DIFFERENTIAL CHANGES OF PLASMATIC MARKERS OF THE ENDOTHELIAL FOLLOWING dDAVP. M.L. Scrobohaci, L. Drouet, B. Baudin, A. Rodriguez. Laboratoire d'Hématologie, Hôpital Saint-Louis, 1 Avenue Claude Vellefaux - 75475 PARIS Cédex 10.

Plasmatic levels of tissue plasminogen activation is commonly assumed to be of endothelial origin; Angiotensin converting enzyme can be of endothelial or monocytic origin; Fibronectin is mostly from hepatic origin but endothelium can participate. Protein S is a newly recognized endothelial protein. Plasmatic von Willebrand factor is mostly from endothelial origin as the factor megakaryocytic origin is stored in platelet & granules.

MDAVP by indirect effect stimulates release of endothelial factors, 13 patients with moderate von Willebrand disease were submitted to an infusion of 0.4 ug/kg dDAVP and were followed for four hours after infusion.

Interstingly the kinetics of release of each of the studied factors is totally different.

- Tissue plasminogen activator is rapidly released and come
- back also quickly to its original level,
 Release of von Willebrand factor is delayed comparatively
 to tPA and stayed for a longer time at increased level,
- Angiotensin converting enzyme is not affected by dDAVP while its level is stimulated by veno-occlusion
- Fibronectin and Protein S are not significantly modified

From these results mechanism of action of dDAVP cannot be hypothesized, but it seems evident that the release (and so the endothelial metabolism) of each of the studied factors is different and not linked.

HAEMOSTATIC RESPONSES TO VASOPRESSIN RELEASE DURING COLONOSCOPY. K.K. Hampton, H. Hariman, P.J. Grant and C.R.M. Prentice. University Department of Medicine, The General Infirmary, Leeds. LS1 3EX, UK.

Vasopressin (aVP) infusions resulting in plasma concentrations comparable to those occurring during stress result in increases in factor VIII coaquiant activity (FVIIIC) and increases in plasminogen activator activity (PAA) as measured by shortening of the euglobulin clot lysis time (ECLT). During major abdominal surgey aVP release is accompanied by similar changes in FVIII, PAA and FPA. The relative contributions of vasopressin release and tissue damage during the surgical procedure are not clear. The aim of this study was to investigate haemostatic changes during colonoscopy where bowel manipulation results in endogenous vasopressin release, but surgical tissue damage is absent. The study was performed in 12 patients undergoing routine colonoscopy. Sedation was achieved with pethidine 50 mg and midazolam 5 mg. Samples were taken after sedation, with the colonoscope in the caecum representing maximal bowel manipulation, and 15 minutes after representing maximal tower manipulation, and 's minutes after the end of the procedure. Samples were taken for aVP, ECLT, FVIII and fibrinopeptide A (FPA). In 8 patients a complete procedure was performed. Median aVP concentration rose from 0.5 before to 153 pg/ml at maximal bowel manipulation (p < 0.02), perfore to 153 pg/mL at maximal bowel manipulation (p < 0.02), PAA rose from 100 to 508% (p < 0.008) and FVIII from 100 to 218% (p < 0.02). The rise in aVP correlated with PAA (r = 0.68 p < 0.004) and FVIIIC (r = 0.74 p < 0.001). In 4 patients the procedure was terminated prematurely after minimal bowel manipulation. Plasma aVP did not change from 0.5 pg/ml and there were no significant changes in PAA and FVIIIC when colonoscopy was abandoned. FPA concentrations did not alter significantly in either group. The results suggest endogenous vasopressin release occurs during colonoscopy and is associated with increased PAA and FVIIIC, providing further evidence that vasopressin has a role in the regulation of haemostasis during stress. The lack of change in FPA suggests vasopressin release does not initiate thrombin generation and that tissue damage is necessary as the stimulus for fibrin formation.

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EFFECTS OF VASOPRESSIN AND ADRENALINE ON FIBRINOLYSIS: SYNERGISTIC OR ADDITIVE? P.J. Grant, P.G. Wiles, M. Boothby, J.A. Davies and C.R.M. Prentice. University Department of Medicine, The General Infirmary, Leeds. LS1 3EX, UK.

