Title: ALTERATIONS IN HEMOSTATIC PARAMETERS IN CRANIOTOMY PATIENTS: LACK OF RELATIONSHIP TO ADH LEVELS.

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Introduction. Postoperative deep venous thrombosis occurs in 29-43% of neurosurgical patients [1]. This high incidence of thromboembolic disease has been attributed to a variety of factors including venous stasis from long surgery and bed rest. Recently, it has become increasingly recognized that antidiuretic hormone (ADH) and its analogue (deamino-8-D-arginine vasopressin) result in increased release of factor VIII and von Willebrand factor (vWF) [2]. Since craniotomy patients (CP) are believed to have increased ADH levels, we were interested to determine if increased levels of ADH might contribute to the increased incidence of thrombosis via increases of factor VIII and von Willebrand factor. The purpose of this study, therefore, was to analyze plasma ADH levels, coagulation screening tests, factors VIII, IX (a non-ADH dependent factor), and vWF, and serum osmolarity in CP patients. We compared those results to a group of general surgery patients (GS) undergoing elective abdominal surgery.

Methods. The study was approved by Mount Sinai's institutional research review board. The patient population consisted of 13 patients (mean age 67 ± 6 years) undergoing elective craniotomy procedures. The control group consisted of 6 GS patients (mean age 72 ± 5 years). No patient in either group had a history of hematologic or hemostasis disorders, or had significant concomitant medical problems. Specimens for laboratory studies were obtained at 3 timepoints: A=prior to surgery, B=immediately postoperatively, and C=2 days following surgery. Prothrombin times (PT), partial thromboplastin time (aPTT), fibrinogen (Fib), CBC's, serum osmolarities and coagulation factor analyses were performed by standard methods. vWF levels determined by Laurell rocket immuno-electrophoresis and by ristocetin cofactor assays. ADH levels were measured by a reference clinical laboratory (Roche Biomedical Lab, Nutley, NJ). Data were analyzed by the Wilcoxon one way method to determine differences between two groups (SAS NPAR1WAY statistical package for microcomputers); $p<0.05$ was significant.

Results. The results of the coagulation studies are summarized in Table 1. Factor VIII, IX, and vWF were significantly increased in both groups following surgery, but not different between groups. aPTT (expressed as % of control aPTT) was significantly decreased in the CP patients postoperatively as compared to both baseline and the GS patients. ADH levels were increased preoperatively in CP patients but not postoperatively.

Discussion. The results of this study demonstrate a significant reduction in aPTT in the craniotomy patients that is not mediated by an ADH effect. In addition, we found that clotting factors are elevated in both groups postoperatively. We had hypothesized that ADH increases might be responsible for coagulation changes in CP patients, but there were no differences in ADH or factor assays between the 2 groups at any of the time-points. Further, factor IX, which is not influenced by ADH levels, was also elevated in both groups following surgery. We conclude that the shortened aPTT in the CP is due neither to elevation of ADH, nor to increases in factor VIII or IX alone. Thus, hypercoagulability, as reflected by reduced aPTT's may contribute to the increased incidence of thrombosis in craniotomy patients.

References.

1. Powers SK, Edwards SB: Prophylaxis of thromboembolism in the neurosurgical patient: a review. Neurosurgery 1982; 10:509.

2. Mannucci PM, Remussi G, Pusineri F, et al: Deamino-8-d-arginine vasopressin shortens the bleeding time in uremia. N Engl J Med 1983; 308:8.

Table 1:

		A	B	C
PT/ CONTROL	GS	1.0 ± 0.04	1.01 ± .01	1.1 ± .01
	CP	1.0 ± 0.03	1.00 ± .04	1.0 ± .05
PTT/ CONTROL	GS	1.0 ± .14	1.00 ± .01	1.01 ± .03[a]
	CP	1.0 ± .14	0.78 ± .12[a,b]	0.87 ± .03[a,b]
FIB	GS	341 ± 118	302 ± 102	415 ± 95
	CP	313 ± 68	285 ± 74	356 ± 96
Fact VIII	GS	239 ± 200	307 ± 104[a]	266 ± 250
	CP	115 ± 51	283 ± 129[a]	190 ± 82[a]
Fact IX	GS	301 ± 118	402 ± 102[a]	415 ± 95[a]
	CP	313 ± 68	515 ± 74[a]	515 ± 96[a]
vWF (electro)	GS	306 ± 133	820 ± 386[a]	614 ± 401
	CP	244 ± 181	1030 ± 480[a]	1280 ± 304[a]
ADH	GS	1.5 ± 1.4	4.1 ± 2.1	3.2 ± 2.2
	CP	4.7 ± 2.1[b]	8.2 ± 11	3.4 ± 2.4
Serum osm	GS	289 ± 12	290 ± 11	284 ± 9
	CP	297 ± 9	311 ± 13[a,b]	294 ± 13[b]

a = Significantly different from baseline $p<0.05$
b = Significantly different from GS group $p<0.05$