Economic Impact of Treating Inhibitor Patients

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Key Words

Cost · Inhibitors · rFVIIa · QALY

Abstract

A literature review of the economics of managing haemophilia patients with inhibitors was conducted. It showed that haemophilia with inhibitors places a burden on the healthcare system and on the patient. Use of rFVIIa compared to 'usual therapy' is associated with improvements on a number of outcomes, including speed of bleed resolution, duration of pain, and quality of life. The extra costs of rFVIIa can be justified by the additional benefits achieved: For example, the extra costs required to achieve a gain of one quality adjusted life year (QALY) in children with inhibitors has been shown to be comparable with that for other reimbursed healthcare strategies. Future research could focus on expanding our understanding of the impact of accelerated bleed resolution on long-term sequelae, including need for surgery and quality of life.

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Introduction

The management of bleeding episodes and surgery in haemophilia patients who develop inhibitors is especially difficult and expensive. As healthcare funding is a limited resource, management of these patients has to compete

with other illnesses that also depend on expensive treatments and specialized staff. But it would be wrong to focus only on costs as new haemostatic agents offer many benefits to these patients. Consideration of the economics (i.e. costs and benefits) of treatment options in patients with inhibitors is, therefore, warranted. This paper reviews current publications on the economics of managing bleeding and surgery in haemophilia patients with inhibitors. A summary of the types and purposes of economic evaluations is presented along with some conclusions that can be drawn about the economics of treating inhibitor patients.

Overview of the Types and Purposes of Economic Analysis

With the exception of cost of illness and budget impact evaluations, economic evaluations invariably attempt to ascertain whether any additional costs associated with particular strategies are justified by additional benefits. Tables 1 summarises the different forms of economic evaluations and how they inform the healthcare decision making process. The specific form of analysis used will be dictated by the question set.

Cost of illness (COI) analysis determines the cost of managing a particular cohort or defined population, identifying cost distribution and main cost drivers. Budget Impact Analysis (BIA) determines the financial impact of purchasing a new treatment for an indication or extending

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Table 1. Economic evaluations inform decisions

Economic evaluation	Costs	Consequences	Decision rule
Cost of illness/budget impact	yes	no	affordability
Cost-consequences	yes	yes list all benefits	subjective
Cost-minimization	yes	yes pre-defined effectiveness outcome	the least costly way of achieving effect is recommended
Cost-effectiveness	yes	yes e.g. controlled bleed on 1st line	if ratio of additional cost to additional benefits less than £x, recommend use
Cost-utility	yes	yes, QALY gained	if additional cost per QALY gained less than £x, recommend use

the use of a currently subsidized drug to other indications/populations. Whilst COI and BIA only consider costs, they complement full economic evaluations because they address one major concern of healthcare decision-makers, remaining within the annual budget [1]! Full economic evaluations examine the costs and benefits of treatments. The simplest form, cost-consequences analysis lists all the costs and consequences associated with alternative treatment strategies [2]. Cost-minimisation analysis compares the cost of alternative treatment regimens producing the same outcome. Total costs, including the price of the drugs and costs associated with administration and management of adverse events, are determined. Cost-effectiveness analysis compares at least two treatment options and benefits are described in terms of illness specific outcomes [e.g. bleeds avoided, bleeds controlled with 1st line treatment]. 'Value for money' is informed by the ratio of additional costs relative to additional benefits. Cost-utility analysis is normally used to compare the cost effectiveness of interventions in one illness with that in other illnesses so that total healthcare resources can be allocated in such a way as to optimize the total health gain from a specified budget. Comparison across a wide number of different illnesses is facilitated by the use of a common currency for the benefits of treatment, called the QALY, a quality adjusted life year gained. Results are described in terms of the additional cost required to gain a QALY.

These forms of economic evaluations have been reported in the still relatively limited but growing international literature on the economics of managing haemostasis in individuals with inhibitors.

Search Details

To compile this review, the author searched Medline and NHS CRD databases and hand reviewed abstracts from the World Federation of Hemophilia meeting (July 2000). Most publications identified examine cost of treatment only. The majority of the published full economic evaluations compare costs and benefits of activated prothrombin complex concentrate (aPCC, FEIBA) and recombinant activated coagulation factor VII (rFVIIa, NovoSeven).