Vasopressin (aVP) and adrenaline both enhance plasminogen activator activity when infused at low doses in man and probably act as physiological regulators of fibrinolysis under certain conditions. The relative contribution changes in fibrinolysis are unknown. The relative contributions of these hormones to This study was carried out to investigate whether aVP and adrenaline act synergistically on plasminogen activator in man. Four normal volunteers were infused with (1) aVP (1.00/h), (2) adrenaline $(420~\mu g/h)$, (3) aVP and adrenaline and (4) 0.9% saline for 1h. Saline (0.9%)was infused for 30 min before and after infusion. There was a minimum of 2 weeks between infusions and the subjects were not aware of the contents of the infusate. Samples were taken after 30 min saline infusion and every 30 min for 1 1/2h for 30 min saline infusion and every 30 min for 1 1/2h for euglobulin clot lysis time (BCLT), factor VIII:C, aVP and adrenaline. During (1) and (3) plasma aVP rose from (median) 0.9 pg/ml to 13.2 pg/ml after 1h. During (2) and (4) plasma aVP remained constant at 0.9 pg/ml. Plasma adrenaline rose from 0.21 nmol/l to 0.62 nmol/l after 1h during (2) and (3) and remained unchanged at 0.20 nmol/l during, (!) and (4). Plasminogen activator activity (10 / PCLTT) rose (%) from 100 to 150% at 1h during adrenaline infusion, (p < 0.05), 100 to 148% during aVP (p < 0.05), 100 to 252% (p < 0.05) when both were infused and from 100 to 123% (N.S) during saline infusion. Factor VIII remained unchanged. The results indicate that at low physiological concentrations, aVP and adrenaline have low physiological concentrations, aVP and adrenaline have additive effects on fibrinolysis but are probably not syner-gistic. This is consistent with the view that aVP and adrenaline mediate this response by different receptors.

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EFFECTIVENESS OF DDAVP IN PATIENTS WITH VON WILLEBRAND'S DISEASE WITH SEVERELY REDUCED BASAL LEVEL OF F VIII/VWF AND NORMAL PLATELET CONTENT (TYPE I, PLATELET NORMAL) UNDERGOING TOOTH EXTRACTION.

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DDAVP has been used for hemorrhage prevention during dental extraction in patient (pts.) with von Willebrand's disease (vWd), usually of type I. However, only about 20 cases have been reported. Moreover, the majority of pts. had basal level of VIII:C and vWf equal to or higher than 20% so that dental procedures could probably have been performed safely also without any specific treatment.

We report the experience with DDAVP for hemorrhage prevention during dental extraction in 14 pts. with type I vWd (confirmed by plasma multimeric analysis, Prof. Mannucci, Milan) and severely reduced basal level of VIII:C (mean 12.9 ± 3 UI%; range 8-18 UI%) and vWf (< 3 UIX), measured as ristocetin cofactor. VWf:Ag and vWf platelet content (UIX/10 platelets; platelets separated by Ficoll-Hypaque and lysed with Triton X) was in normal range (17-35 UI% and 22-68% in pts.; 17-37 UI% and 24-62 UI% in 18 controls). After DDAVP infusion (0.4 $\mu g/m1$), VIII:C and vWf activities increased respectively 8.5 folds (range 6.4-11.8) and 28.2 folds (range 16-40). Return to basal levels occured with an half-life of 60 - 80 minutes for all the activities. Bleeding time, prolonged in 8 pts., was normalized in 7 cases and shortened in 1. All the pts. referred of previous hemorrhage after tooth extraction performed in the past. A total of 50 extractions were performed (3.67 teeth/pts). Mild bleeding occured in only 2 pts. 3-5 days after extraction and was promptly stopped by repeating $\ensuremath{\mathtt{DDAVP}}$ infusion.

In conclusion, DDAVP has proved effective for dental extraction in type I vWd pts. with severely reduced VIII:C and vWf activities in plasma but normal platelet content.