Neonates With Short Bowel Syndrome
An Optimistic Future for Parenteral Nutrition Independence

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IMPORTANCE The introduction of hepatoprotective strategies and multidisciplinary management has significantly improved the outcome of neonates with short bowel syndrome (SBS) who require parenteral nutrition (PN).

OBJECTIVE To determine the probability of weaning from PN based on intestinal length in neonates with SBS amidst the new era of hepatoprotective strategies and multidisciplinary management.

DESIGN, SETTING, AND PARTICIPANTS Retrospective medical record review at a single-center academic institution. Neonates with no more than 100 cm of small intestine at a corrected gestational age of no more than 30 days who were diagnosed with a surgical gastrointestinal disease and PN dependent for at least 2 weeks were included. Data were collected from January 1, 2004, through June 1, 2012.

EXPOSURE Neonates with SBS requiring PN.

MAIN OUTCOMES AND MEASURES The probability of wean from PN without reinitiation for at least 1 year, as determined by logistic regression. Predictors of wean were evaluated using exact conditional logistic regression. Predictors of time to wean were determined by Cox proportional hazards regression.

RESULTS Sixty-three patients with a median (25th percentile, 75th percentile [interquartile range (IQR)]) gestational age of 31 (27, 35) weeks, birth weight of 1423 (895, 2445) g, small intestinal length of 41.0 (24.0, 65.0) cm, and predicted length of 29.0% (17.1%, 45.5%) underwent analysis. Fifty-one patients (81%) received a fish oil-based lipid emulsion (1 g/kg/d), 40 (63%) were weaned, 11 (17%) remained PN dependent, 4 (6%) underwent transplant, and 8 (13%) died while on PN. Excluding patients who underwent transplant or died, the median (IQR) small intestinal length was 55.0 (28.0, 75.0) cm in weaned and 26.0 (14.0, 41.0) cm in PN-dependent patients \((P = .006)\), with 40 of 51 (78%) weaned by study end. The cumulative probability of wean for patients with at least 50 cm of small intestine was 88% after 12 and 96% after 24 months. Patients with less than 50 cm of small intestine had a cumulative probability of wean of 23% after 12, 38% after 24, and 71% after 57 months. Small intestinal length was found to be the primary predictor of wean. Notable predictors of time to wean included the amount of small intestine remaining (hazard ratio, 1.94 [95% CI, 1.45-2.58] per 20 cm of intestine; \(P < .001\)), entirety of care within our institution \((3.27 \ [1.59-6.72]; P = .001)\), and intestinal lengthening procedure \((0.19 \ [0.04-0.84]; P = .03)\).

CONCLUSIONS AND RELEVANCE The majority of patients will wean from PN despite short intestinal length, likely as a result of new management strategies combined with a multidisciplinary team approach.

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In 1968, Wilmore and Dudrick published a report of the first infant whose growth and development was maintained on parenteral nutrition (PN) alone. Since that time, PN has revolutionized the management of intestinal failure. However, long-term use is associated with potentially serious complications, including liver dysfunction, which can be progressive while on PN. Often, and especially in the pediatric population, there is a race between liver failure and bowel adaptation. Liver failure, typically in association with sepsis, has historically been responsible for 67% to 89% of deaths among PN-dependent patients with short bowel syndrome (SBS). As a result of the significant morbidity and mortality associated with prolonged PN, several management strategies have been attempted. The introduction of a fish oil–based lipid emulsion in the management of SBS has dramatically improved the survival of infants by reversing cholestatic liver disease and has allowed for bowel adaptation and growth without progression to liver failure. Recent advances in neonatal intensive care and multidisciplinary management also have contributed to enhanced survival. The objective of the present study was to determine the probability of and factors associated with PN wean in neonates and infants with SBS amidst the new era of hepatoprotective strategies, multidisciplinary management, and an improved understanding of PN-associated liver disease.

