DDAVP, Cryoprecipitate, and Highly 'Purified' Factor VIII Concentrate in Uremia

A.	Allan	Juhl
----	-------	------

Department of Nephrology, University of Copenhagen, Denmark

Allan Juhl, MD, Department of Nephrology, University of Copenhagen, DK-2650 Copenhagen (Denmark)

Dear Sir,

A recent letter [1] dealing with deamino-8-D-arginine vasopressin (DDAVP) in patients with uremia prompted this reply. The authors showed that the bleeding time was not reduced in 5 patients with chronic glomerulonephritis undergoing regular hemodialysis 1 h after the infusion of DDAVP. Furthermore, DDAVP did not produce any important increase in factor VIII: von Willebrand factor activities.

Uremic bleeding reflects a complex disorder of hemostasis commonly associated with variations in the levels of factor VIII: von Willebrand factor activities. Holmberg and Nilsson [2] noted that elevated levels of factor VIII clotting activity accompanied chronic renal failure. Kazatchkine et al. [3] found elevated von Willebrand factor antigen levels, but the ristocetin cofactor activity lower than normal, suggesting that chronic renal failure was accompanied by a functional abnormality of the von Willebrand factor that might partly explain the prolonged bleeding time in chronic renal failure. The study by Janson et al. [4], using cryoprecipitate, known to be enriched in both VIII: C and the larger von Willebrand components of the factor VIII complex, and the study by Mannucci et al. [5], using DDAVP, showed that the bleeding time shortened in uremic patient. The bleeding time is the single test that most closely correlates with clinical bleeding in patients with renal failure [6, 7]. We have evaluated the response of factor VIII: von Willebrand factor and bleeding time to DDAVP (0.3 µg/kg body-weight), cryoprecipitate (50 IU/kg body weight), and highly 'purified' factor VIII concentrates (55 IU/kg body weight) in 1 uremic patient (a 40-year-old woman) undergoing 5 years of regular hemodialysis with a history of complicated postoperative bleedings during the last 4 years (table I). She was planned for a related-donor

Table I. Response of factor VIII: von Willebrand factor and bleeding time to highly purified Hematrate, cryoprecipitate, and DDAVP

Normal range

0.80- 0.70- > 40 1.0 1.20 1.30

3-9.5 0.80- 0.70- > 40 1.0 1.20 1.30

3-9.5 0.80- 0.70- > 40 1.0 1.20 1.30

3-9.5

F = Factor; AHF = antihemophilic factor; n.d. = not determined.

306

Juhl

kidney. After all three infusions we found minor but significant increases in plasma concentrations of factor VIII: von Willebrand factor properties, VIII :C, VIII-R:Ag, VIIIR:RCo, and ristocetin-platelet aggregation. A temporary shortening of the Ivy bleeding time was demonstrated after administration of cryoprecipitate and DDAVP, but not after highly 'purified' factor VIII concentrate. Factor VIII: von Willebrand factor circulates in a multimeric form, of which larger multimers are essential for its biologic interaction with platelets. Only cryoprecipitate and DDAVP increase the larger multimeric factor VIII: von Willebrand factor forms in plasma [5, 8], and the temporal association between the increase and half-life for factor VIII: von Willebrand factor in a specific state of polymerization and shortening of bleeding time is striking. Such a phenomenon is shown to over-come-temporarily-the platelet adhesion defect in uremia. The mechanisms of action of factor VIII: von Willebrand factor in shortening the bleeding time are unclear, but the platelet hypoaggregation demonstrated by raised ristocetin-platelet aggregation values and the elevated levels of factor VIII: von Willebrand factor activities with normal structure of the plasma von Willebrand multimers [4, 5, 9] show a von Willebrand factor receptor defect of uremia. Immunochemical studies of platelet membrane abnormalities in patients with chronic renal failure are in progress.

References

- Vicenti, V.; Alberca, I.; Macias, J.F.; Lopez Barrasca, A.: DDAVP in uremia. *Nephron* 56:145–46 (1984).
- Holmberg, L.; Nilsson, I.M.: AHF related protein in clinical praxis. *Scand. J. Haematol.* 72:221–231 (1974).
- Kazatchkine, M.; Sultan, Y.; Caen, J.P.; Bariety, J.: Bleeding in renal failure: a possible cause. *Br. med. J.* ii:612–615 (1976).
- Janson, P.A.; Jubiliner, S.J.; Weinstein, M.J.; Deykin, D.: Treatment of the bleeding tendency in uremia with cryoprecipitate. *N. Engl. J. Med.* 303:1318–1322 (1980).
- Mannucci, P.M.; Remuzzi, G.; Pusineri, F.; Lombardi, R.; Val-secchi, C.; Mecca, G.: Deamino-8-D-arginine vasopressin shortens the bleeding time in uremia. *New Engl. J. Med.* 308: 8–12 (1983).
- Eknayan, G.; Wacksman, S.J.; Glueck, H.I.; Will, J.J.: Platelet function in renal failure. *New Engl. J. Med.* 280:611–6% (1969).
- Steiner, R.W.; Coggins, C.; Carvalho, A.C.A.: Bleeding time in uremia: a useful test to assess clinical bleeding. *Am. J. Hematol.* 7:107–117(1979).
- Weinstein, M.J.; Deykin, D.: Comparison of factor VHI-related von Willebrand factor proteins prepared from human cryoprecipitate and factor VIII concentrate. *Blood* 55:1095–1105 (1979).