TRANSPLANTATION PROCEEDINGS

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Quadruple-Drug Induction Therapy in Combined Renal and Pancreatic Transplantation—OKT3 Versus ATG

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THE pancreatic allograft rejection remains a major problem in pancreas transplantation. Despite the introduction of cyclosporin and other new immunosuppressive drugs, the incidence of rejection episodes range from 30% to 80%.[1,2] We present here our experience with quadruple-drug induction therapy consisting of CS, azathioprine, "high" doses of steroids and antithymocyte globulin (ATG) or OKT3 for a short period of time.

PATIENTS AND METHODS

In a controlled prospective study (March 1988 to July 1989), 20 diabetics were grafted simultaneously with a pancreas and a kidney. We used the occlusion technique in six patients and the bladder drainage in four patients in each group. Recipients' criteria and number of HLA mean mismatches in both groups were comparable.

Immunosuppressive Protocol

In 10 patients (group I) in addition to triple-drug therapy ATG in a dosage of 4 mg/kg body weight was used. In group II, OKT3 (5 mg/d) was added to the standard regimen. ATG and OKT3 were given for 10 days (Table 1).

Antirejection Therapy

The first rejection episode was treated with 250 mg methylprednisolone for 3 days. The second and third rejection crises were treated with ATG or OKT3 for 7 days. Patients that received ATG as induction therapy were treated with OKT3 and vice versa.

Table 1. Quadruple-Drug Induction Therapy in Pancreatic Transplantation (ATG vs OKT3)

Cyclosporin	1 mg/kg body weight for 24 h per infusion (blood levels, 100 ng/mL), switch to oral medication as soon as possible (6-10 mg/kg body weight)
Azathioprine	1-2 mg/kg body weight/d
ATG	4 mg/kg body weight for 10 d
or	
OKT3	5 mg/d for 10 d
Steroids	500 mg intraoperatively, reduced to maintenance dose of 30 mg/d within 1 wk

RESULTS

In total a pancreatic allograft rejection was observed in 10 of 20 patients (5 in each group). In both groups one pancreatic graft was lost due to an irreversible rejection. A second pancreatic graft loss for an unknown reason was observed in the OKT3-treated group (Table 2).

Kidney graft rejection was observed in four patients in the ATG group and in five patients in the OKT3 group. All

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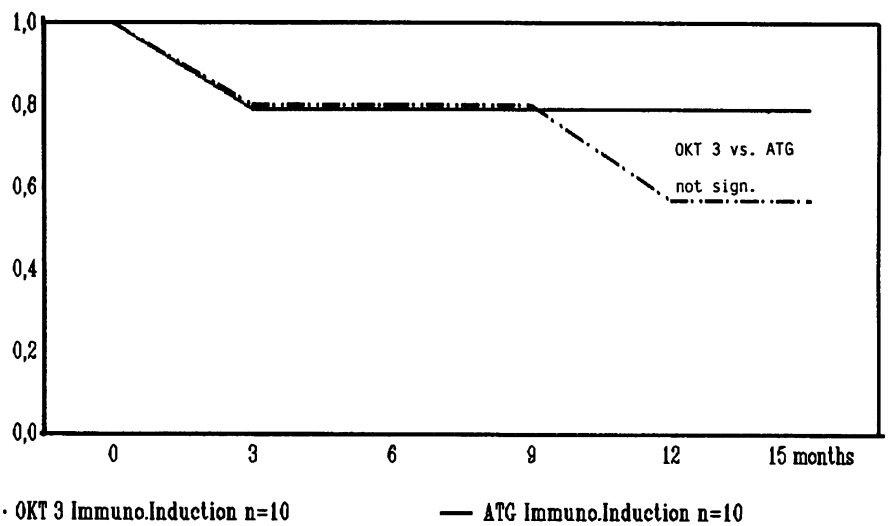

Fig 1. Pancreatic graft survival probability estimated by Cuttler/Ederer using ATG or OKT3.

Table 2. Pancreatic Graft Losses

	ATG	OKT3
Total	2	3
Immunological failure	1	1
Patient death*	1	1
Unknown		1

*None of the patients' death was due to the immunosuppressive protocol.

kidney graft rejection episodes were reversible with antirejection therapy.

Six of 20 patients showed a parallel rejection episode in both organs (three in each group). The rate of infection complications was 60% in the ATG group and 40% in the OKT3 group (one life-threatening event in each group). One patient death (arrosion bleeding) occurred in each group.

Patient and kidney survival probability rate is 90% in both groups. Pancreas survival probability is 60% in the OKT3 group and 80% in the ATG group. The difference is not statistically significant (Fig 1).

CONCLUSIONS

1. Quadruple-drug induction therapy using ATG or OKT3 provides an effective immunosuppression with excellent graft survival and function.
2. In our study the use of the monoclonal antibody OKT3 did not provide an advantage over the use of a polyclonal antithymocyte sera regarding rejection episodes.
3. The infection rate was high, but did not differ in either group.
4. The small number of patients in each group does not allow final conclusions as to whether or not monoclonal antisera are better than polyclonal antisera. Both sera are optimal for treatment of acute rejection episodes.

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