Methods

A research study protocol (M09-12-0640) was approved by the institutional review board at Boston Children’s Hospital to conduct a single-center retrospective review of neonates with SBS. Surgical foundation billing records within the clinical encounter documentation system were queried for codes from the International Classification of Diseases, Ninth Revision (ICD-9) for short gut syndrome (v45.72), intestinal atresia (751.1), necrotizing enterocolitis (777.5, 777.50, 777.51, 777.52, and 777.53), malrotation (751.4), intestinal volvulus (560.2), gastrochisis/omphalocele (756.79), and feeding difficulty (779.3 and 783.3). Departmental databases were also searched to identify neonates from January 1, 2004, through January 1, 2009, with less than or equal to 100 cm of small intestine at no more than 30 days corrected gestational age (CGA), who were diagnosed with a surgical gastrointestinal disease, and who were PN dependent for at least 2 weeks. Electronic and paper medical records were used to confirm inclusion criteria and to collect demographic and clinical data. Reasons for exclusion included CGA of no more than 30 days before January 1, 2004, or after January 1, 2009, small intestinal length of more than 100 cm regardless of CGA or less than 100 cm at 30 days or more CGA, inadequate duration of PN (<2 weeks), and/or incomplete or missing medical record information that prevented identification of intestinal length, age at intestinal resection, or duration of PN.

Data were collected from birth until 1 of the following 4 study end points: wean from PN without reinitiation for at least 1 year, no wean from PN (ie, PN dependence), transplant, or death on or before the study end date of June 1, 2012. Demographic information, including date of birth, sex, gestational age (GA), CGA of 30 days, birth weight, birth length, and diagnoses resulting in short intestinal length were recorded. Operative notes and/or pathology reports were used to determine the residual intestinal length, and when these records were unavailable or ill-defined, intestinal length was estimated. Percentage of predicted small intestinal length based on GA for the most recent operative intervention within 30 days CGA was calculated using data obtained by Strujs et al on mean intestinal bowel length according to postconception age (27-29, 30-32, 33-35, 36-38, 39-40, and ≥41 weeks). Operative data collected included the number, type, and date of major abdominal procedures, number and type of functional intestinal stomas while on PN, and whether and when the ileocecal valve was resected. Procedures documented included exploratory laparotomy, intestinal resection, lysis of adhesions, intestinal anastomosis, strictureplasty, tapering enteroplasty, intestinal lengthening procedure (ie, Bianchi or serial transverse enteroplasty), peritoneal drain placement, and/or liver biopsy. Transplant was separately recorded as a study end point. In addition, documentation of surgical or radiologic placement of a feeding tube was recorded. Nutrition data included the duration of PN and the type of lipid administered. Laboratory data included bloodstream infections and citrulline levels while on PN. Adverse events resulting in death and transfer status were documented.

Data were collected using case report forms, entered into a commercially available statistical software database (SPSS Data Entry Builder, version 4.0, 2003; SPSS Inc), and imported into a different software program for data analysis (SAS, version 9.3; SAS Institute Inc). Continuous outcomes were summarized as median (25th percentile, 75th percentile [interquartile range]) or mean (SD) and compared across groups using a Wilcoxon rank sum test or 2-sided t test for comparison of 2 groups and Kruskal-Wallis test or analysis of variance for comparison of more than 2 groups. Associations between continuous measures were performed with a Spearman rank correlation. Cross-tabulations were evaluated with a Fisher exact test. All tests were 2 sided, with P < .05 established a priori as a threshold for statistical significance.

The predicted probability of weaning based on 10-cm increments of small intestinal length was estimated by logistic regression with an unconditional likelihood function. Analysis was restricted to the 51 patients who survived until the study end (June 1, 2012) and did not undergo transplant. In addition to small intestinal length, several potential predictors of weaning were considered, including (1) major surgical abdominal procedures, (2) components of surgical procedures (eg, ileocecal valve resection), (3) placement of a feeding tube, (4) surgical gastrointestinal diagnosis, (4) type of intravenous lipid administered, (5) bloodstream infection, (6) plasma citrulline levels of no higher than 15 μmol/L (to convert to milligrams per deciliter, divide by 57.081), and (7) demographics. These predictors were evaluated while on PN. Owing to sparse data for several of the predictors, exact conditional logistic regression was used to investigate predictors of weaning.

