A 10 YEARS SBS RETROSPECTIVE STUDY OF NEONATES AND CHILDREN

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Abstract

Introduction: Short bowel syndrome (SBS) neonates have complex management challenges, meaning a significant health care extra cost. This is 10 years retrospective SBS study-based estimate of children and neonates in our hospital. Population estimate of the incidence and mortality rate of neonates with SBS is not so accurate because of the differences in the definition, follow-up and regional referral patterns. The introduction of total parenteral nutrition (TPN) led to a remarkable improvement in the survival of SBS patients, but unfortunately the most common cause of death in SBS patient`s is also TPN-induced hepatic dysfunction. Even though the survival of patients with less than or equal to 40 cm of residual small bowel is now routine. The long term survival of infants with as little as 20 to 30 cm small bowel can be expected. The management goal of these patients is to reduce the duration of TPN and to maximize intestinal nutrient absorption. It is difficult to predict the duration and the type of nutritional support for patients with SBS. Some patients may require permanent parenteral nutrition on either a continuous or intermittent basis depending on the length of the residual bowel. *Objective:* To evaluate the direct and indirect evidence that adaptation occurs after an extensive bowel resection, to review the factors that influence adaptation and to assess the strategies used in attempts to optimize this process. *Methodology:* A retrospective medical record review of newborns and children with SBS treated at our hospital between 2007 and 2017. Medical records of patients studied were retrieved from our archives and analyzed. *Results:* a *p*-value less than 0.05 (*p*-value = 0.033) was obtained, being statistically significant proving that there is a direct correlation between the post-operation intestinal length and the duration of parenteral nutrition. *Conclusion:* The major predictors of weaning from PN are adjusted small bowel length and the amount of energy patient can derive from enteral feeding attempts, also as a result of new management strategies combined with a multidisciplinary team approach, majority of patients will wean from PN despite short intestinal length.

Keywords: short bowel syndrome, incidence, parenteral nutrition, mortality, outcomes

Introduction

Short bowel syndrome (SBS) results from the alteration of intestinal digestion and absorption that occurs after extensive bowel resection. It is a complex disorder with nutritional, metabolic, and infectious consequences. The amount of resection or remaining bowel generally dictates the degree of malabsorption and consequentely the need for specialized enteral nutrition or parenteral nutrition (PN). Intestinal failure in the context of SBS is defined as a dependence on PN to maintain minimal energy and fluid requirement for growth in children. The incidence of extreme SBS in the neonatal age group is around 3-5/100,000 birth/year. The prevalence has improved over the last 2 decades due to an enormous progress in intensive care medicine, while the prognosis of babies with severe intestinal disease and/or following major surgery has drastically improved. Short bowel syndrome occurs when the functioning gut mass is reduced below the amount necessary for adequate digestion and absorption of food and fluid. Although the absorptive function of the intestine does not always correlate with residual bowel length, SBS is usually defined anatomically as less than 30% of normal intestinal length (<75 cm) in children. In the failing intestine the inability to absorb nutrients, fluids, and electrolytes eventually leads to clinical deficiencies and if an increase in oral intake is not sufficient to compensate for this malabsorption, then PN support is required. Short bowel syndrome (SBS) is a devastating condition with a mortality rate of up to 40% in neonates and also with significant morbidity. The causes of SBS are the following: necrotizing enterocoliltis 32%, atresia 20%, volvulus 18%, gastroschizis 17%, aganglionosis 6%, others 7%.

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Institution based estimates of incidence and mortality was carried out using data from our hospital archives 10 years patient`s records. Figure 1 shows the incidence of SBS in the general population (n=53) and in our reference SBS poulation (n=10) per year. While in SBS population the distribution/year was quite homogenous, with mode and median equal to 1, in the general population the distribution shows a decreasing trend, with maximum peak in 2012 (9 SBS cases).

