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Role of an Intestinal Rehabilitation Program in the Treatment of Advanced Intestinal Failure

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ABSTRACT

Objective: To analyze outcomes in children with intestinal failure treated by our Intestinal Rehabilitation Program (IRP) in a 4-year period.

Patients and Methods: A total of 51 parenteral nutrition (PN)–dependent patients (20 male) were enrolled in the IRP. Median age was 1.7 years, with the primary diagnoses being gastroschisis, necrotizing enterocolitis, volvulus, and congenital atresia. Median small bowel intestinal length was 35 cm, with the majority of patients having only jejunum as remaining bowel anatomy. Thirty-six of the 51 patients had liver disease characterized by cirrhosis, advance bridging fibrosis, and portal and periportal fibrosis. Height, weight *z* score, platelet count, albumin, and bilirubin levels were measured at the beginning and end of the study.

Results: Of the 51 patients, 29 had 46 different surgical intestinal repairs. Twenty-nine of the 36 patients with hyperbilirubinemia had normalized serum bilirubin with treatment. Ten patients required transplantation. Five patients died of sepsis, influenza, or complications after intestinal transplantation. Of the remaining 37 patients in the IRP, 31 were weaned from parenteral nutrition (5 with cirrhosis); 6 patients are in the process of weaning. Survival rate of the patients in the IRP was 90%. Growth has continued along the same curve, and some patients have exhibited significant catch-up.

Conclusions: With an aggressive medical/surgical approach, even patients with intestinal failure and advanced liver disease can avoid transplantation. Patients in the IRP showed improved liver function and nutritional parameters with the ability to discontinue PN while maintaining growth. Early referral of these patients to specialized centers before the development of advanced liver disease is recommended. ***JPGN 45:204–212, 2007.*** **Key Words:** Intestinal failure—Intestinal rehabilitation—Short bowel syndrome. © 2007 by European Society for Pediatric Gastroenterology, Hepatology, and Nutrition and North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition

INTRODUCTION

Intestinal failure results from surgical resection, congenital defect, or disease-associated loss of absorption and is characterized by the inability to maintain protein/energy, fluid, electrolyte, or micronutrient balances when receiving a conventionally accepted normal diet (1).

Most individuals maintain nutritional autonomy with 50% of their small bowel. Several variables have been recognized to predict failure in patients undergoing attempts at rehabilitation. Messing et al (1), in a report of 124 adult patients with short bowel syndrome (SBS), concluded that permanent intestinal failure was related to jejunal remnant length <100 cm, end jejunostomy, and absence of terminal ileum. After 2 years of parenteral nutrition (PN), the probability of permanent intestinal failure was 94%. In children, Wilmore et al (2) found that survival with enteral nutrition is possible in newborn infants with a minimum small bowel length of 40 cm and no ileocecal valve (ICV) or 15 cm of small bowel and an intact ICV. Goulet et al (3) reviewed a series of 135 consecutive patients after neonatal intestinal resection. Their results suggest that 40% of the patients with <40 cm of residual small bowel and without an ICV remain dependent on PN after 8 years. Pharaon et al (4) and Vargas et al (5) associated failure of weaning from PN in children with <30 cm of jejunum/ileum, lack of enterocolonic continuity, and lack of feeding tolerance early after birth.

In a recent study Spencer et al (6) determined predictors of survival and of weaning off PN. They found that a conjugated bilirubin level of at least 2.5 mg/dL was the strongest predictor of mortality. Although absolute

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small bowel length was only slightly predictive, the percentage of normal bowel length (for a given infant's gestational age) was strongly predictive of mortality (if $<10\%$ of normal length) and of weaning off PN (if $\geq 10\%$ of normal length). Presence of the ICV was also strongly predictive of weaning off PN; however, ICV was not predictive of survival.

To understand the value of the outcomes of the Intestinal Rehabilitation Program (IRP), it is important to review the indications for liver/small bowel transplantation as established by the Centers for Medicare and Medicaid Services (7). The indications are imminent or evident liver failure due to total PN–induced liver injury, thrombosis of 2 or more central veins, development of 2 or more episodes of systemic sepsis secondary to catheter infection per year that require hospitalization, a single episode of catheter-related fungemia, septic shock and/or acute respiratory distress, and frequent episodes of severe dehydration despite intravenous fluid supplementation in addition to PN (8,9). A total bilirubin level of >7 mg/dL, stage 2 fibrosis, and/or portal hypertension have been recognized as clear indications for liver/intestinal transplantation (8,9).

