Editorial Commentary

Platelet transfusion in the real life

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Platelet transfusion is a common practice in thrombocytopenic patients for preventing or treating hemorrhages. Platelets are mostly transfused to patients diagnosed of onco-hematological diseases and/or undergoing hematopoietic stem cell transplantation (1). With the aim to help physicians to take the most accurate decisions on platelet transfusion, some guidelines have been developed (2-6). The scientific evidence supporting the recommendations included in the guides is stronger for prophylactic platelet transfusion policy in onco-hematologic patients, but much less consistent in many other clinical situations as invasive procedures, lumbar puncture and chronic thrombocytopenia (7-9). Which means that while there are some robust studies to support prophylactic platelet transfusion thresholds in onco-hematological patients (8,9), there is a striking lack of them for other clinical scenarios. However, the limitation in platelet availability and the higher number of patients in need of platelets turn the ideal platelet transfusion into real practice and available guidelines are not as followed as they should (10).

More than two million of platelet components were distributed from collection centers in the United States in 2015, more than 90% having been collected by apheresis (11). Gottschall *et al.* (12) have provided interesting and largest data about platelet transfusion practice in a recent publication. They have performed a retrospective observational data analysis of platelet use in 12 US hospitals that were participants in the Recipient and Donor Epidemiology Study (REDS-III). They collected data from a high number of inpatient (n=28,843) and outpatient (n=2,978) platelet transfusions for a 4-year period, between January 2013 and December 2016. The results provide a general view on current platelet transfusion practice in US. A total of 163,719 platelets representing between 3% and 5% of all platelets transfused in the country, were transfused into 31821 patients of whom 60.5% were males. More than 60% of platelets were from single donor apheresis and 72.5% were irradiated. Percentage of apheresis platelets used was lower than previously published in US national surveys which was more than 90% (11). Authors explain that this is due to one of their four hubs manufactures large number of whole blood derived platelets. Nevertheless, the article do not provide comparative yield data between the two kinds of platelet components. The diagnose codes of patients were hemato/oncology, circulatory system and injury and poisoning. Most patients received at least one other blood product. Forty-six percent of all platelet components were transfused to patients who had a diagnosis of leukemia, myelodysplastic syndrome or lymphoma. These patients, as expected, received more platelet per total study period than patients diagnosed with other diseases. This is consistent with the high use of irradiated platelets.

There are some remarkable aspects in this article (12) that deserve an accurate analysis. The first of all refers to the low percentage of ABO type-specific platelet transfusions. Of all transfusions, only 54.1% were ABO identical, that is a lower rate than expected. In fact, transfusing ABO incompatible platelets is a widespread practice. This strategy has some clear advantages as better availability and better response in emergency situations, avoiding platelets wastage. A survey of a high number of North American and European laboratories showed that more than 19% of transfusion services did not have a clear policy regarding the use of ABO-incompatible platelets (13). Most current guidelines do not make specific recommendations on this

Table 1 Prophylactic platelet transfusion: comparative thresholds for invasive procedures and surgery according to different guidelines

Procedures	Guidelines			
	AABB[2]	ASCO[6]	BSH[5]	SIMTI[23]
Major non-neuraxial surgery	≥50×10^9/L	40-50×10^9/L	>50×10^9/L	>50×10^9/L
Lumbar puncture	≥50×10^9/L	NR*	≥40×10^9/L	>50×10^9/L
Venus central lines placement	≥20×10^9/L	≥20×10^9/L	≥20×10^9/L	>50×10^9/L
Neurosurgery or ophthalmic surgery	NR	NR	>100×10^9/L	>100×10^9/L
Percutaneous liver biopsy	NR	NR	>50×109/L	>50×10^9/L
Insertion/removal of epidural catheter	NR	NR	≥80×109/L	>50×10^9/L
Bone marrow aspirate or trephine biopsy	NR	≥20×10^9/L	Do not give platelet transfusion	NR
Traction removal of tunneled CVCs	NR	NR	Do not give platelet transfusion	>50×10^9/L
Chronic thrombocytopenia from central origin without active treatment	NR	Do not give platelet transfusion	Do not give platelet transfusion	NR

NR*, no recommendation is given. AABB, American Association of Blood Banks; ASCO, American Society of Clinical Oncology; BSH, British Society of Haematoloy; SIMTI, Italian Society of Transfusion Medicine and Immunohematology.

aspect (2-4). Only British guidelines (5) recommend that hospitals should have a strategy to maximize the transfusion of ABO compatible platelets. In this line, some studies have demonstrated higher post-transfusion platelets increments after ABO identical platelet transfusion, supporting this practice (14). A major ABO incompatibility can decrease the platelet transfusion yield more than 40% in patients with hematologic cancers. Higher rate of adverse events in ABO incompatible PLT transfusions as compared to ABO compatible including acute hemolytic reactions have been recently published (15). Major ABO incompatible platelet had the higher rate of adverse reactions: 2%, as compared to 1% in ABO identical platelet transfusions. However, the impact of ABO incompatible transfusion on hemorrhagic and clinical outcome has not been clarified (16). Our group analyzed the ABO compatibility of platelet transfusions in 529 patients who underwent 553 autologous progenitor stem cell transplants at the University Hospital la Fe between January 2000 and December 2013 (17). Patients received a total of 2,772 platelet concentrates, of which 2053 (74.0%) were ABO identical. Transfusion and clinical outcomes were similar for patients who received ABO identical or ABO non-identical platelet transfusions. The isolated fact of receiving ABO non-identical platelets did not influence morbidity or survival. Despite the scarce scientific evidence, an effort to increase ABO compatible PLT transfusions would be made in order to optimize transfusion yield and outcome.

