Financial impact of the introduction of erythropoietin in the treatment of anemia of premature infants in Israel

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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
The use of recombinant DNA produced erythropoietin therapy (EPO) or blood transfusion for the treatment of anaemia in premature infants.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population consisted of very low birthweight infants (weight under 1,500g). Infants in the EPO group had to have reached at least two thirds full enteral feeding by either breast milk or formula.

Setting
Neonatal intensive care unit. The economic analysis was conducted in Tel Aviv, Israel.

Dates to which data relate
Effectiveness and resource data were collected between September 1996 and August 1998. The base price year used was not reported.

Source of effectiveness data
Effectiveness evidence was obtained from a single study.

Link between effectiveness and cost data
Cost data were collected retrospectively using the same patient sample as in the clinical analysis.

Study sample
In the non-EPO group, 25 patients were originally identified, compared with 30 in the EPO group. Power calculations were not used to determine sample size. In the EPO treatment group 5/30 patients (17%) compared with 4/25 (16%) in the pre-EPO group were excluded as they died prior to discharge.

Study design
The study was a single-centre, non-randomised trial with historic controls. Infants were followed up until discharge.
There was no loss to follow-up.

**Analysis of effectiveness**
The analysis of effectiveness was based on treatment completers only. No primary health outcomes were reported, instead the clinical analysis reported the need for blood transfusions in the two groups. The study also monitored the rate of adverse events associated with treatment. At baseline analysis there were no differences in birthweight or gestational age between infants in the two groups.

**Effectiveness results**
No adverse events due to treatment were observed in either group. 3 infants required blood transfusions in the EPO group compared with 9 in the non-EPO group, (p<0.05). The average number of blood transfusions required in the EPO group was also significantly lower, 0.6 +/-1.9 compared with 1.7 +/-2.7 in the non-EPO group, (p<0.006).

**Clinical conclusions**
EPO is both safe and reduces the need for blood transfusions, and the risks associated with such multiple transfusions.

**Measure of benefits used in the economic analysis**
The measure of benefit used in the economic analysis was the need for blood transfusions.

**Direct costs**
All costs associated with blood bank charges, transfusion supplies and EPO were included in the analysis. Data were obtained directly from hospital records. EPO ampoule usage was based on the assumption that each ampoule would be used to treat three patients on any day, and therefore avoid wastage of unused EPO. Units of blood were divided into 4 aliquots and, after initial transfusion, the remaining blood was saved for any future transfusions. The number of transfusions required and ampoules used were recorded separately from costs. The costs of adverse events due to EPO therapy or transfusion were included in the analysis. Costs excluded from the analysis included labour (either physician or nursing time) in administering EPO or blood transfusions, and the costs of using leukocyte filters in transfusion when cytomegalovirus-negative blood was not available. Price years used in the analysis were not reported. Costs and benefits were not discounted, which was appropriate given the short duration of the study. The perspective adopted in the analysis appears to have been that of the study institution.

**Statistical analysis of costs**
No statistical analysis of costs was carried out.

**Indirect Costs**
Indirect costs were not included.

**Currency**
US dollars ($). Conversion from Israeli currency was not reported.

**Sensitivity analysis**
No sensitivity analysis was conducted.

**Estimated benefits used in the economic analysis**
The average need for blood transfusion per infant in the EPO group was 1.1 transfusions less than in the pre-EPO
group, (0.6 +/-1.9 compared with 1.7 +/-2.7, p<0.006), therefore reducing significantly consequential risks associated with multiple transfusions.

Cost results
The average costs per infant in the EPO group for both EPO therapy and transfusion were $128 +/-168 compared with $151 +/-189 for patients in the pre-EPO group, (p<0.01). The cost of blood transfusions alone in the post-EPO group was $57 +/-87. There were no costs for adverse events in either group.

Synthesis of costs and benefits
The authors did not undertake a synthesis of costs and benefits since the intervention was the dominant strategy.

Authors’ conclusions
EPO therapy is an effective intervention that reduces costs for children with anaemia by reducing the need for blood transfusion.

CRD COMMENTARY - Selection of comparators
A justification for the comparator used, usual care, was provided by the authors, since EPO therapy was not a standard regimen. You, as a database user, should consider whether this is appropriate in the context of your own environment.

Validity of estimate of measure of benefit
Benefits were estimated using a non-randomised retrospective approach, which the authors acknowledge, could introduce bias into the study conclusions. However, the authors do argue that the consistency of blood transfusion methods and laboratory procedures across the two study time periods improves the validity of the analysis. The study sample was not determined using power calculations. Both groups were shown to be comparable at baseline analysis, but a larger sample may have detected any statistically significant clinical variations between the two groups. Although the need for blood transfusion is considered by the authors as a measure of benefit, it is unclear whether the length of follow up until discharge was appropriate to identify any consequential risk associated with blood transfusions such as the viral infections noted by the authors. Future analysis may wish to explore this issue in the economic analysis.

Validity of estimate of costs
The perspective adopted in the analysis was not reported, although costs consistent with a study institution perspective were included. Costs were reported separately from resources used in the analysis. The authors themselves noted that the additional costs of leukocyte filters and likely additional labour costs for blood transfusion were not included in the analysis, and that these would increase the cost advantage of EPO therapy. The base price year used in the analysis does not appear to have been reported. A currency conversion from Israeli to US currency appears to have been performed in the analysis but the exchange rate used was not provided. No statistical analysis of quantities was conducted and it would also have been useful to explore any uncertainties associated with the data through sensitivity analysis; for instance the impact of currency fluctuations on cost estimates.

Other issues
The authors did make appropriate comparisons of their findings with those from other studies, and noted that cost implications of the treatment reported in the literature were uncertain. The results of the study do not appear to have been presented selectively.

Source of funding
None stated.
Bibliographic details

PubMedID
10731302

Indexing Status
Subject indexing assigned by NLM

MeSH
Anemia /drug therapy /economics; Blood Transfusion /economics; Cost-Benefit Analysis; Erythropoietin /economics /therapeutic use; Health Care Costs; Humans; Infant, Newborn; Infant, Premature; Infant, Very Low Birth Weight; Israel; Retrospective Studies; Statistics, Nonparametric

AccessionNumber
22000000823

Date bibliographic record published
30/06/2001

Date abstract record published
30/06/2001