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Intended for healthcare professionals

Editorials

Hepatitis C and haemophilia

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Coinfection with HIV is common and will demand great resources

The haemophilic community in Britain, already hit by HIV infection, is now facing the problem of chronic hepatitis C. The high incidence of hepatitis after treatment with clotting factor concentrate from a large pool was first identified by Kasper and Kipnis in 1972.[1] They found that infection was more common in young patients having their first treatment. It is now known that there was virtually a 100% rate of transmission of hepatitis C virus to previously untreated patients with haemophilia until effective procedures to inactivate the virus were introduced in 1985-6.[2] [3] Transmission of hepatitis C occurred with plasma from NHS and commercial sources. Studies of the hepatitis C virus genotype found in British patients with haemophilia who have been treated with concentrates have shown types 1, 2, and 3, reflecting contamination from the British and North American donor pool. Type 4 (reported in the Middle East and Zaire) and type 5 (reported in South Africa) have also, however, been found in a few patients, leading to speculation about the source of some commercial concentrates.[4]

The scale of the problem is large: 232 out of 241 patients at the Royal Free Hospital in London who had received unsterilised clotting factor concentrate from large donor pool were positive for antibodies to hepatitis C.[5] date of first exposure was documented in 183 patients, and from these data it was calculated that over be expected to have liver failure at 20 years. Furthermore, we know that these patients were infected fr and on average 17 years ago. In Britain there are 3122 haemophilic patients who have been treated with unsterilised blood products since 1977 (when the United Kingdom Haemophilia Directors Organisation started its registry). All of these patients must be infected with hepatitis C.

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Two large studies in haemophilic patients have shown that coinfection with HIV could accelerate the development of liver failure.[5] [6] Viral replication of hepatitis C is increased in the presence of HIV (probably because of immune deficiency). From 1978 to 1993 concentrations of hepatitis C RNA in coinfected haemophilic patients increased 58 times compared with a trebling in those infected with HCV alone.[7] The relative risk of developing liver failure in hepatitis C infection increased 21-fold after HIV infection.[5] All patients who are infected with HIV from clotting factor concentrate must, therefore, also be infected with hepatitis C. In our centre 10 out of 11 patients who died of liver failure were infected with HIV. This can cause formidable management problems. The failing liver can cause other clotting factor deficiences that are superimposed on the existing deficiency of factor VIII or IX. A severe haemorrhagic state may develop in the final stages of the illness.

Patients with liver cirrhosis are at an increased risk of developing hepatocellular carcinoma, and the same could be true of patients with haemophilia. A worldwide questionaire sent to 11801 patients with haemophilia identified 10 cases of hepatocellular carcinoma—a risk 30 times higher than normal.[8]

The sexual transmission of hepatitic C virus is an important issue for patients with haemophilia, their families, and those involved in their health care. Studies indicate that transmission is rare.[9] HIV infection has been reported as a cofactor and could reflect the higher viral load of hepatitis C virus in coinfected people.[10] The use of barrier contraception (condoms) is likely to increase safety.

What about treatment? Interferon alfa remains the most promising treatment for hepatitis C. For the patients without haemophilia, liver biopsy is essential in deciding who will benefit from treatment, but this is a hazardous procedure for a patient with haemophilia. Knowledge of other variables, such as hepatitis C virus genotype and viral load, may be helpful as patients with virus types 2 and 3 and with lower viral loads have the greatest chances of responding.[11]

Patients treated with multiple batches of concentrate will have been exposed to a large amount of virus as well as to many viral genotypes.[4] [12] Since patients are infected with multiple species, a change in genotype is likely to be due to a change in dominance. The clinical importance of the change in dominance brought about by treatment with interferon is unclear.[12] The ultimate treatment for liver failure is liver transplantation, and this has successfully been performed in patients with haemophilia, curing not only the liver failure but also the haemophilia. The liver, however, may be reinfected with hepatitis C virus, and transplantation is difficult for patients infected with HIV.

The progression of hepatitis C and coinfection with HIV in haemophilic patients will demand tremendous resources over the next decade. It is important to appreciate the achievements that have been made in treating haemophilia despite their devastating side effects. In 1937 Birch wrote a descriptive monograph on haemophilia; she reported that 82 out of 113 patients died before their 15th year and only 6 out of 113 lived beyond the age of 40.[13] We now have recombinant factor VIII (and soon factor IX), which cannot transmit bloodborne viruses. We need the resources to provide these factors for the children with haemophilia who were born after 1985. They are free of the scourges of hepatitis C virus and HIV, and prophylaxis with a safe clotting factor concentrate could offer them a full life without disability.

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