Mycophenolate mofetil decreases rejection in simultaneous pancreas-kidney transplantation when combined with tacrolimus or cyclosporine

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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
Using (1) tacrolimus (TAC) and mycophenolate mofetil (MMF), TAC-MMF, or (2) cyclosporine (CsA) and mycophenolate mofetil (MMF), CsA-MMF, or (3) cyclosporine (CsA) and azathioprine (AZA), CsA-AZA, as immunosuppression regimens in patients undergoing a first simultaneous pancreas-kidney (SPK) transplantation.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients undergoing a first simultaneous pancreas-kidney (SPK) transplantation.

Setting
Hospital. The economic study was carried out in Denver, USA.

Dates to which data relate
The effectiveness and resource utilisation data relating to the randomised control and intervention group were collected between August 1995 and February 1997. The corresponding data related to the historical control group were gathered in 1993. No date was given for the price data.

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 prospectively performed on the same patient sample as that used in the effectiveness analysis.

Study sample
Power calculations were not used to determine the sample size. A total of 36 patients were randomly assigned either to the TAC-MMF group (18) or to the CsA-MMF group (18). There were 18 patients in the historical CsA-AZA group. One patient was excluded from the initial study sample.

Study design
The study was a single-centre randomised controlled trial whose groups were also compared to a historical control group. The duration of the follow-up was at least 6 months for 29 patients and 1 year for 22 patients in the MMF-treated group. The duration of follow-up for patients in the historical CsA-AZA group was at least 1 year.

**Analysis of effectiveness**
The analysis of the effectiveness data was based on treatment completers only. The main health outcome measures were patient and graft survival, the incidence of acute rejection, the rate of infection, metabolic and drug toxicity. The groups were comparable in terms of age, gender, race, and prognostic features. The effects of two potential confounding variables were discussed viz; a switch from CsA (Sandimmune) in the historical CsA-AZA group to CsA (Neoral) in the CsA-MMF group, and the problems arising from the study being carried out in a single centre.

**Effectiveness results**
The differences in graft or patient survival were not statistically significant for any groups at any time point. Both the TAC-MMF and the CsA-MMF groups had an 11% rate of acute rejection at 3 months (P<0.01) versus a 77% rejection rate in the historical CsA-AZA group. The rate of second rejections was 0% for both MMF-treated groups versus 25% in the historical CsA-AZA group. The CMV infection rates for the TAC-MMF, CsA-MMF, and CsA-AZA groups were 11%, 16.7%, and 5.5%, respectively. In terms of cholesterol level, the difference between the two MMF-treated groups was not significant, but when the average cholesterol level of the TAC-MMF group was compared with the CsA-AZA group the difference was significant: 173.7 (SD=43.7) for the TAC-MMF group versus 218.4 (SD=68) for the CsA-AZA group, P<0.01). There were no significant differences between the groups in terms of Hgb(A1C) and hypertension.

**Clinical conclusions**
The main clinical findings of the study were: “(1) MMF-treatment significantly decreases the incidence of biopsy-proven acute rejection in SPK transplant recipients compared with AZA treated historical controls, and (2) when combined with MMF, TAC and CsA (Neoral) yield similar, low acute rejection rates”.

**Measure of benefits used in the economic analysis**
The main benefit measure was the incidence of acute rejection.

**Direct costs**
The number of hospital days in the first 90 days after transplant and the number of doses of OKT3 administrated to each patients were estimated and reported as the indices of resource utilisation. The cost of doses of OKT3 administered was reported. It was not specified from whose perspective the cost analysis was performed. No information was given on the sources of the cost data. The price date was not specified.

**Statistical analysis of costs**
Statistical tests, using the two-tailed t test, were carried out to compare the alternative groups in terms of resource utilisation and costs of doses of OKT3 administrated.

**Indirect Costs**
Not considered.

**Currency**
US dollars ($).
Sensitivity analysis
No sensitivity analysis was carried out.

Estimated benefits used in the economic analysis
Both the TAC-MMF and the CsA-MMF groups had an 11% rate of acute rejection at 3 months versus a 77% rejection rate in the historical CsA-AZA group (P<0.01). The rate of second rejections was 0% for both MMF-treated groups versus 25% in the historical CsA-AZA group.

Cost results
The OKT3-related costs for the TAC-MMF, CsA-MMF, and CsA-AZA groups were $6,322 (SD=$2,262), $6,554 (SD=$2,204), and $13,050 (SD=$4,292), respectively (P<0.01 for both MMF-treated groups when compared with the historical AZA-treated group).

Synthesis of costs and benefits
No synthesis was carried out since MMF-based treatment was regarded as the dominant strategy.

Authors' conclusions
The results from this study show that MMF treatment significantly decreases the incidence of biopsy-proven acute rejection in SPK transplant recipients compared with AZA-treated historical controls. In addition, the authors concluded that TAC and CsA (Neoral), when combined with MMF, yielded similar, low acute rejection rate with similar graft function and metabolic control.

CRD COMMENTARY - Selection of comparators
A justification was given for the choice of the comparator. CsA-MMF (and CsA-AZA) was used as the comparator since it represented "state-of-the-art" immunosuppression regimen. You should consider whether this is a widely used technology in your own setting.

Validity of estimate of measure of benefit
As acknowledged by the authors, the internal validity of the clinical result is not assured due to a small sample size and the presence of potential confounding variables (a switch from CsA (Sandimmune) in the historical CsA-AZA group to CsA (Neoral) in the CsA-MMF group), and the problems arising from the study being carried out in a single centre.

Validity of estimate of costs
No comprehensive list of all costs involved in using the alternative health technologies was provided, and cost analysis was based only on the doses of OKT3 administered.

Other issues
The issue of generalisability to other settings or countries was not addressed.

Source of funding
None stated.

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