Enhanced oral cyclosporine absorption with water-soluble vitamin E early after liver transplantation


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 liqui-E, a water-soluble vitamin E preparation, to affect cyclosporin A (CyA) whole blood concentration in liver transplant recipients who were unable to achieve and maintain therapeutic CyA whole blood concentration with the standard recommended oral dosages.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Liver transplant recipients unable to achieve and maintain therapeutic CyA whole blood concentration with the standard recommended oral dosages.

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

Dates to which data relate
The effectiveness and resource use data were collected between May 1991 and August 1994. The price year was 1994.

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 study.

Study sample
Power calculations were not used to determine the sample size. The study sample comprised 26 patients (out of 171 liver transplantations for 162 patients) who were unable to achieve and maintain therapeutic CyA whole blood concentrations with the standard recommended oral daily dose in the early post-transplant period. The study sample consisted of adults and children (younger than 10 or weighing less than 30 kg): 19 adults (age 44.5 +/- 15.6 years and weight 72.8 +/- 19 kg) and 7 children (age 1.6 +/- 1.4 years and weight 9.5 +/- 3.4 kg).
Study design
This was a prospective before and after study, carried out in a single centre. The duration of follow-up was not reported. No loss to follow up was reported.

Analysis of effectiveness
The principle (intention to treat or treatment completers only) used in the analysis of effectiveness was not explicitly specified. The primary outcomes used in the analysis were daily oral CyA requirements, intravenous administration of CyA, CyA concentrations before and after Liqui-E and Liqui-E toxicity.

Effectiveness results
With Liqui-E, the daily oral CyA requirements were estimated to decrease in adults from 22.6 (+/- 8.9) to 16.2 (+/- 7.3) mg/kg/day (p<0.001) and in children from 78.6 (+/- 34.1) to 53.7 (+/- 35.0) mg/kg/day (p<0.02). Intravenous administration of CyA was unnecessary. The CyA trough concentrations before and after Liqui-E were 670 (+/- 186) and 1012 (+/- 216) ng/ml, respectively in adults (p<0.001) and 732 (+/- 187) and 1052 (+/- 166) ng/ml respectively, in children (p<0.01). No Liqui-E toxicity was observed.

Clinical conclusions
Oral CyA plus Liqui-E resulted in a significant decrease in the daily CyA dose necessary to achieve therapeutic concentrations. Furthermore, intravenous drug administration were stopped or avoided.

Measure of benefits used in the economic analysis
No summary benefit measure was identified in the economic analysis, and only separate clinical outcomes were reported.

Direct costs
Discounting was not undertaken. Quantities were analysed separately from costs. CyA and Liqui-E costs were included in the analysis. The quantity/cost boundary adopted was the hospital. The date to which the price data referred was 1994. The average wholesale listed price were taken from Drug Topics Red Book, 1994. The cost analysis did not cover the costs of ordering, stocking, dispensing, and administering CyA and Liqui-E.

Statistical analysis of costs
Two-sided paired t test was used to compare the cost per day before and after liqui-E administration.

Indirect Costs
Not considered.

Currency
US dollars ($).

Sensitivity analysis
Not undertaken.

Estimated benefits used in the economic analysis
Not applicable.
Cost results
The before and with Liqui-E total drug costs in adults were $80.09 (+/- 32.99) and $59.29 (+/- 27.37), respectively, (p<0.002). The before and with Liqui-E total drug costs in children were $33.46 (+/- 17.70) and $24.85 (+/- 16.35), respectively, (p<0.025).

Synthesis of costs and benefits
Costs and benefits were not combined since the use of the intervention was the dominant strategy.

Authors' conclusions
Liqui-E administration in the early post-transplantation period can enhance CyA absorption in adults and children who are unable to achieve adequate whole blood concentrations with the usual recommended oral dosages. In addition, a significant cost saving can be realised by coadministration.

CRD COMMENTARY - Selection of comparators
The reason for the choice of comparator is clear.

Validity of estimate of measure of effectiveness
The internal validity of the effectiveness results can not be guaranteed given the limitations of the before and after study design.

Validity of estimate of measure of benefit
In view of the lack of a summary benefit measure, the study may be regarded as a cost-consequences analysis.

Validity of estimate of costs
Quantities were reported separately from the costs and adequate details of methods of cost estimation were given.

Other issues
The issue of generalisability to other settings was not addressed. Some comparisons with other studies supporting the clinical results from the present investigation were reported in the study.

Implications of the study
Further analysis is required in the form of well-controlled pharmacokinetic studies, as mentioned by the authors.

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