Treatment of haemophilia and related disorders in Britain and Northern Ireland during 1976-80: report on behalf of the directors of haemophilia centres in the United Kingdom

C R RIZZA, ROSEMARY J D SPOONER

Abstract

A five year survey of the treatment of patients in the United Kingdom suffering from haemophilia and related disorders was carried out on behalf of the directors of haemophilia centres. The survey showed an increase in the number of patients receiving treatment from the centres, a substantial increase in the total amount of therapeutic materials used, and an increase in the average amount of factor VIII or factor IX used yearly per patient. Home treatment became established for severely affected patients and accounted for roughly half of the total amount of material used. Study of the acquisition of factor VIII or factor IX antibodies (inhibitors) in patients with haemophilia A or haemophilia B showed no increase in antibodies during the survey period, despite the increased use of factor VIII and factor IX concentrates. The occurrence of acute hepatitis in treated patients was also studied and no increased incidence was observed. A near normal median expectation of life in patients with severe haemophilia A was found.

Introduction

ORGANISATION OF TREATMENT

The care of haemophiliacs in the United Kingdom is organised through recognised haemophilia centres situated in National Health Service hospitals throughout the country. The concept of these centres was established in Britain in 1954 to provide specialist diagnostic, registration, and treatment services for haemophilic patients. The present system, which incorporates three types of centres—haemophilia reference centres, haemophilia centres, and associate haemophilia centres—was defined in 1976 by the Department of Health and Social Security in a memorandum (HC(76/4) to regional health authorities and family practitioners. The number of centres gradually increased over the years, and by 1980 there were 10 centres acting as reference centres and nearly 100 other centres.

Each reference centre is responsible for the provision of an advisory clinical and laboratory service to individual haemophilia centres in a wide area (referred to as a "supra region"). Some centres have staff, laboratory and clinical facilities, and funds specifically allocated for the haemophilia work, but most centres are run by the staff of haematology departments, medical departments, or blood transfusion centres as part of their routine service commitment. All haemophilia centres, irrespective of category, are expected to provide 24 hour emergency treatment for haemophilic patients. The number of patients treated each year by centres varies considerably (fig 1). One third of all

![Diagram](image_url)

FIG 1—Numbers of patients treated during 1980 at haemophilia centres in United Kingdom.

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Oxford Haemophilia Centre, Churchill Hospital, Headington, Oxford OX3 7LJ
C R RIZZA, MD, FRCP, consultant physician
ROSEMARY J D SPOONER, research assistant
centres treated fewer than 10 patients in 1980 and two thirds treated fewer than 20.

Since 1969 the directors of the haemophilia centres have collected information about the amount and types of therapeutic materials used to treat patients who have haemophilia A (classical haemophilia: factor VIII deficiency) or haemophilia B (Christmas disease: factor IX deficiency) and about the complications of treatment. In 1976 the directors decided to extend their survey to obtain information on all known patients with haemophilia A or B, including those who had not received treatment, so that more accurate information would be available regarding the total number of patients with the two types of haemophilia in Britain and Northern Ireland. The directors also decided that from 1976 onwards they would collect information on patients receiving home treatment and details about carriers of haemophilia A or B and patients with von Willebrand's disease who required treatment at centres. Reports for the years 1969-75 have been published.1-4 This report is concerned mainly with the treatment of patients during the five years 1976-80, but information from previous years is included where long term trends are being considered.

Report

NUMBERS OF PATIENTS WITH HAEMOPHILIA A AND B

During the study period there was a yearly increase in the numbers of patients known to have haemophilia A and B, and by December 1980 there were 4321 patients with haemophilia A and 777 with haemophilia B known to the directors of the centres (table 1m (miniprint)). The incidences of antibody against factors VIII and IX were 6-0% and 0-9% respectively and had changed little during the period or indeed during the past 11 years except for more intensive treatment with concentrated preparations of clotting factors in later years suffering from severe haemophilia A or B. Twenty of the patients with haemophilia A who died (22%) had factor VIII antibodies in their blood, and one of the patients with haemophilia B who died had factor IX antibodies. The average ages of the patients who died were 46-7 years in the haemophilia A group and 48-3 years in the haemophilia B group. Comparable figures for 1969-74 were 42-3 years and 33-6 years, respectively.