A multidisciplinary IRP formed by a pediatric gastroenterologist, a surgeon, a dietitian, a nurse practitioner, and a nurse coordinator was started at the University of Nebraska Medical Center in October 2000. The philosophy of the program was to use multiple therapies to promote intestinal adaptation and the eventual weaning of patients off PN. Aggressive enteral therapies, along with maintenance of hydration, by trained medical staff were important factors in long-term survival. Treatment options for SBS in children include long-term PN, intestinal rehabilitation, and/or intestinal transplantation. To determine the most appropriate therapy, a comprehensive evaluation is necessary (Fig. 1). This article details the outcomes of children with intestinal failure referred for liver/small bowel transplantation during a 4-year period who, after a complete evaluation, were treated by our IRP.

PATIENTS AND METHODS

Between March 2001 and August 2005, 51 PN-dependent patients with intestinal failure referred for liver/small bowel transplantation were enrolled in the IRP after a complete evaluation. The etiology of the intestinal failure was gastroschisis in 18 patients (35%), necrotizing enterocolitis in 15 (29%), volvulus in 6 (12%), congenital atresia in 6 (11%), congenital short bowel in 1 (2%), intestinal pseudoobstruction in 2 (4%), mesenteric arterial thrombosis in 1(2%), meconium obstruction in fetus in 1(2%), and Hirschsprung disease in 1 (2%).

Indications for Treatment in the IRP

Infants with no liver disease or mild cholestasis who have extreme short bowel as defined by at least 10 cm of small bowel and >50% of their colon. The maximum rate of increase bowel length occurs during the first year of life. The small bowel length doubles during the last trimester of gestation, suggesting that the remaining intestine may have grater potential for increase in length in a preterm infant than a full-term baby. The same difference in growth potential exists between neonates and older children (3). Part of the intestinal adaptation process includes increased wall thickness and bowel dilation. The latter, along with the increase in length, allows for the possibility of bowel lengthening in the future.

Children with more than 35 cm of small bowel with an increased bilirubin level but a normal International Normalized Ratio (INR). Aggressive enteral therapies, maintaining adequate nutrition, hydration, and good control of infections (central catheter and bacterial overgrowth) by trained medical staff have the potential to revert liver disease–associated intestinal failure (2,10–12).

Children with advanced liver disease with portal hypertension–associated hypersplenism or thrombocytopenia but normal INR, who had at least 50 cm of bowel and abnormal but potentially repairable intestinal anatomy, or history of tolerance of at least 30% of caloric needs by the enteral route. Preliminary experience at our institution suggests that PN-dependent patients with advanced liver dysfunction in the setting of SBS may, in some instances, experience functional and biochemical liver recovery. The latter appears to parallel autologous gut salvage in most cases (13,14).

Patients with advanced liver disease and abnormal coagulation with a prolonged INR were considered candidates for a liver/small bowel transplant. If, during evaluation, they demonstrated a tolerance of $>50\%$ of their nutritional needs by enteral feedings, then they were considered possible candidates for an isolated liver transplant and were managed by the transplant team and were not considered IRP patients. Preliminary results have been reported previously detailing the results of isolated liver transplantation in a carefully selected group of patients with SBS (15).

Height, weight z score, platelet count, albumin, and bilirubin measurements were obtained at the beginning and end of the study and are summarized in Figs. 2–5.

Patient Demographics

Fifty-one patients who were PN-dependent (20 males) were enrolled in the IRP. Median age was 1.7 years (range, 0.4–15 y). Our institution is a referral center and 90% of the patients came from different locations throughout the country. When these patients were enrolled in the IRP, all of them stayed in Omaha for at least the first 2 months after evaluation. Eleven of the 51 patients (21%), after an evaluation and partial management, returned to their place of origin to be managed by the primary physician or pediatric gastroenterologist. All of the patients (100%) who were weaned off PN resided in or near Omaha.

All but 2 patients were PN-dependent since birth or within the first month of life; 1 was a teenager who experienced mesenteric thrombosis and was left with 8 cm of bowel. The patient had been dependent on PN for the past 5 years. The other was a patient with intestinal pseudoobstruction who was dependent on PN for 13 months before being enrolled in the IRP and had no history of liver disease.

