

# Intestinal Transplantation in Children: Five-Year Experience

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**T**HE introduction of the new immunosuppressant tacrolimus (FK506, Prograf) in 1989 allowed more consistent survival of human intestinal allograft recipients.<sup>1</sup> We report here the first 41 pediatric patients treated with this drug, all but the last 7 with follow-up of 1 to 5 years (range 0.5 to 5 years).

## MATERIALS AND METHODS

Between 1990 to 1995, 41 children received 44 intestinal transplants under tacrolimus/steroid immunosuppression and included the isolated small bowel (SB) (n = 10), liver/small bowel (LSB) (n = 27) and multivisceral (MV) (n = 7) allografts. There were 19 males and 22 females with ages ranging between 0.5 to 18 years (mean of 4.2 years). Twenty grafts contained a segment of large bowel which was distributed among all three recipient cohorts.

The last four patients, and one additional patient undergoing intestinal retransplantation were also given unaltered adjuvant donor bone marrow. The rationale and methods of simultaneous bone marrow infusion in solid organ transplantation have been reported elsewhere in this issue.<sup>2</sup> Immunosuppression, donor and recipient surgical procedures and nutritional management were as previously described.<sup>3</sup>

## RESULTS

### Patient and Graft Survivals

Twenty-four patients are still alive (58.5%). Twenty-three of these 24 surviving patients still bear their primary allografts, 20 of which are functioning.

Of the 9 SB graft recipients, eight are alive after 0.5 to 48 months (88.9%). Two patients lost their grafts to acute rejection and developed TPN liver dysfunction, one of whom has died of end stage liver disease. One patient underwent retransplantation 8 months after primary graft enterectomy and is at home off TPN, 8 months posttransplantation. This type of graft succeeded in restoring alimentary function at the highest rate at all follow-up times, with the best graft survival (70%).

The LSB and MV composite grafts shared similar patient (50%) and graft survivals (48.2% and 42.9%, respectively). Three patients underwent retransplantation: one patient received an MV retransplant for chronic rejection, another patient received a liver only retransplant after hepatic artery thrombosis, and another patient received LSB retransplant after acute rejection and adenovirus hepatitis (graft survival 48.2%). Another recipient of an MV graft who died was originally a recipient of an LSB graft.<sup>4</sup>

### Complications

Infectious pathogens include bacteria, fungi, and viruses. Of the bacterial pathogens, staphylococci and enterococci are

common, where as gram-negative rods usually accompanied polymicrobial infections. These pathogens may be seen in association with intestinal allograft rejection or PTLD. Fungal infections in children have been mainly yeast organisms in the abdominal cavity and aspergillus infection of the lungs.

Posttransplant lymphoproliferative diseases (PTLD) associated with the Epstein-Barr virus (EBV) has occurred in 11 children with a mean age of 2.8 years (overall incidence of 26.8%); 10 patients presented cytomegalovirus (CMV) disease (24%). These episodes are described more extensively elsewhere in this issue.<sup>5,6</sup>

A total of 31 surgical/clinical complications occurred in 20 recipients (48%). The most common was peritonitis which was usually consequent to another technical event such as hepatic artery thrombosis, biliary or intestinal anastomotic leaks, or intestinal perforation. These complications were significant contributors to morbidity and mortality. Graft associated vascular complications included hepatic artery thrombosis (which was responsible for death in 2 recipients), and portal vein stenosis.

Of the 41 patients, 36 recipients (39 grafts) experienced a mean of 2.6 episodes of rejection of the intestinal allograft. The incidence of rejection when allograft colon was included (90%) was similar to when it was excluded (87.5%). The incidence of rejection of the liver allograft in composite transplants was: LSB 12 of 27 grafts (44.5%), and MV 3 of 5 grafts (60%).

## OUTCOME

Twenty-one (48%) of the 44 grafts were lost by recipient death or as the result of graft removal followed by an immediate (n = 3) or delayed (n = 1) attempt at retransplantation, or return to TPN (n = 2). In five cases the failures stemmed from surgical (n = 4), or clinical (n = 1) misadventures. Two of these five grafts were functioning at or shortly before the time of their loss. The predominant factor for loss of the remaining 16 grafts were infection (n =

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3), PTLD (n = 2), rejection (n = 6), and a combination of PTLD and rejection (n = 5).

Total parenteral nutrition (TPN) was discontinued an average of 56 days posttransplant. Currently 20 children have functioning grafts and are independent of TPN.

#### DISCUSSION

The limitations of intestinal transplantation in children are bordered by technical/clinical, immunologic, and infectious barriers. Though patients suffering from intestinal failure have a mixed and varied etiologic background, the common factor of TPN, with its inherent complications, produces clinical scenarios which stipulate severity of illness. These factors are significant contributors to outcome, and, thus, the development of stringent selection criteria may improve results after intestinal transplantation.

There was no survival difference between the LSB and the MV operations. There is, however, a significant survival difference when compared to the SB type operation. This may reflect the advantage of graft enterectomy and retransplantation. However, it is well known that patients selected for isolated intestinal transplantation are generally not critically ill, nor are they suffering from failure of any other organ systems besides the intestine.

Infectious complications will generally plague this patient population, particularly of viral origin (EBV, CMV). This is

a result of the nature of the transplant procedure and also the immunosuppressive requirements necessary to maintain this type of allograft. The development of tools such as the use of EBV PCR in the peripheral blood<sup>7</sup> may allow for early or pre-emptive therapy, thus preventing the end phase of these diseases. More experience with the treatment of these infections, avoiding concomitant rejection, will likely aid in improving survival.

In spite of the difficulties in management of these complex patients, a small majority is presently enjoying survival with normal growth and development.

#### REFERENCES

1. Todo S, Reyes J, Furukawa H, et al: *Annals of Surg* 222(3): 270, 1995
2. Fontes P, Rao AS, Reyes J, et al: *Transplant Proc* 28:(this issue), 1996
3. Reyes J, Tzakis AG, Todo S, et al: *Seminars in Ped Surg* 2(4):289, 1993
4. Jabbour N, Reyes J, Todo S, et al: *Transplant Proc* 28:(this issue), 1996
5. Reyes J, Green M, Bueno H, et al: *Transplant Proc* 28:(this issue), 1996
6. Bueno J, Green M, Reyes J, et al: *Transplant Proc* 28:(this issue), 1996
7. Greee M, Reyes J, Jabbour N, et al: *Transplant Proc* 28:(this issue), 1996