagents to inactivate pathogens without destroying the membranes of cellular therapeutic products.[12] The results observed in some studies suggest that treating platelets with a riboflavin-and- UV-light-based pathogen reduction process could potentially eliminate window period transmission of screened viruses and greatly reduce the risk of transfusion transmission of unscreened viruses.[13] It is also important to highlight that the platelet concentrates, subjected to inactivation with these new technologies, maintain the same therapeutic efficacy.[14]

However, stakeholders in the field of transfusion medicine have a strong desire to be able to inactivate pathogens in all

blood components in order to increase the safety of the entire blood supply. This implies the need to inactivate RBCs as well as platelets and plasma. Thus, pathogen reduction cannot achieve its full potential for enhancing blood safety as long as pathogen reduction technologies for red blood cells or whole blood will not available.

Transfusion of ABO major incompatible red blood cells (RBCs) may result in severe hemolysis leading to major morbidity or death.[1]The hemolysis is caused by the isoagglutinins (anti-A, anti-B), antibodies directed against the ABO anti-gens that are not expressed on the cells of the transfused individual. Because most of the isoagglutinins are of the immunoglobulin (Ig)M type, and because ABO antigens are present in high density on the surface of RBCs, activation of complement with immediate, intravascular hemolysis often occurs in ABO-incompatible transfusion.

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