Comparison of two different doses of preoperative recombinant erythropoietin in men undergoing radical retropubic prostatectomy

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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
Two different doses of recombinant erythropoietin were evaluated in men undergoing radical retropubic prostatectomy. The regimens studied were two doses of subcutaneous 600 IU/kg (high-dose) epoetin alpha and two doses of subcutaneous 300 IU/kg (low-dose) epoetin alpha.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised men undergoing radical retropubic prostatectomy. The patients were eligible for preoperative epoetin if their baseline haematocrit was 48 or less, and there was no evidence of hypertension or unstable angina.

Setting
The setting was a university hospital. The economic study was carried out at the Department of Urology, New York University School of Medicine in New York, USA.

Dates to which data relate
The effectiveness and resource use data were collected between May 1998 and November 1999. The price year was not reported.

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

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

Study sample
It was not specified as to how the sample size was determined. Two hundred of the 248 patients who underwent radical retropubic prostatectomy by a single surgeon for localised prostrate cancer were selected. The selection was made on the basis of their eligibility for preoperative prostatectomy from May 1998 through November 1999. There were 100 patients in the high-dose group (enrolled from May 1998 through March 1999) and 100 patients in the low-
dose group (enrolled from March 1999 through November 1999). The mean age was 59.9 (+/- 0.7) years in the high-dose group and 60.5 (+/- 0.7) years in the low-dose group. While there were no details of how many patients were actually asked to participate, the authors indicated that some men elected alternative blood management strategies due to insurance reimbursement-related issues.

**Study design**
This was a prospective cohort study carried out in a single centre. The patients were seen at 14 and 7 days before their operation. The length of follow-up was not reported. None of the patients were lost during the follow-up.

**Analysis of effectiveness**
The basis for the analysis of the clinical study (intention to treat or treatment completers only) was not explicitly stated. However, it appears to have been conducted on an intention to treat basis, as all patients included in the study were accounted for in the analysis. The primary health outcome was the effect of the treatment on the haematocrit level. This was measured more than 14 days preoperatively, at day 0 (immediately after anaesthesia), intraoperatively, immediately postoperatively in the recovery room, on the morning of the first postoperative day, and on the day of discharge. The percentages of patients requiring blood transfusions was also reported. The groups were shown to be comparable in terms of their age, weight, serum prostate-specific antigen level and Gleason score.

**Effectiveness results**
The mean haematocrit baseline level was 42.6 (+/- 0.3) for the high-dose group and 43.1 (+/- 0.3) for the low-dose group, (p=0.9223).

The induction levels were 47.7 (+/- 0.5) for the high-dose group and 47.0 (+/- 0.5) for the low-dose group, (p=0.2918).

The recovery levels were 37.4 (+/- 0.5) for the high-dose group and 36.0 (+/- 0.5) for the low-dose group, (p=0.0782).

The discharge levels were 34.8 (+/-0.5) for the high-dose group and 33.8 (+/-0.5) for the low-dose group, (p=0.1604).

There were no statistically significant differences found between the mean haematocrit levels at any point.

The mean change in the haematocrit response from baseline to induction was 4.50 for the high-dose group and 4.69 for the low-dose group. This difference was not statistically significant, (p=0.7225).

The percentages of men exhibiting a marked change, moderate change, slight change, or no change in the haematocrit levels between baseline and induction were:

for the high-dose group, 66% (marked change), 11% (moderate change), 11% (slight change) and 12% (no change); and

for the low-dose group, 65% (marked change), 16% (moderate change), 7% (slight change) and 12% (no change).

The mean haematocrit change per 1,000 IU was 0.09 for the high-dose group and 0.18 for the low-dose group, (p<0.01).

The distribution of the haematocrit responses was not significantly different between the two groups.

Overall, 6% of men in the high-dose group and 7% of men in the low-dose group received blood transfusions. This difference was not statistically significant.