Median remaining intestinal length at the time of evaluation was 35 cm (range, 8–120 cm). The anatomy of the remaining

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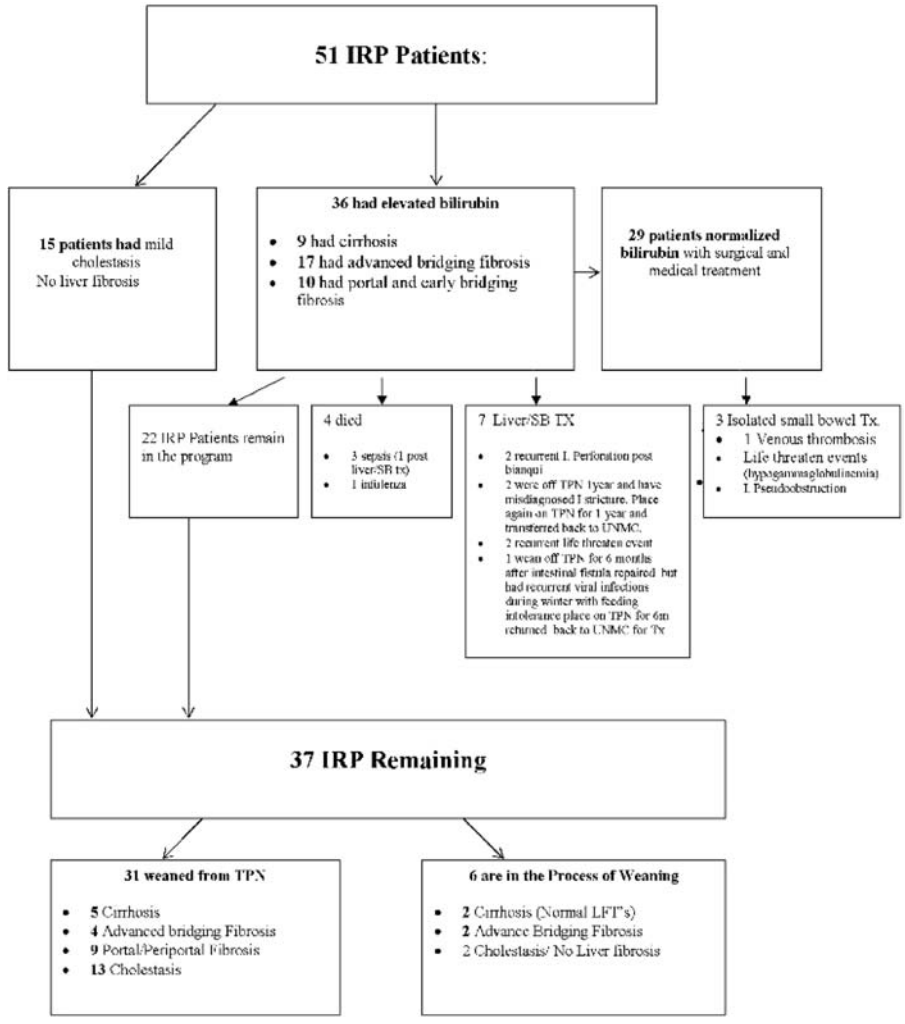

FIG. 1. Summary of results for 51 IRP patients over a 4-year period.

bowel was obtained by radiological studies and surgical reports. Forty-three patients had jejunum and 8 patients had jejunum and some ileum (6 had ICV and the whole colon). Forty-two patients (84%) had partial resection of colon and 1 had an end jejunostomy.

Before enrollment in the IRP, 32 patients (63%) were totally dependent on PN with no history of enteral tolerance. The median daily energy requirement by PN was 100% (range, 55%–100%). Thirty-six patients (70%) had hyperbilirubinemia at the time of initial evaluation. The median conjugated bilirubin level was 5.0 mg/dL (range, 0.1–26 mg/dL). On liver biopsy, 9 had cirrhosis, 17 had advanced bridging fibrosis, and 10 had portal and periportal fibrosis.

Treatment of the Patients in the IRP

The components of the IRP in children are summarized as follows (16,17):

1. Physical, biochemical, radiological, and histological evaluation of patients' condition, identifying the anatomy and possible abnormalities of the intestinal tract
2. Parent/patient education
3. Enteral tube feedings
4. Parenteral nutrition management/weaning
5. Management of complications of intestinal failure (eg, sepsis, catheter-related, bacterial overgrowth)
6. Psychosocial support
7. Surgical options to restore intestinal continuity, repair enterocutaneous fistulas, and resect strictured/obstructed bowel, including intestinal lengthening (Bianchi procedure) and serial transverse enteroplasty (17); the decision of any surgical options depends on the age, intestinal length, and intestinal anatomy, as well as bowel diameter.
8. Investigational pharmacological agent

At the end of the initial assessment there is a more comprehensive understanding of the cause of intestinal failure,

