Financing the rising cost of haemophilia care at a large comprehensive care centre

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ABSTRACT - Haemophilia affects 1 in every 6,000 males. Patients with haemophilia A receive treatment with factor VIII (FVIII) and those with haemophilia B receive factor IX (FIX). In the UK, patients receive their treatment from comprehensive care centres (CCCs) or haemophilia centres. Over the last two decades the amount of clotting factor used per patient has increased; the quality of the clotting factors available and the methods of administration have also improved. As a consequence, the cost of providing care has increased substantially. In theory, the nature and level of haemophilia treatment is specified in contracts between purchasers and providers, ensuring that the costs of treating patients are fully recovered. However, at our large CCC, which has 1,700 registered patients with inherited bleeding disorders, the costs of care regularly exceed contract revenue. This paper describes the cost pressures and difficulties faced by a North London Trust in an attempt to maintain, and in some instances improve, the services provided within its CCC.

Haemophilia affects 1 in every 6,000 men. A patient has either mild, moderate or severe haemophilia. Those with mild haemophilia will experience few problems. However, those with severe haemophilia may spontaneously bleed. In 1994 in the UK 2,300 patients were registered as severe. Patients receive treatment from comprehensive care centres (CCCs) or haemophilia centres. To qualify as a CCC, a centre must provide treatment for 40 or more severely affected patients per year and offer other specialist services, eg orthopaedic units, HIV and hepatitis expertise, counselling and physiotherapy. In most cases treatment is used to abort a bleed once it has occurred (on-demand therapy) although in children and adults there is increasing interest in giving clotting factor prophylactically to prevent bleeds from occurring.

The cost pressures

New clotting factors

The provision of clotting factors is believed to account for up to 93% of the total cost of care. As a result, total costs are sensitive to the unit price of clotting factors, and to the amount of clotting factor used. Because plasma-derived products continue to transmit hepatitis A and B19 parvovirus, and because of concern over as yet unknown viruses, most haemophilia treating specialists consider recombinant (synthetic) clotting factors as the treatment of choice. A recombinant FVIII was first licensed in the UK in 1994. Recombinant FIX is currently under clinical trial and, once licensed, is likely to become the recommended treatment for patients with haemophilia B. Whilst increased purity probably reduces the risk of viral transmissions, it is more expensive. For example, one particular clotting factor of intermediate purity currently costs 18 pence per i.u to purchase and, because it is derived from human plasma, it is exempt from VAT. However, recombinant FVIII is currently purchased at 48 p/i.u and is subject to VAT (these acquisition prices are lower than corresponding list prices). In 1994, 146 severe patients at our CCC required a median of 72,000 (range 20,000-640,000) i.u of clotting factor. Table 1 demonstrates the effects of variations in the amount of clotting factor used and the price of clotting factor on the costs of acquisition.

 Patients with von Willebrand’s disease (vWD) may also need treatment with FVIII. Previously, they were treated with desmopressin or cryoprecipitate. However, the early 1990s saw the introduction of high purity FVIII concentrates containing large quantities of von Willebrand factor (vWF). Concentrates that are rich in vWF, along with pure vWF, are now purchased regularly. In 1980, six patients with vWD were treated with clotting factor, but by 1994 this number had increased to 28. Total clotting factor usage in these patients had increased from 0.08 million i.u in 1980 to 2.35 million i.u by 1994 (Fig 1). Additionally, whilst no pure vWF had been purchased before 1993, in 1995 0.25 million i.u were used.
Table 1. Clotting factor cost (£) per patient per year by units required and product type.

| Clotting factor usage (iu) | Intermediate purity | Recombinant excl. VAT | Recombinant incl. VAT* |
|---------------------------|---------------------|-----------------------|------------------------|
| 20,000                    | 3,600               | 9,600                 | 11,280                 |
| 72,000                    | 12,960              | 34,560                | 40,600                 |
| 640,000                   | 115,200             | 307,200               | 361,000                |

