Effects and Timing of Tranexamic Acid on Transfusion Requirements in Patients Undergoing Cardiac Surgery with Cardiopulmonary Bypass

To the Editor:

Sigaut et al.[1] published a double-blind, randomized, controlled trial comparing low-dose and high-dose tranexamic acid (TA) bolus injections followed by continuous infusion in patients undergoing cardiac surgery with cardiopulmonary bypass.

The primary study endpoint was the incidence of overall blood products transfusions during surgery and up to 7 days postsurgery, which was not different between the two groups, a part from a lower transfusion of platelets concentrates during surgery in the high-dose TA group. The high-dose TA group showed also lower amounts of blood losses during day 1 and reduced administration of fresh-frozen plasma and platelets concentrates during the first postoperative week. Moreover, in the high-dose TA group, the rate of bleeding-related reexploration was less than half. Interestingly, although not statistically different, the 7-day and 28-day mortality rates were lower in the high-dose compared with low-dose TA group.

These results are very interesting and may partially support the use of high-dose TA. However, concerns may be raised against the protocol and design of the study. The primary outcome of transfusion at day 7 seems rather inappropriate for several reasons.

First, the half-life of TA (in order of a couple of hours)* and the need to maintain appropriate levels to ensure antifibrinolytic efficacy (>10 μg/ml)[2] are not consistent with a 7-day evaluation.

Second, during the first week, many other factors influence the risk of bleeding and transfusion requirements, for instance, postoperative strategies for antiplatelets therapy after coronary artery bypass grafting, for anticoagulation after valve surgery, or in patients developing atrial fibrillation. The authors did not clarify about the presence of standardized protocols for postoperative antiplatelet and anticoagulant therapy, and the incidence of postoperative atrial fibrillation was not reported.

Last, acute kidney injury is a well-known complication after cardiac surgery, with different incidence according to the criteria used and up to 5% of patients requiring postoperative renal replacement therapy.[3] The anticoagulation associated with renal replacement therapy is another factor that may increase the risk of bleedings and incidence of transfusions. Importantly, in this study, the baseline creatinine was higher in the high-dose group. The peak postoperative creatinine was not different between the groups, but the incidence of postoperative renal replacement therapy is not reported what hampers the interpretation of the results.

It may be speculated that significantly less blood loss and lower incidence of bleeding-related repeat surgery during the first 24-h postsurgery in the high-dose group was related to TA effects, considering the half-life of the drug, whereas the 7-day outcome could have been influenced at least by these three factors: strategies for antiplatelets/anticoagulation, development of atrial fibrillation, and need of renal replacement therapy and the related anticoagulation.

Further data analysis in this regard in both groups may be very useful to clarify the difference between the two groups.

Competing Interests

The authors declare no competing interests.

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In Reply:

We thank Dr. Sanfilippo *et al.* for their interest in our recent study published in Anesthesiology[1] about the comparison of two doses of tranexamic acid in adults undergoing cardiac surgery.

They criticize the choice of the primary outcome in our study, which was the number of patients who received at least 1 unit of blood product during the first postoperative week (including the intraoperative period).[1] They would have preferred a shorter period of observation for the primary outcome because of the half-life of tranexamic acid which was discontinued at the end of surgery. We disagree with their point of view. First, transfusion at day 7 includes the first day, when the majority of the transfusions occurred: 62% of the transfused patients were transfused only on the first day, 77% of the packed erythrocytes and 71% of the fresh-frozen plasma were given during day 1. Furthermore, transfusion during the first day, including the intraoperative period is reported

* Available at: http://labeling.pfizer.com/ShowLabeling.aspx?id=556. Available July 11, 2014.

 Anesthesiology 2014; 121:902-7