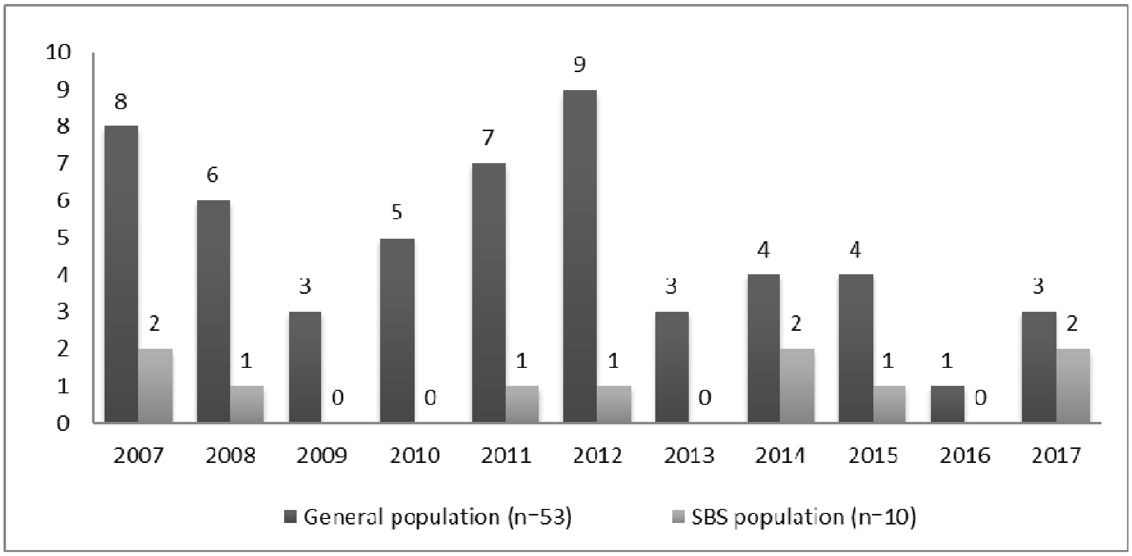

Figure 1. The incidence of SBS patient`s (number) within the reference 10-years period of time, histogram.

In the general population, the incidence of SBS was much higher in the premature infants (less than 37 weeks) representing 35.84% (19 patients). In our reference group, however, the rate of premature patients was 40%, out of which 30% were male and 10% female, thus proving that SBS is multifactorial and not influenced by prematurity alone as a single factor. SBS fatality case rate was 3 out of 53 patients studied (5.66 %). The specific cause of death (for children less than 4 years old) was mainly cardio-respiratory arrest, acute respiratory insufficiency and multiple organ failure Syndrome (MOFS). Table 1 defines the frequency rate of the main pathologies leading to SBS in the general studied population (n=53) and in the SBS studied population (n=10). In the general population study (n=53) gastroschisis was reported as the principal diagnosis in 17 patients (32 %), while in the specific population studied (n=10) gastroschisis was reported in 4 patients (40%). However, intestinal atresia represented 37 % in the general population cases studied (n=53) and just 20 % in the specific population cases studied (n=10).

Table 1. Comparison between rates of main diseases producing SBS in the general studied population (n=53) and the SBS reference population (n=10).

Frequency (%)	*General studied population (n=53)*	*Disease*	*SBS studied population (n=10)*	*Frequency (%)*
32.07547	17	***Gastroschisis***	4	**40.0**
7.54717	4	***Volvolus***	2	**20.0**
9.433962	5	***Intussusception***	0	**0**
37.73585	20	***Small intestine Atresia/Stenosis***	2	**20.0**
13.20755	7	***Others (Necrotizing enterocolitis, etc)***	2	**20.0**
100	***53***	***TOTAL***	***10***	***100***

Extensive intestinal resection leading to SBS is rarely necessary in older children.

Age was the first data analyzed and the mean age on admission in the SBS reference population was 896.7 ± 1818.87 hours. We calculated age in hours because majority of our patients (40%) were admitted in the first 24 h of life. Another 40% were admitted in the first one month, out of which 20% in the first week another 20% during the first month. Admission in the first 6 months of life and/or later in life was very rare. Table 2 illustrates the age on admission in both population studied.

Table 2. Age on admission in the general studied population (n=53) and the SBS reference population (n=10).

%	*Nr of pts*	*Age*	*Nr of pts*	*%*
30.18868	16	***< 24 h***	4	40
41.50943	22	***1 - 30 days***	4	40
9.433962	5	***1 - 6 months***	1	10
3.773585	2	***6 - 12 months***	1	10
3.773585	2	***> 12 months***	0	0
11.32075	6	***unknown***	0	0
100	***53***	***TOTAL***	***10***	***100***

