A Surgical Perspective of the Outcome of a Multidisciplinary Intestinal Rehabilitation Program for Children With Short Bowel Syndrome in the Netherlands


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ABSTRACT

Aim. In 2001, a multidisciplinary intestinal rehabilitation program, prompted by a nationwide collaboration on intestinal failure (Dutch Registry for Intestinal Failure and Intestinal Transplantation), was started for children who have short bowel syndrome (SBS). This study evaluates this program, focusing on children who have SBS after extensive bowel resection.

Design. This is a retrospective cohort study.

Method. Demographic data, general information on disease status, and outcome of intestinal rehabilitation of patients treated between 2001 and 2009 were collected. Outcome measures were intestinal autonomy, intestinal and/or liver transplantation, and survival.

Results. Ten boys and 9 girls, median gestational age 36 weeks, were treated. Eight were referred, 3 times as many as in the period 1991–2000. Causes of SBS were intestinal atresia (3), gastroschisis (2), volvulus (9), necrotising enterocolitis (3), and strangulation (2). The median remaining small-intestinal length was 35 cm (range, 10 to 70 cm). In 14 patients the ileocecal valve was still present. In all patients at least 25% of colon was still present. The median follow-up was 25 months (range, 50 days to 9 years). After a median of 138 days (range, 41 days to 11 years) on total parenteral nutrition, 16 patients (84%) reached intestinal autonomy. Central venous catheter-related complications occurred in all; there were liver function disorders in 68%, and a failure to thrive in 26%. One patient underwent intestinal lengthening. No patient needed intestinal transplantation, but one underwent liver transplantation for intestinal failure-associated liver disease. Overall mortality was 11%: those 2 patients died of abdominal sepsis.

Conclusion. This specialized intestinal rehabilitation program led to intestinal autonomy in 84% of the patients who had SBS. None of the patients underwent an intestinal transplantation.

IN 2001, a multidisciplinary intestinal rehabilitation program, prompted by a nationwide collaboration on intestinal failure (Dutch Registry for Intestinal Failure and Intestinal Transplantation; DRIFT) was implemented in the University Medical Center Groningen (UMCG) along with a coinciding receipt of governmental permission to perform intestinal transplantations [1].

The rehabilitation program consisted of a systematic approach of determining the functional ability of the bowel of patients suffering from intestinal failure. Optimizing both enteral and parenteral feeding (total parenteral nutrition; TPN), prevention of (worsening of) cholestasis and central venous catheter (CVC)–related infections were among the main goals of the program. Non-transplant surgical


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360 Park Avenue South, New York, NY 10010-1710
Interventions, such as restoration of bowel continuity and intestinal lengthening procedures, were performed when deemed necessary. As a tertiary transplantation center, liver and/or intestinal transplantations completed the full spectrum of therapeutic possibilities.

Intestinal failure is a clinical condition characterized by temporary or permanent malabsorption of body nutrient and fluid requirements. In short bowel syndrome (SBS), one of the causes of intestinal failure, this malabsorption is caused by loss of functional intestinal mass. Incidence is estimated at 2 per million, but because in literature numerous definitions for SBS are given, the exact number is unknown [2]. In an attempt to clarify this issue, the Dutch Committee on Short Bowel Syndrome drafted criteria to better define the condition. These Dutch criteria are summarized in Table 1 and acknowledge both anatomical and functional aspects of SBS. In functional SBS, bowel length per se is sufficient for adequate digestion and absorption of food and fluids, but the ability to do so is disturbed by a myopathic, neuropathic, or epithelial disorder. This results in a (lifelong) dependence on parenteral nutrition. The anatomic version of SBS is characterized by a critical reduction of functional bowel mass, caused by extensive bowel resection [3].

In the past, the intra-operative finding that after resection only a very limited length of bowel would remain (ie, less than 10 to 20 cm) would undoubtedly have lead to the decision to discontinue further treatment. With the advent of home parenteral nutrition, the prognosis of SBS has improved substantially. Nowadays, prognosis is not so much determined by residual bowel length, but by TPN-related complications such as sepsis and liver failure (with an incidence of 15% to 50%, respectively) [4].

The main objective of this study was to evaluate the effect of implementing a multidisciplinary intestinal rehabilitation program for children with anatomical SBS.

METHODS

Data from all patients treated from 2001–2009 in our hospital with an anatomic SBS were collected and analyzed. These included demographic data such as gender, gestational age, and birth weight, as well as other patient characteristics related to the cause and severity of the SBS, treatment, and the result of the intestinal rehabilitation.

