Mycophenolate mofetil (MMF)/tacrolimus/single shot ATG versus azathioprine/cyclosporine (CsA)/ATG in immunosuppression after pancreas/kidney transplantation: results of a prospective randomized study

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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
Immunosuppressant drugs used in pancreas renal transplantation. Group I (neo-quadruple) received preoperative prednisolone (250mg), preoperative ATG(6mg/Kg/KG) and for 10 days postoperatively, azathioprine (2-3mg/Kg/KG) and cyclosporine A to a level of 220-270ng/ml all on the day of operation. Group II (MMF/tacrolimus) received preoperative prednisolone (250mg), preoperative ATG-single shot (6mg/Kg/KG), preoperative MMF 4g and preoperative tacrolimus 5mg. During days 1 to 7 after the operation, Group II patients received prednisolone (100-40mg/day), MMF (4g/day) and tacrolimus to a level of 12-15ng/ml. In days 8 to 12 after the operation Group II patients were given prednisolone (30mg/day), MMF (3g/day) and tacrolimus to a level of 8-12ng/ml.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with Type I diabetes with a mean age of 39, mean duration of diabetes 26 years and an average duration of dialysis treatment of 26 months.

Setting
Hospital. The study was carried out at the university hospital Bochum, Germany.

Dates to which data relate
The effectiveness data were collected between November 1995 and August 1996. The price year was not stated.

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

Link between effectiveness and cost data
The costing was carried out on the same patient sample as that used in the effectiveness analysis. The collection of cost data was undertaken prospectively.

Study sample
No power calculations determined the sample size. 24 patients were randomly divided into two groups of 12 patients.
each. The specific method of randomisation was not stated.

**Study design**
The study was a randomised control trial carried out in a single-centre. The duration of follow-up was between 1 and 12 months with an average of 4 months with no losses.

**Analysis of effectiveness**
The analysis of effectiveness was based on intention to treat. The primary health outcomes were survival of patients, including pancreas and kidney grafts. In addition, the study looked at acute rejections of the transplants and the occurrence of infections during treatment.

**Effectiveness results**
Patient and transplant survival was 100% after an average observation of 4 months. The initial functioning of the pancreas was 100% in both groups, while initial kidney functioning was 100% in Group I and 91% in Group II. Acute rejection occurred 3 times in Group I and 0 times in Group II. The rejections in Group I could be successfully treated with steroids in 2 cases and OKT3 in 1 case. No severe bacterial infections resulted in either group with 3 cases of cytomegalovirus infections reported in both groups. The average duration of stationary treatment in hospital was 28 days for Group I and 32 days for Group II.

**Clinical conclusions**
The authors conclude that the high incidence of acute rejections, that occur with a probability of 55%-83.5% after pancreas and kidney transplants, can be substantially reduced by using either the standard quadruple therapy used with Group I and neo-quadruple therapy used with Group II. In the study both forms of prevention were treated as equally good.

**Modelling**
No modelling was employed.

**Measure of benefits used in the economic analysis**
The measure of benefits was the number of successful immunosuppressions. As both the intervention and the comparator had identical effectiveness the principal benefit was in cost savings.

**Direct costs**
The direct costs consisted of medication and in-patient hospitalisation costs.

**Statistical analysis of costs**
Not stated.

**Indirect Costs**
Not assessed.

**Currency**
German marks (DM).
Sensitivity analysis
No sensitivity analysis was performed.

Estimated benefits used in the economic analysis
Both preventative methods of avoiding acute rejections were 100% successful.

Cost results
The costs were not discounted. The average cost of immunosuppression in Group I was DM31,696 versus DM4,497 in Group II.

Synthesis of costs and benefits
Since prevention was 100% successful in both groups, the cost per successful immunosuppression was DM31,696 in Group I and DM4,497 in Group II.

Authors’ conclusions
The reduction of the ATG induction from 10 days (Group I) to a perioperative single-shot administration (Group II) lowered the cost from more than DM31,000 to less than DM5,000 with equal medical success during the first 4 weeks.

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

Validity of estimate of measure of benefit
There were differences in the medical effectiveness of both immunosuppressants. While Group I experienced initial acute rejections, Group II experienced no such problems. Additionally, hospitalisation was, on average, 4 days longer in Group I compared with Group II. Neither difference was accounted for in the estimated medical benefits.

Validity of estimate of costs
The authors do not go into detail about the derivation of costs. Indirect costs were not accounted for.

Other issues
The sample size of 24 is very small and as no power calculations were used to determine the sample size the results need to be treated with a degree of caution.

Implications of the study
The results should be considered with some caution as the sample size is relatively small and the fact that both prevention methods are treated as being equally effective is questionable. Nevertheless, the results strongly indicate that the single-shot administration of ATG in Group II is superior in terms of cost-effectiveness to Group I with ATG induction over 10 days.

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