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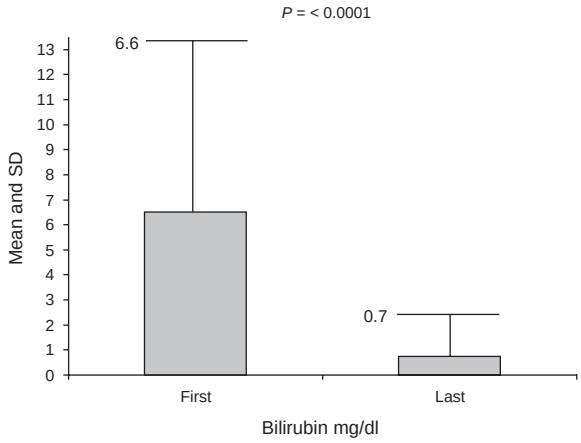

FIG. 2. Patients' bilirubin levels measured at the beginning (First) and end (Last) of the study show significant improvement through the treatment course.

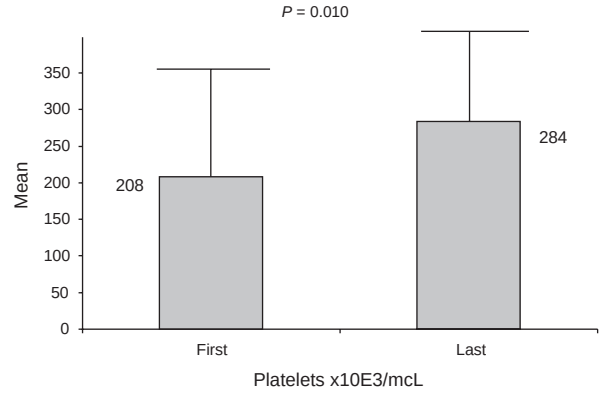

FIG. 4. Patients' platelet count increased considerably even though the majority had moderate to advanced liver disease.

along with knowledge of the anatomy and length of the remaining bowel. The reasons for feeding intolerance and possible causes are delineated; anatomic problems such as intestinal stricture, obstruction, and fistulas are identified; and other complications such as bacterial overgrowth, recurrent catheter infections, and gastroparesis/dysmotility are systematically reviewed. With this first evaluation, the grade of the liver disease is also estimated.

Medical Management

The medical treatment of patients in the IRP is focused on an aggressive dietetic management with precise control of the metabolic balance as well as prompt and effective treatment of patient complications. Continual parent education and support is an important part of the program because they are vital members of the team. When the patients are enrolled in the IRP they are followed at least weekly by a pediatric gastroenterologist, a dietitian, a nurse coordinator, and a nurse practitioner. The surgeon follows them closely postoperatively and then as needed. All of the patients are initially treated directly by our IRP at least for the first 2 months after evaluation. For the families who do not live in Omaha, the Nebraska Medical Center offers them different possibilities of lodging at no or very low cost.

Most patients are placed on continuous tube feeding using elemental formulas, which is started slowly and advanced according to tolerance. Even a minimal amount of 1 mL/hour may be beneficial for a newborn baby in attempting to achieve intestinal adaptation. A continuous enteral infusion permits a greater percentage of total nutritional requirements to be delivered by constant saturation of carrier proteins and reduces the tendency for emesis (19,20). Reduction in thermal energy loss has also been found in normal patients fed continuously compared with patients fed with boluses (21). Amino acid formulas are beneficial in reducing the risk of secondary protein intolerance, which may occur more commonly in children with SBS because of conditions that predispose them to enhanced intestinal permeability (19,20,22). When the patient tolerates a certain amount of tube feeding without emesis, the patient is additionally started on small boluses of the prescribed formula to stimulate normal development of oral feeding and prevent

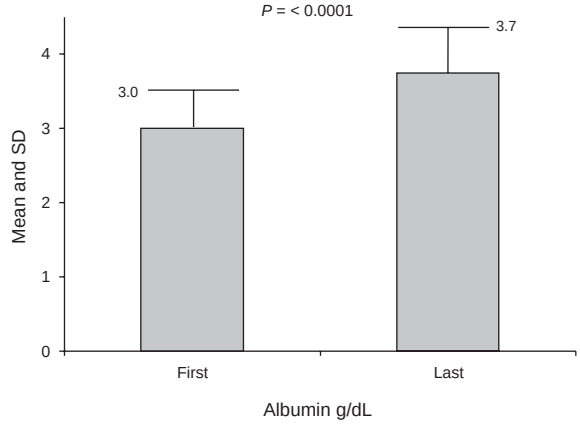

FIG. 3. Patients' albumin levels measured at the beginning (First) and end (Last) of the study show significant improvement.