Table 1. Criteria for Short Bowel Syndrome*

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<th>Condition</th>
<th>Definition</th>
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<tr>
<td>&gt;70% of total small bowel length resected</td>
<td>or</td>
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<td>After resection remaining bowel length⁴ is:</td>
<td>&lt;50 cm in a premature neonate (&lt;36 weeks of gestation)</td>
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<td></td>
<td>&lt;75 cm in a at term neonate</td>
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<td></td>
<td>&lt;100 cm in a 1-year old</td>
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<td>Intestinal failure necessitating feeding by</td>
<td>total parenteral nutrition during &gt;6 weeks</td>
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*Criteria according to the Dutch Committee on Short Bowel Syndrome [1].

Intestinal failure (defined as being no longer dependant on TPN for maintaining fluid, electrolyte, and nutrient balance in the combination with growth), intestinal and/or liver transplantation, and survival were main outcomes measures. Figure 1 shows a schematic flow chart of the rehabilitation program.

After patient admission to our center, intestinal rehabilitation started by analyzing the remaining bowel function. Systematically, anthropometric data were collected in combination with quantitative data on malabsorption of macronutrients (ie, proteins, lipids, and carbohydrates) and micronutrients (ie, vitamins and trace elements). At first, TPN was given in a standard solution of the above-mentioned nutrients. If signs of TPN-induced liver failure became apparent, the composition of TPN was altered according to the specific dietary needs. Simultaneous with parental administration of calories, the limits of the digestive and absorptive capacity of the bowel were assessed by steadily expanding and optimizing enteral feeding. By conducting daily to weekly analyses of bowel movements and/or stoma production and frequent laboratory tests (eg, serum electrolytes, fat soluble vitamins and albumin level), a good estimation of the remaining bowel function could be given.

CVC-related complications were avoided as much as possible by training medical personnel as well as (parents of) patients in catheter maintenance and insertion site hygiene. A prophylactic lock with tauradoline was used on a routine basis.

If optimizing the bowel function was inhibited in any way by anatomical factors, such as a stoma or intestinal stenosis, a surgical procedure was performed to solve the problem. Besides procedures such as restoration of bowel continuity or adhesiolysis, autologous gastrointestinal reconstructions were performed if necessary [5].

This intensive intestinal rehabilitation was performed by a multidisciplinary dedicated team of pediatric gastroenterologists, dieticians, pediatric surgeons, and pharmacists. It is important to consider that, although such a rehabilitation program is firmly based on guidelines and protocols, the key to success lies in an individual approach of every patient. By implementing the online, web-based registry from DRIFT, individual patients could be monitored nationwide to facilitate and optimize this complex care.

RESULTS

During the study period, 19 patients with an anatomical SBS were treated (10 boys and 9 girls). Of these 19 patients, 8 (42%) were referred to our tertiary care center because of disappointing results from treatment of intestinal failure elsewhere (n = 4) or screening for intestinal and/or liver transplantation (n = 4). This is a clear increase in the number of referred patients when compared with the decade before implementation of DRIFT and our intestinal rehabilitation program (14% referred patients). Other patient characteristics are summarized in Table 2.

All causes of SBS are summarized in Fig 2. The median length of remaining bowel was 35 cm (range, 10 to 70 cm). In 14 of 19 patients, the ileocecal valve was present; in 14 of 19 patients the whole colon was in situ (Table 2). After a median follow-up of 25 months (range, 50 days to 9 years) 16 of 19 (84%) patients reached intestinal autonomy after a median of 138 days (range, 41 days to 11 years).

CVC-related complications occurred in every patient and liver function disorders, such as cholestasis, in 13 of 19...
(68%) patients. Five patients (26%) suffered failure to thrive: in one patient the weight-for-age ratio deviated more than 2.5 SD. In one patient, an intestinal lengthening procedure was performed: this so-called Bianchi procedure will be discussed in detail in the next paragraph. None of the patients required small bowel transplantation; however, due to intestinal failure–induced liver failure, a liver transplantation was performed in one patient. Overall mortality was 11%. Two patients died because of abdominal sepsis.
Dutch Committee on Short Bowel Syndrome has drafted (Table 1). When SBS is caused by extensive bowel resection, SBS is the most common cause of intestinal failure[2]. The Severity of Disease and Prognostic Factors

DISCUSSION

Severity of Disease and Prognostic Factors

SBS is the most common cause of intestinal failure [2]. The Dutch Committee on Short Bowel Syndrome has drafted criteria for pediatric patients to better define this condition (Table 1). When SBS is caused by extensive bowel resection, length of the remaining bowel is important. Severity of disease is related to that length: the less mucosal surface remains, the greater the dependency of parenteral nutrition and difficulty of reaching intestinal autonomy will be [2,6,7]. In our study population, the median length of remaining bowel was 35 cm (range, 10 to 70 cm). Even with only 10 cm of small bowel remaining, intestinal autonomy could be reached.

