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CONCENTRATED DDAVP: FURTHER IMPROVEMENT FOR THE TREATMENT OF MILD F.VIII DEFICIENCIES. A. Ghirardini, T. DiPaolantonio, S. Solinas, M. Papacchini, C. Cutrera and G. Mariani. Dept. of Human Biopathology - Section of Hematology, University "La Sapienza", Rome, ITALY.

We have evaluated the pharmacological efficacy of a concentrated DDAVP preparation (40 µg/mL) (herein referred to as C-DDAVP) administered subcutaneously (s.c.) in mild (n=23) and moderate (n=2) hemophilia A patients. A comparison between the response to s.c. C-DDAVP and the "dilute" DDAVP (4 µg/mL) (administered s.c. in 16 patients with mild (n=13) and moderate (n=3) hemophilia A and i.v. in 18 patients with mild (n=16) and moderate (n=2) was also carried out. In all instances Desmopressin was given at a dose of 0.3 µg/kg b.w. in absence of bleeding. The increase of F. VIII:C (expressed as post/pre bleeding) after s.c. C-DDAVP was 2,55 at 30', 3,50 at 60' and 3,21 at 120'. The comparison among the three schedules of DDAVP administration showed that s.c. C-DDAVP elicited an increase of F. VIII:C at least as high as that induced by the dilute DDAVP with differences not statistically significant.

	Patients (n)	F.VIII:C (u/dL)			
		baseline		60 min.	
		$\bar{x}$	S.D.	$\bar{x}$	S.D.
C-DDAVP s.c.	25	11.78	5.07	39.92	22.03
DDAVP s.c.	16	11.67	5.86	37.12	25.55
DDAVP i.v.	18	10.6	6.8	28.9	16.8

C-DDAVP was also administered s.c. in 4 patients with type I vWD (platelet normal subtype) with a normalization of bleeding time 60' after s.c. C-DDAVP, concomitant with a rise of activities related to F. VIII/vWF complex. Side effects were modest and transient. We can conclude that s.c. C-DDAVP is equally effective and safe in comparison with the dilute brand with the advantage of the minimal administration volume (<1 mL).

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THE FIBRINOLYTIC, FACTOR VIII:C, VON WILLEBRAND FACTOR AND HEMODYNAMIC RESPONSES TO DDAVP IN PATIENTS WITH HEREDITARY NEPHROGENIC DIABETES INSIPIDUS. BRINK S (1), DERKX F (1), BROWWER E (2), STIBBE J (1), KOLSTEE A (3), SCHALEKAMP M (1). Departments of Internal Medicine 1 and Hematology Erasmus University Rotterdam (1), Gaubius Institute Leiden (2), Stichting Crayenburch, Wootdorp (3), The Netherlands.

The pressor response of vasopressin (AVP) is mediated by a calcium-dependent mechanism (V1-receptor), whereas its antidiuretic effect depends on c-A<sub>2</sub>P (V2-receptor). DDAVP (1-desamino-8-D-arginine vasopressin) is a synthetic V2 analog of AVP. AVP and DDAVP also increase FVIII:C vWF:Ag and tissue-type plasminogen activator (t-PA) in plasma. The mechanism by which AVP and DDAVP elevate these factors is unclear. Patients with X-linked nephrogenic diabetes insipidus (NDI) are resistant to the V2-mediated antidiuretic action of AVP and DDAVP. We therefore have studied the effect of DDAVP (0.4 µg/kg iv infusion in 10 min) in 2 brothers with NDI, their mother and an unrelated patient.

In control subjects (n=12) FVIII:C rose 122 (6) % (mean (SE)), vWF:Ag 104 (4) % and t-PA 115 (7) % over basal levels. This rise was associated with a fall in diastolic blood pressure -11 (3) mmHg and an increase in heart rate from 62 (4) to 91 (5) bpm. Plasma noradrenaline rose from 252 (34) to 590 (84) pg/ml and renin from 15 (3) to 42 (5) uU/ml. Ten out of 12 controls showed facial flushing. The patients with NDI had normal basal FVIII:C, vWF:Ag and t-PA levels. Plasma noradrenaline and renin were within the normal range. The patients with NDI were also resistant to the stimulatory effect of DDAVP on the release of FVIII:C, vWF:Ag and t-PA. They also showed no change in blood pressure, heart rate, plasma noradrenaline and renin and had no facial flushing. The carrier had normal responses to DDAVP.