The second issue to highlight is that more than 60% of platelets administered to RhD negative patients were RhD positive. The higher the transfusion requirements of RhD negative patients the greater the probability of receiving RhD positive platelets. Unfortunately, the article do not provide data about D alloimmunization rate and neither about if prophylaxis protocols against alloimmunization were used. This is also a controversial issue, alloimmunization rate after RHD positive platelet transfusions in RhD negative patients is low in most studies, and much lower when apheresis platelets are transfused (18-20).

Third interesting issue to be discussed is about platelet transfusion thresholds reported in the study (12). The most common pre-transfusion platelet count range was 20,000 to 50,000/μL for inpatients, and 10,000 to 20,000/μL for outpatients. Prophylactic transfusion strategy using low dose platelets and threshold of 10,000/μL is the current recommendation for hematological patients undergoing chemotherapy or allogeneic stem cell transplantation. This threshold should be increased to 20×10^9/L if there are some additional risk factors for bleeding (3-9,21). *Table 1* summarizes the platelet thresholds for prophylactic transfusions recommended in some guidelines. For therapeutic platelet transfusions in severe bleeding, the recommended threshold is 50,000/μL (2,5). In the inpatient setting, only 20% of platelet transfusions were transfused to patients with threshold of ≤10,000/μL, 22% were transfused with threshold between 10,000 and 20,000/μL, and 28%

between 20,000 and 50,000/μL. Patients who receive platelet transfusion with threshold between 20,000 and 50,000 should be with therapeutic or prophylactic intention before some invasive procedure, then a clinical condition should justify the transfusion. There is no information about specific clinical conditions of patients as the presence of active bleeding or not, but in the view of the results, one could hypothesize that a variable percentage of platelets were not transfused according to the current guidelines. As reported in the literature, the degree of guidelines compliance of platelet transfusions is variable (10). In an audit performed by Etchells and colleagues 78% (95% CI: 72–84%) of PLT transfusions were adjudicated as appropriate. Prophylactic transfusions for non-bleeding patients had the highest proportion of appropriateness, and therapeutic transfusions for bleeding patients had the lowest.

On the contrary, for outpatients the pre-transfusion platelet count range was 10,000 and 20,000/μL, lower than for inpatients. In this subset of patients, probably with better clinical conditions, adherence to guidelines is greater.

In the intensive care unit (ICU) setting there were a larger number of platelet transfusions performed to patients with platelet counts of 50,000 to 100,000/μL (12). More severe conditions and invasive procedure requirements are reasons that could explain the higher thresholds used for platelet transfusions in ICU. But in this range of platelet counts, is where the scientific evidence is weaker, therefore, the adequacy of transfusions to guidelines should be analyzed to find out the improvement points.

The median post-transfusion platelet increments were lower for inpatients (ranged from 12,000 to 20,000/μL) than for outpatients (ranged from 17,000 to 27,000/μL). The median time from transfusion to post-platelet count was 6.9 hours (maximum 24 hours). These counts are quite similar to those previously reported in patients with hypoproliferative thrombocytopenia (16) and even higher than in critically ill patients (22). Worse clinical condition of inpatients could explain this. Platelet transfusion refractoriness is defined as the lack of adequate post-transfusion platelet count increment Platelet refractoriness is a quite frequent condition in some subsets of patients, as those underwent hematopoietic stem cell transplantation (23). The study (12) do not collect information about this common and severe complication of platelet transfusion.

Another remarkable aspect refers to there were 5,983 episodes of platelet transfusions to patients receiving antiplatelet medications (12). The median pre-transfusion platelet count for these patients was 83,000/μL, much higher than 19,000/μL that was the median pre-transfusion platelet count for patients without antiplatelet therapy. Again, the clinical conditions of patients are not provided, but we assume that these patients suffered severe bleedings. Although widespread, there is no scientific evidence to support this practice. Some of the guidelines (6,7) do not provide recommendations about the topic. British Guidelines (5) recommend that platelet transfusion must be considered as additional measure to general hemostatic measures and tranexamic acid in patients with critical bleeding. The guidelines from the AABB (2) specify that can not recommend for or against platelet transfusion for patients receiving antiplatelet therapy who have intracranial hemorrhage (traumatic or spontaneous). Therefore, this is a topic where the lack of scientific evidence is clear, and studies are needed to clarify the role of platelet transfusion in the control of hemorrhage and the patient outcome.

In summary, the article published by Gottschall *et al.* (12) provide interesting and largest data about platelet transfusion in real life, that is in some aspects quite different of recommendations summarized in the main guidelines. However, they provide a basis on which to design studies to improve the scarce available scientific evidence on platelet transfusion practice.

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