

Cryoprecipitate and Hepatitis

Background

Cryoprecipitate was introduced for the treatment of haemophilia A in the mid-1960s. Transmission of hepatitis by cryoprecipitate in the UK was first reported in 1969, with two cases being described.

In the first case reported, a 41-year old patient with haemophilia A was treated with a total of 162 units of cryoprecipitate in the period January-March 1969. He presented with clinical symptoms of hepatitis in May 1969 and died about one week later. Hepatitis infection was confirmed at post-mortem.¹

In the second case reported, a 51-year old haemophiliac had been treated with 72 units of cryoprecipitate in December 1967 and a further 52 units in February 1968. He was diagnosed with clinical hepatitis in May 1968.²

The timescale for development of clinical symptoms suggests that both of these patients were infected with hepatitis B virus. Screening of donors for hepatitis B infection was introduced in the UK in 1970/71.

After this it was apparent that cases of abnormal liver function continued to occur, and this syndrome became known as non-A, non-B hepatitis [NANB]. Almost all cases of NANB hepatitis were attributed to Hepatitis C after this virus was identified in 1989 and a test developed soon afterwards. The proportion of donations that caused NANB hepatitis was 0.3% [Prof Howard Thomas evidence to the Inquiry, p7 of the transcript]. When testing of blood donors for Hepatitis C commenced in the UK, the initial prevalence of Hepatitis C in blood donations was lower than that at nearer 0.1%. It is now significantly lower than that.

Theory

The probability of a patient being infected by a blood product, which has not been treated to eliminate the infective agent, is related to the prevalence of

the infection in the blood donor population and the amount of treatment received.

The probability of exposure to an infective agent via treatment with blood products can be calculated using the following equation³

$$P = 100 - 100 (1 - i)^n$$

Where:

P = the probability of exposure

i = the incidence of infection in the donor population

n = the number of donations.

Hepatitis C risk from cryoprecipitate

The probability of infection with hepatitis C via treatment with cryoprecipitate has been estimated for two scenarios, a lower level of treatment and a higher level of treatment. These are both based on documented treatment programmes from the relevant period. The figure for the prevalence of Hepatitis C in blood donations in Scotland prior to testing of 0.3% has been used to calculate the risk of acquiring Hepatitis C during the period before testing started in 1991. Alternative scenarios using a figure of 0.1% hepatitis C prevalence are also provided.

Lower level of treatment

In 1974, patients with haemophilia A in the South East of Scotland were treated on average with 500 IU factor VIII/kg body weight /year.⁴ On this basis a typical adult haemophiliac would have received 313 units of cryoprecipitate per annum.

Assuming an incidence of hepatitis C in the donor population of 0.3%, it can be calculated that the probability of exposure to infection would have been 60% after one year and 85% after two years of treatment.

This level of treatment did not encompass home therapy, nor did it include major reconstructive surgery, nor other elective or general surgical procedures, nor treatment of inhibitors with large amounts of factor VIII.⁴ At this time, the average age at death of a person with haemophilia A in the UK was 42 years.⁵ If the prevalence was 0.1% in donations, then 27% of patients would be exposed to hepatitis C at 1 year and 46 % at 2 years, reaching 95% after 10 years.

Higher level of treatment

With modern treatment, a person with haemophilia A receives on average 2000 IU of factor VIII thirty times per annum. This higher level of treatment would have required treatment with about 600 units of cryoprecipitate per annum, giving a probability of exposure to hepatitis C (assuming a hepatitis C prevalence of 0.3% in the donor population) of 83% after one year of treatment. After many years of treatment, for example from 1977 until effective heat treatment against Hepatitis C in the mid 1980's, this figure would approach 100% exposure, although it is known that 15% of people appear not to become chronically infected with Hepatitis C. For a lower prevalence of Hepatitis C of 0.1%, these figures would be a probability of exposure of 45% at 1 year, 70% at 2 years, and 95% at 5 years.

Transmission of Hepatitis C

Treatment with Factor VIII concentrate largely superseded the use of cryoprecipitate in the UK from about 1975. However, in a detailed examination of hepatitis C infection in haemophilia, the Scottish Executive determined⁶ that a total of six patients had been infected in Scotland in the period 1985-1987 – that is, the period between the technique of 80°C being invented in England and all patients in Scotland receiving such a product. Of these, two had been treated only with cryoprecipitate, one had received cryoprecipitate and concentrate and three had been treated only with SNBTS concentrate⁶ (dry-heat treated at 68°C). Neither the total number of susceptible patients treated, either with cryoprecipitate or with concentrate,

nor the amount of treatment provided is known to SNBTS. Therefore we cannot estimate the relative risk of infection associated with each type of product. Nevertheless, it can be concluded from these data that the risk of infection with hepatitis C via cryoprecipitate was not insignificant, given that most patients received concentrate at that time.

Conclusion

The available data demonstrate that the risk of exposure to hepatitis C via cryoprecipitate was very substantial. Our calculations suggest that an adult haemophiliac would have had a probability of exposure to hepatitis C infection of 60% to 80% within one year of treatment, depending on the level of treatment provided.

References

1. Whittaker, JA And Brown, MJ. *British Medical Journal* 1969; **3**: 597.
2. Fitzpatrick, J and Kennedy, CC. *British Medical Journal* 1969; **4**: 299.
3. Woods, K and Horowitz B. *Vox Sanguinis* 1980; **38**: 113-117.
4. Cash JD. *British Medical Journal* 1976; **ii**: 682-684.
5. Biggs R. *British Journal of Haematology* 1977; **35**: 487-504.
6. Cachia P. *Letter to Scottish Executive Health Department, 17th March 2000*. Released by Scottish Executive Health Department December 2005.

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