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The Costs of Treating Febrile Neutropenia in Six U.K. Hospitals

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The cost of treating an episode of febrile neutropenia (FNE) in patients with solid tumours was estimated from the expert opinions of six consultant oncologists in six hospitals in England. Hospital, antibiotic, therapeutic and diagnostic test costs were collected. Hospitalisation, representing 62% of costs, was the largest single factor contributing to the mean cost per FNE of £1541. If granulocyte colony-stimulating factor (filgrastim) can reduce the length of stay of such patients, then the savings will partly offset the cost of the drug.
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INTRODUCTION

FEBRILE NEUTROPENIA (FNE) is said to occur when the total neutrophil count falls below $1.5 \times 10^9/l$ [1]. This is a significant problem in patients receiving cytotoxic chemotherapy in cancer treatment. There is a mortality rate of 10–20% [2]. Moreover, infection accounts for up to 65% of deaths in lymphoma patients and 40% of deaths in solid tumour patients [3–5]. The standard method of treatment is hospitalisation and antibiotic therapy [6, 7]. Neutropenia may result in dose modifications and delays in chemotherapy treatment. Recombinant granulocyte colony-stimulating factor (filgrastim) can reduce the incidence and duration of febrile neutropenia, so alleviating the susceptibility of patients to life-threatening infections, and allowing chemotherapy to continue rather than being curtailed.

Clinical trials have shown that the number of days of hospitalisation and antibiotic treatment are reduced by approximately 50% when filgrastim is given, compared with placebo [8]. There were no major side-effects other than mild to moderate bone pain in approximately 20% of patients receiving filgrastim, which could be relieved by analgesic treatment [2, 8].

There have been few studies assessing the costs of neutropenia and the effect of filgrastim treatment on these costs [9, 10]. Glaspy *et al.* [9] calculated the costs for febrile neutropenia in the U.S.A., and found that savings of 28% could be made if patients were treated with filgrastim. The costs of filgrastim itself were not, however, included. Faulds *et al.* [11] noted that the costs of treating neutropenia varied widely among institutions and that the major cost savings of filgrastim treatment were in avoidance of hospital accommodation, and of antibiotic treatment for infections. Chaplin [10] summarised the financial implications of neutropenia management, and concluded that detailed studies of costs were urgently required.

This study attempts to remedy this gap by estimating the costs of neutropenia from the expert opinions of six consultant oncologists in six hospitals in England. Consultants completed a questionnaire about the treatment received by patients admitted for febrile neutropenia following chemotherapy. Costs were then collected from the hospitals in which each consultant worked. The paper also sets out some of the difficulties involved in collecting such costs.

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MATERIALS AND METHODS

In order to assess the impact of filgrastim on the costs of treating cancer patients with chemotherapy, a study was undertaken to assess the costs of an episode of febrile neutropenia in patients with solid tumours.

The study took place in six individual hospitals in England, and the expert opinions of six consultant oncologists were sought. Clinicians were interviewed using a detailed structured questionniare which sought their opinion on how they would treat a patient admitted for febrile neutropenia following chemotherapy. Factors covered were average length of stay in a general ward and in intensive care, outpatient visits, antibiotic medications prescribed, diagnostic tests performed and therapy administered. Costs were then collected, where available, for each aspect of treatment from the hospital at which each consultant had beds available. This allowed the calculation of a mean cost per FNE. Using information from clinical trials it was then possible to estimate the impact of filgrastim on these costs.

RESULTS

Hospitalisation costs

Hospitalisation costs are obviously influenced to a large extent by the length of stay in hospital, and these are set out for each hospital in Table 1. Length of stay for routine care was similar in all six hospitals, with a mean of 6.3 days. Hospital E was the exception with an estimated average length of stay of only 4 days. There was greater variation for patients requiring critical care, with estimates ranging from 0 to 21 days, with a mean of 5.3 days, although this affected, on average, only 2% of patients.

