Journal of Pediatric Surgery 50 (2015) 289–292

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

Intestinal Rehabilitation of Infantile Onset Very Short Bowel Syndrome

Mikko P. Pakarinen [a,b,*], Niklas Pakkasjärvi [a,b], Laura Merras-Salmio [b,c], Antti Koivusalo [a], Risto Rintala [a]

[a] Section of Pediatric Surgery, Children's Hospital, University of Helsinki, Finland
[b] Pediatric Liver and Gut Research Group, Children's Hospital, University of Helsinki, Finland
[c] Section of Pediatric Gastroenterology, Children's Hospital, University of Helsinki, Finland

ARTICLE INFO

Article history:
Received 25 October 2014
Accepted 2 November 2014

Key words:
Adaptation
Autologous intestinal reconstruction
Bowel lengthening
Neonatal

ABSTRACT

Aim: The aim of this study was to evaluate treatment and outcomes of infantile very short bowel syndrome (SBS).
Methods: A retrospective review of 42 consecutive children treated for infantile onset SBS defined as remaining small bowel length less than 30% of predicted or more than 3 months of parenteral nutrition (PN) was performed. Surgical treatment and outcomes were compared between very SBS (VSBS, small bowel length less than 25 cm, n = 12) and SBS (more than 25 cm, n = 30).
Main results: Median follow-up was 5.7 years (IQR, 2.8 to 11). Absolute initial small bowel length (cm), presence of ileocecal valve (%), and proportion of remaining colon (%) was 15 (10 to 21) vs. 48 (32 to 60) ($P < 0.0001$), 58 vs. 50 ($P = 0.74$), and 95 (76 to 100) vs. 78 (60 to 100) ($P = 0.27$) in VSBS and SBS, respectively. More autologous intestinal reconstruction procedures per patient were performed in SBS group (27/30 vs. 5/12; $P = 0.002$) leading to intestinal autonomy in 2 of 4 VSBS patients in relation to 9 of 11 SBS patients ($P = 0.52$). Cumulative 5-year probability of weaning from PN was 46% (95% CI, 16 to 77) in VSBS and 92% (95% CI, 81 to 100) in SBS ($P < 0.01$). Five-year cumulative survival was 80% (95% CI, 54 to 100) in VSBS and 93% (95% CI, 83 to 100) in SBS ($P > 0.30$). No patients were transplanted. At final follow-up, plasma alanine aminotransferase (29 U/L [21 to 47]), bilirubin (6.0 μmol/L [3.0 to 8.0]), height (−1.4 SD [−2.5 to 0.1]), and relative weight (−5% [−12 to −2]) were similar between the groups.
Conclusion: Although survival, well-preserved biochemical liver function, and growth in VSBS patients are comparable to their counterparts with longer remaining bowel, regaining intestinal autonomy remains challenging in children with the shortest small intestinal remnant.

Short bowel syndrome (SBS) is characterized by reduced enterocyte mass, leading to failure of the intestine to provide sufficient fluid and energy absorption to meet the body's demands [1]. Intestinal failure is most often caused by SBS as a result of massive small intestinal resection [2]. The management of intestinal failure relies on parenteral nutrition (PN) to maintain adequate growth, hydration and nutritional status [3]. Prolonged PN predisposes to increased morbidity and mortality because of associated complications, such as central line–derived blood stream infections and cholestatic liver disease [2,3]. Weaning from PN is the single most important positive prognostic factor in SBS, and is mainly predicted by remaining small bowel length [1,4,5]. Recent developments in multidisciplinary intestinal rehabilitation with application of hepatoprotective PN, efficient infection control and autologous intestinal reconstruction (AIR) surgery to optimize function of the remaining bowel together with intestinal transplantation have improved overall outlook of pediatric SBS [3]. However, it is unclear how these improvements in management modalities have influenced outcomes of the infants with the shortest remaining small intestine. To this end, we have here analyzed intestinal rehabilitation outcomes of infantile onset SBS. All consecutive infants who had undergone greater than 70% small intestinal resection or who required PN for longer than 3 months without a primary intestinal motility disorder were included.

