The cost effectiveness of mycophenolate mofetil in the first year after primary cadaveric transplant

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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
Immune suppressant therapy post-renal transplant using mycophenolate mofetil (MMF) or azathioprine.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population was primary cadaveric renal allograft patients, enrolled prior to transplant. The average age (approximately 45 years) and gender distribution (approximately 60% male) were similar in the control group and the MMF group.

Setting
Hospital. The economic analysis was conducted in Seattle, Washington, USA.

Dates to which data relate
The effectiveness analysis data and prices were from 1995.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was undertaken on the same sample as in the effectiveness study. Although not specifically stated, it appears that costing was done retrospectively.

Study sample
166 patients were enrolled in the standard therapy group and 167 in the MMF group. Patients were randomized prior to transplantation. Power calculations were not reported.

Study design
The clinical study was a randomized controlled blinded trial in 14 centres. The clinical trial was planned for three years duration. These data referred to the results of the clinical trial at one year post-transplantation. Premature withdrawal...
occurred in 22.6% of subjects on standard therapy and 21.2% on MMF. The primary reason for withdrawal in the standard therapy group was lack of expected effect, while in the MMF group adverse effects, new illness and laboratory abnormalities were the primary reasons. Assessment of outcomes was performed by blinded clinicians.

**Analysis of effectiveness**

The analysis of effectiveness was based on the patients who completed six months of therapy and not on ‘intention to treat’. The health outcomes assessed were acute graft rejection rates, graft failure rates, and medical care utilization including length of hospital stay, rejection-related treatments, and cytomegalovirus infections.

**Effectiveness results**

The acute rejection rate in the standard group was 47% and 27.9% in the MMF group. Graft failure occurred in 9.8% on standard treatment and 4.2% on MMF. Cytomegalovirus infections requiring treatment occurred in 6.1% of the standard treatment group and 9.1% in those on MMF. Other effectiveness results and confidence intervals were not reported from the original study.

**Clinical conclusions**

At six months post-transplant, MMF therapy was superior to standard therapy using azathioprine in reducing acute rejection rates.

**Measure of benefits used in the economic analysis**

The health outcomes assessed were acute graft rejection rates, graft failure rates, and medical care utilization including length of hospital stay, rejection-related treatments, and cytomegalovirus infections. These health states were measured directly by the physicians at the 14 sites. The total number of physicians was not stated.

**Direct costs**

Not all costs and quantities were reported separately.

The quantities/costs measured were: rejection treatment rate/costs, graft failure rate/costs (including subsequent dialysis), azathioprine or MMF use/costs, and the rate/cost of treating cytomegalovirus infections (considered as an adverse effect). The societal boundary was used. The estimation of quantities was based on a single RCT. The estimation of most costs was based on published standard costs (i.e. American Hospital Association Annual Summary of hospital costs). Outpatient rejection treatment costs were estimated based on sample data from one centre in the RCT. Quantity data were obtained from the RCT data. Sources of price data included Medicare fee schedule, IMS National Prescription Audit, Roche Inc., Health Care Financing Administration ESRD Annual Report, the Midwestern Transplant Center, and the American Hospital Association Annual Summary of hospital costs. Quantity data were from a study published in 1995. Price data were from sources ranging from 1994 to 1995. Cost data were all adjusted to 1995 values but the method was not reported. The initial cost of transplantation (including surgical fees and the cost of organ procurement) was excluded as being common to both groups.

**Statistical analysis of costs**

Costs were treated stochastically, in that mean costs were presented. Statistical analysis was carried out.

**Currency**

US dollars ($).

**Sensitivity analysis**

A one-way simple sensitivity analysis was carried out on acute rejection, graft failure and adverse effect rates, as well as
Estimated benefits used in the economic analysis
The acute graft rejection rate was 27.9% on the standard regimen and 40.6% on MMF. Graft failure occurred in 9.8% on standard treatment and 4.2% on MMF. Cytomegalovirus infections requiring treatment occurred in 6.1% of the standard treatment group and 9.1% in those on MMF. These benefits were those seen in the first year post-transplant.

Cost results
Total mean first year costs in the standard therapy group were $29,158, and $27,807 for the MMF group.

Synthesis of costs and benefits
Since the effectiveness in acute graft rejection was better in the MMF group than the standard group, and the costs were less in the MMF group, MMF therapy was dominant and combination of costs and benefits was unnecessary. The results remained stable under plausible variations of the parameters tested in the sensitivity analysis.

Authors’ conclusions
This study demonstrated that an immunosuppressive regimen that included MMF was cost-effective compared with azathioprine for the prevention of acute rejection of primary cadaveric renal allografts, because the improved therapeutic benefits were obtained at a somewhat lower overall cost of treatment.

CRD COMMENTARY - Selection of comparators
Selection of azathioprine as the comparator was appropriate. You, as a user of this database, should consider whether these are relevant interventions in your own setting.

Validity of estimate of measure of benefit
The study was based on a review of an interim report of a single randomized controlled trial, planned to last three years. The data are from patients who are one year post-transplant. The authors note that this one year period of follow-up may have some limitations in relation to long-term potential outcomes (e.g. rejection and graft survival) but that the 3 year US trial in progress may provide additional information at a later date. It was also noted that a higher dosage for MMF (3g/d) may bring benefits to higher risk patients and further trials are required to validate this.

Validity of estimate of costs
The authors note that the use of average patient costs rather than hospital charges may have resulted in conservative estimates. Moreover, potential savings may have been obtained by the lower rejection rate with MMF due to reductions in procedures such as renal biopsies, which were not addressed by the cost analysis.

Implications of the study
Based on one-year data, MMF was superior. A longer study is necessary to clarify its role beyond the first year.

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Bibliographic details