A more useful statistic was the median expectation of life. This was calculated from life tables derived from the information on the number of deaths in each age and severity group and total numbers at risk in each age and severity group during the five years of the survey. Surprisingly the calculations yielded a median expected life expectancy of 69-1 years for severely affected haemophiliacs as compared with 72-8 years for normal males (appendix 1m (miniprint)). Those figures must clearly be viewed with caution; since the numbers in the calculations were relatively small and also because of the possibility that deaths in haemophiliacs may not all be reported to haemophilia centre directors. Median expectation of life for the group of patients with factor VIII values greater than 10% of average normal were not calculated because of the small number of deaths which had occurred. Also many such patients probably go undetected owing to the mildness of their clinical symptoms. It is therefore difficult to be sure of the total number in the group "at risk" for the purpose of calculating "probability of death" rates.

Cerebral haemorrhage was the commonest cause of death in haemophilia A and accounted for 26 of the 89 deaths (29%). Two thirds of the cerebral haemorrhages occurred in severely affected patients. Other types of haemorrhage accounted for 11 deaths (12%). Hepatitis was recorded as the cause of death in one patient with haemophilia A and one with haemophilia B, and there were five suicides. In 11 cases (12%) the cause of death was not known. As expected, there was a greater incidence of deaths in patients with antibodies than in those without antibodies: bleeding accounted for 55% of deaths in patients with antibody and 38% of deaths in patients without antibody.

AMOUNT AND TYPES OF THERAPEUTIC MATERIAL USED

Figures 2 and 3 show the long term changes in usage of the different blood products, and tables VI and VII show in more detail the type and amount of the various therapeutic materials used in the management of haemophilia A and B during 1976-80. The total amount of factor VIII used steadily increased each year from 33·716 x 10^6 units in 1976 to 57·0 x 10^6 units in 1980. In 1976 nearly

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1977-80 some centres reported that desmopressin (DDAVP) had been used to treat mild haemophilia A. The numbers of patients treated with this drug were 8, 10, 20, and 12 in successive years from and including 1977.

With regard to amounts of factor IX used in the treatment of haemophilia B this also showed a trend upwards, rising from 5.96 x 10^9 units in 1976 to 8.27 x 10^9 units in 1980 (table VIIa). This increase was accounted for in part by the increase in number of patients treated but also by an increase in the yearly amount received per patient. Some 99% of the factor IX concentrate used was prepared by NHS fractionation laboratories. Enough factor IX is made by those laboratories to meet the needs of patients with haemophilia B in Britain and there seems little if any need to purchase factor IX from commercial companies.

**MATERIALS USED FOR TREATMENT OF PATIENTS WITH ANTIBODY AGAINST FACTOR VIII OR FACTOR IX**

Information on the use of factor VIII or IX replacement was available only for 1977, 1978, 1979, and 1980 (table VIIIa). The therapeutic material used included human factor VIII concentrate, activated and non-activated human prothrombin complex concent-

**MINIPRINT TABLES VIIa-VIIx**

Table VIIa: This table shows the total usage of factor VIII and factor IX concentrates in the United Kingdom during 1976-1980, with data for patients treated in 1976-1980 included in the figures for 1979 and 1980.

Table VIIb: This table provides details of the number of patients treated with factor VIII and factor IX concentrates, showing the distribution by age group and sex.

Table VIIc: This table presents the data on the number of patients treated with factor VIII and factor IX concentrates by age group and sex, with further breakdowns by hospital and region.

Table VIIid: This table includes information on the number of patients treated with factor VIII and factor IX concentrates, broken down by age group, sex, and hospital.

Table VIIe: This table shows the distribution of patients treated with factor VIII and factor IX concentrates by sex and hospital.

Table VIIf: This table provides data on the distribution of patients treated with factor VIII and factor IX concentrates by hospital and region, with further breakdowns by age group and sex.

Table VIIg: This table includes information on the number of patients treated with factor VIII and factor IX concentrates, broken down by age group, sex, and hospital.
At the time of reporting there had been remarkably few sequelae of acute hepatitis. Over the six years only two patients had died from illness related to the complications of acute hepatitis. The problem of chronic hepatitis remains unsolved. Several patients have been seen with symptomatic evidence of chronic liver disease, but only further studies of these patients as a whole over the next 10 years will disclose the true incidence.

