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DDAVP IN DIABETES INSIPIDUS. V.Vicente, J.Corrales, J.Miralles, I.Alberca. Departments of Hematology and Endocrinology. University Hospital. Salamanca.Spain.

In order to investigate whether the response of von Willebrand factor (vWF), Factor VIII (FVIII) and tissue plasminogen activator (t-PA) to DDAVP infusion is governed by the integrity of the hypothalamo neurohypophyseal axis, we studied the behaviours of these proteins (FVIII, one stage; vWF antigen by electroimmunoassay and t-PA was measured in the plasma auglobulin fraction with added C-1 inactivator on fibrin plates) after DDAVP infusion (0.3 ug/Kg) in five patients with cranial diabetes insipidus, comparing them with the responses obtained in six healthy subjects.

In spite of receiving a daily therapeutic dose of 10-20 ug of DDAVP the patients with diabetes insipidus showed normal basal levels of FVIII, vWF and t-PA. The increase in these parameters following DDAVP infusion were not significantly different in the two groups. These findings suggest that the integrity of the hypothalamo-hypophyseal axis is not neccessary for a response by vWF, FVIII and t-PA to occur after DDAVP infusion.

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EFFECT OF DDAVP ON MYOCARDIAL INFARCT SIZE: P.Pabón, V.Vicente, I.Alberca, C. Martin Luengo, A. Lopez Borrasca. Department of Cardiology and Haematology. University Hospital. Salamanca. Spain.

Infarct size, estimated by electrocardiographic changes (the QRS Scoring System, developed by Wagner et al, Circulation 65,342, 1982) and enzymatic analysis (creatinine kinase, CK) was studied in 45 patients with no history of previous infarcts. 25 received an intravenous dose of DDAVP (0.3 ug/kg) and 20 received a placebo solution (saline). The time between the onset of symptoms and DDVAP administration was less than 12 hours. The results showed no significant differences between the two groups in maximal or acumulative activity of creatinine kinase (CKr) or the QRS score peak. However, in patients with a mean evolution time of less than 1 hour, the CK peak was significantly lower in the DDAVP group than in the placebo group ($p<0.05$). Furthermore the percent of maximal increase in the QRS score was lower in the DDAVP group than in the patients receiving the placebo ($p=0.1$). On admission, the fibrinolytic activity of euglobulin fractions (measured by fibrin plates) was higher in the patients in both groups than in a group of healthy subjects (n=40). Also, DDAVP significantly increased fibrinolyric activity whereas no changes were found in patients receiving the placebo. The mean CKr value was lower in patients with an increase in fibrinolysis than in those who showed no changes in it. Finally, in the DDAVP group the QRS score peak was strongly dependent on the initial QRS score and, regarding this, our results suggest that small infarcts on admission may represent a potential indication for DDAVP therapy.

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HAEMOSTATIC CHANGES IN CIRRHOSIS AFTER REPEATED DOSES OF DESAMINO D-ARGININE VASOPRESSIN (DDAVP). Burroughs A,* Taylor L, Sprengers D,* Hutton RA, McIntyre N,* Kernoff PBA. Academic Dept of Medicine* and Haemophilia Centre, Dept of Haematology, Royal Free Hospital, London, NW3 2QG, England.

Eight patients with stable cirrhosis received DDAVP (0.3ug/kg I.V. of Desmopressin acetate, Ferring Pharmaceuticals) and this dose was repeated after 4h and 24h. Blood for haemostatic studies was collected immediately before and 1h after each dose. Results, shown below as medians (expressed in u/dl), with ranges in parentheses, were analysed using the Wilcoxon signed rank test for paired data. One hour after the first dose, von Willebrand factor antigen (VW:ag) and Ristocetin co-factor activity (Ricof) rose from 380 (182-1060) to 502 (230-1000), $p<0.01$ and from 400 (154-1200) to 494 (180-1600), $p<0.01$ respectively. This rise was sustained at 4h but increased further 1h after the second dose: VW:ag to 540 (305-1000) and Ricof to 570 (420-1150), $p<0.01$. Levels were significantly above baseline ($p<0.01$) at 24h but rose again after the third dose: VW:ag to 540 (300-1180), $p=<0.01$ and Ricof to 479 (277-625). A similar but less marked response was seen in factor VIII:C from 220 (112-300) to 300 (128-360) $p=0.01$ at 1h, which was maintained up to 4h but not 24h. The rise after the second and third dose was not significant. Multimeric analysis of VWF showed an increase in the very high MW oligomers after DDAVP. Irrespective of the basal value, the euglobulin lysis time shortened consistently after DDAVP and platelet aggregation showed an enhancement with ristocetin, a decrease with adrenaline and no change with adenosine diphosphate and collagen. The bleeding time shortened in half the patients but did not correlate with other changes. We conclude that rises in VW:ag and Ricof are sustained with repeated doses of DDAVP despite the high initial levels in cirrhotics, whereas rises in VIII:C and fibrinolytic activity are transient.

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EFFECT OF DDAVP ON PRIMARY HEMOSTASIS WITH CONGENITAL AFIBRINOGENEMIA. M. Taki (1), M. Inagaki (1), T. Miura (1), N. Saito (1), T. Meguro (2) and K. Yamada (2). Department of Pediatrics, School of Medicine, Keio University, Tokyo (1) and Department of Pediatrics, School of Medicine, St. Marianna University, Kawasaki (2), Japan.

It has been reported recently that DDAVP might be an useful tool in the therapy and prevention of bleeding in patients with congenital afibrinogenemia (CA).
To study the mechanism of its efficacy, changes in the platelet functions of a patient with CA were examined prior to, and one hour after, the infusion of DDAVP (0.4 μg/Kg). A patient with Glanzmann's thrombasthenia (GT) was also examined, to allow a study of the role of platelet membrane glycoprotein IIb/IIIa (GP IIb/IIIa), a deficient platelet in GT, in the resulting effects of the drug. When both patients were infused with DDAVP, the level of plasma von Willebrand factor (vWF) increased two- to fourfold, accompanied by an enhancement of ristocetin-induced platelet agglutination. The level of plasma fibrinogen was never changed. The prolonged bleeding time observed was markedly improved only in the CA patient, remaining unchanged in the GT patient, after the infusion of DDAVP. This indicates that DDAVP is effective in diminishing the bleeding tendency in CA, but not in GT. Among the platelet functions tested, only the platelet retention rate on glass beads, ADP-induced platelet aggregation and collagen-induced platelet aggregation improved in CA, each remaining unchanged in GT. In particular, collagen-induced platelet aggregation was markedly improved in the CA patient. However, the platelet adhesion to collagen (50 μg/ml)-Sepharose remained normal, both before and after the infusion of DDAVP in CA.
These results suggest that an increase in the plasma vWF level and the existence of platelet membrane GPIIb/IIIa may be necessary for the improvement of primary hemostasis, after the infusion of DDAVP. The vWF-mediated platelet aggregation by collagen or ADP may produce this effect in the CA patient.