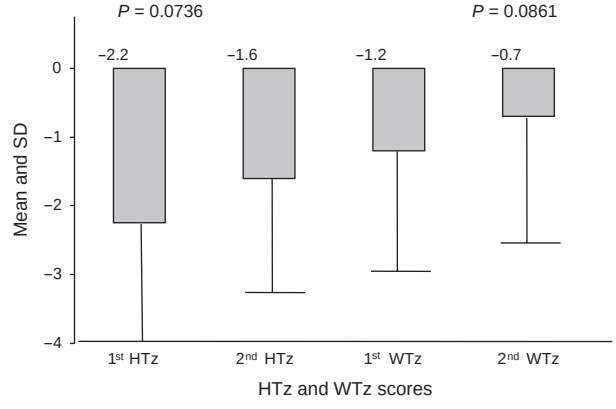

FIG. 5. Height and weight *z* scores continued along the same curve during the months spent in the IRP, while some exhibited significant catch up.

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feeding aversion. Children older than 6 months of age are administered solid food initially in small amounts. Solid food is beneficial in stimulating normal oral skills as well as adaptation. Oral feeding is more physiological, stimulating gallbladder motility and gastrointestinal secretions and perhaps contributing to reduction in PN-related liver disease (2,20–22). Although solid food feedings are traditionally initiated with high-carbohydrate foods, children with SBS do better with high-fat, high-protein foods. Meats are probably the best food group to start because they provide less osmotic load to the small bowel and the fat provides an additional stimulant for the intestinal adaptation (20). Older children are taught to eat frequent meals (6 times per day) in small portions, avoiding sugars and juices.

As enteral feedings are tolerated, PN is weaned proportionally. The calculations of the energy intake requirements for patients with SBS include the Recommended Daily Allowance for age multiplied by a factor of 1.2 to 1.5 to account for malabsorption. Parenteral nutrition infusion time is progressively weaned during the day as the child gets older. Careful monitoring of glucose and hydration status throughout this time is important. When the total volume and energy intake requirements by PN and/or the number of hours infused are low, PN is eliminated 1 or 2 nights per week or may only necessitate hydration fluids. Progressive advancement of days without PN is performed as the patient continues to tolerate enteral nutrition. This entire process is gradual and may take weeks, months, or even years to complete.

As noted, a small number of patients tolerate the necessary enteral feedings to maintain nutritional balance, but still need extra fluids for the maintenance of good hydration and electrolyte status. With time, this fluid/electrolyte deficit is replaced using the gut. Normal or half-normal saline solution is added to the patient's formula, increasing the tube feeding rate accordingly to meet patient's fluid needs.

All of the patients in the IRP have an esophagogastroduodenoscopy as part of their evaluation. Samples of duodenal fluid for colony count and cultures are obtained. Treatment of small bowel bacterial overgrowth (SBBO) commonly involves rotating broad-spectrum oral antibiotics, which are often effective in reducing the number of bacteria. Ideally, the choice of the antimicrobial agent should reflect in vitro susceptibility testing, but is sometimes impractical because many different bacterial species with different antibiotic sensitivities coexist (23). A trial of empiric antibiotic covering aerobic and anaerobic bacteria may be attempted to evaluate the improvement of symptoms associated with SBBO such as lessening of diarrhea, weight gain, and reduction of gas-related symptoms. Because the underlying mechanism(s) responsible for causing SBBO are unlikely to change in patients with SBS, a periodic treatment of 7 to 14 days or more of continuous use of alternate antibiotics may be necessary. The most frequently used are metronidazole (10 mg/kg every 8 hours), trimethoprim/sulfamethoxazole (5 mg/kg every 12 hours), oral gentamicin (5–10 mg/kg every 8 hours), extended-spectrum penicillins, and cephalosporins. When significant intestinal inflammation coexists, antiinflammatory therapy with corticosteroids may be used.

Probiotics (lactobacillus and *Bifidobacterium*) are live microorganisms that, when ingested, colonize the intestine, establish themselves as part of its flora, and are beneficial to human health by preventing or treating certain pathological processes (24). Several mechanisms of actions have been identified with the use of probiotics, such as production of substances that prevent bacterial proliferation (25), competitive inhibition of bacterial adhesion (26), competitive consumption of nutrients, modification of toxin receptors through enzymatic mechanisms, and stimulation of the immune system (27). *Lactobacillus* species produce nutrients, mainly short-chain fatty acids, and antimicrobial products such as pyroglutamate, and also remove potentially toxic substances from the intestine (28). All of these factors lead to the observation that probiotic therapy in SBBO may be effective in reducing the use of antibiotic therapy and in controlling symptoms related to bacterial overgrowth. The majority of our patients are administered lactobacillus GG as part of the bacterial overgrowth treatment. In patients younger than 3 months of age, we avoid probiotics because of previous experience with central catheter infection in small infants.

