Effective utilization of erythropoietin with intravenous iron therapy
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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 iron therapy for haemodialysis patients on erythropoietin (EPO).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with end-stage renal disease receiving regular haemodialysis (two to three times weekly for 4 hours) were followed prospectively. Patients were both male and female and their ages ranged from 24 to 80 years with an average age of 62.4 years.

Setting
Hospital setting. The study was carried out at the renal unit in Leeds General Infirmary in the UK.

Dates to which data relate
No dates were reported for either the effectiveness or the cost data.

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

Link between effectiveness and cost data
The costing was carried out prospectively on the same patient sample as that used in the effectiveness study.

Study sample
It was not reported whether power calculations were used to determine the sample size. 22 patients were included, all of whom completed the study for up to at least three months and were included in the final analysis. After 3 months one patient received a cadaveric renal transplant and another was converted to CAPD due to poor vascular access. Patients were selected on the basis of having a SF of less than or equal to 60 micro.g/litre despite oral iron supplements (three times daily). Patients with high aluminium levels, elevated parathyroid hormone (PTH) levels, underlying bleeding/haematological disorders, malignancy or active chronic inflammatory diseases (as indicated by a raised C-reactive protein) were excluded from the study.
Study design
This was a case series study (before and after cohort) carried out in a single centre. The patients were followed up for four months. There was no loss to follow up as all patients completed three months of study. The study was non-blinded.

Analysis of effectiveness
Although it was not clearly stated, the study was based on intention to treat, as all patients were included in the final analysis. The outcome was a more effective utilization of EPO in patients. No analysis was carried out to show what influence demographic factors had on the results and there was no explicit mention of confounding variables.

Effectiveness results
Both serum iron and transferrin saturation increased with the administration of iron. Serum iron increased significantly in the first month from $15.3 \pm 2.3$ micro.mol/litre to $24.1 \pm 3.1$ micro.mol/litre and rapidly reduced to the baseline value ($14.6 \pm 1.3$ micro.mol/litre) after a month and then remained stable ($P=0.0001$). For TS a significant difference only arose at the end of the study ($P=0.00047$), when the level dropped to a mean of $20.2\% \pm 2.3$ from that at 4 weeks ($38.3\% \pm 4.3$). The median EPO dose was $4000$ units/week (mean $6050$ units/week) pre-treatment and $2000$ units/week (mean $3700$ units) post intravenous iron therapy, ($P=0.03$).

Clinical conclusions
The authors indicated that their data, like that of others, indicated that intravenous iron therapy was highly effective in the reduction of EPO requirements in haemodialysis patients.

Modelling
No model was used.

Measure of benefits used in the economic analysis
The benefits outcomes were reductions in the EPO dose used and better haemoglobin levels, which would imply better quality of life.

Direct costs
The costs measured for EPO therapy included the cost of erythropoietin s/c (per 1000 units), swabs, needles and the total cost of mean weekly treatment. The cost of intravenous iron therapy included intravenous iron 100mg, 100ml normal saline, giving set and the total cost of loading dose for 7 treatments. The costs considered were mainly hospital costs and were not discounted due to the short study period. Some quantities were mentioned separately from costs although, generally, details were not provided of actual quantities used by individuals. The price year was not stated.

Statistical analysis of costs
Not undertaken.

Indirect Costs
There was no mention of indirect costs as the study focussed mainly on a health service perspective.

Currency
UK pounds sterling ().
Sensitivity analysis
No sensitivity analysis was undertaken.

Estimated benefits used in the economic analysis
The benefits were the reduction in amounts of the EPO dose. The pre-treatment median dose was 4000 units per week (mean 6050 units/week) and 2000 units/week (mean 3700 units) post-intravenous iron therapy. Mean haemoglobin (Hb) levels remained constant at 6 and 12 weeks, (p=0.087).

Cost results
Intravenous iron was available at grossly elevated prices, the cost being 11.26 for 100mg of intravenous iron. EPO treatment using ESPREX (Cilag Biotech) cost 9 per 1000 units given. According to data provided this amounted to a saving for EPO of 21.45 per week per patient (128.68 at 6 weeks) at the expense of an initial cost of 176.70 per 3 months of iron. The authors envisaged that once iron loaded, patients would only intermittently require further iron therapy at doses of 200mg, approximately every 3 months (23.64) thus reducing the long term savings.

Synthesis of costs and benefits
Not undertaken.

Authors’ conclusions
The authors concluded that their data, like that of others, demonstrated that intravenous iron therapy is both economic and safe with a very effective reduction of EPO requirements in haemodialysis patients.

CRD COMMENTARY - Selection of comparators
The selection of comparator was stated to be oral iron therapy, as administered prior to the study.

Validity of estimate of measure of benefit
The benefit was stated in terms of the reduced EPO therapy. No explicit mention was made of other health benefits to the patients, although Hb level was included which implicitly increased quality of life.

Validity of estimate of costs
There was a lack of detail as far as the costs were concerned; in particular the price year was not reported. Details regarding the before-study (oral therapy) period could have been more comprehensively reported.

Other issues
The study concentrated on the clinical effectiveness of the intervention and more detail could have been given on the cost analysis. The authors noted that their costs for intravenous iron therapy were ‘grossly elevated’ and this may affect the generalisability of the results to other settings. They did make good comparisons with other similar studies which produced similar findings.

Implications of the study
This is a new method of treating patients which appears to be at an experimental stage. The authors indicated that intravenous iron was only available at their unit at grossly elevated prices. This study therefore raises many issues and provides a basis for future research into the use of intravenous iron therapy for haemodialysis patients on erythropoietin.
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