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Pediatric Kidney Transplantation at the University of Pittsburgh

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THE RESULTS of pediatric kidney transplantation have varied over the years, with outcomes ranging from fair to excellent.[1] The majority of centers performing pediatric kidney transplantation in the United States have shown patient and graft survival rates of 92% to 96% and 74% to 89%, respectively.[2] We describe here our own results with cadaveric and living related pediatric renal transplant recipients over a 5-year period.

MATERIALS

Sixty-three consecutive kidney transplants were performed in 62 patients at Children's Hospital of Pittsburgh between Jan 1, 1988, and Jan 1, 1993 (Table 1). Children with previous or simultaneous liver transplants were excluded. Thirty-five (56%) patients had living donors, while 28 (44%) received cadaveric kidneys. The mean age was 9.8 ± 4.8 years (range, 0.8 to 17.4 years). Primary transplants were performed in 47 patients (75%), while 16 (25%) underwent retransplantation. Only 9 patients (14%) had panel-reactive antibody levels of >40%. Thirty-three patients (52%) received cyclosporine as their main immunosuppression, while 30 patients (48%) received FK 506 (Table 1).

Living related transplants performed with cyclosporine (20 patients) initially received induction Minnesota antilymphoblast globulin (MALG), 20 mg/kg/d for 2 weeks along with azathioprine and prednisone. Cyclosporine was introduced at 5 mg/kg twice a day starting at day 7. For cadaveric transplants performed with cyclosporine (13 patients), 4 patients received induction OKT 3 at 5 mg/d for 2 weeks and 1 patient received induction MALG. Azathioprine was also used in 11 patients on cyclosporine therapy. Thirty patients (15 living donors and 15 cadaveric) received FK 506 and this was given at 0.1 mg/kg/d as a continuous infusion followed by a 0.30 mg/kg/d oral dose in two divided doses. Twelve patients (40%) received azathioprine initially with FK 506, and all patients received steroids.

RESULTS

The median follow-up was 38 months (range, 6 to 67 months). The 1- and 4-year actuarial patient survival rates were 100% and 98%, respectively. The 1- and 4-year actuarial graft survival rates were 98% and 86% (Table 2). When cadaveric and living related patients were separated, patient survival rates were not significantly different at 1 and 4 years (100% and 96% vs 100% and 100%, respectively). Graft survival was shown to be a bit better for living related transplant recipients at 1 year and at 4 years when compared to cadaveric transplant recipients. Patient survival was essentially the same for cyclosporine-treated patients and FK 506-treated patients. There was also little difference in graft survival at 1 and 4 years with cyclosporine (100% and 85%) vs 1 and 3 years with FK 506 (96% and 89%).

One patient died, 1.5 years after his second cadaveric transplant, with a functioning graft. This patient had been treated with cyclosporine and died of cardiac abnormalities. Five other patients lost their grafts: 2 to noncompliance at 1.5 and 3 years after transplantation (with cyclosporine), and 3 to recurrent disease (hemolytic uremic syndrome, focal segmental glomerulosclerosis, and membrane proliferative glomerulonephritis) at 1 week and 3.5 and 2.5 years after their transplants.

Rejection was seen in 46% of the patients. Eighteen cadaveric transplant patients experienced rejection (64%), while 11 (31%) living related transplant patients rejected their grafts (P = .01). Cyclosporine-treated patients had

Table 1. University of Pittsburgh Pediatric Kidney Transplantation (Jan 1, 1988, to Jan 1, 1993): Recipient Characteristics

Number of patients	62
Number of grafts	63
Living donor	35 (56%)
Cadaveric donor	28 (44%)
Mean recipient age	9.8 ± 4.8 years
Primary transplants	47 (75%)
Retransplantation	16 (25%)
Panel-reactive antibodies >40%	9 (14%)
Cyclosporine	33 (52%)
FK 506	30 (48%)

Table 2. University of Pittsburgh Pediatric Kidney Transplantation (Jan 1, 1988, to Jan 1, 1993): Survival Rates

	Patient Survival		Graft Survival	
	1 Year	4 Years	1 Year	4 Years
Overall	100%	98%	98%	86%
Cadaveric donor	100%	96%	96%	76%
Living related donor	100%	100%	100%	95%
Cyclosporine	100%	97%	100%	85%
FK 506	100%	100%*	96%	89%*

*Three years rather than 4.

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39% rejection vs 53% for those patients who received FK 506 ($P = .237$).

Eighteen (60%) patients treated with FK 506 had prednisone discontinued. No patient on cyclosporine was successfully taken off prednisone long term.

Six patients (10%) developed cytomegalovirus (CMV) infections (3 cadaveric and 3 living related patients). Five of 6 (83%) patients received FK 506 ($P = .07$), and nearly all patients (5 of 6) were at high risk for CMV infection (seropositive kidneys to seronegative recipients).

Posttransplant lymphoproliferative disease was seen in 6 patients (10%), 3 cadaveric and 3 living related. One patient had been treated with cyclosporine (3%), and 5 patients (17%) received FK 506 immunosuppression ($P = .07$). All patients were treated with cessation or diminution of their immunosuppression, along with intravenous acyclovir or ganciclovir. No grafts were lost, and all patients recovered.

Four patients were switched from cyclosporine to FK 506: 1 for rejection and 3 for proteinuria. The patient with rejection was successfully rescued and 1 patient with proteinuria had significant improvement in protein excretion with FK 506. The remaining 2 patients lost their grafts to recurrent disease.

DISCUSSION

Pediatric patient survival after kidney transplantation did not vary significantly regardless of donor source or type of immunosuppression. Results of graft survival at 4 years for cadaveric transplants, although above average, were not as good as for those patients who received a kidney from a living related donor (76% vs 95%). Likewise, more episodes of rejection were seen in the cadaveric patients when compared to the living related patients. Although FK 506-treated patients had slightly more rejection episodes, 60% of this group had the ability to discontinue prednisone. For pediatric recipients, this allows for long-term growth and development after transplantation, and there are some preliminary data from this center suggesting that there is improvement in growth for those patients treated only with FK 506 in the long term.[3]

The increased incidence of CMV infection and posttransplant lymphoproliferative disease seen with patients treated with FK 506 is significant when compared to that in the cyclosporine-treated patients. Fortunately, these complications all resolved without any significant sequelae or graft losses. These findings may represent a learning curve with the use of FK 506 in renal transplant recipients, as described in our own experience with adult patients.[4]

Overall, our data support the improved results of pediatric kidney transplants and suggest that newer agents such as FK 506, with the ability to discontinue the use of steroids after transplantation can be very useful, especially for this population of patients. Further work to decrease the long-term side effects of chronic immunosuppression should still be a primary focus to optimize the long-term outcome of pediatric kidney transplantation.

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