Cost-effectiveness impact of iron dextran on hemodialysis patients' use of epoetin alfa and blood

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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
Iron dextran administration in hemodialysis patients. The iron dextran protocol was as follows: for ferritin concentrations less than 100ng/mL, transferrin saturation less than 20%, and hematocrit less than 30%, load with 100mg every dialysis session for five sessions and follow with weekly 100mg doses; for ferritin concentrations between 100ng/mL and 800ng/mL, transferrin saturation greater than 20%, and hematocrit 30-36%, continue 100mg weekly doses and adjust epoetin alfa dosage per period; for ferritin concentration greater than 100ng/mL, transferrin saturation greater than 20%, and hematocrit 30-36%, withhold iron dextran until ferritin concentration is below 800ng/mL.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Ambulatory patients who had been receiving hemodialysis for at least six months before the start of an iron dextran protocol.

Setting
Hospital. The economic analysis was carried out in the USA.

Dates to which data relate
Effectiveness and resource use data were collected in the period July 1997 to June 1998. The price year appears to have been 1997-98.

Source of effectiveness data
The evidence for the final outcomes was based on a single study.

Link between effectiveness and cost data
Costing was conducted prospectively on the same patient sample as that used in the effectiveness analysis.

Study sample
Power calculations were not used to determine the sample size. The study sample was 33 patients with a mean (SD) age of 62 (16) years (range: 25 - 83 years) who completed the entire 12-month study period.
Study design
This was a before-and-after study, carried out in a single centre. The duration of the follow-up was 6 months. The number of patients who did not complete the study (loss to follow-up) was not reported. The study was completed in a real-life clinical setting in which the nephrologist, staff, and patients were aware of all therapies being given. No attempts were made to alter prescribing patterns, except to encourage the use of dosage protocols for epoetin alfa and iron dextran.

The epoetin alfa dosage protocol that was in place before this study, was as follows:

for hematocrit above 37%, reduce dosage by 50% if hematocrit increases by 4% or more, and reduce dosage by 25% if hematocrit increases by 3% or more;

for hematocrit below 30%, ferritin concentration below 100ng/mL, and transferrin saturation greater than 20%, initiate iron dextran protocol;

for hematocrit below 30%, ferritin concentration over 100ng/mL, and transferrin saturation above 20%, increase dosage by 50% to a maximum of 10,000 units three times a week.

Before the initiation of the iron dextran protocol at the end of the six-month baseline period, iron dextran was administered randomly at doses ranging from a total of 100 to 500mg. Blood prescribing was at the nephrologists' discretion throughout the study.

Analysis of effectiveness
The principle used in the analysis of effectiveness appears to have been treatment completers only. The primary outcome measure was success rate. Successful treatment was defined as a hematocrit of 33-36%, a transferrin saturation above 10%, a ferritin concentration of more than 100ng/mL, and no blood use except for acute blood loss. The following clinical variables were also reported: ferritin level, transferrin saturation, hematocrit, number of units of blood, epoetin alfa doses, and untoward reactions due to receiving blood.

Effectiveness results
The overall success rate was 30% (10 patients) in the pre-protocol period versus 82% (27 patients) in the post-protocol period, (p<0.001). There was a statistically significant difference in success rate for ferritin (54% versus 97%, (p<0.001)) and blood use (39% versus 91%, (p=0.004)). Fifty units of blood were used in the first six months, and nine units of blood were used in the second six months. There was significant improvement in the mean values for hematocrit, ferritin, and transferrin saturation after the protocol was instituted. The mean epoetin alfa dose decreased, but the difference was not statistically or clinically significant. None of the patients receiving blood had any untoward reactions.

Clinical conclusions
Iron indices were borderline for many of the patients in the pre-protocol period. Once the iron dextran protocol was implemented, ferritin and transferrin saturation improved markedly. Several studies have documented that intravenous iron dextran can reduce the need for epoetin alfa. That result was not seen in this study, possibly because the whole blood was used in the first half of the study. Furthermore, epoetin alfa resistance may have been present in the 4 patients who received high doses of epoetin alfa.

Measure of benefits used in the economic analysis
The benefit measure was the success rate.

Direct costs
 Costs were not discounted due to the short time frame of the cost analysis. Some resource use quantities were reported.
separately from the costs. Cost items were reported separately. Cost analysis covered the cost of drugs, laboratory tests, blood, and supplies. The perspective adopted in the cost analysis was that of the hospital and dialysis unit. The costs were reported in terms of average monthly values. The price year appears to have been 1997-98. The cost analysis did not cover the costs of nursing time and pharmacy time because there would be no changes in staffing whether these protocols were in place or not.

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

**Currency**
US dollars ($).

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

**Estimated benefits used in the economic analysis**
The overall success rate was 30% (10 patients) in the pre-protocol period versus 82% (27 patients) in the post-protocol period, \( p<0.001 \).

**Cost results**
The mean monthly total cost was $13,498.80 (pre-protocol) compared to $14,205.44 (post-protocol), a difference of $707.41.

**Synthesis of costs and benefits**
The average and incremental cost-effectiveness ratios were calculated in terms of cost per successful treatment. Monthly cost-effectiveness costs for the pre-protocol and post-protocol periods were $1,350 and $526 per successful treatment, respectively. The incremental cost-effectiveness of iron dextran was $42 per successful treatment.

**Authors’ conclusions**
Iron dextran improved iron indices and reduced the need for blood transfusions but did not reduce the average dose of epoetin alfa. The additional cost of therapy per month seemed justified by the clinical benefits.

**CRD COMMENTARY - Selection of comparators**
The strategy of not using iron dextran was explicitly regarded as the comparator. This allowed the active value of the intervention to be evaluated.

**Validity of estimate of measure of effectiveness**
The internal validity of the effectiveness results can not be guaranteed due to the before-and-after nature of the study design and the effectiveness analysis being based on treatment completers only. It is not clear how many patients were eligible for the study and why some did not complete it and were thus excluded from the analysis. The study sample size may have been insufficient to identify changes in the use of epoetin alfa. The study sample appears to have been representative of a broad range of patients with end-stage renal disease (ESRD).

**Validity of estimate of measure of benefit**
The estimate of the benefit measure was directly obtained from the effectiveness analysis. Other widely used benefit
measures such as life-years gained or quality-adjusted life-years gained can be used in the economic analysis.

Validity of estimate of costs
Positive aspects of the cost analysis, which are likely to have enhanced its validity, were that some resource use quantities were reported separately from the costs, cost categories were reported separately, the price year and the perspective adopted in the study were specified and resource use data were collected prospectively. However, it is not entirely clear whether cost data were based on charges or true costs. The effects of alternative procedures on indirect costs were not addressed and statistical analyses were not performed on cost data. Cost results may not be generalisable outside the study setting.

Other issues
Given the inherent limitations of the study design, and the lack of sensitivity analysis and statistical analysis of the costs, the study results should be interpreted with some caution. The issue of generalisability to other settings or countries was not addressed, although, appropriate comparisons were made with other studies.

Implications of the study
The consensus of the study dialysis unit is that avoiding epoetin alfa in favour of blood transfusions could have a devastating impact on some patients in terms of disease transmission and allergic reactions. The additional cost of epoetin alfa and iron dextran seems well justified to attain the overall clinical edge.

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