Weight on admission was also studied and it was essential for subsequent postoperative follows-ups. Surprisingly, the mean weight calculated at 2522 ± 656.51 g falls within the normal weight range for newborns (2500 to 5000 g). However, when compared with the calculated mean weight for the general population (n=53) the value was much lower (mean weight value being 3640 ± 2948 g). SBS is the main cause of intestinal failure (IF) in children and has a higher morbidity and mortality rate. The adaptation changes that takes place after an extensive intestinal resection depends on the resected intestinal length, the location of the residual intestine and the nature of the disease responsible for the decision to resect a relatively large portion of the intestine. The length of residual intestine was measured in 10-cm segments from the ligament of Treitz advancing along the anti-mesenteric border of a slightly stretched intestine. The length of residual small bowel varied from 37 to 75 cm. Patients with residual intestine above 75 cm were excluded from the SBS reference group since their PN did not exceed a period of two weeks. While some patients received daily trace elements (added to the standard nutrient formulas) and lipids every other day, others received standardized formulas with or without lipids. During the immediate post-operation phase, continuous TPN was introduced until the first bowel movement occurred. This protocol assured an adequate circulating fluid volume with an acid-base and electrolyte balance. Patients received per kilogram body weight per day: dextrose, 3-4 g; lipids, 0.7-1 g. Nitrogen requirements were met by 0.10-0.15 g nitrogen contained in an amino acid solution (25 g of nitrogen per liter). Vitamins were administered separately twice a week. PN was delivered using a subcutaneous tunneled silicone catheter emptying into the internal jugular vein. EN was initiated gradually, starting with a strict non-fiber diet which was followed by a normal diet with or without intermittent or continuous TPN. Nutritional status was evaluated weekly. The body weight, urine, stool and serum albumin, pre-albumin, and transferring were frequently analyzed.

Aim

To evaluate the direct and indirect evidence that adaptation occurs after an extensive bowel resection, to review the factors that influence adaptation and to assess the strategies used in attempts to optimize this process.

Methodology

A retrospective medical record review of neonates and children with SBS treated at the Children`s Hospital "Louis Ţurcanu", between 2007 and 2017. First we analyzed the medical records of patients with preliminary diagnosis of SBS after an extensive intestinal resection in the *general population* (n=53), this was trimmed down further to a small cohort of patients that met our criteria for SBS referred to as *SBS population* (n=10). Dependency on PN for at least 25 days after surgery for congenital or acquired intestinal diseases and a minimal admission length of 30 days were parts of the criteria considered for a true short bowel syndrome. Microsoft Excel Worksheet was used for data collection and statistical analysis.

Results

Attention was focused first on the correlation between the length of the residual bowel (cm) and the duration of the exclusive/complementary PN and then the correlation between the length of the residual bowel (cm) and the initiation of total EN after surgery (days). In the reference SBS population (n=10) data analysis, the average length of the resected intestine was 122 ± 43.82 cm, these varied from 15 cm to 175 cm, while the mean length of post-operation residual intestine was 55.20 ± 11.28 cm, these varied from 37 cm to 75 cm. However, the average duration of PN alone was 40.1 ± 26.33 days, while the mean period of time needed to restore a complete EN was 42.5 ± 29.45 days. Using regression statistics, we calculated the correlation (R) between the residual bowel length and the time needed for the restoration of a complete EN. Tables 3 and 4 illustrate the steps taken towards this calculation.

Table 3. Regression Statistics.

Multiple R	**0.701299489**
R Square	0.491820974
Adjusted R Square	0.428298595
Standard Error	8.994559521
Observations	10

Table 4.

	df	*SS*	*MS*	*F*	*Significance F*
Regression	1	626.3831921	626.3831921	7.742483625	0.02383128
Residual	8	647.2168079	80.90210099		
Total	9	1273.6			

Table 5.

	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*Lower 95.0%*	*Upper 95.0%*
Intercept	66.62054297	4.993603002	13.34117729	9.52577E-07	55.1052738	78.13581214	55.1052738	78.13581214
EN	-0.268718658	0.096573434	-2.782531873	**0.02383128**	-0.491417396	-0.04601992	-0.491417396	-0.04601992

Our *p*–value being equal to 0.023 is statistically significant at a $p < 0.05$, so it was assumed that with a confidence interval (*C.I.*) of 95% with 1 degree of freedom (*df*), the post-operation residual intestinal length has direct correlation with the time needed for a complete restoration of EN.

The same formula and statistical calculation was used to find the correlation between post-operation intestinal length and the duration of PN, as illustrated in Tables 6, 7 and 8.

Table 6. Regression Statistics.

