Pharmacoeconomic study of tacrolimus-based versus cyclosporine-based immunosuppressive therapy following liver 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
Two therapies to prevent acute cellular rejection after liver transplantation were studied. The first was a tacrolimus-based immunosuppressive regimen with an initial dose of 0.1 mg/kg per day, taken orally in two doses. The second was a cyclosporine-based immunosuppressive regimen with an initial dose of 10 mg/kg per day, also taken orally in two doses.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients receiving liver transplants. Further inclusion and exclusion criteria were not reported.

Setting
The setting was a hospital. The economic study was conducted at Oregon Health Sciences University and the Portland Veterans Affairs Medical Center in Portland (OR), USA.

Dates to which data relate
The dates during which the data were gathered were not reported. The price year was not given.

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

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

Study sample
Power calculations to determine the sample size were not performed. A sample of 31 consecutive patients (18 men and 13 women) received tacrolimus for 6 months after transplantation. Their median age was 48 years. These patients were compared with a sample of 29 matched liver transplant recipients (20 men and 9 women) who received cyclosporine (historical control group). Their median age was 46 years. Sixty-two transplants were performed in the overall sample of 60 patients.
Study design
This was an open-label, prospective clinical trial, which was carried out at Oregon Health Sciences University and the Portland Veterans Affairs Medical Center in Portland. No randomisation was performed. The patients were followed for 6 months after transplantation. No loss to follow-up was reported.

Analysis of effectiveness
All patients included in the study were accounted for in the effectiveness analysis. The primary health outcomes estimated in the analysis were:

- the mortality rate;
- re-OLTx;
- the incidence of rejection at 6 months;
- HCV patients and biopsy-proven HCV recurrence;
- HTN;
- hyperglycaemia (new onset PTDM), oral hypoglycaemic agent, insulin, and PTDM at 6 months;
- seizure;
- CVM infection; and

The comparability of the study groups was not discussed.

Effectiveness results
The mortality rate was 16% in the tacrolimus group and 24% in the cyclosporine group.

The rate of re-OLTx was 3% in both groups.

The incidence of rejection at 6 months was 10% in the tacrolimus group and 38% in the cyclosporine group.

Seventy per cent of the tacrolimus group and 48% of the cyclosporine group were HCV patients.

Biopsy-proven HCV recurrence was 23% in the tacrolimus group and 14% in the cyclosporine group.

HTN occurred in 57% of the patients in the tacrolimus group and 51% of those in the cyclosporine group.

Hyperglycaemia (new onset PTDM) was found in 44% of the patients in the tacrolimus group and 34% of those in the cyclosporine group.

The use of an oral hypoglycaemic agent was 39% in the tacrolimus group and 34% in the cyclosporine group.

The use of insulin was 29% in the tacrolimus group and 27% in the cyclosporine group.

PDTM at 6 months was 19% in the tacrolimus group and 24% in the cyclosporine group.

Seizure occurred in 9.6% of the patients in the tacrolimus group and 10% of those in the cyclosporine group.

CVM infection did not occur in the tacrolimus group and occurred in 7% of the patients in the cyclosporine group.
The duration of hospital stay was 8 days in the tacrolimus group and 9 days in the cyclosporine group.

The duration of ICU stay was 2 days in both groups.

**Clinical conclusions**
The effectiveness analysis showed that tacrolimus-based immunosuppressive therapy was more effective than cyclosporine in terms of transplant outcomes, as it led to a reduction in both the number of acute rejections and the use of anti-lymphocyte antibodies.

**Measure of benefits used in the economic analysis**
The health outcomes were left disaggregated and no summary benefit measure was used in the analysis. A cost-consequences analysis was therefore conducted.

**Direct costs**
Discounting was not performed since the costs were incurred during 6 months. The unit costs were reported only for calcineurin inhibitors. The economic analysis included the costs of calcineurin inhibitors and steroid responsive rejection. The cost/resource boundary of the analysis was not stated. The quantities of resources used were collected alongside the trial, while the source of the cost data was not stated. No price year was reported.

**Statistical analysis of costs**
The costs were treated deterministically.

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

**Currency**
US dollars ($).

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

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

**Cost results**
In a group of 100 patients, the average daily cost was $10.53 with tacrolimus and $28.09 with cyclosporine.

The total costs of the calcineurin inhibitor were $384,000 with tacrolimus and $1,025,300 with cyclosporine.

The total costs of rejection were $50,000 with tacrolimus and $280,000 with cyclosporine.

Consequently, the overall costs were $434,300 with tacrolimus and $1,305,300 with cyclosporine. Thus, tacrolimus led to cost-savings of $871,000 in comparison with cyclosporine.

**Synthesis of costs and benefits**
Irrelevant as a cost-consequences analysis was performed.

**Authors’ conclusions**
Tacrolimus proved to be both more effective and less costly than cyclosporine as an immunosuppressive agent in liver transplantation.

**CRD COMMENTARY - Selection of comparators**
The comparators were chosen on the grounds that no pharmacoeconomic comparison between the two study drugs had been carried out. Thus, the authors conducted a head-to-head comparison of the two therapies. You should decide whether they represent widely used health interventions in your own setting.

**Validity of estimate of measure of effectiveness**
The analysis of effectiveness used a prospective trial. No randomisation was performed and the method used to allocate the patients to the study groups was not reported. In addition, power calculations were not performed, and there was no evidence that the initial sample was appropriate for the clinical study question. The period during which the effectiveness data were collected was not reported. All of the patients were included in the analysis. The main limitations to the internal validity of the analysis were the small sample size and the lack of appropriate statistical analyses to take account of potential biases and confounding factors. Also, the study groups were not shown to be comparable and the study population was not defined in detail.

**Validity of estimate of measure of benefit**
No summary benefit measure was used in the economic analysis. The analysis was therefore categorised as a cost-consequences study.

**Validity of estimate of costs**
The perspective adopted in the study was not stated, but it is likely to have been that of the hospital. The unit costs were reported for drug use. The costs and the quantities were treated deterministically and no sensitivity analyses were conducted. The source of the cost data was not stated, and overall, details of the cost analysis were lacking.

**Other issues**
The authors made several comparisons of their findings with those from other studies. However, they did not address the issue of the generalisability of the study results to other settings. Sensitivity analyses were not conducted, thus the external validity of the analysis is relatively low. The study referred to a sample of patients receiving liver transplant and this was reflected in the conclusions of the study.

**Implications of the study**
The authors suggest that further research should be based on long-term follow-up studies of tacrolimus in patients suffering from hepatitis C.

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