At any stage of treatment, and particularly the late stage, monitoring of weight gain and growth is the most beneficial tool to evaluate nutritional status and nutrition absorption. Efforts to identify malabsorbed nutrients in the stool are rarely helpful. It is important to ensure that the patient's weight gain is appropriate for his or her height and not excessive. As the enteral feeding becomes the primary nutritional supply, the child is monitored more frequently for micronutrient deficiencies. Macronutrients such as fat, proteins, and carbohydrates are usually absorbed in adequate amounts. Micronutrients such as zinc, magnesium, fat-soluble vitamins, vitamin B_{12}, and iron are frequently deficient in patients with SBS. Enteral feedings are supplemented with the specific deficient micronutrient, although magnesium supplements often result in osmotic diarrhea. In this case, frequent small doses may be required. Liquid preparations may be necessary because tablets or capsules are usually excreted intact.

During later therapy, administration of many other additional dietary supplements may be attempted to enhance enteral tolerance. Soluble fiber can be useful in slowing transit time and increasing stool consistency. In addition, aerobic bacteria of the colon metabolize unabsorbed fiber (ie, pectins) to short-chain fatty acids. These short-chain fatty acids are rapidly absorbed by the colonic mucosa and used for energy (29) and may have some added anti-inflammatory effect. In PN-dependent patients with SBS, the use of high-dose recombinant human growth hormone in controlled (30,31) and uncontrolled studies (32) has led to variable results. Clearly, the dose, the optimal time frame of administration, and the safety of long-term treatment with growth hormone need to be determined.

Surgical Management

Although the primary management of SBS is medical, there are many circumstances in which surgical intervention may offer great therapeutic benefits. Patients with SBS may develop high ostomy outputs, anastomotic strictures, and/or severe bowel dilation and regularly have problems with recurrent emesis, dysmotility, bacterial overgrowth, and severe diarrhea. Proadaptive surgery, such as stoma closure, stricturoplasty, enteroplasty, and tapering or lengthening procedures may produce dramatic clinical improvement (14,18). The main indications for surgical intervention in the IRP for children with SBS

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are failure to progress in enteral feedings, a decrease in the previous level of enteral tolerance, life-threatening complications such as liver disease intestinal failure–associated and recurrent septic episodes with enteric bacteria in a child with a dilated bowel.

Two different bowel-lengthening surgeries are performed at the IRP; these include the serial transverse enteroplasty (STEP) and the Bianchi procedure. The Bianchi procedure involves transecting the bowel longitudinally, preserving the blood supply to both sides of the small bowel, thereby creating a segment of bowel twice the length and half the diameter of the original segment. A STEP procedure is based on the anatomic principle that the blood supply to the bowel comes from the mesenteric border of the bowel and transverses the bowel, remaining perpendicular to the long axis of the bowel. A stapler is applied sequentially from alternating and opposite directions in a transverse, partially overlapping fashion, creating a zigzag-like channel approximately 2 to 2.5 cm in diameter. Because all staple lines are kept perpendicular to the long axis of the bowel, all of the segments of the bowel should remain well vascularized. Alternating the direction of the stapler from side to side creates a channel of bowel that is smaller in diameter and longer in length than the original bowel (33).

The choice of operation in SBS is influenced by 3 principal factors: intestinal remnant length, intestinal function, and caliber of the intestinal remnant. In patients with jaundice, an aggressive approach is used to look for bowel dilation unless the patients are weaning off total PN rapidly without intervention. The dilated bowel segment should be at least 2 times the normal diameter for a Bianchi procedure to be effective and could be slightly less than that if a STEP is performed. In patients who require a small increase in enteral energy intake tolerance to wean off PN, the STEP is indicated as a primary procedure because the Bianchi procedure probably poses higher risks and the patient will probably experience the modest benefit from the STEP procedure alone. In patients with injury to the vascular anatomy of the mesentery or other anatomic reasons that make the Bianchi procedure not possible or associated with higher risk, primary STEP is indicated. Patients with shortest lengths of remnant bowel should likely first undergo the Bianchi procedure with the hope that recurrent dilation will be achieved and the patients will then be candidates for the STEP procedure.

Statistical Analysis

Patient survival was calculated using the Kaplan-Meier method. Weight and height z scores were calculated using National Center for Health Statistics growth data. The mean and standard deviation results of bilirubin, albumin, platelet, and height and weight z score measurements obtained from the patients at the beginning and at the end of the study were compared using a 2-tailed unpaired t test. $P < 0.05$ was considered significant.

