Cost-minimization analysis of prophylactic granulocyte colony-stimulating factor after induction chemotherapy in children with non-Hodgkin's lymphoma

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Children with non-Hodgkin's lymphoma receiving chemotherapy.

Setting
Hospital. The economic study was carried out in France.

Dates to which data relate
Effectiveness and resource use data were collated during the period January 1994 to June 1996. 1996 prices were used.

Source of effectiveness data
The evidence for final outcomes was derived from a single study.

Link between effectiveness and cost data
The costing was undertaken partially prospectively on the same patient sample as that used in the effectiveness study. Some resource use data were retrospectively collected from medical records from the Gustave Roussy Institute study patients.

Study sample
Power calculations were used to determine the sample size. It was necessary to examine a total of 150 patients to detect a minimum difference of 20% (incidence rate of 90%; type I error = 0.05; power = 80%; and two-sided test). 149 children with newly diagnosed non-Hodgkin's lymphomas were enrolled into the clinical trial. 75 were randomly assigned to the G-CSF group and 74 to the control group. To be eligible for inclusion, participants had to be 17 years of age or younger and to have a diagnosis of either non-Hodgkin's B-cell, T-cell or anaplastic large-cell lymphomas.
Study design
The study was a multi-centre randomized controlled clinical trial undertaken in 28 centres of the French Society of Pediatric Oncology. Patients were monitored throughout the two consecutive induction courses of chemotherapy. Loss to follow-up was not reported. Children were randomly assigned either to receive subcutaneous G-CSF with the use of a randomisation procedure stratified according to the type of lymphoma (B-cell, T-cell or anaplastic large-cell). In addition, patients with B-cell lymphomas were stratified according to the prognostic subgroup which determined the chemotherapy protocol administered.

Analysis of effectiveness
The analysis was based on intention to treat. The primary clinical endpoint was the incidence of febrile neutropenia, which was defined as an absolute neutrophil count of $5 \times 10^5$ cells or fewer per millilitre and a rectal temperature greater than 38 degrees C monitored two or more times within 2 hours. The incidence of severe infection, World Health Organisation grade 3 or 4 infection, was also reported.

Effectiveness results
The incidence of febrile neutropenia during the two courses, 95% in the G-CSF group and 99% in the control group, did not differ significantly between the two groups. However, the median total duration of febrile neutropenia was 2 days shorter ($p<0.01$) in the G-CSF group. The incidence of severe infection was 21% (16/75) in the G-CSF group and 22% (16/72) in the control group, (NS).

Clinical conclusions
G-CSF did not reduce either the rate of febrile neutropenia or the incidence of severe infection, and it was apparently of limited clinical benefit.

Measure of benefits used in the economic analysis
Since the effectiveness analysis showed no difference in effectiveness between the intervention and the comparator, the economic analysis was based on costs only.

Direct costs
Costs were not discounted due to the short time frame of the study. Quantities were reported separately from the costs. Some of the resource use data were collected prospectively from the study patients and some retrospectively from medical records from the Gustave Roussy Institute study patients. The cost analysis was based on a health care point of view; both total inpatient costs and costs of G-CSF treatment administered at home were taken into account. Four sources were used for unit costs: hospitalization from the accounts department of one study hospital, G-CSF from the acquisition prices paid by the central pharmacy of one of the study hospitals, laboratory costs from the 1996 NHS unitary point value for all laboratory tests as applied to the current quotation of laboratory tests, and blood products from the official 1996 prices for blood products as directly fixed by the government each year. All costs were calculated for each patient separately. 1996 price data were used.

Statistical analysis of costs
The use of medical resources by the two groups was compared by employing nonparametric tests.

Indirect Costs
Not included.

Currency
US dollars ($) (converted from French francs (Ffr) at a rate of Ffr6 = $1).
Sensitivity analysis
Three sources of cost variation were incorporated into the pharmacoeconomic study: the acquisition cost of a packaged paediatric dose for G-CSF, health care costs from two of the other study hospitals were calculated, and the daily hospital cost per patient in intensive care in another study hospital was also used.

Estimated benefits used in the economic analysis
Not applicable.

Cost results
The total cost for induction chemotherapy with G-CSF was $29,765. In this group, the cost of a 31-day hospital stay was $22,103, and the acquisition cost of 17 days of treatment with G-CSF was $2,175. G-CSF represented 7% of the total cost per patient. G-CSF was the most expensive treatment, accounting for about half of the total cost incurred for drugs ($4,489), including the induction chemotherapy regimen. In the control group, the total cost was $30,774, with a 33-day hospitalization making up most of the cost ($24,675). The G-CSF treatment strategy was slightly less expensive than the treatment strategy without G-CSF (mean difference of $1,009). Overall, the acquisition price of lenograstim by the G-CSF group was almost balanced by the expense incurred for an additional 2 days of hospitalization by the control group.

Synthesis of costs and benefits
A synthesis of costs and benefits was not applicable since the study was a cost-minimisation analysis. The results of the sensitivity analyses remained nearly the same for each of the three sources of cost variation tested. G-CSF became more expensive only when the per diem inpatient cost weighted with the value of the other study hospital was taken into account with the adult dosage and the cost of hospitalization in the pediatric care unit. The results of the two treatment procedures were practically equivalent after exclusion of four outliers.

Authors' conclusions
Treatment with G-CSF following chemotherapy in children with non-Hodgkin's lymphoma (previously shown to be of limited clinical benefit) also does not appear to reduce the costs of chemotherapy.

CRD COMMENTARY - Selection of comparators
The reason for the choice of the comparator is clear.

Validity of estimate of measure of benefit
The estimate of the measure of effectiveness is likely to be internally valid due to the randomized design and the intention to treat principle used in the effectiveness analysis. The study was a cost-minimisation analysis.

Validity of estimate of costs
Resource quantities were reported separately from prices and adequate details of the methods of cost estimation were given. The authors noted that the study was too underpowered to detect differences in cost.

Other issues
The authors’ conclusions were justified, given the uncertainties in the data. The issue of generalisability in costs (but not in effectiveness) was addressed by performing sensitivity analysis. Appropriate comparisons were made with other studies.
Implications of the study
Daily and subcutaneous administration of prophylactic CSFs is an additional painful procedure. When used to treat children, it should therefore be restricted to those likely to benefit. The authors were unable to show a significant clinical benefit with the use of G-CSF. The economic advantage gained was too limited to propose systematic G-CSF treatment in this context.

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Other publications of related interest
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