The method of Kaplan and Meier was used as a nonparametric estimator of time to wean. Comparisons between pa-
patients with at least 50 cm of small intestine (vs <50 cm) or with at least 50% of predicted small intestine for age (vs <SO%) were made using a log-rank test. Cox proportional hazards regression was used to investigate predictors of time to wean. The same effects investigated in the logistic regression analysis were considered in this analysis. Surgical procedures were incorporated into the model as time-varying covariates by defining a dichotomous predictor for each procedure equal to 1 on day t of PN if the patient already had the procedure before day t and 0 otherwise. The aforementioned surgical procedures and procedural components were considered. A stepwise modeling procedure was used to select the most parsimonious model, after forcing remaining intestinal length to be included in the final model. Variables were selected into the model iteratively using 0.10 and 0.05 probabilities for entry and retention, respectively.

Results

Six hundred seventy-five patients were identified initially by ICD-9 codes and surgical departmental databases. After further review, 581 patients were excluded with a small intestinal length of greater than 100 cm, 19 with missing medical record information, 9 with a small intestinal length of less than or equal to 100 cm at a CGA of 30 days or more, and 3 who never initiated PN (Figure 1). Sixty-three neonates met inclusion criteria of having a surgical gastrointestinal disease, small intestinal length of no more than 100 cm at a CGA of 30 days or less, and PN dependence for at least 2 weeks. The median GA was 31 (27, 35) weeks and birth weight was 1423 (895, 2445) g. Sex distribution included 40 boys (63%). Of the 63 neonates, 46 (73%) were transferred to our institution. Diagnoses resulting in short intestinal length were necrotizing enterocolitis (34 [54%]), jejunal atresia (16 [25%]), intestinal volvulus (11 [17%]), gastroschisis (8 [13%]), and ileal atresia (8 [13%]). Median small intestinal length at a CGA of 30 days or less was 41.0 (24.0, 65.0) cm with a range of 5.0 to 100.0 cm. Median percentage of predicted small intestinal length remaining based on CGA was 59.0% (17.1%, 45.5%) and ranged from 4.3% to 94.8%. Patients with a CGA of at least 40 weeks were found to have shorter predicted small intestinal length remaining than those with a CGA of less than 40 weeks (P = .03; Table 1). After omitting patients with a CGA of 40 weeks or more, no differences in predicted small intestinal length were found among the remaining age groups. Six of 63 patients (10%) had small intestinal length estimated based on previously published guidelines.

All neonates underwent at least 1 major abdominal procedure while on PN with a median of 2.0 (2.0, 4.0) and a range of 1.0 to 8.0 procedures. The frequency of each procedural type is included within Table 2. Fifty of 63 neonates (79%) had a functional stoma (duodenum, jejunum, ileum, or colon) while on PN. A feeding tube was placed in 50 neonates (79%), including surgical gastrostomy, 5 gastrostomy-jejunostomy, and 1 jejunostomy placement. The ileocecal valve was resected in 26 patients (41%) during the study period while on PN.

The median duration of PN was 10.3 (4.4, 28.3) months, ranging from 0.5 to 86.0 months. In association with PN, 51 patients (81%) received a fish oil-based lipid emulsion at 1 g/kg/d. Bloodstream infections were found in 43 neonates (68%) while on PN during the study period, with 11 (26%) having 1 infection, 10 (24%) having 2 infections, and 21 (50%) having 3 or more infections.

