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A prospective study of cryoprecipitate administration: absence of evidence of virus infection

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Summary In a prospective study of cryoprecipitate administration to patients who had never received large pool concentrates, no evidence of hepatitis or HIV infection was detected in a follow up period of one year. Following the introduction of screening of blood donors for anti-HIV in the UK in October 1985 the use of cryoprecipitate in selected cases should be reconsidered.

Keywords: cryoprecipitate, virus infection

After first treatment with large pool factor VIII concentrates in patients with haemophilia A or Von Willebrand's Disease (VWD), the development of non-A, non-B hepatitis is almost inevitable (Fletcher *et al.* 1983; Kernoff *et al.* 1985a). Attempts to prevent hepatitis by heat treatment of the concentrates have usually proved disappointing (Colombo *et al.* 1985) although some batches of heated concentrates appear not to have transmitted hepatitis (Kernoff *et al.* 1985b; Colvin *et al.* 1986). Until the recent epidemic of the Acquired Immune Deficiency Syndrome (AIDS), cryoprecipitate was widely used as the safest form of treatment for patients with mild coagulation defects who were unsuitable for DDAVP injection.

The association of Human Immunodeficiency Virus (HIV) infection with the use of NHS factor VIII concentrate has also provoked reluctance to use cryoprecipitate. We are now reporting a prospective study of patients with mild haemophilia A or VWD treated with cryoprecipitate between October 1982 and July 1984, in an attempt to establish the risk of transfusion hepatitis in this group and have also tested the sera retrospectively for evidence of HIV infection.

Patients, methods and results

Six patients (three with haemophilia A and three with VWD) were selected for study. None had a previous history of jaundice, had received treatment in the

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previous year or had ever received large pool concentrates. Three had occasionally received cryoprecipitate in the past and three were untreated. One patient was treated for a severe knee haemarthrosis and the other five underwent elective surgery. The mean dose of cryoprecipitate was 100 bags (range 47–250). At the start of treatment and at the times shown in Table 1, blood samples were collected and were tested for serum alanine (ALT) and aspartate (AST) aminotransferase levels by routine methods. Sera were also tested for hepatitis B surface antigen (HBsAg) by immunoradiometric assay (Hepatube: Burroughs Wellcome Ltd), anti-HBs by radioimmunoassay (Ausab: Abbott Laboratories Ltd), anti-HBc by a blocking enzyme immunoassay (Organon Laboratories Ltd) and anti-HAV by antiglobulin enzyme immunoassay (Central Public Health Laboratory, Colindale, London NW9). Anti-HIV tests were done using a competitive enzyme immunoassay (Wellcome Laboratories Ltd). All the patients remained well without clinical or laboratory evidence of hepatitis. All patients were positive for anti-HAV, but negative for HBsAg, anti-HBs, anti-HBc and anti-HIV. ALT and AST values are shown in Table 1.

Discussion

This small prospective study of cryoprecipitate treatment showed no evidence of infection with hepatitis or HIV viruses after careful follow-up of each patient for one year. These findings agree with those of Kernoff *et al.* (1985a) in which five patients treated exclusively with cryoprecipitate showed no evidence of viral hepatitis. In that series the dose used was lower (mean 37 bags, range 5–70) and evidence of HIV infection was not sought. It is important to establish the relative

Table 1. Liver enzyme values in patients treated with cryoprecipitate

Patient and enzyme values iu/l	Week										
	0	2	4	8	12	16	22	28	32	38	50
ALT	41	38	32	16	23	22	16	11	22	18	27
AST	39	18	29	23	29	28	32	27	27	25	30
ALT	14	28	1	16	8	18	25	23	12	9	23
AST	30	23	9	14	19	27	27	17	24	19	25
ALT	11	29	18	29	14	4	16	12	—	14	13
AST	10	26	22	13	17	26	30	28	—	25	30
ALT	30	32	29	24	24	28	19	21	20	28	25
AST	26	18	15	20	22	16	14	17	17	28	27
ALT	4	14	9	7	7	14	5	—	10	11	14
AST	23	13	11	18	7	18	22	—	13	13	17
ALT	15	20	12	8	7	12	14	5	16	18	17
AST	17	16	19	13	11	17	15	15	14	18	16

safety of cryoprecipitate and large pool concentrates because not all patients with VWD are suitable for treatment with DDAVP and highly purified factor VIII concentrate may not contain enough Von Willebrand Factor to produce a clinical response in this condition (Nilsson & Hedner 1977).

The emergence of HIV infection in haemophiliacs has prompted the suggestion that cryoprecipitate should not be used as it cannot be heat treated (Bloom, Forbes & Rizza 1985). More recently doubt has been expressed as to the absolute safety of heat treated concentrates with respect to HIV infection (White *et al.* 1986; van den Berg *et al.* 1986), but the data so far published are by no means conclusive. A survey of HIV antibody in haemophiliacs in the UK conducted in August 1985 showed that only two of 166 patients (1.2%) treated only with cryoprecipitate between 1980 and 1984 had seroconverted compared with 20 out of 198 (10%) of those treated only with NHS (unheated) factor VIII over the same period (AIDS Group of UK Haemophilia Centre Directors 1986). The introduction of the screening of blood donors for anti-HIV in the UK in October 1985 should further reduce the risk of HIV infection from cryoprecipitate, and its use should now be reconsidered in selected cases. Careful follow-up will be needed to confirm its safety.

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