**Clinical conclusions**
There were abundant data demonstrating the effectiveness of epoetin as a blood management strategy for men undergoing radical retropubic prostatectomy, irrespective of the dose selected.
Measure of benefits used in the economic analysis
The main outcome measure was the reduction of the mean haematocrit levels of the two groups being compared. This was derived directly from the effectiveness analysis.

Direct costs
Discounting was not carried out since the costs were incurred over a specified period of less than one year. The quantities and the costs were not reported separately. The cost/resource boundary appears to have been that of the hospital. The cost data estimates came from a Medicare reimbursement rate of $11.40 per 1,000 IU epoetin alpha, and an administrative fee of $30 per injection. The cost of autologous blood was obtained from the literature for a group of 52 men undergoing radical retropubic prostatectomy, who preoperatively donated 3 U autologous blood. The costs of autologous blood donation per patient were calculated using an average transfusion rate of 1.4 U/case and a cost of $409 for the transfusion of a single unit. The price year was not reported. The indirect costs were not considered as the study was conducted from a provider perspective.

Statistical analysis of costs
Statistical analyses of the total costs were carried out. A paired student t-test was used to determine significant differences within the groups and an unpaired student t-test was used to determine the statistical significance between the groups.

Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis was not carried out.

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

Cost results
The mean cost of two doses of recombinant erythropoietin was $1,218 in the high-dose group and $656 in the low-dose group, (p<0.01).

The difference in the cost per unit change in haematocrit between the two dose groups was statistically significant.

Synthesis of costs and benefits
An average cost-effectiveness analysis was carried out to combine the costs and the benefits of the two interventions. The mean cost per percentage point change of haematocrit was $267 for the high-dose group and $146 for the low-dose group. This difference was statistically significant (p<0.01).

Authors' conclusions
The administration of epoetin alpha on preoperative days 14 and 7 was a safe and effective treatment strategy for reducing the risk of allogeneic blood transfusions, regardless of the dose selected. The results of the study demonstrated that the low-dose epoetin alpha regimen was more cost-effective than the high-dose regimen.

CRD COMMENTARY - Selection of comparators
The authors justified the comparator on the grounds that they sought to gain insights into the dose-dependent response of epoetin alpha in men undergoing radical prostatectomy. The comparators used were also based on current practice. You should assess if the recommended doses represent widely interventions in your own setting.

Validity of estimate of measure of effectiveness
The study used a prospective cohort design, which was appropriate for the study question. The study sample was representative of the study population, and the groups of patients were shown to be comparable at analysis. However, some issues have to be taken into account. First, power calculations were not performed. Second, confounding factors and selection bias could have occurred due to the lack of randomisation. Third, the effectiveness data were collected in two different periods of time, and thus some other factors could have affected the estimated outcomes. Finally, the authors noted that the absence of a double-blind design allowed for potential investigator bias.

Validity of estimate of measure of benefit
The benefits were estimated directly from the effectiveness analysis. The authors justified their choice of estimate. However, the change in haematocrit level appears to have been an intermediate outcome measure.

Validity of estimate of costs
The categories of costs relevant to the provider perspective were included in the analysis, although no details were given of the actual amounts of resources used to arrive at the cost estimates. Discounting was unnecessary since all the costs were incurred in one year. The indirect costs were not considered as the study appears to have been conducted from a provider perspective. No price year was reported. The costs were derived using Medicare reimbursement rates, and they appear to have been somewhat specific to the study setting. Statistical analyses were only carried out on the total costs.

Other issues
The authors made appropriate comparisons of the effectiveness findings with those from other studies. They reported a number of limitations to their study, but indicated that their conclusions were justified based on the safety, effectiveness and cost data used. They identified that there was a lack of data as far as the dosing regimens were concerned.

Implications of the study
The authors highlighted the need of a multi-centre, randomised double-blind trial to examine the different doses of epoetin alpha that should be initiated to define the optimal dosing schedule.

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