In England, there is a lack of information on hospital costs,

Table 1. Average estimated length of stay per FNE

Hospital	Average length of stay (days) Routine care	Critical care	% patients in critical care
A	7	Up to 21	2
B	6	0	0
C	8	8	1
D	7	0	0
E	4	3	10
F	6	0	0
Mean	6.3	5.3	2.2

Table 2. Estimated costs of days in hosptial per FNE patient (£)

Hospital	Routine I.P.	I.C.U.	O.P.	Total
A	744	45	45	834
B	831	—	31	862
C	1002	10	—	1012
D	1064	—	33	1097
E	559	42	39	640
F	1297	—	20	1317

IP, inpatient; ICU, intensive care unit; OP, outpatient.

although with the recent National Health Service changes [12], the situation is improving. Inpatient and outpatient costs per day or per visit were available for some hospitals, but in other cases, it was necessary to use general figures compiled for the health region in which the hospital was situated [13]. Hospital costs included nursing, medical and paramedical services and supplies, and general services such as catering and laundering. Pathology and pharmacy services were excluded to avoid double counting. In this study, costs per inpatient day of £106 for hospital A, £152 for hospital D and £216 for hospital F were obtained directly from the hospitals themselves. For hospitals B, C and E, costs of £138, £125 and £140, respectively, were taken from regional data. The variations in hospital costs reflect the lack of information currently available.

Table 2 sets out the total cost for each hospital, of inpatient stay, intensive care unit accommodation and outpatient attendance after discharge. All except hospital C expected patients to return for a single outpatient visit.

Hospitalisation costs ranged from a low of £640 to a high of £1317, with a mean of £960, figures which are heavily influenced by the length of stay. Intensive care and outpatient costs were only a small part of this total cost. Hospitalisation costs were by far the highest single cost per FNE.

Antibiotic treatment and costs

Table 3 sets out the medications prescribed at each hospital for treatment of FNE, together with the cost of treatment at each hospital. A range of antibiotics is used to reduce mortality, which can be as high as 10% [2]. Broad spectrum antibiotics are essential, as are aminoglycosides, against the most common, potentially fatal bacteria [6]. Table 3 shows that all clinicians prescribed broad spectrum antibiotics and aminoglycosides.

Table 3. Costs of antibiotic treatment for patients with FNE (£)

Drug	Hospital A	B	C	D	E	F
Piperacillin	92	243	214	176	144	290
Gentamicin	7	13	5	—	2	2
Netilmicin	—	—	—	23	—	—
Ceftazidime	181	—	3	—	—	—
Cefuroxime	—	—	—	111	—	—
Amphotericin B	—	—	1	—	—	—
Oral nystatin	—	—	—	21	—	—
Oral acyclovir	—	—	—	113	—	—
Ciprofloxacin	—	—	1	—	—	—
Total (inc. dispensing)	309	258	246	489	161	321

Thereafter, treatment varied. Cephalosporins were prescribed by three clinicians, in varying amounts. In hospital C, ceftazidime, amphotericin B and ciprofloxacin were prescribed only for the 1% of patients who required intensive care. In hospital A, ceftazidime was prescribed routinely. Hospital D, which prescribed the relatively expensive oral acyclovir, was a specialist cancer hospital, which might explain its different regime and higher costs.

Drug costs were available from pharmacies in all six hospitals and included value added tax (VAT), but not usually a dispensing cost. This might either be because internal costing procedures had not yet reached this stage of refinement, or because such charges are not made for patients at their own hospital. However, for the purposes of this study, 10% has been added, where appropriate, for dispensing costs.

The mean estimated antibiotic cost per FNE was £297, with a range from £161 at hospital E to £489 at hospital D.

Diagnostic tests and costs

The diagnostic tests requested by physicians at each hospital are listed in Table 4. This table also shows the costs of individual tests at each hospital. These show considerable variation, and it was not always clear whether overheads were included. For the purposes of the study, actual costs were used where available. Where they were not available in specific locations, mean figures from the final column in Table 4 were substituted. Where no costs were available from any source, a figure from the literature was used [14], but this was only necessary for urine culture, mouth swabs, ECG (electrocardiogram), LFT (liver function tests) and blood gases which were requested only rarely (Table 5).