A working party of haemophilia centre directors has been set up to look into the incidence of both acute and chronic post-transfusion hepatitis. A separate report on the incidence of acute hepatitis in haemophiliacs in Britain is in preparation.

Discussion

The number of haemophiliacs known and treated at haemophilia centres in Britain continues to rise, as does the amount of factor VIII used in their treatment.

If the amount of factor VIII used continues to increase at the present rate some 120 x 10^8 units of the factor will be required by 1990. Should there be any major change in treatment policy...
such as the administration of larger doses for the management of haemarthroses or the widespread use of prophylactic treatment the total amount of factor VIII used will be still greater.

During 1980 commercial factor VIII constituted 60% of the total factor VIII used and cost the NHS some £2.5 million. If the proportion of commercial factor VIII used in 1990 remains the same as today, the cost at today’s prices will be of the order of £5 million. But if, as seems likely from recent trends, there is an increase in the proportion of commercial factor VIII used the cost will be even higher. It is unlikely that the upward trend in the use of commercial factor VIII will be reversed before the middle to late 1980s, when the NHS fractionation laboratories are expected to increase greatly their output of factor VIII.

As in other reports intracranial bleeding is the commonest cause of death in patients suffering from haemophilia A. Other types of bleeding constituted the second largest cause of death. The finding of a near normal median expectation of life in severely affected haemophiliacs and a greater than normal expectation in mildly affected patients is interesting and encouraging. The numbers concerned are relatively small, so that the above results must be interpreted with caution. Clearly there has been a noticeable improvement in the management of haemophilia since factor VIII has become widely available and bleeding to death from trivial injury—to common in the past—is now rarely seen. We should therefore not be surprised at some increase in life expectation, but whether the improvement observed in this survey is an overestimate will remain to be seen.

The directors of haemophilia centres in Britain are continuing with their collaborative studies, and it is hoped that further information collected over the next few years will answer this question.

In view of the widespread concern about the transmission of hepatitis viruses by giving blood products it is interesting to note that only two deaths were attributed to hepatitis during the five year period. There have been several reports recently of persistently abnormal liver function values and abnormal histological findings in liver tissue from haemophiliacs treated with blood products. Most of these patients are asymptomatic but it remains to be seen how many will develop severe chronic liver disease with the passage of time.

We are grateful to Dr A Barr and Mr J Ennis, of the Oxford Regional Health Authority’s statistics department, for constructing the life tables (see appendix IIm) and for much useful advice and discussion. We thank the directors and staff of the haemophilia centres for their help with the survey (see appendix IIm). We are also grateful to the staff of the Oxford Regional Computer Unit for setting up and maintaining a confidential computer system for handling the patient data, Mrs Patricia Lawrence for typing the manuscript, and Mr R H Matchett for drawing the diagrams.

References

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GARDEN TANSY FLOWERS in June and July.

Dame Venus was minded to pleasure women with child by this herb, for there grows not an herb, fitter for their use than this is; it is just as though it were cut out for the purpose. This herb bruised and applied to the navel, stays miscarriages; I know no herb like it for that use: Boiled in ordinary beer, and the decoction drank, doth the like; and if her womb be not as she would have it, this decoction will make it so. Let those women that desire children love this herb, it is their best companion, their husbands excepted. Also it consumes the phlegmatic humour, the cold and moist constitution of Winter most usually affects the body of man with, and that was the first reason of eating tansies in the Spring. The decoction of the common Tansy, or the juice drank in wine, is a singular remedy for all the griefs that come by stopping of the urine, helps the strangury and those that have weak reins and kidneys. It is also very profitable to dissolve and expel wind in the stomach, belly, or bowels, to procure women’s courses, and expel windiness in the matrix, if it be bruised and often smelted unto, as also applied to the lower part of the belly. It is also very profitable for such women as are given to miscarry. It is used also against the stone in the reins, especially to men. The herb fried with eggs (as is the custom in the Spring-time) which is called a Ty blox, helps to expel and carry downward those bad humours that trouble the stomach. The seed is very profitably given to children for the worms, and the juice in drink is as effectual. Being boiled in oil, it is good for the sinews struck by cramps, or pained with colds, if thereto applied. (Nicholas Culpeper (1616-54) The Complete Herbal, 1850.