Epoetin in haemodialysis patients: impact of change from subcutaneous to intravenous routes of administration

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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
Haemodialysis patients suffering from anaemia associated with chronic renal failure were given intravenous (IV) epoetin (EPO) (EPREX; Janssen-Cilag, Berchem). The comparator treatment was subcutaneous (SC) EPO.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The main characteristics of the study population were that they were suffering for anaemia associated with chronic renal failure and were cared for by haemodialysis. The patients had undergone dialysis three times a week for more than 6 months.

Setting
The setting was secondary care. The economic study was carried out in Lille, France.

Dates to which data relate
The effectiveness evidence was collected between July and November 2002. The resource use evidence referred to 2002 to 2003. The price year was 2002/03.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The patients who provided the effectiveness data were also the source for some of the cost data but, as the cost data were given on a ward basis, other patients were probably included as well. The costing was carried out retrospectively.

Study sample
No power calculations were reported. There was no sample selection. The treatment was given to patients according to the protocol operating at the time. Therefore, the patients were divided into two groups, the SC/IV group and the IV group. Patients in the SC/IV group received SC EPO until July 2002 and were then switched from SC to IV EPO after July 2002. This group contained 69 patients with a mean age 69.5 (+/- 1.44) years, and the male-to-female was 0.82. Patients in the IV group had already received IV EPO before July 2002. This group contained 30 patients with a mean
age of 70.1 (+/- 1.8) years, and the male-to-female ratio was 0.50.

**Study design**
This was a single centre, retrospective cohort study in which treatment was allocated on the basis of the treatment that the hospital thought best. Prior to July 2002, EPO was preferentially administered by the SC route, with the IV route being used only for patients for whom the SC route was contraindicated. This view changed in July 2002 following recommendations of the European Medicines Evaluation Agency. The patients were followed up for 6 months after the change from the SC route to the IV route. No blinding of the assessment was reported.

**Analysis of effectiveness**
No patients were excluded for incomplete data. The health outcomes used to assess the patients were haemoglobin (Hb) concentration, serum ferritin and transferrin saturation. Demographic and biological data at baseline were given for each group. Age, gender ratio and weight were similar in the two groups. However, serum ferritin was higher in the SC/IV group and the doses of EPO administered tended to be lower (130.19 +/- 11.75 UI/kg per week versus 160.65 +/- 19.10 UI/kg per week in the IV group), but this difference was statistically insignificant, (p=0.1650).

**Effectiveness results**
The Hb concentration went from 11.27 (+/- 0.14) g/dL to 11.67 (+/- 0.12) g/dL in the IV group, (p<0.05), and from 11.52 (+/- 0.13) to 11.14 (+/- 0.13) in the SC/IV group, (change not statistically significant).

Transferrin saturation went from 26.91% (+/- 2.22) to 21.82% (+/- 2.11) in the IV group, and from 26.55% (+/- 1.50) to 28.06% (+/- 1.64) in the SC/IV group, (the changes in each group were not statistically significant).

Serum ferritin went from 373 (+/- 51.1) microg/L to 277.16 (+/- 43.87) microg/L in the IV group, (change not statistically significant), and from 500.2 (+/- 33.9) microg/L to 398.53 (+/- 28.40) microg/L in the SC/IV group, (p<0.05).

**Clinical conclusions**
The authors concluded "there were no significant clinical and biological changes associated with the change in method of administering epoetin" and "there was no biological modification between July and November 2002 in the IV group", although the serum ferritin levels decreased significantly in the SC/IV group and the Hb concentration increased significantly in the IV group.

**Measure of benefits used in the economic analysis**
No summary measure of benefits was produced. Therefore, the authors carried out a cost-consequences analysis.

**Direct costs**
No discounting was carried out as the costs were incurred during less than 2 years. The quantities of EPO used per patient and the associated costs were assessed; no other information on any other costs was given. The total expenditure on EPREX and total quantity used (by the dialysis ward) was given so that the price of EPREX could be deduced. The estimation of costs was based on data provided by the hospital. The resources were measured between 2002 and 2003. The authors calculated the change in costs between 2002 and 2003 when considering a decrease in the overall price of EPO and when using constant 2002 prices.