The total costs of diagnostic tests at each hospital are shown in Table 5. These will depend on the numbers of each test performed per patient per episode of FNE, and this accounts for much of the variations in cost. They ranged from a low of £90 at hospital B to £322 at hospital D, with a mean of £210.

Therapeutic costs

The main therapeutic costs associated with the treatment of FNE were for blood and platelets, intravenous fluid and TPN (total parenteral nutrition). Other procedures mentioned were subclavian catheterisation and central venous pressure (CVP) monitoring, but these were used rarely and only in intensive care units, and were not included in the costs.

The cost of TPN was estimated at £150 per day. Intravenous fluid was £1.20 per litre with continuous infusion estimated at an average of 3 litres per day. These costs were used in all calculations.

Table 6 sets out the total costs of therapeutic procedures, where used, for patients at each of the six hospitals. Total costs ranged from £25 at hospital E to £132 at hospital A, with a mean estimated cost of £75.

Total cost of treating FNE

The total estimated cost of treating patients with FNE in six hospitals in England in terms of hospitalisation, antibiotics, diagnostic tests and therapeutics is set out in Table 7. The estimated mean cost at 1989/1990 prices is £1542 (£1649 at 1990/1991 prices).

Hospitalisation costs account for 62% of the total, with antibiotics contributing a further 19%. Diagnostic tests contribute 14% and therapeutics only 5% of total estimated costs. If treatment with filgrastim can reduce average length of stay and

Table 4. Diagnositc test costs provided by hospitals (£)

Test	A	B	C	D	E	F	Mean
Complete blood count	4.50	2.00	—	6.00	5.00	15.00	4.30
Global blood clot testing		—	—	—	22.00		22.00
Creatinine clearance	—	1.74	—	—	6.00	—	6.00
Electrolytes (Panel)	4.50		1.62	9.00	5.00	7.50	4.66
Urinalysis	7.50	—	1.50		3.50	9.00	4.50
Urine culture and sensitivity	—	—	—	—			6.75 (lit)
Blood culture and sensitivity	—	—	—	—	7.50	12.00	9.75
Sputum culture and sensitivity	—	—	—	—	—	9.00	9.00
Aminoglycosides	—	—	—	—	5.00	—	5.00
Chest X-ray	15.00	—	—	—	15.00	—	15.00

Table 5. Type and total costs (£) of diagnostic tests at each hospital

Diagnostic test	A	B	C	D	E	F
Complete blood count	42.30	14.00	39.04	54.00	36.50	75.00
Global blood clot	—	—	0.22	—	13.20	—
Creatinine clearance	—	8.70	—	9.00	19.20	—
Electrolytes	24.30		8.23	198.00	50.00	30.00
Urinalysis	63.00	4.50	3.02		17.50	63.00
Urine culture	13.64	6.75	13.57	6.75		
Blood culture	29.84	29.25	19.60	9.75	—	24.00
Sputum culture	3.78	9.00	9.09	9.00	—	—
Aminoglycosides	37.10	—	0.05	10.00	25.00	10.00
Chest X-ray	51.00	18.00	30.15	15.00	61.50	15.00
Additional tests						
EGG	4.53	—	—	—	—	—
Swab	2.23	—	6.75	—	—	—
Blood gases	2.84	—	0.07	—	—	—
LFT	—	—	—	10.13	—	—
Total cost	275	90	130	322	223	217

ECG, electrocardiogram; LFT, liver function tests.

Table 6. Estimated costs of therapeutic procedures per FNE (£)

Therapy	Hospital A	B	C	D	E	F
TPN	3.00	—	12.00	—	—	—
Intravenous fluid	9.31	28.80	28.80	7.80	14.76	14.64
Blood	81.30	—	18.85	35.30	6.10	35.00
Platelets	38.00	—	7.90	41.70	4.00	59.00
Total	132	29	68	85	25	109

TPN, total parenteral nutrition.

