TITLE: PROPHYLACTIC TRANEXAMIC ACID DECREASES BLOOD LOSS AFTER EXTRACORPOREAL CIRCULATION

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INTRODUCTION: Significant hemorrhage remains a complication after surgery utilizing extracorporeal circulation (ECC)[1]. Primary fibrinolysis may contribute to this coagulopathy.[2] Epsilon aminocaproic acid (EACA), an inhibitor of fibrinolysis, can decrease post-operative bleeding.[3-4] Another anti-fibrinolytic agent, tranexamic acid (TA), has greater potency, fewer unwanted effects, and a longer half-life than EACA.[5] We evaluated the ability of prophylactic TA to decrease bleeding after ECC.

METHODS: With institutional review board approval, 36 patients for elective open heart surgery gave informed consent for this double-blind, randomized study. We excluded patients with known bleeding diatheses, those receiving aortic balloon counterpulsation, and those medicated within one week of surgery with heparin, warfarin, persantine, aspirin, or nonsteroidal anti-inflammatory drugs. The radial arterial catheter provided blood for PT, PTT, platelet count, fibrinogen, fibrin split products (FSPs), and plasminogen availability. This coagulation profile was done immediately upon catheter placement and again 4 hours after arrival in the ICU.

After induction with narcotic or volatile anesthesia but prior to incision, patients received either a saline placebo or TA, 10 mg/kg over 20 minutes IV followed by 1 mg/kg/hr for 10 hours. To insure adequate anticoagulation, the activated clotting time (ACT) was determined in duplicate prior to and every 30 minutes after administration of 400 Units/kg of beef lung heparin. Pump prime included an additional 5000 Units of beef lung heparin.

Adequate heparin neutralization was insured by administering protamine sulfate 1 mg for each 100 Units of prior heparin, including that in the pump. We gave an additional 0.3 mg protamine per 100 Units heparin after sternal closure to prevent heparin rebound. Blood loss was measured as the total chest tube drainage for the first 12 hours after surgery. Parametric data were analyzed with the unpaired Student's t-test; Fisher's exact test was utilized for FSP data.

RESULTS: Six patients with an abnormal pre-induction coagulation profile were excluded from analysis. Of 14 patients in the TA group, 8 underwent CABG, 4 valve replacement, and 2 a combined procedure; of 16 in the placebo group, 15 underwent CABG and 1 valve replacement. One patient in each group underwent re-operation. Post-operative PT, PTT, platelet count, and fibrinogen were not different between TA and placebo groups (see table). Plasminogen availability was decreased by more than half in the TA group ($p<0.001$). FSPs were present less frequently in the TA group ($p<0.00005$). Blood loss was nearly 50% greater in the placebo group ($p<0.05$).

DISCUSSION: TA inhibited activation of the fibrinolytic system, as seen by the significant decreases in plasminogen availability and FSPs in the TA group. The decrease in blood loss in the TA group suggests that fibrinolysis is a significant cause of bleeding after ECC and that inhibiting fibrinolysis reduces blood loss. Recently, EACA was shown to decrease blood loss minimally (273 vs 332 ml) after elective CABG.[4] We attribute the superior reduction of blood loss in our study to use of a better drug (TA)[5] and to administration prior to ECC.

Owing to an inability to develop strict criteria for the need to transfuse, this study did not address whether TA permits transfusion of fewer units of banked blood. In summary, prophylactic TA significantly decreases blood loss after ECC, which may lead to a decreased exposure to potentially infectious blood components in patients requiring ECC.

TABLE: Coagulation Test Results (mean ± SD)

	PLACEBO	DRUG	P-VALUE
Number of pts	16	14	
PT (% of nl)	45±13	53±13	NS
PTT (secs)	46±11	45±7	NS
PltCt (K/ul)	305±166	220±61	NS
Fibrinogen	177±43	173±25	NS
Plasminogen	98±77	37±18	<0.001
FSP Neg	2	11	
(# pts) >10	10	3	<0.00005
>40	4	0	
Blood loss	748±359	508±246	<0.05

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