1. Patients and methods

1.1. Study design

Helsinki University Children's Hospital is a nationwide referral center for intestinal failure and has run the only intestinal transplantation program in the country since 2009 [6]. Prospectively collected database and medical records of all children treated for intestinal failure during 1988 to 2013 in our institution were retrospectively reviewed. From this group (n = 79), children with infantile onset SBS with the initial remaining small bowel length less than 30% of predicted or duration of PN more than 3 months were included. This cohort was subdivided based on absolute bowel length into 2 groups with (i) less than or equal to 25 cm or (ii) greater than 25 cm remaining viable small intestine. Patients with a primary intestinal motility disorder were excluded [6].

Collected data consisted of gestational age and birth weight, etiology of SBS, type and time of surgical procedures, anatomy of the remaining bowel, nutritional history, dependence of PN and survival. Growth

* Corresponding author at: Department of Pediatric Surgery, Children's Hospital, University of Helsinki, PL 281, 00029 HUS, Helsinki, Finland. Tel.: +358 50 4272981.
E-mail address: mikko.pakarinen@hus.fi (M.P. Pakarinen).

http://dx.doi.org/10.1016/j.jpedsurg.2014.11.018
0022-3468/

indexes and plasma levels of alanine aminotransferase (ALT) and bilirubin were measured at last follow-up. Growth data are expressed as height *z* score (SD) and height-adjusted weight (%) based on age- and sex-specific reference values of the Finnish population. Relative height-adjusted weight expresses percentage deviation from the population-based reference value. Percentage of age-adjusted predicted small bowel length was assessed based on available reference values and proportion of remaining colon as described previously [7,8]. Long-term outcomes of AIR surgery in 10 of these patients have been published previously [8].

1.2. Principles of medical treatment

Composition, volume and weekly number of cyclic nocturnal PN infusions were adjusted according to individual needs based on weight gain, growth and hydration status aiming at energy provision of 80 to 90 kcal/kg/day [6,8]. Always less than 30% of parenteral calories were provided as olive oil–based fat aiming at 1 g/kg/day. When increased risk (anticipated prolonged PN or infections) or biochemical signs of liver dysfunction were observed, lipid administration was further reduced by increasing proportion of lipid-free days. During the recent years olive oil–based PN lipid preparation was combined with fish oil and antimicrobial central venous line locks were employed [9]. By reducing the number of weekly infusions proportionally to increasing enteral intake the amount of PN was gradually tapered. Breast milk was initially used for enteral feeding and combined with lactose-free hydrolyzed iso-osmolar preparations when needed. Enteral formula was gradually changed to a more energy-dense low-osmolar whole protein preparation and solid feeds were initiated at the age 6 months to improve eating skills and adaptation. Percutaneous endoscopic feeding gastrostomies were used liberally, but continuous tube feeding was restricted during nights only if progression with preferred oral bolus feeding failed. To control high-volume intestinal excretions proton pump inhibitors and enteral sodium supplementation were used routinely.

1.3. Surgical management

Surgical management of SBS aimed at rapid reestablishment of intestinal continuity [8]. Longitudinal intestinal lengthening and tailoring (LILT) and serial transverse enteroplasty (STEP) were performed as described in detail previously [8,10,11]. Depending on a child's age, small bowel diameter above 4 to 5 cm was considered suitable for bowel lengthening. Simple tapering was performed with a linear stapler parallel to the long axis of the dilated small bowel segment when remaining bowel length was not critical. Enteric fistulas and strictures were dealt according to general surgical principles. The main indication for AIR surgery consisted of small bowel dilatation with or without obstruction in contrast examination and simultaneous symptoms of bacterial overgrowth including worsening tolerance of enteral feeds and increased intestinal secretions or D-lactate acidosis.

1.4. Ethics

The hospital's ethical committee approved this study.