Table 3 depicts other prognostic factors. Total bowel length doubles in the last 15 weeks of pregnancy and further lengthening occurs postnatally [2,6]. Regenerative capacity is therefore highest in young children. This holds true especially for premature children in whom bowel length can increase to a large extent. Relative bowel length (bowel length in relation to age) is therefore a more important prognostic factor than absolute bowel length.

Anatomical characteristics and functional integrity of the remaining bowel are also prognostic factors: the ileum can compensate for loss of jejunum (especially regarding the absorption of micronutrients) but not the other way around [6,7]. Therefore, prognosis is better when ileum remains as compared to when jejunum remains in situ.

Presence of the ileocecal valve (ICV) and (part of the) colon is also of paramount importance [7]. The ICV has a dual function: controlling passage of fluids and nutrients (the “ileal brake”) and preventing reflux from the colon. The latter prevents colonic micro-organisms in reaching the ileum [8]. Although resection of the ICV might induce an increased transition speed and bacterial overgrowth, conserving it may increase the survival of children with SBS [8,9]. However, it might be that this improved survival is not due to the presence of the ICV itself, but due to the presence of the distal ileum. As stated above, the function of the distal ileum, eg, absorption of bile acids and vitamin B12, cannot be compensated by more proximal small bowel [10]. A bowel resection should therefore be performed as conservatively as possible. Bowel continuity should be aimed for to make maximal use of the remaining bowel.

Finally, prognosis of patients with SBS is also influenced by the occurrence of complications such as sepsis and TPN-related liver failure (see below) [4].

Bowel Rehabilitation

In almost 50% of cases, intestinal rehabilitation was initiated by patient referral to our center. In three cases, the indication for referral was screening for bowel transplantation. Eventually, none of the cases required bowel transplantation because they all reached intestinal autonomy.

The Dutch Intestinal Failure Foundation, comprising the only Dutch bowel transplantation center and both home TPN centers for children and adults, has established the Dutch Committee on Short Bowel Syndrome. After establishing this nationwide collaboration, referral to our center increased significantly when compared to the decade before [1]. Therefore, concentration of expertise seems an important aspect for referring centers. The fact that a relatively large number of patients was not referred from other...
Table 3. Prognostic Factors for Short Bowel Syndrome

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<th>Factor</th>
<th>Percentage</th>
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<tr>
<td>Gestational age (and age at onset of short bowel syndrome)</td>
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<tr>
<td>Length of remaining bowel</td>
<td></td>
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<tr>
<td>Anatomic location (jejunum and/or ileum)</td>
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<tr>
<td>Presence or absence of ileocecal valve</td>
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<tr>
<td>Length of remaining colon</td>
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<tr>
<td>Presence or absence of stoma</td>
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<tr>
<td>Infectious complications (especially sepsis caused by a central venous catheter infection)</td>
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<tr>
<td>Total parenteral nutrition-induced cholestasis</td>
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centers reflects the fact that the UMCG serves 2 to 3 million inhabitants of the country.

Although not all studies on intestinal rehabilitation programs show a clear survival benefit, it seems that a dedicated program invariably decreases TPN-induced liver failure and resulting deaths. A dedicated program also leads to fewer CVC infections, an improved nutritional state, a higher chance of decreasing or even ending TPN, integration and continuity of highly specialized care, higher patient (and parent) satisfaction, and improved communication with patients and their parents [11–14].

Enteral Feeding

To stimulate bowel adaptation, minimal enteral feeding is started as soon as bowel motility occurs after surgery. Choice of feeding is related to several factors, such as age and anatomical factors of the remaining bowel [15]. By starting as soon as possible with small amounts of oral feeds (liquids or solids) suction and swallowing reflexes are stimulated and an aversion for food is prevented. TPN-related liver function disorders might also be diminished by early enteral feeding [5,6,10].

Central Venous Access

CVC-related complications (eg, infection, thrombosis, occlusion, and dislocation) occurred on average 4 times per patient, which is in accordance with the literature [6,16,17]. Each complication necessitating renewed CVC placement increases the importance of venous access, as recurrent CVC-related sepsis and absence of an adequate venous access are indications for bowel transplantation.

