Five-Year Experience With Tacrolimus Rescue for Renal Allograft Rejection


Tacrolimus is safe and effective for primary renal transplantation, but perhaps even more striking is the utility of this drug as a salvage agent for refractory renal allograft rejection. We previously reported that graft salvage with tacrolimus conversion was achieved in 74% (57 of 77) of patients with refractory acute rejection. We previously reported that graft salvage with tacrolimus conversion was achieved in 74% (57 of 77) of patients with refractory acute rejection on baseline cyclosporine (CyA) therapy. Since then, we have entered an additional 92 patients for a total of 169 renal transplant recipients who have been converted to tacrolimus.

MATERIALS AND METHODS

Between July 14, 1989 and May 24, 1994, 169 patients (98 male, 71 female; 132 cadaveric donors, 37 living donors) with a mean age of 36.2 ± 13.1 years with ongoing allograft rejection under baseline CyA immunosuppression were converted to tacrolimus. One hundred thirty-eight patients (82%) were primary transplant recipients and 31 (18%) had been retransplanted. Maintenance immunosuppression had consisted of CyA and prednisone in all patients, with either (n = 117, 69%) or without (n = 52, 31%) azathioprine (AZA). All patients had previous antirejection therapy (high-dose corticosteroids) and 144 of 169 patients (85%) had also received at least one course of an antilymphocyte preparation. Acute cellular rejection (ACR) was present on biopsy in all 169 patients prior to conversion. Tacrolimus was started at 0.2 to 0.3 mg/kg/d in divided doses every 12 hours starting 12 to 24 hours after the last CyA dose. Data were analyzed for significance by two-tailed Student's t test or chi-square analysis when appropriate.

RESULTS

With a mean follow-up of 30.0 ± 2.4 months, 159 of 169 patients (94%) are alive and 125 of 169 patients (74%) have achieved graft salvage. A total of 28 of 169 patients (17%) were dialysis dependent at the time of tacrolimus conversion. Thirteen of these (46%) currently have functioning grafts with a mean serum creatinine (sCr) of 2.15 ± 0.37 mg/dL at a mean follow-up of 37.3 ± 16 months. Excluding these 13 patients, the overall mean sCr in the remaining 112 patients with preconversion graft function improved from 3.1 ± 1.7 mg/dL to 2.3 ± 1.1 mg/dL postconversion (P = .0002). The average preconversion prednisone dose of 28.0 ± 9.0 mg/d has been lowered to 6.6 ± 5.1 mg/d, and 28 of 125 patients (22%) are on tacrolimus monotherapy. Of the 144 patients receiving preconversion antilymphocyte preparations (average length of treatment 14.2 ± 5.8 days), 117 (81%) were salvaged by tacrolimus conversion. There were 44 failures in the 169 patients (26%); 22 due to ongoing renal allograft rejection and 22 due to repeat rejection episodes after initial successful rescue.

DISCUSSION

The profile of patients in this expanded study is very similar to that reported previously. The majority (144 of 169, 85%) of the patients had failed prior treatment with antilymphocyte preparations and a subset of 28/169 (17%) of the patients had rejections so severe as to necessitate ongoing dialysis therapy prior to conversion. Graft salvage was obtained in 125 of 169 patients (74%) with a 30-month follow-up, identical to the salvage rate we previously reported but with a larger group of patients with longer follow-up. The previously reported ability to taper and even stop prednisone in approximately 20% of patients successfully salvaged was maintained in this expanded experience. In addition to the now well-established graft salvage effects of tacrolimus, several other agents have shown initial promise as rescue agents, including mycophenolate mofetil, 15-deoxyspodergualin, and perhaps sirolimus. Whether these agents will provide long-lived salvage rates and afford the opportunity to wean steroids after rescue (such as is possible with tacrolimus) remains to be determined. We currently recommend that tacrolimus conversion be considered an alternative to antilymphocyte preparations for steroid-resistant rejection in CyA-based regimens.

REFERENCES


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