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Early Structured Surgical Management Plan for Neonates with Short Bowel Syndrome May Improve Outcomes

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Abstract
Background In children with short bowel syndrome, maximal adaptation of the bowel after extensive resection is thought to occur during the first 2 years of life. The aim of the present study was to review children with short bowel syndrome from two intestinal rehabilitation centers, comparing those undergoing lengthening procedures <365 days of age (early) versus those whose lengthening procedure was carried out >365 days of age (late).
Methods Retrospective data collection was performed from January 2004 to December 2010 in Manchester, UK, and from December 2006 to December 2010 in Brussels, Belgium. Both medical centers follow a similar intestinal rehabilitation program (IRP). Data collected included population demographics, bowel length preoperatively and postoperatively, age at operation, parenteral nutrition (PN), central access, and complications.
Results Complete data were available for eight children who underwent lengthening surgery at <365 days of age, and six who underwent the procedure at >365 days of age. Diagnoses were similar. Groups were matched for gestation and birthweight, with no statistical difference in preoperative and postoperative bowel lengths. The mean duration of PN postoperatively was 378 days in the early cohort and 589 days in the late cohort. This trended toward statistical significance ($p = 0.071$). Full enteral autonomy was achieved at 17 months (early) and 59 months (late) ($p = 0.01$). Patients in the early group required fewer central lines than those operated on later ($p = 0.035$).
Conclusions Enrolling children into an IRP involving early (<365 days of age) lengthening surgery allows a shorter postoperative time to allow weaning to full enteral nutrition, as well as fewer central lines. Both outcomes provide benefits for the child and family, allowing an earlier return to normal life.

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Introduction

Short bowel syndrome (SBS) is a multisystem disease secondary to loss of bowel [1]. The adaptation process after bowel resection starts within 48 h, allowing for an increase in intestinal surface area [2]. Adaptation is continuous and may take up to 4–7 years to complete [3], with changes being the most rapid during the first postoperative year of life. Patients left to wait for adaptation without attempting to enhance their potential to adapt are more prone to severe complications resulting in high morbidity and mortality [4]. Particularly this approach tends to ignore the deleterious effects of PN on liver function. With all these potential complications it is ideal to wean the infant off PN as soon as possible. Managing this relatively small population of patients with severe SBS is challenging and requires a structured multidisciplinary intestinal rehabilitation program (IRP) [5] encompassing the management of central venous lines with vein preservation, hepato-sparing

parenteral nutrition (PN), early introduction of oral feeding, formation of tube stomas for controlled bowel expansion, and autologous gastrointestinal reconstruction (AGIR) surgery [6]. If PN is prescribed on the basis of the child's centile chart, deleterious effects on the liver may develop, resulting in a higher morbidity and mortality. Thus every effort should be made to preserve liver function even if that means a suboptimal increase in weight for a period of time [1]. We hypothesized that early AGIR surgery performed during the 1st year of bowel adaptation increases significantly the outcome of patients affected by SBS, particularly in terms of weaning them from parenteral nutrition. To confirm our hypothesis, the aim of the present study was to compare outcomes in two cohorts of children who underwent AGIR before and after 1 year of age.

Methods

Patient Population

Retrospective data collection concerning pediatric patients affected by SBS starting in the neonatal period and undergoing AGIR procedures from January 2004 to December 2010 in Manchester and Brussels was performed (in Manchester and from December 2006 to December 2010 in Brussels). Inclusion criteria were neonatal SBS and AGIR surgery. Data collected included patient demographics, initial diagnosis of SBS, age at AGIR, preoperative and postoperative bowel length, duration of PN, presence of ileocecal (IC) valve and colon, number of central lines required, and complications. Children were separated into two groups depending upon the timing of lengthening surgery, either less than 365 days of life (early) or more than 365 days of life (late).

Children from both medical centers were enrolled into an IRP either at birth or upon referral. The two centers followed similar standardized intestinal rehabilitation programs that included the use of central vein preservation, hepato-sparing total PN, minimal surgery at birth (if enrolled at birth), early enteral feeding, AGIR surgery, and social integration [1].

Data Analysis

All data were tested for normality with the Shapiro–Wilk test. Differences in both gestation and birthweight between the groups were determined with the Mann–Whitney *U*-test. In addition, the Wilcoxon rank correlation and the Kruskal–Wallis tests were employed to analyze the differences between bowel length before and after surgery and differences between groups, respectively. The Mann–Whitney *U*-test was used to determine any further differences between groups. Statistical significance was accepted at $p < 0.05$, and all statistical analysis was performed with PASW 17 for Windows (SPSS, IBM, New York).

Results

From the two centers, data were collected on 14 children with completed episodes. Eight of these children underwent operation during the first 365 days life (early), and six children after 365 (late). There were six male and two female children versus three male and three female children in the early and late cohorts, respectively. Mean gestational ages for early and late children were 33.75 weeks versus 35.6 weeks (ns), and mean birthweights were 2,244 g versus 2,122 g (ns) (Table 1). The primary etiologies leading to SBS were gastroschisis ($n = 2$), gastroschisis and atresia ($n = 2$), gastroschisis and volvulus ($n = 2$), jejunoileal atresia/multiple atresias ($n = 4$), NEC ($n = 1$), and volvulus ($n = 2$). In the early group four children underwent a LILT (longitudinal intestinal lengthening and tapering) procedure, and four underwent the STEP (serial transverse enteroplasty) procedure. In the late group, four underwent LILT and two had the STEP procedure. Mean preoperative bowel lengths were 39 cm (early) versus 48 cm (late) ($p = 0.475$). Postoperative bowel lengths were not significantly different between groups ($p = 0.796$), although in both groups there was a significant increase in length after operation ($p = 0.032$). Age at surgery was statistically different ($p = 0.002$), and the number of central lines each group required was statistically different, with means of 3