RESULTS

Of the 51 patients, 29 had 46 different surgical intestinal repairs, among them 12 Bianchi procedures, 11 STEP procedures, 13 repairs of intestinal stricture/obstruction, 6 ostomy takedowns, and 4 intestinal fistula repairs. Others surgeries performed were cholecystectomies in 6 of the patients. Ten patients required transplantation. Five patients died (1 after transplantation).

Among the remaining 37 patients in the IRP, 31 were weaned from PN through surgical and/or dietary manipulations, with an average length of 6 months. Of these 31 patients, 5 had stable cirrhosis with current normal liver function test results, 4 had advanced bridging fibrosis, 9 had portal and periportal fibrosis, and 13 had cholestasis but not fibrosis. Six of the remaining 37 patients in the IRP were in process of weaning: 2 had cirrhosis but normalized bilirubin, 2 had bridging fibrosis, and 2 had normal liver/cholestasis (Fig. 1). Of the 6 patients who were still receiving PN, nutritional support by PN decreased from a median of 100% to a median of 32% (range, 7%–80%). Two of these patients were teenagers and had been PN dependent for 5 and 15 years, respectively. The first is a patient with 8 cm of bowel who was evaluated as a result of recurrent catheter infections and feeding intolerance, but had no catheter infections during the past 2 years was tolerating 30% of enteral feedings. The other patient was a 15-year-old with SBS secondary to gastroschisis, severe feeding aversion, and a history of feeding intolerance. The patient was evaluated for a lack of venous access with multiple thromboses and no liver disease. The patient had a STEP procedure, and after multiple medical attempts, a thorough teaching of an adequate oral diet, and nutritional and psychological support, the patient was weaned off PN before being sent back home. Unfortunately, the patient decided to quit eating by mouth (ie, feeding aversion) and was placed once more on PN, but is still receiving >50% of nutritional support by enteral feedings. All of the laboratory parameters evaluated (albumin, platelet count, and bilirubin) improved in the remaining 37 patients in the IRP (Figs. 2–5). Growth continued along the same curve, with some exhibiting significant catchup.

Among the 29 patients who underwent intestinal repair, 24 had hyperbilirubinemia and chronic liver disease but normal coagulation. Fifteen of the 29 patients achieved full enteral feedings (51%), and 6 (20%) were in the process of weaning off PN. Seven of the 12 patients who underwent a Bianchi procedure were weaned off PN (2 required transplantation 1 year later) and 4 had reduced PN by 50%. Four of 11 patients who received STEP were weaned off PN and 5 were in the process of weaning, reducing PN needs by >50%. Five of the 29 surgical patients (17%) had complications. Two patients developed intestinal fistulas or perforations after Bianchi procedures, which were successfully repaired. Two other patients (1 after a Bianchi procedure and 1 after a STEP/intestinal obstruction repair) had recurrent intestinal perforations and required liver and small bowel transplantation. One patient had an intestinal perforation repaired after a surgical closure of an intestinal fistula. Eight of the 29 surgical patients (27%) required transplantation.

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Thirty-six of the initial 51 patients had hyperbilirubinemia and chronic liver disease associated with intestinal failure. Twenty-nine of them had normalized serum bilirubin levels with medical and surgical treatment. Ten patients required transplantation (7 liver/small bowel transplant and 3 isolated small bowel transplants). The cause of the liver/small bowel transplants were as follows: 2 patients had recurrent intestinal perforation after Bianchi or STEP procedures, 2 had partial intestinal obstructions (misdiagnosed) after being off PN 1 year after a Bianchi procedure, and 2 had recurrent life-threatening central catheter infections. One patient was weaned off PN for 6 months after having an intestinal fistula repaired but had recurrent viral infections during the winter with feeding intolerance and were administered PN for 6 months before returning for transplantation.

Of the 3 patients who received an isolated small bowel transplant, 1 patient had a Bianchi procedure, decreasing his total PN needs by 50%. His liver function test results normalized and he achieved adequate weight for his age but had a history of multiple venous thromboses that required an isolated small bowel transplant. The second patient had 15 cm of bowel and an intestinal stricture repaired. While in the IRP, the patient's total PN requirements decreased by 45% and liver function test results were normalized. He started in the program at 6 months of age weighing 4 kg with advanced liver disease (stage 3 fibrosis). He received a transplant with an isolated small bowel at 1 year of age with a normal weight (9.6 kg) as a result of recurrent catheter infections. The third patient had the diagnosis of intestinal pseudoobstruction and a 13-month history of total dependence on PN. The patient was initially weaned off PN, but had recurrent urinary tract infections with subsequent episodes of intestinal pseudoobstruction and life-threatening central catheter infections.

