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Intestinal Transplantation in Humans Under FK 506

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A CLINICAL trial of intestinal transplantation under FK 506 was instituted in our center in May 1990. As of the end of June 1992, 23 patients have received either isolated intestinal grafts (n = 9), combined intestine and liver grafts (n = 12), or abdominal multivisceral grafts (n = 2). Described herein is the clinical course of the intestinal transplant patients that have a minimum follow-up of 2 months. Preliminary results of the initial cases were reported previously.[1,2]

METHODS

Of the 23 patients, 12 were adult, with a mean age of 27.9 years (20 to 50 years), and 11 were children, with a mean age of 3 years (0.6 to 10.2 years). Indications for intestinal transplantation, duration of total parenteral nutrition (TPN), and type of transplant are listed in Table 1.

The principles and steps for intestinal harvesting and transplantation have been described previously in detail.[3,4] The grafts were obtained from ABO-matched cadaveric donors who were of similar or smaller size than the recipients. HLA matching was not considered and was universally poor. Selective decontamination of the intestine was performed in all donors before procurement, but immunomodulation, by graft irradiation or antilymphocyte antibody administration, was not attempted. Grafts were preserved with the University of Wisconsin solution for mean duration of 7.6 hours (2.8 to 10.9 hours). Luminal flushing of the intestine was not performed.

The type of intestinal grafting (ie, isolated, combined, or multivisceral) was determined by the cause of intestinal failure and associated extraenteric organ failure. Patients who have short-gut syndrome or incorrectable intestinal disease but have normal liver function were given isolated intestinal transplants. Patients with short-gut syndrome and accompanying liver failure were given combined intestine and liver transplants. Two patients who had thromboses of both the celiac axis and the superior mesenteric artery, caused by deficiencies of protein S or antithrombin-III, were given multivisceral transplants.

Details of postoperative immunosuppression and nutritional management are described by Abu-Elmagd et al, and Reyes et al

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Table 1. Clinical Features of the 23 Small Bowel Transplant Recipients

Pt.	Age	Sex	Cause of Short-Gut Syndrome	TPN Duration*	Graft†	Patient Survival‡	Graft Survival‡	TPN Status	Current Location
1	31.1	M	Gunshot wound	6	SB	776	684	Died, sepsis	
					SB		71		
2	3.2	F	Necrotizing enterocolitis	38	SB/L	>754	>754	Free	Home
3	26.7	F	SMA thrombosis	30	SB/L	>744	>744	Free	Home
4	4.3	M	Gastroschisis	52	SB/L	>631	>631	Free	Home
5	2.8	M	Intestinal atresia	33	SB/L	385	385	Died, LPD	
6	0.6	F	Intestinal atresia	6	SB/L	23	23	Died, GVHD and Sepsis	
7	1.1	F	Volvulus	12	SB/L	>372	>372	Free	Home
8	1.7	F	Volvulus	18	SB/L	>370	>370	Free	Surgical ward
9	21	M	Traffic accident	12	SB/L	>361	>361	Partial	Surgical ward
10	32	M	CA and SMA thrombosis	36	MV	>307	>307	Free	Home
11	2.5	F	Microvillus inclusion disease	29	SB	>290	>290	Free	Home
12	1.3	M	Intestinal atresia	15	SB	>235	>235	Free	Home
13	50	F	Crohn's disease	120	SB	>232	>232	Free	Home
14	34	F	Desmoid tumor	1	SB	>195	>195	Partial	Surgical ward
15	38	M	Crohn's disease	120	SB	>165	>165	Free	Home
16	10.2	F	Pseudo-obstruction	132	SB	>163	>163	Free	Home
17	22	F	Crohn's disease	36	SB	>157	>157	Free	Home
18	25	M	Crohn's disease	15	SB/L	>141	>141	Free	Home
19	1.5	M	Necrotizing enterocolitis	18	SB/L	70	70	Died, MOF, sepsis	
20	29	F	Desmoid tumor	17	SB/L	>83	>83	Free	Surgical ward
21	24	M	SMV thrombosis	3	MV	>80	>80	Partial	Surgical ward
22	20	F	SMA injury, MVA	24	SB	>70	>70	Free	Home
23	4.2	F	Gastroschisis	50	SB/L	>67	>67	Free	Home

*Pretransplant TPN duration in months; †SB: small bowel; SB/L: small bowel/liver; MV: multivisceral; ‡Survival in days as of 8/16/92.

in this issue. Briefly, immunosuppression was with FK 506 (intravenously 0.1 to 0.15 mg/kg/d, or orally 0.3 mg/kg/d), tapering of steroids and prostaglandin-E_1 (0.6 to 0.8 μg/kg/min), and occasionally supplemented by Imuran. Intestinal graft rejection was monitored clinically and histopathologically, using endoscope-guided biopsies. Treatment of graft rejection was either by increasing the FK 506 dose, steroid bolus, tapering of steroids, or OKT3.

RESULTS

Of the nine isolated small bowel recipients, eight (88.8%) are alive for a median duration of 6.5 months, ranging from 2 to 23 months. One patient (case 1), who had a stormy immediate postoperative course and several episodes of drug-noncompliant rejection, lost his graft by chronic rejection at 22 months and was retransplanted (graft survival eight of ten). This patient died 71 days after retransplantation by overwhelming sepsis. The median duration of ICU stay and hospitalization of isolated graft recipients was 6 days and 79 days, respectively.

Nine of the 12 combined intestine and liver recipients (75%) are well for median follow-up of 12 months, ranging from 2 to 25 months. Three pediatric combined intestine and liver recipients died; at 23 days by sepsis and possible graft-versus-host disease (GVHD), at 70 days by sepsis, and at 385 days by postoperative lymphoproliferative disease. Diagnosis of GVHD was made by immunohistopathologic study of a skin biopsy taken at 22 days; however, the immunohistopathology of a skin biopsy taken at 19 days did not show any signs of GVHD. Technical complications, intestinal anastomotic leak, and biliary anastomotic leak, were major causes of sepsis in the first two patient deaths. The median duration of ICU stay and hospitalization of combined graft recipients was 14 days and 80 days, respectively.

Two multivisceral transplant recipients are well for 2 months and 10 months, respectively (100%).

Of the 19 surviving patients, 14 are home and are completely free from TPN. The remaining five patients are in the hospital, either for postoperative management or routine examination, of which two are free from TPN and the other three are supported by TPN partially.

DISCUSSION

In spite of improved nutritional management of patients with short-gut syndrome or incorrectable intestinal disease, transplantation of the intestine has been considered as a theoretical modality of treatment for these patients.[5] However, the results with such attempts using conventional immunosuppression have been unsatisfactory. Our experience has shown that small bowel transplantation in humans is feasible under improved immunosuppression, FK 506. In addition, three different types of intestinal grafting (isolated, combined, or multivisceral) are needed to treat patients depending upon the cause of intestinal failure and associated extraenteric organ dysfunction. Contrary to past experimental and clinical findings,[6,7] the results associated with isolated intestinal transplantation are not inferior to the results obtained from transplantation of combined grafts. Thus, our experience suggests that before severe, life-threatening TPN-related complications occur, an isolated intestinal transplantation should be considered for patients who would be on TPN for life.

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