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CORRESPONDENCE

Dual-route tranexamic acid to reduce blood loss in coronary artery bypass graft surgery: a randomized controlled trial

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To the Editor,

A 2009 systematic review and meta-analysis[1] suggested that topical anti-fibrinolytic agents can reduce postoperative bleeding and transfusion requirements in patients undergoing on-pump cardiac surgery. Systemic administration of lysine analogues, including tranexamic acid (TXA), has become the standard of care in patients undergoing on-pump coronary artery bypass graft (CABG) surgery to diminish perioperative blood loss and transfusion requirements.[2] Here, we report the findings of a double-blind, randomized trial in low-risk CABG surgical patients that evaluated whether co-administration of intravenous and topical TXA has a significant impact on blood loss and transfusion requirements. Approval from our institutional ethics board was obtained, and written informed consent was given by each participant.

Between December 1, 2011 and April 30, 2012 all patients scheduled for cardiac surgery at our institution were prospectively screened for trial participation. To limit participant heterogeneity, we recruited low-risk surgical candidates defined according to EUROScore criteria[3] scheduled for elective or urgent CABG.

Our primary outcome was the total volume of postoperative blood loss, determined by measuring mediastinal chest tube drainage. We calculated that a total sample size of 74 participants allowed 80% power to detect a 200 mL difference in total blood loss (type I error of 0.05) between groups. Secondary outcomes included chest tube losses at six and 12 hr, postoperative red blood cell transfusion requirement, and length of intensive care unit (ICU) stay. Adverse events of a thrombotic nature were recorded.

Participants were randomized to receive an intraoperative topical TXA solution (study arm) or normal saline (control arm) prepared by our institutional clinical trials pharmacy according to a non-blocked randomization list generated before patient enrollment began.

After general anesthesia, but prior to initiation of cardiopulmonary bypass, the study participants received a single intravenous bolus dose of TXA 30 $mg \cdot kg^{-1}$ over two minutes. Following removal of retractors and sponges prior to sternotomy closure, participants in the study arm received a cardiac bath of TXA solution containing 2 g TXA (1 g in 10 mL; Pfizer Canada, Saint-Laurent, QC, Canada) plus 50 mL of pre-warmed (42°C) normal saline. The control arm received 70 mL of pre-warmed normal saline only. This fluid remained within the pericardial cavity during placement of mediastinal chest tubes and chest closure. It was subsequently drained to the intraoperative cell-salvage machine by suction. The chest

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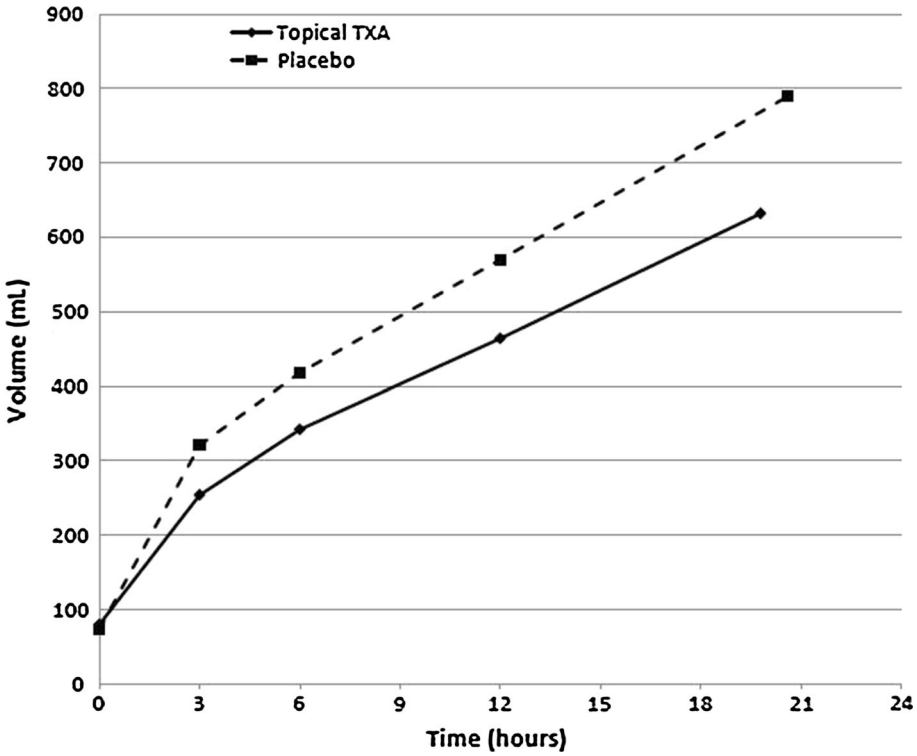

Figure Chest tube drainage over time. Mediastinal chest tubes were removed at a mean (standard deviation) of 19.8 (2.3) hr in the topical tranexamic acid (TXA) arm and 20.6 (2.9) hr in the control arm

tubes were connected to a portable drainage unit with continuous suction prior to ICU transfer.

The amount of chest tube drainage was recorded by the nursing staff beginning at ICU admission. Chest tubes were removed once the output fell below 200 mL over six hours.

Overall, 96 of the 149 patients scheduled to undergo cardiac surgery during our study were not eligible. The remaining 41 patients, randomized to the topical TXA arm (n = 23) or the control arm (n = 18), were included in the final analysis (recruitment into this trial stopped early because of resource constraints). There were no differences in baseline characteristics.

The mean (SD) postoperative chest tube loss at removal (Figure) was 632 (265) mL in the topical TXA arm *vs* 789 (216) mL in the control arm, with a difference of 157 mL (95% confidence interval, 0.5 to 312; P = 0.049). Differences in chest tube drainage were not significant at any other time points. No patients required postoperative red blood cell transfusion. The mean (SD) length of the patients' ICU stay was 24.7 (6.1) hr in the study arm and 24.4 (2.7) hr in the control arm. No significant adverse outcomes were reported.

The primary limitation of our study was its small sample size, which leads to the possibility that our results were due to chance. However, a recent retrospective study[4] with a similar study population also suggested that combined-modality TXA administration may be a superior blood conservation strategy. At our institution, we continue to utilize dual-route TXA administration in patients undergoing CABG surgery.

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Conflicts of interest None declared.

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