A randomized, prospective, pharmacoeconomic trial of tacrolimus versus cyclosporine in combination with thymoglobulin in renal 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
The study examined tacrolimus (TAC) and cyclosporine modified (CsA), two medications used for immunosuppression in renal transplant recipients, in a regimen of Thymoglobulin induction, an antimetabolite and prednisone.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised renal transplant patients. The inclusion and exclusion criteria adopted in the original trial were not reported in this study.

Setting
The setting was a hospital. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness and resource use data were gathered from December 2000 to October 2002. The price year was 2003.

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

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients as that used in the effectiveness study.

Study sample
The study sample was based on power calculations that were carried out with the aim of verifying equivalence for rates of rejection, new onset of diabetes, treated hyperlipidaemia, and hypertension. Overall, 200 patients were included. There were 134 patients (64% men) in the TAC group and 66 (61% men) in the CsA group. The mean age was 44 (+/- 13) years in the TAC group and 46 (+/- 13) in the CsA group. It was not stated whether some patients refused to participate or were excluded from the study sample.
**Study design**
This was a prospective, open-label, randomised, clinical trial that was carried out at a single centre. The patients were randomised to study groups in a 2:1 ratio. The length of follow-up was 12 months. No patient appears to have been lost to the follow-up assessment.

**Analysis of effectiveness**
All of the patients included in the initial study sample were taken into consideration. Thus, the clinical analysis appears to have been conducted on an intention to treat basis. The main outcome measures used were:

- the rates of patient survival and graft loss,
- the rates of acute rejection,
- event-free survival,
- malignancy,
- post-transplant lymphoproliferative disorder (PTLD),
- cytomegalovirus (CMV) infection,
- serum creatinine levels,
- blood pressure medications,
- dyslipidaemic medications, and
- post-transplant diabetes mellitus (PTDM).

The study groups were comparable at baseline in terms of their demographics and clinical characteristics.

**Effectiveness results**
The rate of patients free from graft loss was 95% with TAC and 100% with CsA, (p=0.059).

The rate of patient survival was similar between the two groups (99% with TAC versus 100% with CsA).

The serum creatinine level was 1.3 (+/- 0.3) mg/dL with TAC and 1.6 (+/- 0.7) mg/dL, (p=0.03).

No statistical significant differences were found in the rates of acute rejection, event-free survival, malignancy, PTLD, CMV infection or PTDM.

At 12 months, use of medications was comparable.

Ten patients (1 in the TAC group and 9 in the CsA group) required discontinuation or change of their calcineurin inhibitor during the study (0.7% versus 14%; p=0.001).

Five patients in the CsA group required calcineurin inhibitor crossover.

Five patients (1 in the TAC group and 4 in the CsA group) required sirolimus conversion (0.7% versus 6%; p=0.008).

**Clinical conclusions**
The effectiveness analysis showed that the two treatments were comparable in terms of their efficacy and safety.
Measure of benefits used in the economic analysis
No summary benefit measure was used in the economic evaluation since the two treatments were considered to be equally effective. In effect, a cost-minimisation analysis was carried out.

Direct costs
The perspective adopted in the study was unclear and only the costs of immunosuppressive and other medications were included. Antibodies, antiviral medication agents and short-term antibiotic treatments were excluded from the analysis. The unit costs were not presented separately from the quantities of resources used. The resource use data were estimated prospectively from the sample of patients included in the effectiveness study. The costs came from average wholesale prices. The price year was 2003. Discounting was not relevant as the costs were incurred during only 12 months.

Statistical analysis of costs
Conventional statistical analyses were carried out to test whether differences in the costs reached statistical significance.

Indirect Costs
The indirect costs were not considered.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were not performed.

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

Cost results
The total medication costs increased from $8,324 (+/- 8,411) before transplant to $17,723 (+/- 11,647) after transplant in the TAC group, and from $7,870 (+/- 7,388) before transplant to $16,515 (+/- 10,189) after transplant in the CsA group.

The total immunosuppression costs were $6,866 (+/- 3,184) in the TAC group and $7,410 (+/- 2,801) in the CsA group.

The differences in costs were not statistically significant. The two groups were comparable in terms of the length of stay and readmission rates.

Synthesis of costs and benefits
A synthesis of the costs and benefits was not relevant since a cost-minimisation analysis was performed.

Authors' conclusions
When combined with Thymoglobulin induction, an antimetabolite, and corticosteroids, tacrolimus (TAC) and cyclosporine modified (CsA) were comparable in safety, efficacy and costs.
CRD COMMENTARY - Selection of comparators
The authors did not provide a justification for their choice of the comparators. The comparators appear to have represented two widely used immunosuppressive treatments for renal transplant patients. You should decide whether they would be valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness data were derived from a clinical trial, which was appropriate for the study question. The strengths of the analysis were its randomised design and the baseline comparability of the study groups. However, since the study was based on a published clinical trial, only limited information on the trial was reported in the current pharmacoeconomic study. For example, details of the method of sample selection were not provided. Moreover, the lack of blinding and the single-centre design of the study might limit the robustness of the analysis. Also, although power calculation were reported, the methods used to determine the final sample size were not totally clear. A standard statistical analysis was performed to estimate the significance of differences between the treatment groups.

Validity of estimate of measure of benefit
No summary benefit measure was used in the analysis because a cost-minimisation analysis was conducted. Please refer to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

Validity of estimate of costs
The analysis of the costs was restricted to medication costs. No specific justification was provided for the exclusion of other relevant categories of costs. The unit costs and the quantities of resources used were not reported separately, which might limit the possibility of replicating the analysis in other settings. The cost estimates were specific to the study setting and the impact of alternative costs was not investigated. However, statistical tests were carried out to assess the significance of cost-differences. The price year was implicitly stated, which will facilitate reflation exercises in other time periods.

Other issues
The authors did not make extensive comparisons of their findings with those from other studies. They also did not address the issue of the generalisability of the study results to other settings. In effect, sensitivity analyses were not performed. The authors acknowledged that a limitation of the study was the short time horizon. The study referred to renal transplant patients and this was reflected in the authors' conclusions.

Implications of the study
The study results suggested that TAC and CsA are comparable when used in renal transplant patients in combination with Thymoglobulin induction, an antimetabolite, and corticosteroids. The authors stated that longer follow-up studies are required.

Source of funding
Supported in part by NIH and by Fujisawa, Inc.

Bibliographic details

PubMedID
16003231
Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Antilymphocyte Serum /economics /therapeutic use; Costs and Cost Analysis; Cyclosporine /economics /therapeutic use; Female; Graft Rejection /epidemiology /prevention & control; Humans; Immunosuppressive Agents /economics /therapeutic use; Kidney Failure, Chronic /etiology /surgery; Kidney Transplantation /immunology; Male; Middle Aged; Missouri; Survival Analysis; Tacrolimus /economics /therapeutic use

AccessionNumber
22005001204

Date bibliographic record published
30/04/2006

Date abstract record published
30/04/2006