The increase in FVIII:C, vWF:Ag and t-PA and the hemodynamic responses after DDAVP infusion probably appear to depend on extrarenal V2-receptor activation. DDAVP cannot be used in identifying carriers in families at risk.

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THE EFFECT OF DDAVP ON PLASMA AND PLATELET VON WILLEBRAND FACTOR MULTIMERIC PATTERN AND BLEEDING TIME IN PATIENTS WITH CONGENITAL PLATELET FUNCTION DEFECTS. K.Oksanen, R.Kekomäki, A.Lindbom, G.Myllylä, V.Rasi and E.Vahtera. Finnish Red Cross Blood Transfusion Service, Kivihaantie 7, Helsinki, Finland.

Eleven patients with congenital platelet function defects and prolonged template bleeding time (BT) were studied. All patients had significant bleeding tendencies and were classified as having platelet release defects.

After initial blood sampling and BT measurement, tranexamic acid (10 mg/kg) and DDAVP (0.3 µg/kg over 15 minutes) were infused, followed by second blood sampling at 30 minutes and BT measurement at 60 minutes.

Plasma vWF multimeric patterns were analyzed from 11 and platelet vWF multimeric patterns from 7 patients. vWF multimers were identified by electrophoresis of plasma or platelet lysates in agarose containing 0.1% SDS and visualized by immunoblotting using alkaline phosphatase-conjugated anti-antibody.

Bleeding time was normalized by DDAVP in 5 patients, partly corrected in 3, and unchanged in 3. Those 4 patients with longest BT (more than 20 minutes) either showed no response (3) or were only partially corrected (1).

Plasma F VIII:C, vWF:Ag, and F VIII:Rcof all increased similarly in responders, partial responders, or non-responders. The multimeric patterns of plasma vWF were initially normal in all patients and showed increases of the largest multimers in all three groups. Platelet vWF analysis also showed increase of larger multimers after DDAVP infusion; these changes usually paralleled those of plasma vWF. Increase of the large multimers was observed as well in responders and partial responders as in non-responders.

DDAVP was effective in correcting the prolonged bleeding time of several patients with platelet release defect. The analysis of plasma or platelet vWF multimeric pattern seemed not to predict this response.

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DOES DESMOPRESSIN ACETATE REDUCE BLOOD LOSS AFTER CARDIOPULMONARY BYPASS SURGERY? E. Rocha (1), R. Llorens (2), J.A. Páramo (1), R. Arcas (2), B. Cuesta (1), A. Martín Trenor (2). Hematology (1) and Cardiovascular Surgery (2) Services, University Clinic, University of Navarra, Pamplona, Spain.

It has been suggested that desmopressin acetate (DDAVP) administration reduces blood loss after cardiac surgery. We have investigated the effect of DDAVP administration in a double-blind, randomized, prospective trial including 60 patients undergoing cardiopulmonary bypass surgery. Thirty patients received 0.3 µg/kg DDAVP and 30 patients a placebo. The infusion was administered in a 50 mL saline solution over 15 min when cardiopulmonary bypass had been concluded. Blood samples were taken before surgery, immediately before and 90 min after DDAVP or placebo administration, and 24 hours postoperatively. The following parameters were measured in each sample: hematocrit, hemoglobin, platelet count, VIII:C and factor VIII:vWF. Bleeding time was also measured before operation and 90 min after treatment administration. Blood loss and transfusion requirements were evaluated from the beginning of treatment until 72 hours after surgery. Results showed no significant differences neither in total blood loss (833 ± 363 ml in the DDAVP group vs. 907 ± 646 in the placebo group) nor in blood transfusion (1633 ± 676 ml in the DDAVP group vs. 1643 ± 720 in the placebo group). The prolongation of bleeding time and the decrease of factor VIII:vWF, 90 min after treatment, were significantly lower (p < 0.05) in the DDAVP group as compared with the placebo group. We conclude that DDAVP administration does not reduce blood loss in patients undergoing cardiopulmonary bypass surgery, which would suggest a more complex mechanism to explain the increased bleeding in these patients.