Successful Rehabilitation in Pediatric Ultrashort Small Bowel Syndrome

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Objective To examine treatment outcomes in pediatric patients with ultrashort small bowel (USSB) syndrome in an intestinal rehabilitation program (IRP).

Study design We reviewed IRP records for 2001-2011 and identified 28 children with USSB (≤20 cm of small bowel). We performed univariate analysis using the Fisher exact test and Wilcoxon rank-sum test to compare characteristics of children who achieved parenteral nutrition (PN) independence with intact native bowel and those who did not. Growth, nutritional status, and hepatic laboratory test results were compared from the time of enrollment to the most recent values using the Wilcoxon signed-rank test.

Results Of the 28 patients identified, 27 (96%) survived. Almost one-half (48%) of these survivors achieved PN independence with their native bowel. The successfully rehabilitated patients were more likely to have an intact colon and ileocecal valve ($P = .01$). Significant improvements in PN kcal/kg, total bilirubin, and height and weight *z*-scores were seen in all patients, but serum hepatic transaminase levels did not improve in the nonrehabilitated patients.

Conclusion Enrollment in an IRP provides an excellent probability of survival for children with USSB. The presence of an intact ileocecal valve and colon are positively associated with rehabilitation in this population, but are not requisite. Approximately one-half of patients with USSB can achieve rehabilitation, with a median time to PN independence of less than 2 years. The USSB population can attain reduced PN dependence, improvement of PN-associated liver disease, and enhanced growth with the aid of an IRP. *(J Pediatr 2013;163:1361-6)*.

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Short bowel syndrome, the most common cause of intestinal failure in the pediatric population, is characterized by an inability of the gastrointestinal tract to absorb sufficient nutrients and water to maintain adequate hydration, nutrition, and ultimately growth, secondary to loss of surface area. Greater residual small bowel length after initial resection has been consistently associated with improved survival in these children.[1,2] Ultrashort small bowel (USSB) syndrome has been defined as approximately 20 cm of remaining small bowel.[3] Massive resections leading to USSB syndrome have been reported in the literature for several years,[4] although to date the outcomes of these patients have been documented only in case reports and small case series.[3,5-10]

The concept of rehabilitating patients with USSB syndrome began with the development of parenteral nutrition (PN) and has since evolved to encompass advances in enteral nutrition, hormone therapy, medical treatments, and autologous reconstruction procedures.[11] The development of these technologies has fostered the idea of intestinal adaptation, which strives to enable the remaining gut to undergo compensatory changes, including mucosal hyperplasia, villus lengthening, and increases in crypt depth, that allow successful enteral feeding. The concept of intestinal rehabilitation programs (IRPs) as specialized centers promoting intestinal adaptation in children with USSB syndrome is a recently introduced paradigm. These centers have raised expectations for all children with USSB syndrome in terms of achieving not only improved overall survival, but also enteral autonomy, obviating the need for intestinal transplantation.[12]

Children with USSB syndrome after an initial insult are considered to have higher mortality and less chance of achieving enteral autonomy compared with those with less substantial bowel loss. Because these children are subject to prolonged periods of dependence on PN, they are especially prone to the development of PN-associated liver disease (PNALD), which further hinders intestinal adaptation. Historically, USSB in infants has been considered an indication for termination of life support, with the prognosis viewed as futile. At best, USSB may lead to early referral for intestinal transplantation in cases in which enteral autonomy might have been possible without transplantation. Even though significant advances have been made in

ALT	Alanine aminotransferase
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IRP	Intestinal rehabilitation program
PN	Parenteral nutrition
PNALD	Parenteral nutrition–associated liver disease
STEP	Serial transverse enteroplasty procedure
USSB	Ultrashort small bowel

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increasing the survival of intestinal transplant recipients and allografts, the need for lifetime immunosuppression remains a reality, and a substantial number of grafts continue to be lost to rejection. Organ Procurement and Transplantation Network data from 2010-2011 indicate an intestinal graft failure rate of 16% at 6 months and 26% at 1 year. The 5-year graft failure rate for intestinal transplants in 2006-2007 was 48%.[13] In view of these statistics, we believe that it is important to better define the possible impact of IRPs on outcomes in patients with USSB syndrome.