Table 7. Estimated costs of febrile neutropenia (£)

Hospital	Antibiotics	Diagnostic	Therapeutics	Hospitalisation	Total
A	309 (20)	275 (18)	132 (9)	834 (54)	1550 (100)
B	258 (21)	90 (7)	29 (2)	862 (70)	1239 (100)
C	246 (17)	130 (9)	68 (5)	1012 (70)	1456 (100)
D	489 (25)	322 (16)	85 (4)	1097 (55)	1993 (100)
E	161 (15)	223 (21)	25 (2)	640 (61)	1049 (100)
F	321 (16)	217 (11)	109 (6)	1317 (67)	1964 (100)
Mean	297 (19)	210 (14)	75 (5)	960 (62)	1542 (100)

Percentage values are in parentheses.

cut antibiotic costs, then the cost savings incurred will contribute significantly towards offsetting the cost of the drug.

The cost of treating FNE with filgrastim

Using data from Green [15], who did a study on small cell lung cancer (SCLC) patients, it is possible to calculate the cost savings attributable to filgrastim treatment of neutropenic patients. Green found that the incidence of FNE with placebo was 41% and with filgrastim was 20%, i.e. there was a reduction of 50% in the number of patients developing FNE when treated with filgrastim compared with placebo. The cost savings attributable to filgrastim treatment, based on these data, are

Table 8. Cost savings attributable to filgrastim treatment (£)

	Mean cost	Range
1. Cost FNE/patient/cycle without filgrastim (incidence FNE × cost per event = 41% × 1542)	632	430–817
2. Cost FNE/patient/cycle with filgrastim (incidence FNE × cost per event = 20% × 1542)	308	210–399
3. Cost saving with filgrastim (632 − 308)	324	220–418
4. Cost of filgrastim (7 days at £79 per day)	553	—
5. Excess cost of filgrastim treatment (554 − 324)	229	333–135

shown in Table 8. If 41% of patients with placebo develop FNE then cost per cycle becomes £632 and for 20% of patients treated with filgrastim the cost is £308. This gives a mean cost saving with filgrastim of £324 per patient per episode of FNE. It is, however, possible that the incidence of FNE in patients with solid tumours may differ from that found by Green.

The cost of a vial (30 million units/ml) of filgrastim in the U.K. is £79, and is comparable across other countries within ± 10%. There are no plans for the U.K. price to change in the near future. Substitutes are being developed such as granulocyte–macrophage colony-stimulating factor (GM-CSF), which has a similar mode of action to filgrastim. The cost of filgrastim treatment must be included, and for 7 days is £553, giving an excess cost of filgrastim treatment of £229 per patient per FNE. Filgrastim may, however, be administered for longer or shorter periods than 7 days, so changing the cost.

DISCUSSION

The study originated with the need to cost FNE with the advent of filgrastim treatment. The few studies in the literature have tended to be superficial [10] or not directly relevant in the U.K. situation [9].

The study described in this paper also has its limitations in that it is based on the expert opinions of consultant oncologists and not on actual patient experience. It does, however, serve to highlight some of the difficulties involved in assessing treatment costs and provides a basis on which future research can build.

The difficulties involved in collecting hospital costs in the U.K. are well known, but the situation is improving. Antibiotic costs were comparatively easy to collect, but diagnostic and therapeutic costs were much more difficult and variable, but contributed only a small amount to total costs.

The major cost is that of inpatient stay, representing an average of 62% of the total costs of FNE. Antibiotic costs represent 19% of the total, and together these constitute 81% of the total costs of an FNE event. In clinical trials, filgrastim has been shown to have a significant impact on both of these parameters [10]. It has been shown that using filgrastim to reduce the length of an FNE can have a major effect on treatment costs for this group of patients. This is particulary important because it is not common that the use of a drug helps to recapture the cost of its purchase and administration. Most drugs are additive to the cost of care. Filgrastim provides significant clinical, as well as economic impact.

Moreover, treatment with filgrastim may allow increased chemotherapy or delivery of standard doses on time, perhaps improving chances of recovery, but this has yet to be evaluated. There may also be a reduction in nursing costs, and the important issues of patient quality of life and the side-effects of this treatment, including the costs of treating bone pain with analgesics, have yet to be evaluated.

Studies are underway to follow a group of patients throughout their treatment, to measure the actual cost of FNE. Now that filgrastim is licensed in the U.K., trial data are needed so that a more detailed assessment of the overall benefits of filgrastim can be made.

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