*at current level of 17.5%

Different treatment strategies

After a bleed, patients used to receive clotting factor at a dose of 30 iu per kg body weight, and they could expect to need treatment for 30-35 bleeds per year\(^9\). However, spontaneous bleeding and chronic joint arthropathy seldom occur in patients with mild or moderate haemophilia. Thus prophylactic regimes have been introduced in an attempt to convert severe haemophilia A and B to a milder form. A prophylactic regime will typically comprise 25–40 iu per kg body weight of the appropriate clotting factor three times a week\(^9\). Long-term results have been at their best when prophylaxis is started before any signs of joint damage\(^13,14\). Therefore, since the early 1990s it has been policy to place, whenever feasible, all previously untreated patients with severe haemophilia on prophylaxis. For the most part they will be young children. Assuming the above treatment protocols, a change to prophylaxis for a patient would require a four-fold increase in clotting factor.

Fig 1. Total FVIII usage 1980–94 by patients with vWD at the CCC.

Antibodies (inhibitors)

The development of antibodies that inactivate FVIII remains a serious and continuing complication in the management of haemophilia A. Treatment involves achieving immune tolerance with massive doses of clotting factor and is therefore extremely expensive\(^13\). In the UK the incidence of inhibitors developing in previously untreated patients with severe haemophilia is 20–25%\(^15\). However, in our experience with a cohort of boys exposed to a single FVIII concentrate (BPL 8Y) since 1985, there have been no high titre inhibitors\(^16\) and thus no additional costs.

Unpredictability

Haemophilia is a highly unpredictable disorder\(^4\). Individual clotting factor requirements can vary dramatically from year to year and from patient to patient. This complicates the contracting process, as is shown in Fig 2 which illustrates yearly FVIII usage in a typical patient.

Human immunodeficiency virus (HIV)

In the early 1980s, many patients became infected with HIV through the use of plasma-derived clotting factor\(^19\). The CCC has provided care for approximately 130 HIV infected patients. There have been no new HIV transmissions secondary to clotting factor since 1986\(^20\), as all products are now sterilised. Patients who are known to be HIV positive receive monoclonally purified products as there is reason to believe that this slows the deterioration of the immune system\(^20, 21\).

Fig 2. Total amount of FVIII needed by a 27 year old patient with severe (<2 u/dl) haemophilia A during period 1980–94.
Patients who are HIV negative are placed on standard intermediate products. In 1993 it was estimated that the additional hospital costs attributable to HIV infection amounted to £6,050 per patient year\textsuperscript{22}, although treatment protocols have since been revised and average treatment costs are likely to be higher. Although additional AIDS funding provides financial cover for placing patients on high purity products, there is evidence to suggest that patients with end stage AIDS need upwards of 50% more clotting factor than when they were asymptomatic\textsuperscript{22}.

**Hepatitis C virus (HCV)**

The majority of patients with severe haemophilia who received untreated, large pool blood products in the years 1965–85 became infected with HCV\textsuperscript{23}. The CCC has identified 255 patients infected with this virus. Over 100 of these patients are co-infected with HIV which can accelerate the rate of progression of HCV\textsuperscript{24}. Studies indicate that 20% of patients infected with chronic HCV have a prolonged response to treatment with interferon alpha\textsuperscript{25}. A six month course of treatment with 6 million units of interferon alpha three times per week costs £6,000; however, responsiveness to treatment remains unpredictable\textsuperscript{26}. After 20 years’ infection with HCV, it is calculated that 10% of these co-infected patients will have progressed to chronic liver failure. As they reach a terminal phase, patients are likely to be admitted to hospital. They may also need increased amounts of the clotting factors normally made by the liver (including FVII, FVIII and FIX). It is expected that there will be at least two patients with HCV-related liver failure per year at the CCC for the foreseeable future. No additional funding for this group of patients is available.

**An increase in the numbers of patients**

The CCC has witnessed a steady increase in the number of registered patients and the percentage of patients who are treated with clotting factor in each year. In 1980, 30% of patients received at least one iu of clotting factor; by 1994 this had increased to 60%. This may be the result of a combination of the introduction of prophylaxis, the incidence of AIDS- and HCV-related illnesses, and the availability and use of more appropriate clotting factors.