Methods

Inclusion criteria included residual small bowel length ≤20 cm after initial resection and age <2 years at time of referral to the IRP. Medical records for the period May 2001 to May 2011 were reviewed, and 28 patients were selected for inclusion in this study. Bowel length was established by operative report or transfer paperwork from another hospital. Patients with unclear bowel length on available records were included if an operation (eg, bowel-lengthening procedure, stricturoplasty, ostomy takedown) performed at our center after referral demonstrated a length of ≤20 cm after the initial resection. Although this operation often was separated by days to weeks from the initial resection, we posited that the passage of time would only serve to lengthen the bowel, which by default would indicate that the initial length of remaining bowel was sufficiently short.

Institutional Review Board approval was obtained in accordance with the protocol of the University of Nebraska Medical Center. After identification, a further review of each patient's records was undertaken. Along with small bowel length, data collected for each patient included sex, date of birth, ethnicity, date and cause of death (if applicable), primary cause of USSB, presence of an ileocecal valve, presence of colon, small intestine transplantation or bowel-lengthening procedure, PN independence, time on PN, time enrolled in the IRP, presence of primary anastomosis, and prematurity (defined as gestational age <37 weeks). In addition, values at time of referral to the IRP and the most recent values on record were obtained for aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, height, weight, and kcal/kg supplied by PN. Our indications for intestinal or multivisceral transplantation included intestinal failure deemed "irreversible," as indicated by advanced PNALD with portal hypertension, recurrent life-threatening central venous line infections, loss of vascular access sites, or a nonreconstructable gastrointestinal tract.

Values associated with patient characteristics are expressed as number and percentage or mean ± SD. The Fisher exact test was used to compare categorical data between the adapted and nonadapted groups of survivors. The Wilcoxon rank-sum test was used for comparisons of continuous variables. Cumulative incidence methods were used to examine the time to adaptation. The competing event for this analysis was transplantation, and patients still on PN at last follow-up were treated as censored.

The *z*-scores for height and weight were calculated for standardization purposes using the methodology of the National Health and Nutrition Examination Survey.[14] The Wilcoxon rank-sum test was used to compare initial measurements of liver function, growth, and nutritional variables between the adapted patients and the nonadapted patients, and the Wilcoxon signed-rank test was used to compare the initial and most recent values for these variables within each group. A P value of <.05 was considered to indicate statistical significance. SAS software (SAS Institute, Cary, North Carolina) was used for data analysis.

Results

Demographic data of the study group are presented in **Table I**. The mean age at enrollment into the IRP was 5.3 months. Age was determined for all patients at the time of data collection in June 2011. Of the 28 patients enrolled, 27 (96%) were still alive at the time of this study. The patient who died expired as a result of overwhelming resistant *Candida tropicalis* infection several months after combined liver/small bowel/pancreas transplantation.

The group of surviving patients with USSB was divided into a cohort of 13 patients (48%) who had gained enteral autonomy with native bowel by the time of this study and 14 (52%) who had not done so. Enteral autonomy, or "adaptation," was defined as cessation of PN without intestinal transplantation. A cumulative incidence curve depicting the time to adaptation is shown in the **Figure**. The cumulative incidence of adaptation at 2 years was 37% (95% CI, 9%-66%). The median time on PN was 1.13 years. The characteristics of the study group, along with the adapted and nonadapted cohorts, are summarized in **Table II**.

Fourteen patients (52%) underwent at least 1 bowel-lengthening procedure, including 3 Bianchi procedures and 11 serial transverse enteroplasty procedures (STEPs). Two of these patients had an initial STEP performed at the referring facility. All repeat bowel-lengthening procedures were STEPs. Only 3 Bianchi procedures were performed; this procedure was largely abandoned by our program around 2004, because it was more technically difficult and appeared to offer no measurable advantages, and carried the disadvantage of possible late intraloop fistula formation, which is not seen with STEP.

There were also no significant differences in the primary diagnosis between the 2 cohorts. The adapted cohort had a significantly higher rate of intact ileocecal valve and colon (P = .013). Four of the adapted patients (31%) did not have an intact colon and ileocecal valve. The nonadapted cohort included 3 children who underwent isolated small bowel transplantation and 1 child who underwent combined liver/small bowel/pancreatic transplantation. Of the 4 nonadapted patients who underwent transplantation, 1 patient suffered severe graft rejection necessitating explantation and is now receiving PN. The other 3 patients achieved enteral autonomy following transplantation.

The adapted cohort started PN between March 8, 2002, and April 24, 2010, and was referred between April 14,