1.5. Statistical analyses

Unless otherwise stated, data are presented as median and interquartile range (IQR). The Mann–Whitney U test was used to compare continuous variables, and the Fisher's Exact test for frequencies between groups. The Kaplan–Meier method with Mantel–Cox log-rank test was utilized in evaluation of cumulative risks of remaining on PN and survival. Duration of PN was calculated from the date of PN start to end of follow-up, cessation of PN, or death. Survival time extended from birth to the end of follow-up or death. Statistical significance was considered with $P < 0.05$.

2. Results

2.1. Patient characteristics

Altogether 42 patients fulfilled the inclusion criteria, including 12 VSBS and 30 SBS patients. The groups were comparable in terms of birth weight, gestational age, underlying etiology of SBS, and follow-up time (Table 1). Onset of SBS occurred during the neonatal period, except for 3 SBS patients, who underwent bowel resection leading to SBS later on during the first year of life. No cases were lost to follow-up.

Individual data on VSBS patients are shown in Table 2. In VSBS group median absolute and percentage of predicted initial remaining small bowel length was 15 cm (range, 7 to 25) and 11% (range, 3 to 29), respectively. The respective figures were 48 cm (range, 30 to 123) and 23% (range, 15 to 91) in SBS group ($P < 0.0001$ for both). No statistically significant differences between groups were observed for percentage of patients with preserved ileocecal valve and jejunoileocolic continuity or proportion of remaining colon (Table 3).

2.2. AIR surgery

As shown in Table 3, the percentage of patients who received AIR surgery was identical within the groups: 4/12 and 12/30 ($P = 0.74$). However, when all AIR operations in addition to bowel lengthening (STEP and LILT), such as tapering, resection of dilated small bowel segment, closure of enteric fistula and stricture removal were included, the overall frequency of AIR procedures per patient was significantly higher in SBS group (27/30 vs. 5/12; $P = 0.002$). The median age at the first AIR surgery was 27 months (12 to 61) in VSBS group and 13 months (11 to 41) in SBS group ($P = 0.76$). Four VSBS children underwent 5 AIR procedures (Table 2), whereas 11 SBS children underwent 1 to 5 separate procedures in 1 to 4 different operations. AIR reoperations were performed in 1 VSBS child and in 3 SBS children ($P > 0.99$). The 1 VSBS child underwent reSTEP for bowel redilatation after 11 months. Three SBS patients were reoperated. Of them, 1 underwent resection of anastomotic stricture and associated segmental bowel redilatation 17 years after the initial tapering enteroplasty, 1 underwent 2 STEPs and tapering enteroplasty owing to bowel redilatation 8 and 10 years after the initial tapering, and 1 underwent tapering enteroplasty 2 years after 2 STEPs performed in a referring hospital.

2.3. Parenteral nutrition dependence and survival

The overall duration of PN was 2.5 years (1.1 to 7.1) in VSBS and 0.8 years (0.4 to 1.2) in SBS group ($P < 0.01$). In total, 50% (6/12) of VSBS children weaned from PN after median of 1.5 years (range, 0.3 to 10) (Table 2), whereas 90% (27/30; $P < 0.01$) of SBS children weaned from PN after median of 0.8 years (0.4 to 1.0) ($P = 0.15$). Two of the 4 VSBS patients who received AIR surgery weaned off PN in comparison to 9 of 11 in SBS group ($P = 0.52$). Within VSBS group the median absolute length of the remaining small bowel was 19 cm (15 to 25) among the

Table 1
Characteristics of short bowel patients.

Variable	VSBS	SBS controls
Number	12	30
Birth weight (kg)	1.2 (0.7–3.3)	2.2 (0.9–3.5)
Gestational age (w)	30 (27–36)	35 (28–37)
Etiology of SBS		
NEC	5 (42)	14 (47)
Volvulus	3 (25)	7 (23)
Atresia	2 (17)	5 (17)
Gastroschisis	2 (17)	4 (13)
Follow-up time (y)	6.9 (2.3–11)	4.7 (3.2–11)

Data are median (interquartile range) or frequency (percentage).
NEC, necrotizing enterocolitis; VSBS, very short bowel syndrome.
$P > 0.05$ for all comparisons between groups.