Long-Term Follow-Up of Tacrolimus Rescue Therapy for Renal Allograft Rejection


The efficacy of tacrolimus in primary renal transplantation led us to evaluate this agent for rescue of resistant allograft rejection in 77 patients under primary cyclosporine (CyA)-based immunosuppression, in whom we reported a 74% salvage rate with a 13.9-month follow-up. To evaluate the longevity of the observed effects of tacrolimus rescue, we herein present a report and the long-term follow-up of this group of patients. Between July 14, 1989 and April 16, 1993, 77 patients (44 male, 33 female) with a mean age of 33.3 ± 12.4 years (range 2 to 59 years) failing CyA-based immunosuppression were converted to tacrolimus. Fifty-nine patients (77%) were primary transplant recipients and 18 (23%) had been retransplanted. Fifty-two patients (68%) were recipients of cadaveric grafts and 25 (32%) live donor grafts. All patients considered for tacrolimus conversion had uncontrolled biopsy-proven rejection. Previous antirejection therapy had been administered to all 77 patients in the form of bolus high-dose corticosteroids and 61 (79%) had also received at least one course of an antilymphocyte preparation. Tacrolimus was given at a standard daily dose of 0.3 mg/kg/d in divided doses every 12 hours starting 12 hours after the last CyA dose. Statistical significance was calculated by Student’s t test or chi-square analysis as appropriate. Successful tacrolimus conversion was defined as a return to baseline serum creatinine (sCr), and/or improvement on postconversion renal allograft biopsy, and/or freedom from dialysis if the patient was dialysis dependent at the time of conversion. In our initial report on these 77 patients, we reported successful allograft salvage with tacrolimus conversion in 57 of 77 patients (74%) with a follow-up of 13.9 ± 9.1 months (range 2 to 34 months). Of the 57 patients whose grafts were successfully rescued initially, 48 (84%) continue to have functioning grafts with a mean sCr of 2.1 ± 0.85 mg/dL at a mean follow-up of 41.9 ± 12.1 months (range 16 to 62 months). There have been nine late graft losses due to patient death (n = 3; two patients with functioning grafts and 1 with unknown allograft function), chronic rejection (n = 5), and patient noncompliance (n = 1). Of the 18 patients on dialysis at the time of conversion, 9 (50%), continue to have functioning grafts with a mean sCr of 2.1 mg/dL (mean follow-up 45.1 ± 11.9 months). Among 61 patients who had received antilymphocyte preparations, 39 (64%) continue to have functioning grafts (mean sCr 2.15 ± 0.9 mg/dL). In all 48 patients rescued, prednisone doses have been lowered from 22.2 ± 7.2 mg/d preconversion to 4.6 ± 4.0 mg/d postconversion, and 18 (38%) patients are not currently on steroids.

Since its introduction in the early 1980s, CyA has become the mainstay of contemporary posttransplant immunosuppression. Unfortunately, even with triple and quadruple-drug CyA immunosuppression, a significant number of allografts are lost to resistant rejection. Tacrolimus is an immunosuppressant that has been used with encouraging results in renal transplantation. The utility of tacrolimus as a potential rescue agent was initially shown in 57 of 77 (74%) patients with a follow-up of 14 months, including 9 of 18 patients (50%) who were on dialysis at the time of conversion, 4 of 10 (40%) whose graft had never functioned from the time of transplantation, and 48 of 61 (79%) who had received at least one course of an antilymphocyte preparation prior to rescue. Further decreases in steroid doses were achieved in 56 (98%) and prednisone was stopped completely in 12 (21%). At a mean follow-up of 41.9 ± 12.1 months (range 16 to 62 months), 48 (84%) of the 57 patients whose grafts were successfully rescued continue to have functioning grafts with a mean sCr of 2.1 ± 0.85 mg/dL. Hence, long-term success with tacrolimus rescue is observed with a low (11%) incidence of late graft loss, which appears to be primarily due to chronic rejection. Tacrolimus is therefore an effective long-term rescue agent and should be part of the transplant clinician’s armamentarium for resistant renal allograft rejection.

REFERENCES

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