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LETTER TO THE EDITOR

Use of tranexamic acid in pediatric cardiac surgery: we really need more

David Faraoni · Caroline Van Aelbrouck · Christophe Cacheux

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To the Editor:

I read with interest the recent article of Shimizu et al. [1]. First, I congratulate the authors for their work and their wish to improve our knowledge about the use of tranexamic acid (TXA) in congenital heart surgery (CHS). It appears more and more evident that if TXA could reduce blood loss, the clinical benefit of this drug does not appear so evident. Indeed, if we analyze the available literature comparing TXA to placebo in terms of blood loss but also transfusion requirement, the results of the analysis indicate that TXA marginally decreases blood-product transfusion compared with placebo in the pediatric population. The results obtained for postoperative blood loss and other outcomes, such as re-exploration, are generally too heterogeneous, and no clear results could be interpreted [2]. As the authors wrote, the variability in the dosage schemes used in the different studies is striking. Moreover, the choice of TXA dosage was not based on pharmacokinetic (PK) data regarding the fibrinolytic inhibiting activity of the drug; instead, dosage choice was empirical based on its effects on blood loss. In fact, no pharmacological data on TXA are available in the pediatric cardiac surgery population. PK data have been determined in adults, and suggest the administration of a loading dose of 12.5 mg/kg given over 30 min, a maintenance infusion of 6.5 mg/kg/h, and a cardiopulmonary bypass (CPB) priming dose of 1 mg/kg to maintain TXA concentration in blood >345 μM/ml [3]. This dosage scheme is clearly smaller than those used in the different pediatric trials. Another lack of evidence in the use of TXA is the pharmacodynamic (PD) evaluation. Indeed, no randomized controlled trials have evaluated the effect of CPB on fibrinolysis activation with the currently available monitoring (thromboelastography, rotation thromboelastometry, or standard biological tests). What is the exact frequency rate of hyperfibrinolysis during CPB in CHS? What is the minimal effective concentration of TXA require to inhibit this fibrinolysis? Does TXA mechanism of action only work by fibrinolysis inhibition or by a combination with inflammatory pathway inhibition, and/or platelet function improvement [4]?

In the pediatric population, side effects related to TXA administration are not well established. Most of the studies available have evaluated the effect on bleeding and blood-product requirements, but none were designed to evaluate postoperative outcomes in the population. Actually, only two retrospective cohort studies reported side effects related to TXA administration during pediatric cardiac surgery [5]. They found 9.6% renal injury, 1.8% renal failure, 3.5% seizure, and 2.6% other neurological events. According to their results, more than 500 patients per group are needed to evaluate side effects related to TXA administration.

In conclusion, the article by Shimizu et al. offers another study and another reason to believe that we need more evaluations! We need to describe the PK in the pediatric population; we need to evaluate the PK/PD relation and the

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D. Faraoni (✉)
Department of Anesthesiology, Centre Hospitalo-Universitaire Brugmann, HUDERF, Place A. Van Gehuchten, 4, 1020 Brussels, Belgium
e-mail: David.FARAONI@huderf.be

C. Van Aelbrouck · C. Cacheux
Department of Anesthesiology, Erasme University Hospital, Brussels, Belgium

best dose scheme needed to reach the effective concentration. Finally, larger studies are needed to evaluate the benefit/risk balance with the administration of TXA during CHS.

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