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Tacrolimus Versus Cyclosporine in Primary Simultaneous Pancreas-Kidney Transplantation: Preliminary Results at 1 Year of a Large Multicenter Trial

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SIMULTANEOUS PANCREAS-KIDNEY (SPK) transplantation is emerging as the state-of-the-art treatment for diabetic patients scheduled to receive a kidney transplant.

PATIENTS AND METHODS

Ten European and one Israel transplant centers enrolled 205 patients undergoing simultaneous kidney-pancreas transplantation into this open, parallel-group study. Following antithymocyte globulin (ATG) induction, patients were randomized to receive either tacrolimus (Tac) or cyclosporine-microemulsion (CyA) together with mycophenolate mofetil (MMF) and steroids. Despite randomization the patient population of the two groups differed significantly concerning two baseline characteristics: the recipients in the Tac group had more portal venous drained grafts than those in the CyA group (9% vs 2%, $P = .03$) and were less likely to receive dialysis before transplantation (9% vs 19%, $P = .04$).

RESULTS

At 1 year posttransplant patient and kidney survival was excellent in both treatment arms (98.0% and 95.0% for Tac, and 96.8% and 92.0% for CyA, respectively.[1] However, there was a significant difference in pancreas survival: 91.2% for Tac and 73.9% for CyA ($P = .00048$). The main cause of pancreas graft loss was thrombosis: two in the Tac group versus 10 in the CyA group. Mean CyA trough level during week 1 was 336 ng/mL for the patients with pancreas thrombosis versus 226 ng/mL for the patients with no pancreas loss ($P = .0107$).[2] The incidence of rejections trended to be lower and less severe in the Tac arm, despite the fact that patients were receiving significantly less concomitant MMF at 6 months and 1 year posttransplant. At 1 year, the mean daily MMF doses was 1364 mg in the Tac group and 1670 mg in the CyA group. Rejection-free survival rate was 57.6% in the Tac group compared with 45.8% in the CyA group. According to the Banff classification, grade 2 and grade 3 biopsy-proven rejections occured in one patient in the Tac group versus 12 in the CyA group ($P = .0015$). The safety profile between both treatment arms was comparable. Other important finding was that, irrespective of the immunosuppressive regimen used, the incidence of urinary tract infection differed significantly between patients with bladder drainage of the pancreatic graft and patients with enteric drainage (71% vs 31%, $P < .00001$, respectively). Also independent of the immunosuppressive regimen used was the impact of the type of pretransplant dialysis: The incidence of peritonitis after transplantation in patients previously treated with peritoneal dialysis was significantly higher compared to previous treatment with hemodialysis or no dialysis (24% vs 11%, $P < .0253$). At 1 year, steroid withdrawal was achieved in 35% of the Tac group and 33% of the CyA group. Thereafter, only one patient (3%) in the Tac group and two (6%) in the CyA group experienced an acute rejection episode.[3] At 1 year, the serum creatinine level was 1.4 ± 0.6 mg/dL in the Tac group and 1.5 ± 0.6 mg/dL in the CyA group. Fasting glucose, C-peptide, and HbA1C were 91 ± 18 mg/dL, 3.3 ± 1.4 ng/mL, and 5.5 ± 0.7% in the Tac group compared with 98 ± 47 mg/dL, 3.8 ± 2.4 ng/mL, and 5.7 ± 1.4% in the CyA group. The total cholesterol was 181 ± 38 mg/dL (Tac) and 186 ± 42 mg/dL (CyA). The mean length of initial hospital stay was 33 ± 19 days in the Tac group and 40 ± 24 days in the CyA group ($P = .025$).

CONCLUSIONS

At 1 year, using a ATG, tacrolimus, MMF-based immunosuppression, combined with an optimized pre- and posttransplant patient management (ie, type of dialysis, type of drainage), excellent 1-year pancreas survival rates can be achieved. There were significantly fewer pancreatic graft losses and grades 2 and 3 biopsy-proven rejections with Tac-based therapy. Moreover, the duration of the first hospitalization is shorter. Based on these findings the EUROSPK study group strongly advises to enlist diabetic patients with end-stage renal disease not for solitary kidney, but rather for simultaneous pancreas-kidney transplantation.

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