As CVC-infections are among the most important complications, preventing of such complications will improve outcome. In our center, tauroidine locks are routinely used. Tauroidine has a broad spectrum activity against bacteria and fungi, preventing adhesion of the micro-organism to the surface of the line [16]. Other measures for prevention of infectious or thrombotic complications are prophylactic anticoagulants, eg, with low molecular heparins. In a recent study, 3-year infection- and thrombosis-free survival was 46% and 93%, respectively, with prophylaxis versus 19% and 48% without prophylaxis, respectively [18].

TPN-induced Cholestasis

TPN-induced cholestasis is a frequent complication of children on TPN. It can progress rapidly to liver failure, necessitating liver transplantation. One of the factors contributing to cholestasis is nutrients reaching the liver via the systemic blood flow as opposed to the portal circulation. Other important factors are recurrent septic episodes, bacterial translocation, and changes in the enterohepatic circulation [19]. Factors such as prematurity, low birth weight, and immaturity of the liver also play a role [3,20].

In our population, a more or less severe form of TPN-induced cholestasis occurred in 68% of patients. This percentage is higher than the 50% mentioned in the literature [3]. Cholestasis occurred after a median of 20 weeks, which is relatively late when compared to the 4 to 12 weeks mentioned in the literature [3]. The relatively high incidence might therefore be due to the long duration of TPN in our population. The incidence of end-stage liver failure ranges from 25% to 85% in neonates receiving long-term TPN. In our population, one patient underwent a liver transplantation due to end-stage liver failure.

TPN is administered in a standard composition of carbohydrates, proteins, and lipids. When there were signs of TPN-induced cholestasis, the composition was altered: 100% fish oil (Omegaven: Fresenius Kabi) was added and soy oil (Intralipid: Fresenius Kabi) was removed. The use of omega-3 fatty acids has a protective and therapeutic effect in TPN-induced cholestasis [20,21]. In our center, fish oil-based emulsions are now used to prevent further deterioration of intestinal failure–associated liver damage.

Surgical Options Not Including Bowel Transplantation

Surgical interventions such as adhesiolysis or correction of stenoses can significantly improve bowel function. Of course, one should always aim at restoration of bowel continuity to maximize functional capacity of the bowel. Bowel function might also be improved by an autologous gastrointestinal reconstruction (AGIR) [22], AGIR comprises a multitude of procedures, of which the longitudinal intestinal lengthening procedure (LILT procedure, also called Bianchi procedure) and the serial transverse enteroplasty (STEP procedure) are currently the most performed [23,24]. During the LILT procedure the widened bowel is spliced longitudinally in the midline. This can safely be done due to the vasculature of the bowel which bifurcates in the midline of the bowel. After longitudinal closure of each half of the bowel, they are anastomosed in a serial fashion. This leads to a doubling of the bowel length and a reduction of the bowel diameter. During a STEP procedure, the bowel is stapled partially in a transverse way to decrease the passage of luminal content. Long-term survival after both procedures is excellent, exceeding 85% [25]. Among the other less frequently used procedures are the reversed segment technique, tapering of the dilated bowel, or the construction of a valve [26–29].

The goal of these surgical procedures is to avoid stasis of luminal contents and thereby prevent bacterial overgrowth, while also increasing contact time between mucosa and luminal contents and thus improving absorption of nutrients. In our series, one patient underwent a LILT...
procedure, thereby doubling the remaining jejunum to 60 cm. This led to intestinal autonomy after more than 11 years of TPN.

Small Bowel Transplantation

Indications for small bowel transplantation are end-stage liver failure; loss of venous access; recurrent line sepsis; and frequent, severe dehydration [6]. There is no consensus regarding the optimal timing of transplantation. Five-year survival rates do not exceed 50%. Small bowel transplantation is therefore only warranted when there are no other therapeutic options. In the present series, bowel transplantation has not been necessary. During the same time frame, 5 children were transplanted because congenital forms of intestinal failure, eg, for microvillus inclusion disease. The analysis of this category of patients is beyond the scope of the present paper.

Patient Survival

Bowel rehabilitation was not successful in three patients. Two of them died as a result of abdominal sepsis. The overall mortality in the present cohort (11% after a median follow-up of 25 months) is comparable with the literature [7–9].

CONCLUSION

Multidisciplinary treatment of intestinal failure by a dedicated team has resulted in intestinal autonomy in SBS patients, for many of whom the prognosis would have been deemed inauspicious preoperatively in the past. Limiting length of bowel resection, liver function preserving–TPN, preservation of venous access, and early enteral feeding are all essential factors in the treatment of children with an anatomical SBS. Implementation of a multidisciplinary intestinal rehabilitation program in 2001 has led to 84% intestinal autonomy with majority of patients showing adequate growth and development. Treatment of patients with SBS should therefore be limited to a specialized center.

REFERENCES