**Confounding issues**

**Patient base and size**

In 1994 (Fig 3) 42 out of the 85 haemophilia centres sending information to the United Kingdom Haemophilia Centres Directors Organisation treated fewer than 10 patients with severe haemophilia A, B and severe vWD\textsuperscript{2}. Only three centres treated more than 110 such patients: the CCC treated 153 [haemophilia A 112, haemophilia B 34 and vWD 7]. This group represents the largest drain on resources. In the UK in 1994, 2,855 patients with haemophilia A, B or vWD of all grades of severity received clotting factor; almost 8.5% of them were treated at this North London Trust. The remainder were treated at one of 92 other centres in the UK.

**Contracting**

The Trust has contracts with several different purchasers to treat haemophilic patients. At present, they are divided over the decision to purchase plasma-derived clotting factors or the new recombinant

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**Fig 3.** The number of severe patients treated in CCCs and haemophilia centres in 1994 (*Royal Free Hospital*). (Reproduced from reference 2 by permission of the UK Haemophilia Centres Directors Organisation).
clotting factors, presumably because they are uncertain whether recombinant products represent value for money and whether they can afford them. Purchasers can decline to pay for recombinant products, and some have chosen to do so. Therefore, whether a patient at the CCC receives recombinant FVIII depends upon their place of residence. However, there is considerable pressure on the Trust, from patients and doctors, to treat patients according to clinical diagnosis and in accordance with new guidelines rather than specific contractual arrangements. Compliance with these demands has a large financial implication for the Trust.

The current situation

In the past, the Trust has offered purchasers the option of a fully inclusive block contract, where a specified amount of activity is provided for an agreed amount of money. This approach, however, is no longer sustainable. The rapidly escalating and unpredictable level of costs has meant that expenditure on haemophilia treatment is often not covered within the block contract sum and as a result, the Trust is faced with an unacceptable level of financial risk (even in light of significant and successive annual uplifts to the CCC's budget). It has, therefore, become increasingly difficult for the Trust and its purchasers to ensure that haemophiliacs patients receive the appropriate care, while at the same time sustaining the level of service provision in other specialties.

Discussion

This paper has demonstrated the serious problems that haemophilia and its treatment pose for both the purchasers and providers of a large CCC. These pressures derive from a number of different sources but the order of magnitude of these pressures on a Trust's financial position increases dramatically in relation to the number of cases of severe haemophilia. The same difficulties apply for other rare and expensive disorders that are disproportionately spread around the country.

Different contract formats have been explored in order to identify a mechanism that ensures the desired clinical treatment and at the same time manages the very high levels of financial risk. Central funding may be a better way of commissioning haemophilia services, particularly in respect of severe haemophilia. However, such adjustments to contractual arrangements simply shift the burden of cost elsewhere, and unless agreed care plans are negotiated and adhered to by all CCCs, central funding alone is unlikely to stop the costs of treatment from increasing. We believe these conclusions can be generalised beyond haemophilia care to all other rare and expensive conditions.

Useful information on the cost-effectiveness of prophylaxis is beginning to emerge but no hard information is as yet available on the cost-benefit of using recombinant clotting factors. Purchasers are, therefore, unable to compare the true costs and benefits of newer treatment options and interventions with those that have been evaluated in the past. Purchasers and providers should be encouraged to perform complete economic evaluations of prophylaxis and the use of recombinant clotting factors so that the costs and benefits of improving haemophilia care and the priority setting of clinical interventions can be rationalised.

Whether it is economically desirable to increase spending now is open to argument, but adopting a longer perspective within the constraints and pressures of an annual contracting round is often difficult. Should we be looking for alternative ways of reducing costs by evaluating new approaches to the management of haemophilia care such as continuous infusion and gene therapy? What are the costs and benefits associated with liver transplantation which can cure haemophilia?

In the short run we are left with new contractual arrangements between purchasers and providers to prevent haemophilia services being a drain on their own hospital budgets. In the long run it may be necessary to revert to central funding for this and other rare, expensive, unpredictable and lifelong conditions.

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