Five patients died, 4 from sepsis. Three died after moving back to their homes, 1 of whom had achieved 80% of enteral feeding after a Bianchi procedure. One patient died of influenza, who had a Bianchi procedure and had achieved >50% of enteral tolerance. The fifth patient died of sepsis after a liver and small bowel transplant. The survival rate among patients in the IRP was 90% (Fig. 6).

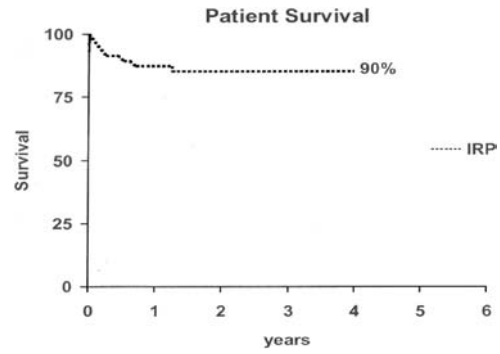

FIG. 6. Kaplan-Meier curve shows an impressive 90% survival throughout the 4-year treatment course.

DISCUSSION

Small bowel syndrome is a complex condition that requires a multidisciplinary approach. The likelihood that a patient with SBS will have his or her enteral autonomy restored is influenced by the length, location, and function of the remaining bowel. In the past decade investigations have been focused on trophic factors to enhance intestinal adaptation, but it is still not clear whether the use of these factors alone or combined with diet modification will provide better benefits than the use of dietary intervention with careful medical management.

With the results obtained during the past 4 years in our IRP, we have demystified the idea that patients with chronic liver disease cannot be rehabilitated or undergo surgical repair. With intestinal lengthening procedures (Bianchi procedure and STEP procedure), patients showed a notable increase in their enteral feeding tolerance. Although patients undergoing the Bianchi lengthening procedure have more severe complications, the overall improvement in enteral tolerance was also greater after the Bianchi procedure than after STEP. It is important to note that 58% of patients with intestinal stricture/obstruction were misdiagnosed by an upper gastrointestinal and small bowel series; among them, 1 intestinal atresia was missed as well. This fact shows the importance of performing an initial esophagogastroduodenoscopy and colonoscopy in patients with SBS with persistent symptoms of emesis and small amounts of stool.

The survival rate of patients in the IRP, even counting the patient who died after transplantation (ie, on an intent-to-treat basis) was 90%. Our experience contradicts previous reports in the literature. The majority of our patients had levels of bilirubin of at least 2.5 mg/dL with a median of 5.0 mg/dL (range, 0.1–26 mg/dL). Additionally, many of our patients had <40 cm of intestinal length or <10% of normal bowel length.

Even in the patients whose treatment in the IRP failed and subsequently needed transplantation, during the time they were treated in the IRP, their general state of health improved before transplantation. None of the patients in the IRP on the waiting list have died or have received a transplant in critical condition. All of the transplant recipients were in clinically stable condition with good nutritional status.

With surgical innovations, novel immunosuppressive protocols, and better postoperative management, the efficacy of liver/intestinal transplantation has

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significantly improved in the past 5 years, such that survival after transplantation is currently similar to that with isolated liver transplantation (80%–90% 1 year after transplantation). Despite this trend toward improving results after intestinal transplantation, immunosuppression therapy is required on a lifelong basis, with its attendant complications. Our experience with the IRP demonstrates that more aggressive attempts at intestinal rehabilitation are warranted in many patients with SBS who have risk factors previously identified for poor prognosis in terms of total PN weaning or survival. In 75% of these selected patients, we have achieved long-term survival, weaned patients from PN, and avoided the need for long-term immunosuppression.

The success of the program can be related mostly to a comprehensive medical/surgical approach and close follow-up by trained medical staff. The medical treatment of patients in an IRP is focused on an aggressive dietary management with precise control of the metabolic balance, as well as prompt and effective treatment of patient complications. Continual parent education and support is also an important part of the program. The advantage of having a rehabilitation program in a transplant center is that the line between the 2 programs is contiguous, making it possible for a patient to move from 1 program to the other in a timely fashion.

In conclusion, with an aggressive medical and surgical approach, even patients with intestinal failure and advanced liver disease can avoid transplantation. The patients in the IRP at the Nebraska Medical Center showed improved liver function and nutritional parameters with the ability to discontinue PN while maintaining growth. Early referral of patients with intestinal failure to specialized centers before the development of advanced liver disease is recommended.

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