Table 1 Descriptive and surgical outcome data for the early and late surgery groups (mean ± SD)

	Early	Late	*p* Value
Gestation, weeks	33.8 (3.8)	35.6 (2.7)	0.42
Birthweight, g	2,244 (725)	2,122 (449)	0.66
Age at surgery, days	171 (52)	879 (395)	0.002
Preoperative small bowel length, cm	39.1 (20.1)	48.3 (32.2)	0.48
Postoperative small bowel length, cm	72.0 (34.1)	90.0 (64.76)	N0.80
No. central lines required	3.6 (1.2)	5.5 (2.0)	0.035
Postoperative PN, days	361 (225)	916 (847)	0.071
Age at full enteral nutrition, months	17 (7.4)	59 (39)	0.01

(early) versus 5 (late) $p = 0.035$. A trend to significance was found between the age at surgery and the number of days of postoperative PN required ($p = 0.054$), as well as the number of postoperative days of PN (early: 361 days $\pm$ 225; late: 916 days $\pm$ 847) between the groups as a whole ($p = 0.071$). In one child in the early group it was possible to retain the IC valve, and all children had at least half of their colon. One child within the late group required liver transplant for intestinal failure associated liver disease (IFALD).

Discussion

Only a few decades ago severe SBS was a terminal diagnosis, with the first patient surviving massive bowel resection being described in 1880 by Koeberle [7]. There was no effective nutritional support or surgery and withdrawal of care was often taken into consideration. The advent of PN allowed survival and growth [8]. Nevertheless, the current course for patients with SBS is far from smooth, with many children experiencing several complications related to the use of PN and dysmotility of bowel remnants [9]. Intestinal transplantation, isolated or combined with liver transplant, considered when autologous intestinal rehabilitation fails, is not a risk-free option [10]. The key for long-term survival of patients with SBS depends on the adaptation time of the residual bowel, and consequently on the time the child is dependent upon PN and related complications (infections, IFALD, etc.).

Flint in 1912 documented functional adaptation after massive resection [7]. Survival and adaptation appear to be greatly affected by short bowel length (SBL) [11–13], and ileocecal valve (ICV) preservation. In children, the ICV appears to be crucial for adaptation, especially if the SBL < 15 cm [11]. The extent to which the colon aids adaptation is still not clear [11, 12], although fermentation, which occurs within the colon, appears essential for absorption of nutrients in this group of patients [14]. In SBS the adaptive response is a hyperplastic process that involves the villus and crypt structures, as well as the musculature. There is evidence of upregulation of transporters, as well as brush border enzyme activity and an increase in the variety of gene products [7]. These changes reduce diarrhea, increase absorption, and improve nutrition [7]. Increases in jejunoileal length of up to 450 % have been reported to occur after massive resection with aggressive nutritional support alone [14]. Adaptation can arguably be enhanced through a three-pronged approach encompassing nutrition, pharmacologic manipulation, and surgery [15]. Enteral nutrition with lactose-free protein hydrolysate given either as a continuous or bolus feed enhances the adaptive response while PN supports growth and development during adaptation. Medications can treat the complications of SBS which impair adaptation, such as bacterial overgrowth, diarrhea, gastric hypersecretion, and gastrointestinal dysmotility. Surgical procedures such as the tube stoma to encourage dilatation followed by a serial transverse enteroplasty (STEP) or longitudinal intestinal lengthening and tapering (LILT) procedure can increase mucosal surface area and improve motility while reverse colonic segments slow transit time. Two studies have shown a postoperative increase in tolerance for enteral feeds, with enhanced bowel growth and nutrient absorption and fewer cather-related infections [16, 17].

All aspects of SBS care can be administered at any time, but it appears that early surgical intervention as described in the present study takes advantage of normal growth and development. This would suggest a benefit toward earlier adaptation when AGIR surgery within an IRP is offered during the first 365 days of life. Certainly it appears that children are able to adapt and survive with shorter lengths of bowel than their adult counterparts. It is possible that the high rate of growth from birth to $\sim$4 years of age provides an advantageous postsurgery recovery adaptation period.

Figueroa-Colon et al. [16] classically recommended surgical intervention be performed only after a period of adaptation, as the natural process may obviate the need for any other interventions. Although this may still be the case for many individuals, cases of early neonatal intestinal lengthening procedures in patients with dilated bowel at diagnosis have been reported in the literature to good effect [18]. With increased experience with the IRP we have become more aggressive with surgery, thus allowing earlier reduction in PN requirements. Although the numbers in the current study are low and the study data were collected in a retrospective manner, there appears to be a trend toward earlier AGIR surgery (<365 days) and a commensurate benefit from shorter postoperative periods of PN. The shorter requirement for PN generally equates to fewer numbers of central lines and earlier progression to enteral autonomy. Therefore intestinal rehabilitation programs that include early surgery are likely to improve quality of life (QOL) through these inferred benefits, as QOL has been shown to be reduced while patients are receiving PN [19–21] and to improve following AGIR surgery [22]. The inherent cost of therapy is also important in the current economic climate in which we practice [23]. With all these considerations, the more rapid the adaptation, the more complication-free the treatment of SBS is, the more the child and family will benefit.

Conclusions

Early structured intervention appears to improve the clinical outcome in infants with SBS by reducing the morbidity and mortality associated with PN. Improvement in these

factors secondary to early active management in neonates with SBS who are unlikely to be weaned from intravenous nutrition could improve QOL and cost-effectiveness in a group of children otherwise requiring meticulous long-term care while on PN [24]. Indeed, one of the fundamental goals of the program is life without PN.

Conflicts of Interest None.

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