The cost effectiveness of mycophenolate mofetil in the first year after living related renal transplantation
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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
The health intervention examined in the study was mycophenolate mofetil (MMF), an immunosuppressive drug used for prevention of acute rejection in renal transplant patients. It acts as a reversible inhibitor of inosine monophosphate dehydrogenase, with the result of limiting the ability of lymphocytes to proliferate and destroy foreign tissue, which may determine the rejection of transplanted organs. MMF in combination with corticosteroids and cyclosporine may reduce the incidence of renal allograft rejection after transplantation.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients receiving living related renal transplant.

Setting
The setting was hospital. The economic study was carried out at the Akdeniz University in Antalya, Turkey.

Dates to which data relate
No dates were reported. No price year was given.

Source of effectiveness data
Effectiveness data were 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 analysis.

Study sample
Power calculations and the method of sample selection were not reported. A sample of 34 patients receiving living related renal transplant were included in the study: 17 patients were allocated to the MMF group (recipient age: 32.35 +/- 2.69 years; donor age: 43.58 +/- 3.49 years; recipient gender: 6 women; donor gender: 8 women) and 17 patients to the AZA group (recipient age: 33.17 +/- 2.40 years; donor age: 44.23 +/- 3.59 years; recipient gender: 4 women; donor gender: 5 women).
Study design
This was a prospective, case-controlled study carried out in a single centre. Patients were followed for one year and assessed weekly for three months post-transplant, every 15 days between three to six months post-transplant, and every three weeks for six to twelve months post-transplant. All patients were also administered cyclosporine and prednisolone. During each assessment, a physical examination and a laboratory assessment based on measurement of creatinine and cyclosporine A blood levels were carried out. No loss to follow-up was reported.

Analysis of effectiveness
All patients included in the study were accounted for in the analysis, in effect intention to treat. The primary health outcomes assessed in the analysis were presence of hyperlipidemia, statin usage, hypertension, antihypertensive medication, acute rejection, levels of serum creatinine after discharge and at one year, duration of hospitalisation after transplant, rate of graft loss, need for antilymphocytic antibody treatment, and mortality. Study groups were comparable at baseline in terms of renal function, episodes of acute rejection, requirement of antilymphocytic antibody treatment, and incidence of opportunistic infections.

Effectiveness results
The effectiveness results were as follows:

Hyperlipidemia was present in 10 patients in the AZA group and 8 patients in the MMF group, (p=0.491).

Statin usage was carried out in 9 patients in the AZA group and 7 patients in the MMF group, (p=0.491).

Hypertension was present in 8 patients in the AZA group and 12 patients in the MMF group, (p=0.163).

Acute rejection was observed in 7 cases (41.1%) in the AZA group and 3 cases (17.6%) in the MMF group, (p=0.130).

Levels of serum creatinine were 1.32 +/- 0.06 in the AZA group and 1.46 +/- 0.09 in the MMF group after discharge, (p=0.243) and 2.3 +/- 0.5 mg/dL in the AZA group and 1.4 +/- 0.1 mg/dL in the MMF group at one year, (p=0.010).

Duration of hospitalisation after transplant was 15.8 +/- 5.7 days in the AZA group and 2.5 +/- 1.4 days in the MMF group, (p=0.037).

The rate of graft loss was 2 cases in the AZA group and no cases in the MMF group, (p=0.144).

The need for antilymphocytic antibody treatment was 5 cases in the AZA group and 1 case in the MMF group, (p=0.197).

Mortality was 1 case in the AZA group and no cases in the MMF group, (p=0.310).

Antihypertensive medication was similar in both study groups.

Clinical conclusions
The effectiveness analysis showed that the use of MMF was associated with better renal function (as shown by serum creatinine levels at one year), lower hospitalisation and reduced incidence of acute rejection in comparison with AZA treatment.

Measure of benefits used in the economic analysis
Health outcomes were left disaggregated and no summary benefit measure was used in the economic analysis, thus a cost-consequences analysis was carried out.

Direct costs
Discounting was not relevant as costs were incurred over a period of one year. Unit costs and quantities of resources were not reported separately. A breakdown of costs was not given as only total costs of the treatments were reported. The cost/resource boundary adopted was not stated. The source of cost data was not reported. Quantities of resources used were presumably derived from the single study. No price year was reported.

**Statistical analysis of costs**
Statistical analyses of total costs were carried out to test for statistical significance of the results.

**Indirect Costs**
Indirect costs were not included.

**Currency**
US dollars ($).

**Sensitivity analysis**
No sensitivity analyses were performed.

**Estimated benefits used in the economic analysis**
Please refer to the effectiveness results reported earlier.

**Cost results**
Total costs were $16,697 +/- 2,998 in the MMF group and $14,614 +/- 1,228 in the AZA group, but the difference did not achieve statistical significance, (p = 0.525).

**Synthesis of costs and benefits**
Costs and benefits were not combined as a cost-consequences analysis was carried out.

**Authors' conclusions**
The authors concluded, "MMF-based triple therapy seems to be cost effective in the first year after living related renal transplantation". The intervention resulted in shorter hospitalisation and better renal function. Although MMF was more expensive than AZA, total costs were similar for both drugs, due to shorter hospitalisation and fewer episodes of acute rejection.

**CRD COMMENTARY - Selection of comparators**
As regards the rationale for the choice of the comparator, the authors stated that MMF was often compared with AZA in previous trials. Further justification of the comparison was not provided. You, as a user of this database, should assess whether it represents a currently used treatment in your own setting.

**Validity of estimate of measure of effectiveness**
The analysis of effectiveness was based on a prospective case-control study carried out in a single centre, which was appropriate for the study question. Study groups were comparable at baseline. The analysis took into account all patients included in the analysis. However, the internal validity of the analysis could have been limited by several factors, such as the fact that the sample size was small and power calculations were not performed to ensure that the sample was adequate to ensure the detection of statistically significant differences between the study groups. In addition, the method of sample selection was not reported and no dates were given. Finally, due to the lack of randomisation in the
allocation of the patients to the study groups, confounding factors and selection bias cannot be excluded.

Validity of estimate of measure of benefit
Health outcomes were left disaggregated and a cost-consequences analysis was carried out. The use of a summary benefit measure combining quality of life and survival after transplantation would have been useful as the intervention affected both dimensions.

Validity of estimate of costs
The analysis of costs was somewhat limited. The cost items included in the analyses and the quantities of resources used were not reported. The perspective of the study was not stated, although it might have reflected that of the hospital. The price year was not given, thus hindering any reflation exercise to other settings. The source of cost data was not reported, but it should have been the hospital where the study was carried out. Finally, statistical analyses were carried out only on total costs to test for statistical significance of results.

Other issues
The authors made some comparisons of their findings with those from other studies. The issue of the generalisability of the study results to other settings was not addressed as sensitivity analyses were not carried out, thus the external validity of the analysis was quite limited. The study enrolled a sample of patients receiving living related renal transplant and this was reflected in the conclusions of the study.

Implications of the study
The study results suggest that MMF-based triple therapy should be recommended for the prevention of acute rejection episodes after renal transplant. However, these conclusions must be viewed in the light of the limitations of the analysis reported above.

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