TITLE: TRANEXAMIC ACID, NOT DESMOPRESSIN OR BOTH, DECREASES BLEEDING AFTER OPEN HEART SURGERY.

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Desmopressin (DDAVP) releases plasminogen activator (t-PA) from endothelial cells.[1] Might fibrinolysis resulting from t-PA release explain DDAVP's inability to limit bleeding after cardiac surgery?[2] We determined if prophylactic tranexamic acid (TA), an antifibrinolytic drug, could unmask the hemostatic effect of DDAVP.

103 cardiac surgical patients (single surgeon) gave informed consent with IRB approval. Recent therapy with aspirin or heparin did not exclude patients. Patients received, randomized & double-blinded, either placebo, TA, DDAVP, or both. IV TA began prior to skin incision with 10 mg/kg loading dose, followed by 1 mg /kg/hr for 12 hr. IV DDAVP, 0.3 µg/kg over 20 min, began after completion of protamine infusion. Beef-lung heparin, 400 U/kg iv plus 5000 U in clear fluid pump prime, provided anticoagulation. ACT ≥480 s determined the need for additional heparin. CPB utilized non-occlusive roller pumps and membrane oxygenators (Maxima).The 1st protamine dose was 4 mg/kg+ 1 mg/200 U additional heparin given. After chest closure and infusion of remaining pump blood, we gave additional protamine (30% of 1st dose). Mass of blood drained via mediastinal tubes for the first 12 hrs determined blood loss. Daily visits sought evidence of myocardial infarction, venous thrombosis, and stroke. Prior to incision and 2 hr after chest closure, we measured aPTT, platelet count, plasma fibrinogen, fibrin split products (FSP), Factor VIII, plasminogen, and thromboelastograph. Two-way ANOVA determined the effects of TA, DDAVP, and their interaction on blood loss.

99 patients completed the protocol. CPB lasted 96±37 min. Reinfused pump blood weighed 670±157g. Prior to incision, aPTT was 5±12s over control and platelet count 333±129 K/µL. Final aPTT (6±10 s over control), platelet count (230±135K/µL), fibrinogen (195±60) and Factor VIII (110±44%) did not differ among groups. The table displays blood lost, RBCs given, and incidence of FSP >10µg/mL. ANOVA showed TA (P <.005) but not DDAVP (P=.31) or their interaction (P=.71) affected blood loss. Groups TA and BOTH had less frequent post-op FSP (P<0.02). Fifteen variable stepwise regression showed RBCs given varied only with initial Hct (r=.35) and administration of TA (r=.39).

TABLE.	PLACEBO	DDAVP	TA	BOTH
Blood lost(g)*	508±284(SD)	450±197	354±191	327± 99
RBCs given	83±193 mL	157±240	72±171	51±195
+ FSP (#pts)	11/26	8/24	4/23‡	3/26‡

* Newman-Keuls test: (BOTH = TA) < (DDAVP = PLACEBO)
‡ P <0.02 compared to other groups.

These data confirm lack of DDAVP's hemostatic effect,[2] as well as the efficacy of antifibrinolytics[3,4] in decreasing blood loss. TA did not unmask a salutary effect of DDAVP, suggesting that t-PA release is not relevant. Prophylactic TA might inhibit a lytic state caused by Factor XII activation or it might preserve platelet function during CPB via platelet plasmin receptors.

References

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TITLE: IMPROVED NEUROLOGIC OUTCOME USING NALOXONE AND SPINAL FLUID DRAINAGE IN SURGERY OF THE THORACOABDOMINAL AORTA

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Introduction: Previous anesthetic and surgical interventions to reduce neurologic deficits associated with repair of thoracic and thoracoabdominal aneurysms (TAA) have been ineffective. Cerebrospinal fluid (CSF) drainage has been advocated to reduce the incidence of neurologic deficits following these procedures. Endorphin antagonists have been proposed as protective to the spinal cord in trauma and ischemia. Our recent experience with intraoperative CSF drainage by lumbar catheter and postoperative intravenous infusion of the endorphin antagonist naloxone suggests that it is possible to improve neurologic outcome with these interventions. This report reviews our 5 year experience in the surgical treatment of TAA patients with and without the use of spinal fluid drainage and naloxone.

Methods: Fifty-two consecutive patients were analyzed. Twenty (39%) were acute (13 ruptures, 4 dissecting aneurysms, 3 acute pain). Operative technique was uniform in all patients, employing simple aortic crossclamping and graft inclusion. Anesthetic technique in all patients consisted of fentanyl-benzodiazepine-muscle relaxant. Hemodynamic manipulations using inotropic agents and vasodilators were performed intraoperatively to maximize cardiovascular status when high thoracic aortic crossclamping was required. Spinal fluid was drained to keep CSF pressure below 14 mm/Hg. Naloxone was administered as a continuous intravenous infusion for 48 hrs after surgery.

Twenty-four patients treated from 1/84 to 12/86 did not receive spinal fluid drainage or naloxone (group A) and 28 patients treated from 1/87 to 10/89 had spinal fluid drainage (group B); the last 17 of these group B patients also received naloxone. Group A and B were comparably matched for age, sex, extent of aortic involvement, aortic crossclamp time, intraoperative hemodynamics, clinical presentation (acute or elective), prior cardiac and aortic surgery, and preoperative renal function.

Results: Neurologic deficits occurred in seven group A patients (29%) but in only one group B patient (3.5%) (who did not receive naloxone). This significant reduction ($p < 0.02$) in neurologic deficit was associated with lower operative mortality (12% in group A vs. 3.5% in group B) and increased one year survival (71% in group A, 93% in group B).

Conclusion: We conclude that adjunctive use of naloxone and spinal fluid drainage can significantly reduce the incidence of neurologic deficits associated with repair of thoracoabdominal aneurysms.

	Number Deficit (%)	Operative Mortality (%)	12 mo Survival
Group A N = 24	7 (29%)	3 (12%)	17 (71%)
Group B N = 28	1 (3.5%)*	1 (3.5%)	26 (93%)

*Did not receive Naloxone