Risk-benefit of OKT3 prophylaxis in immunologic high-risk cadaver kidney transplant recipients
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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
OKT3 prophylaxis in immunologically high-risk patients receiving cadaver kidney transplants.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
OKT3 prophylaxis was deemed suitable for patients receiving transplants who were likely to reject the transplant.

Setting
Hospital. The study was carried out at the University of Montreal, Canada.

Dates to which data relate
Patients were admitted to the study between June 1991 and June 1996. No dates were given for the collection of resource use data or the prices used.

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

Link between effectiveness and cost data
The costing was undertaken on the same patient sample as that used in the effectiveness study although it is not clear whether this was undertaken prospectively or retrospectively.

Study sample
100 patients were recruited into the study of whom 26 entered the high-risk group (receiving the OKT3 prophylaxis) and 74 the low-risk group. Since the patients entered these groups on the basis of their immunological risk status, no randomisation was performed. No power calculations were undertaken and there is no evidence that the samples were of adequate size to demonstrate statistically significant differences. It is not stated whether any patients refused to participate nor whether any patients were excluded from the initial samples.

Study design
This was a non-randomised trial. Although two groups were studied one cannot classify this as a controlled trial since the groups, by their nature, were not comparable. In the results section the authors compare the present high-risk group with a historical high-risk group but no details were given about this historical group, including its size. The study appears to have been conducted at a single centre. Follow-up appears to have been conducted, among some patients, for up to 60 months following transplantation although the authors report in the results section that mean follow-up was 29 months.

**Analysis of effectiveness**
The method of analysis (intention to treat or completers only) was not stated. However, it was not reported that medication was withdrawn from any patients. The primary health outcomes measured were patient survival, graft survival rates, rejection episodes and infections. Aside from immunological risk status, patient characteristics were reported to be similar in both groups except for the higher female to male ratio in the high-risk group.

**Effectiveness results**
In the high-risk group patient survival was 92% at months 6 to 24 and 86% at months 36 to 60 as compared with 97% at months 6 to 12 and 95% at months 24 to 60 among the low-risk group. This was not statistically different. Neither were there any statistically different results for graft survival rates between the two groups. In the high-risk group graft survival rates were 88% at months 6 to 24 and 82% at months 36 to 60. This compares with 85% at months 6 to 12, 83% at month 24, 81% at month 36 and 77% at months 48 to 60 among the low-risk group (not statistically significant). Among the historical group of high-risk patients who did not receive OKT3, graft survival rates were 64% at month 12 and 60% at month 36. The incidence of rejection episodes and infections were reported not to have been statistically different. 6 patients in the low-risk group and none in the high-risk group developed cancer. 3 patients died in the high-risk group and 5 in the low-risk group.

**Measure of benefits used in the economic analysis**
No summary benefit measure was used by the authors. Therefore the benefits were assumed to be equal to the effectiveness results.

**Direct costs**
With the exception of length of initial hospital stay, quantities and costs were not analysed separately. The following costs were measured: laboratory, radiology, surgery, dialysis, medication, medical personnel and service costs. The cost of organ procurement was not considered. Data sources for these costs were the hospital medical records, financial report of the hospital activity centre and national data on physicians' fees. It was reported that a detailed investigation of the costs borne by the health ministry was undertaken during the initial hospital stays for transplantation in 5 high-risk and 20 low-risk patients. Patient costs were not included.

**Statistical analysis of costs**
A statistical analysis of costs was performed.

**Indirect Costs**
Indirect costs were not measured.

**Currency**
Canadian dollars (Can$).

**Sensitivity analysis**
No sensitivity analysis was undertaken.
**Estimated benefits used in the economic analysis**
No summary benefit measure was used by the authors. Therefore the benefits were assumed to be equal to the effectiveness results.

**Cost results**
According to the text, the total cost of the initial hospitalisation per patient was significantly higher in the high-risk than the low-risk group (Can$19,188 versus Can$12,313, p=0.0001). It should however be noted that Table 2 in the paper reports the costs in the low-risk group to be Can$12,674. Immunosuppressive drug costs were, not surprisingly, higher among the high-risk group (Can$7,148 versus Can$730, p=0.0001). There were no statistically significant differences among the other cost components. Initial length of hospital stay was significantly greater among the high-risk patients (28 versus 21 days).

**Synthesis of costs and benefits**
There was no synthesis of benefits and costs.

**Authors' conclusions**
The authors concluded that OKT3 prophylaxis is efficacious among high-risk patients receiving cadaver kidney transplants, which is shown by the improved graft survival rate when compared with the historical high-risk group and the fact that the results among the high-risk group approached those of the low-risk group. In the discussion the authors drew on other studies commenting that, although patient costs in the first year after a transplantation may be similar to those associated with dialysis, the costs in future years are dramatically lower with transplantation. Lastly the authors concluded that the improvement seen in the graft survival rate compared with the historical group offsets the higher costs associated with prophylaxis OKT3.

**CRD COMMENTARY - Selection of comparators**
The choice of the comparator (no prophylaxis) is clear. It is, however, unclear why the authors compared a group of high-risk patients with a group of low-risk patients.

**Validity of estimate of measure of benefit**
As mentioned above, the groups in the present study were not comparable. The authors did briefly compare the results of the present high-risk group with a historical control group of high-risk patients although no details were provided about this patient sample, added to which historical control groups are unreliable. No power calculations were reported and the groups were not comparable with regards to the sex distribution, although no comment was made as to whether this would be likely to affect the outcome. How many patients were followed-up and for how long also remains unclear.

**Validity of estimate of costs**
Too few data were provided on the method of calculation of the costs and quantities and costs were unfortunately not reported separately. Costs were only calculated for the initial hospitalisation with follow-up costs not being included. It would also be useful to consider the effect of prophylaxis on costs borne by patients.

**Other issues**
It is not possible to draw firm conclusions from this paper; a randomised controlled trial with equivalent groups of patients would really be required along with a more thorough examination of the costs.

**Implications of the study**
The authors point out that the question of whether immunologic low-risk patients would also benefit from OKT3 prophylaxis or whether other antithymocite/antilymphocyte preparations would achieve the same results remains to be answered.

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