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MEMORANDUM

OVERVIEW OF THE INCREASING COSTS OF TREATMENT FOR PATIENTS WITH CONGENITAL COAGULATION DISORDERS AT THE ROYAL FREE HOSPITAL

The Haemophilic Condition

Health Service Guidelines - NHS Management Executive HSG(93)30
"The haemophilic population in the United Kingdom comprises a group of patients whose medical management is both complex and costly. Some of the complexity arises due to the rarity of the condition, its lifelong nature, its variable severity, and the fact that patients do not appear "ill" in the accepted sense of the term. It may not always be understood that the lack of prompt, appropriate treatment may lead to prolonged hospitalisation and the misuse, or even on occasions, the wastage of expensive blood products."

Home Treatment for Adult Patients

Patients with severe haemophilia (A) Factor VIII deficiency or severe haemophilia (B) Factor IX deficiency, or severe von Willebrand's disease treat themselves at home in order to have prompt treatment. The majority of such patients treat themselves "on demand" only when they experience a bleeding episode. They treat according to a protocol of a dosage of units per kg body weight. Older patients with severe haemophilia may have extensive and painful joint damage; such joints can be more vulnerable to bleeding and therefore may require larger doses of treatment. Some younger patients have been on prophylaxis or regular treatment since their teenage years. This regular prophylaxis prevents bleeding into target joints.

Children on Prophylaxis

The right treatment for children is regular dosage of clotting factor concentrate in order to prevent joint damage. This has been practised in Sweden since 1958 and has resulted in a group of patients without any disability. Children are given regular treatment, three times a week for Factor VIII deficiency and twice a week for Factor IX deficiency, with a dose according to their body weight. Although this results in an increasing amount of clotting factor concentrate being used in the short term, it will prevent these children having chronic pain and disability in the future.

At the present time at The Royal Free Hospital, all children are treated with the lowest cost intermediate purity Factor VIIIY made by BPL. However, it is the view of haemophilia treaters, both in the UK, Europe and the United States, that all children should be offered recombinant Factor VIII. The move to such treatment would result in a doubling of the

cost for these children. Furthermore, since the dosage is given according to body weight, the cost will increase.

Types of Replacement Product

Factor VIII and IX clotting factor concentrates are either made from plasma or are genetically engineered - the latter so called "recombinant products". The plasma derived products are of intermediate purity or high purity monoclonal products. All individuals who are infected with HIV are given plasma-derived monoclonal produced products because there is evidence that this slows the deterioration of their immune system. At the present time other patients are given intermediate purity products - however, it is felt that previously untreated patients (particularly pregnant women) should have the advantage of recombinant clotting factor concentrate. Plasma derived concentrates continue to transmit viruses, particularly parvo virus which can cause miscarriage for women. Severe von Willebrand's disease is a very rare condition, but, because the Royal Free Haemophilia Centre is very large, a number of these patients attend. These patients require high purity clotting factor concentrate which is very rich in von Willebrand's factor. It is generally agreed amongst people treating haemophilia that individuals with Factor IX deficiency should have high purity Factor IX concentrates, because the less pure Factor IX concentrates have in the past been associated with thrombosis.

Therapeutic Trials

The Haemophilia Centre at The Royal Free Hospital is one of the largest in Europe and is an International Haemophilia Training Centre of the World Federation of Haemophilia. We therefore from time to time have the opportunity of conducting therapeutic trials which may reduce the cost of clotting factor concentrates to purchasers.

Surgery

It has recently been established that the way to make surgery safe for people with haemophilia is to use constant infusion of clotting factor concentrate. This means that there is a constant adequate level of the clotting factor concentrate in the blood throughout the surgery and post-operative period. However, any surgery will require treatment with large amounts of clotting factor concentrate, often two to three times that of the annual consumption of clotting factor concentrate for the individual patient. At the present time, we are conducting all surgery for those with severe haemophilia, by constant infusion; this is an experimental phase and it is likely we will be able to reduce the amount of concentrate used by about one-third of that used previously when surgery was conducted under twice-daily dosing.

HIV Infection

At the Royal Free Haemophilia Centre about 130 patients with HIV infection have been cared for. Approximately 50 of these patients have died and there are 70-80 in regular follow-up. These patients often require more clotting factor concentrate in order to investigate and diagnose their HIV related problems. Often in their terminal illness they may use up to 50% more clotting factor concentrate per annum than when they were asymptomatic. If such individuals have to be admitted with severe infection, they may have daily treatment with clotting factor concentrate over a period of many months.

Because these patients were infected during the years 1979-1985, we now have a group of patients who are entering the symptomatic and terminal phases of their infection. It is likely over the next few years that this will result in an increase in consumption of clotting factor concentrate by these patients.

Hepatitis C Infection

We have identified 255 patients who were infected via blood products during the years 1965 to 1985. Over a hundred of these individuals with hepatitis C have co-infection with HIV and HCV. We know that HIV accelerates the progression of hepatitis C infection, and we know that after 20 years of infection with hepatitis C about 10% of individuals will have chronic liver failure. The vast majority of these patients are likely to have co-infection with HIV and HCV when they enter their terminal phase, and have to be admitted to hospital. They may consume vast amounts of clotting factor concentrates, not only because they need the Factor IX or Factor VIII required for their clotting factor deficiency, but also because their failing liver cannot make necessary clotting factors. We feel that when such patients die they are entitled to have a dignified death. This may result in many months of treatment with clotting factor concentrate, in order to prevent overt bleeding from varices or the nose.

Acquired Haemophilia

This is an unpredictable condition and is difficult to treat. It is an auto-immune condition where individuals have antibodies to Factor VIII, Factor IX, or von Willebrand factor, which results in severe bleeding, and it ofen requires treatment with Porcine Factor VIII which is very expensive. Occasionally this fails and it is necessary to give Factor VIIa which costs up to £50,000 per day per treatment episode. This condition predominantly occurs in older people but it can also occur post-natally in association with pregnancy.

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