Intravenous iron dextran treatment in predialysis patients with chronic renal failure

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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
Intravenous (IV) iron dextran (IVID), 500 mg/wk for two doses, for the treatment of iron deficiency anaemia in patients with chronic renal failure (CRF), not undergoing haemodialysis.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population consisted of patients with chronic renal failure (CRF) (creatinine clearance less than 50 mL/min), not undergoing dialysis who had iron deficiency anaemia (ferritin level less than 100 ng/mL or transferrin saturation (TSAT) less than 0.20%/100). Patients were excluded or removed from the study if they had a history of hypersensitivity or adverse reaction to iron supplementation, were pregnant, or started dialysis therapy or required blood transfusion or other iron infusion during the study period.

Setting
The setting was primary care. The economic analysis was carried out in Virginia, USA.

Dates to which data relate
No dates were given for effectiveness, resource use and price year data.

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 on the same patient sample as that used in the effectiveness analysis. It was not reported whether costing was performed prospectively or retrospectively.

Study sample
Power calculations were not used to determine the sample size. A total of 22 patients (aged 45 to 85 years) were randomly assigned to group I (n=8) to be administered 200 mg/week of IVID for 5 consecutive weeks or to group II (n=14) to be administered 500 mg/week of IVID for 2 consecutive weeks.
Study design
The study took the form of a randomised controlled trial carried out in a single centre. The duration of the follow-up was 6 months after the last dose of iron dextran. Regarding the number of patients who were lost to follow-up, it was reported that at three months, two patients were removed from the study to initiate dialysis, and at 6 months, four more patients were removed, three requiring dialysis and one for a blood transfusion for severe anaemia and myocardial ischaemia. Randomisation was performed using medical record numbers; even numbers being assigned to group I and odd numbers assigned to group II. A standard test dose of 25 mg of IVID diluted in 100 mL of normal saline was administered over 30 minutes during the initial visit, monitoring very closely for adverse reactions. If this dose was well tolerated, a second infusion was administered to complete the full weekly dose of 200 or 500 mg, depending on the group, diluted in 250 mL of saline over 60 to 90 minutes.

Analysis of effectiveness
The principle (intention to treat or treatment completers only) used in the analysis of effectiveness was not explicitly specified. The clinical outcome measures were haemoglobin (Hb) concentration, ferritin concentration, and TSAT. Adverse reactions were also recorded.

Effectiveness results
All patients tolerated IVID infusions without serious adverse reactions. Over the 6-month follow-up, both groups experienced an increase in haemoglobin levels from baseline. Ferritin levels in both groups increased, (p<0.005), peaked at 2 weeks, then declined thereafter. Over the 6-month follow-up, both groups experienced significant improvement, although the beneficial effects of group II declined at a significantly faster rate than group I, (p=0.003). There was no significant difference in change in ferritin levels between groups. TSAT peaked at 2 weeks in both groups, (p<0.001). Group I experienced a significant increase in TSAT throughout the 6-month follow-up, (p<0.03), and group II achieved a significant increase in TSAT at 2 weeks, but not at 3 and 6 months. There was no significant difference in pretreatment to posttreatment change in TSAT.

Clinical conclusions
This study shows that a 500-mg dose of IVID administered twice is as safe and effective in improving iron status in predialysis patients with iron deficiency anaemia as a 200-mg dose of IVID administered five times.

Measure of benefits used in the economic analysis
No summary benefit measure was identified in the economic analysis, and only separate clinical outcomes were reported. The economic analysis appears to have been conducted on the basis of cost-minimisation based on the equal efficacy of the two alternative treatment approaches.

Direct costs
Costs were not discounted due to the short time frame of the cost analysis. Some quantities were reported separately from the costs but cost items were not reported separately. The cost analysis covered the costs of iron dextran, facility use fees, professional fees, IV catheter placement, and saline solution. The price year was not explicitly specified. The cost analysis did not cover the costs of transportation and travel expenses.

Indirect Costs
Indirect costs were not considered.

Currency
US dollars ($).
Sensitivity analysis
No sensitivity analysis was conducted.

Estimated benefits used in the economic analysis
Not applicable due to the cost-minimisation approach adopted. See effectiveness results reported above.

Cost results
The average total cost of treatment was $965 in Group I versus $1,490 in Group II, and was therefore 35.2% less costly in group I compared with group II.

Synthesis of costs and benefits
Costs and benefits were not combined since the economic analysis was performed on a cost-minimisation basis.

Authors' conclusions
The authors concluded that IVID, 500 mg/week, for 2 weeks is as effective and safe as 200 mg/wk for 5 weeks, but much less costly.

CRD COMMENTARY - Selection of comparators
A justification was given for the choice of the comparator; it was the recommended regimen for iron replacement. You, as a database user, should consider whether this regimen is a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
Despite being a randomised study, the internal validity of the effectiveness results is not likely to be high due to the small sample size, the lack of reporting on the comparability of the study groups and the fact that the basis for the analysis of effectiveness (intention to treat or treatment completers only) was not specified. Furthermore, no report was given regarding whether the study was blinded or not. The study sample appears to have been representative of the study population. The dates during which the effectiveness data were collected were not reported.

Validity of estimate of measure of benefit
The analysis of benefits appears to have been based upon the therapeutic equivalence of treatment alternatives. The economic analysis therefore included only costs.

Validity of estimate of costs
The following features may have adversely affected the validity of the cost analysis: the resource use profile was not fully reported separately from the costs; the cost breakdown was not reported; the price year and perspective adopted in the cost analysis were not specified; the cost data appear not to have been based on true costs; the direct cost analysis was not comprehensive as some cost elements were omitted from the analysis; statistical analyses were not performed on resource use and cost data; the effects of alternative treatment strategies on indirect costs (productivity loss) were not addressed, but may have been relevant; the cost results may not be generalisable outside the study setting.

Other issues
Given the above limitations of the study design, some caution may need to be exercised in interpreting the study results. The issue of generalisability to other settings or countries was not addressed, although the authors did make appropriate comparisons with other studies. The degree to which the study sample was representative of the study population was not addressed in the authors' comments.
Implications of the study
Within the caveats identified above, the results appear to support the intervention from both clinical and economic perspectives. The authors indicate that, during the study period, the only IV iron preparation available in the United States was iron dextran. A major safety problem is the risk for anaphylaxis, causing an impediment to more aggressive use. Other parenteral iron preparations will be available in the near future and are considered to be as effective but safer than iron dextran.

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