Multiple R	**0.671784622**
R Square	0.451294578
Adjusted R Square	0.382706401
Standard Error	9.346330998
Observations	10

Table 7.

	df	*SS*	*MS*	*F*	*Significance F*
Regression	1	574.768775	574.768775	6.579772104	0.033380701
Residual	8	698.831225	87.35390313		
Total	9	1273.6			

Table 8.

	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*Lower 95.0%*	*Upper 95.0%*
Intercept	66.7460514 4	5.384809 059	12.395249 43	1.67411 E-06	54.328659 48	79.163443 39	54.328659 48	79.163443 39
PN	-0.28793145 7	0.112249 312	-2.5651066 46	**0.03338 0701**	-0.5467788 36	-0.0290840 79	-0.5467788 36	-0.0290840 79

In this case a *p*-value less than 0.05 (*p*-value = 0.033) was obtained, being statistically significant, thus proving that there is a direct correlation between the post-surgery intestinal length and the duration of PN, at a confidence interval of 95%, with 1 degree of freedom. These results clearly demonstrated how the post-operation intestinal length can influence the quality of life and the evolution of a SBS pediatric patient. On the contrary, applying the same calculation, no statistically significant relationship was found neither between the length of the resected intestine and the duration of PN (*p*-value = 0.555, for $p < 0.05$, $df = 1$, *C.I.* = 95%) nor between the resected intestine and the time needed for restoration of a complete EN (*p* –value = 0.561, for $p < 0.05$, $df = 1$, *C.I.* = 95%).

Discussions

Pediatric SBS remains a management challenge with significant mortality. In order to improve the survival rate of patients we need to create an Advanced Intestinal Rehabilitation Center which includes dedicated surgery staff, gastroenterologists, neonatologists, nutritionists, pharmacists, nursing staff and social workers (3). Although absolute small bowel length is only slightly predictive of mortality, the percentage of normal bowel length (for a given infant's gestational age) is strongly predictive of mortality (if < 10% of normal bowel length) (1). The presence of the ileocecal valve (ICV) also strongly predicted weaning from PN; however, ICV was not predictive of survival. Death rate was just 5.66%, representing 3 out of 53 patients in the general population studied, while in the SBS population studied (n=10), there were no death observed.

Multiple nutritional, hormonal, and surgical therapies have evolved in the management of SBS patients in an attempt to improve life and decrease the duration of TPN dependency (5). Indirect evidence that intestinal adaptation takes place comes from the fact that patient`s with very short bowel lengths can become independent of PN after a period of months or even years (12). Whether a patient can be weaned from PN is dependent on a number of factors. The length of small bowel and the presence of colon are very important. Other factors that are useful in predicting whether intestinal failure is permanent are the time on PN (> 2 years) and the amount of energy the patient can derive from enteral feeding (13). PN associated liver failure (PNALF) or venous thrombosis with loss of vascular access, result in failure of PN therapy (2). Patients who can no longer receive PN may still have intestinal transplantation as the only therapeutic option left (4). The result of transplantation due to intestinal failure using either an isolated intestine or composite grafts (liver and intestine or multi-visceral including intestine), has improved considerably but remains disappointing (6). The introduction of hepato-protective strategies and multidisciplinary management has significantly improved the outcome of neonates with SBS who require PN (7). Successful and reproducible strategies to increase adaptation remain elusive despite an abundance of experimental data (13). More than 90% of infants now survive after extensive small bowel resection with PN and the remaining small intestine will adapt with time (11). Home-based PN allows children to be treated in the best psychosocial environment (8). The residual small bowel length remains an important predictor for the duration of PN in infants and children with SBS. Prompt restoration of intestinal continuity is associated with low risk of intestinal failure and subsequent cholestatic liver disease (9). Early enteral feeding after surgery is associated with reduced duration of PN and less cholestasis (10). Cholestasis (conjugated bilirubin ≥ 2.5 mg/dl) remains the strongest predictor of mortality (9).

Conclusions

The major predictors of weaning from PN are adjusted small bowel length and the amount of energy that patient can derive from enteral feeding attempts, while the major predictors of mortality in pediatric SBS are cholestasis and age adjusted small bowel length. These data permit better prediction of outcomes of pediatric SBS and may help to direct future management of these challenging cases, while accurate estimates will assist clinicians in counseling parents, allocating resources, and planning clinical trials. Also, as a result of new management strategies combined with a multidisciplinary team approach, majority of patients will wean from PN despite short intestinal length.

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