**Statistical analysis of costs**
No statistical analysis was carried out.
Indirect Costs
No indirect costs were calculated.

Currency
Euros (Euro).

Sensitivity analysis
No sensitivity analysis was carried out.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
A significant mean increase in EPREX doses between July and November was observed in the SC/IV group (+46.83 +/- 10.20 UI/kg per week, +34.9%; p=0.001). This increase was not observed in the IV group (+2.17 +/- 20.14 UI/kg per week, +1.3%; p=0.939).

Overall EPREX consumption showed an increase of 37.0% between 2002 and 2003 (40,006 kUI between January and July 2002 versus 54,831 kUI between January and July 2003; extrapolated difference at one year 25,414 kUI).

The increase in dosage led to an increase in cost per patient per year of Euro 1,841 (+/- 401) after July 2002 and to an overall increase in cost for the hospital of Euro 213,905 (+26.3%) a year. If the price had remained unchanged, the overall increase in cost would have been 32.7% (Euro 265,905).

The costs of adverse effects were not considered in the costing.

Synthesis of costs and benefits
The costs and benefits were not combined as the study was a cost-consequences analysis.

Authors' conclusions
Changing the administration of epoetin (EPO) from a subcutaneous (SC) route to an intravenous (IV) route resulted in an increase in EPO dosage and in substantial additional costs.

CRD COMMENTARY - Selection of comparators
The choice of the comparator, SC administration of EPO, was implicitly justified by it having been current practice in the recent past in the authors' setting.

Validity of estimate of measure of effectiveness
The effectiveness data were derived from a single study. The study design, a retrospective cohort study, was not appropriate for the hypothesis. This is because the patients were not randomly allocated to treatment, instead being allocated according to a particular protocol operating before July 2002 and another protocol operating after July 2002. Therefore, the IV patients were different from the SC/IV patients and were not shown to be comparable at baseline. These confounding factors were not taken into consideration in the analysis of effectiveness. The analysis of the SC/IV patients could be seen as a before-and-after study in which the patients were those who had, in the past, seemed suitable for SC administration of EPO.

The analysis of effectiveness was not handled credibly for several reasons. First, no sample size was determined in the
planning phase of the study. Second, the authors did not confine themselves to examining similar patients before and after a change. Third, the authors did not record the frequency of erythroblastopenia before and after the change (the occurrence of which as an adverse effect of EPO was initially given as the justification of the change from SC to IV administration). Finally, the authors concluded that there were no significant biological modifications associated with the changes in the route of EPO administration, although changes occurred in each group.

Validity of estimate of measure of benefit
The authors did not derive a summary measure of health benefit. The health benefits are therefore those associated with the effectiveness outcomes.

Validity of estimate of costs
The cost data were very limited in scope. From the cost perspective adopted (i.e. the hospital), it seems that only the cost of EPO was included. It was unclear whether the cost of administering EPO was included or not. The quantity of EPO was assessed separately from the costs. However, the costs were not clearly broken down into costs and quantities, and often the costs were given for the whole ward rather than per patient in the IV or SC/IV groups. The quantities were taken from a single study, while the prices were taken from the authors' setting. The authors did not report any statistical analysis of resource use or costs, and this introduces uncertainty into the results. The price year was reported, which will aid future reflation exercises and allow comparisons with other interventions assessed at different time periods. Discounting was not necessary as the costs were incurred during less than 2 years.

Other issues
The authors made appropriate comparisons of their results with the findings from other studies. The issue of generalisability to other settings was not addressed. The authors did not present their results selectively and their conclusions did not reflect the scope of the analysis (for the reasons already reported). The authors did not present any limitations of their study.

Implications of the study
The authors did not make any recommendations for policy or practice following their study, or suggestions for further work.

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