Cost of Illness Studies

Cost of illness evaluations have been conducted for patients with inhibitors in a number of European countries including, France [3, 4] and Italy [5]. Their results highlight the burden haemophilia with inhibitors places on the healthcare system and on the patient. Figure 1 summarizes the results from the French study that compared the cost of managing adult patients without inhibitors (0inh, n = 103), with low responding inhibitors (LR, n = 24) and high responding inhibitors (HR, n = 17), between 1988 and 1998 during two periods: 1988–1995 and 1996–1998, before and after the introduction of rFVIIa in France (1996) [4]. In both periods, the mean cost of managing of patients with high responding inhibitors (HR) was considerably higher than that for patients with no inhibitors (0inh) and low responding inhibitors (LR). In the period 1988–95, hospitalisations and deaths

Fig. 1. Burden is greater in haemophilia patients with inhibitors: French study [4].

due to uncontrolled bleeds were more frequent in patients with high responding inhibitors than the other groups. Use of rFVIIa contributed to the increased cost in the period 1996–1998. However, the authors point out that rFVIIa was used in spontaneous severe bleeds, which in the past would not have been controlled and led to death. In addition, rFVIIa was used in eight surgical procedures that would not have been undertaken in its absence.

The Cost of Home versus Hospital Treatment in Severe Haemophilia Patients with Inhibitors

A recent case report of the economics of implementing a home treatment protocol with rFVIIa for a particularly severe inhibitor patient showed that over a 2 year period, rFVIIa was associated with lower overall treatment costs than in the 2 years previously during which the patients received aPCC (FEIBA) [6]. Whilst on rFVIIa the patient experienced considerably fewer days in hospital, suggesting better control of haemostasis.

Long Term Costs of Using rFVIIa in Surgery

As indicated in the French COI study [4], there is increased interest in the use of rFVIIa in surgery. The use of a decision analysis model to estimate the cost of haemostasis (with rFVIIa treatment) in patients undergoing surgical procedures in the UK and predict the costs of

managing bleeds in these patients for 5 years post treatment has recently been published [7]. For a person weighing 75 kg, experiencing 1 bleed per month in the affected joint, the costs for haemostasis associated with total hip replacement were estimated to be £322,911. But when the reduction in future regular bleeds is accounted for, the model predicted a net saving of £298,401 over 5 years.

Can the Additional Costs be Justified by Additional Benefits?

The COI and BIA studies hinted at some of the benefits of treatment with the new haemostatic agents, however, no quantitative evaluation of benefits was carried out. The following published studies have examined the ‘value for money’ of these agents.

Cost Minimization Analysis in Adults with Inhibitors

Two cost minimization analyses comparing the cost of managing a minor bleed in adult inhibitor patients in hospital- [8] and home-based settings [9] using either rFVIIa or aPCC have been published. Based on a decision analysis model that described the management of bleeds using either drug, both analyses showed that in the 1st line treatment of bleeds, rFVIIa is less costly than aPCC. In addition, using rFVIIa as the initial treatment, instead of aPCC, is expected to resolve a minor bleeding episode in about half the time (30 versus 58 h). However, a major limitation of the analyses was the absence of randomized control trial data comparing the two products, necessitating the data required for the decision analysis model (describing the management of bleeds using either drug) to be taken from historical published efficacy data on both drugs, supplemented with information from a panel of haematologists.

Cost Utility Analysis in Children with Inhibitors

A cost utility analysis has been reported examining the cost-effectiveness of rFVIIa in six Australian children with long standing inhibitors to factor VIII or IX compared with usual treatment [10] (fig. 2). Using validated questionnaires, the quality of life and utility was measured in addition to medical resource use and associated costs for 3 phases: 6 months prior to rFVIIa (phase 1), first

Fig. 2. Cost per QALY gained for one year of rFVIIa vs. 'usual treatment' in Australia [10].

6 months of rFVIIa and second six months of rFVIIa treatment. Patient QoL and utility improved significantly on treatment with rFVIIa, resulting in an average gain of 0.58 QALY. The additional cost per QALY gained was A\$ 51,553 which is comparable with that derived for currently reimbursed healthcare strategies, including hospital dialysis (i.e. \$ 57,053).

Future Research

As rFVIIa accelerates the resolution of bleeding, future research could expand our understanding of the impact of accelerated bleed resolution on long-term sequelae, including need for surgery and quality of life. The availability of a disease specific QoL instrument would be useful in this regard.

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