Of 63 neonates, 40 (63%) were weaned from PN, 11 (17%) remained PN dependent at the end of the study, 4 (6%) underwent multivisceral transplant, and 8 (13%) died while on PN (Table 3). These 4 cohorts did not differ according to patient demographics, diagnosis, and/or PN initiation (data not shown). Excluding those infants who underwent transplant (n = 4) or who died (n = 8), the median small intestinal length in patients weaned from PN (n = 40) was 55.0 (28.0, 75.0) cm compared with 26.0 (14.0, 41.0) cm in PN-dependent patients (n = 11) (P = .006). To qualify as weaned, patients required PN independence for at least 1 year, with the exception of perioperative reinitiation after the documented PN end date if the

**Table 1. Percentage of Predicted Small Intestinal Length**

<table>
<thead>
<tr>
<th>Age, wk</th>
<th>No. (%) of Patients</th>
<th>Mean (SD)</th>
<th>Median (IQR) [Range]</th>
</tr>
</thead>
<tbody>
<tr>
<td>27-29</td>
<td>5 (7.9)</td>
<td>41.0 (31.9)</td>
<td>35.0 (21.0, 40.0) [14.0-94.8]</td>
</tr>
<tr>
<td>30-32</td>
<td>9 (14.3)</td>
<td>25.4 (25.2)</td>
<td>18.8 (7.7, 29.8) [4.3-85.1]</td>
</tr>
<tr>
<td>33-35</td>
<td>22 (34.9)</td>
<td>37.5 (16.5)</td>
<td>41.4 (21.5, 48.3) [9.9-69.5]</td>
</tr>
<tr>
<td>36-38</td>
<td>13 (20.6)</td>
<td>34.5 (21.2)</td>
<td>31.6 (17.5, 52.6) [9.8-70.1]</td>
</tr>
<tr>
<td>39-40</td>
<td>1 (1.6)</td>
<td>60.4</td>
<td>60.4 [60.4]</td>
</tr>
<tr>
<td>≥41</td>
<td>13 (20.6)</td>
<td>20.6 (10.2)</td>
<td>23.0 (10.9, 29.3) [5.9-35.1]</td>
</tr>
</tbody>
</table>

Abbreviation: IQR, interquartile range.
Total duration was no more than 3 weeks. Figure 2A displays the predicted probability of wean based on 10-cm increments of small intestinal length in patients who were weaned vs patients who remained PN dependent. Eleven patients (28%) with small intestine of no more than 30 cm and 23 (58%) with small intestine of less than 60 cm were weaned. Overall, 40 of 51 patients (78%) weaned by study end, after excluding patients who underwent transplant and who died. Figure 2B displays the predicted probability based on percentage of predicted small intestinal length. Patients who died (n = 8) or underwent transplant (n = 4) were excluded.

Table 2. Residual Small Intestinal Length and Procedural History

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. (%) of Patients</th>
<th>Residual Small Intestinal Length</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Small intestine</td>
<td>63 (100)</td>
<td>45.2 (26.2)</td>
</tr>
<tr>
<td>Absolute length, cm</td>
<td></td>
<td>32.3 (20.3)</td>
</tr>
<tr>
<td>Predicted length, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Procedure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exploratory laparotomy</td>
<td>63 (100)</td>
<td></td>
</tr>
<tr>
<td>Intestinal resection</td>
<td>62 (98)</td>
<td></td>
</tr>
<tr>
<td>Anastomosis</td>
<td>50 (79)</td>
<td></td>
</tr>
<tr>
<td>Strictureplasty</td>
<td>5 (8)</td>
<td></td>
</tr>
<tr>
<td>Tapering enteroplasty</td>
<td>8 (13)</td>
<td></td>
</tr>
<tr>
<td>Bowel lengthening</td>
<td>9 (14)</td>
<td></td>
</tr>
<tr>
<td>Liver biopsy</td>
<td>25 (40)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: IQR, interquartile range.

Table 3. Study End Points

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No. (%) of Patients</th>
<th>Length of Residual Small Intestine, cm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Weaned from PN</td>
<td>40 (63)</td>
<td>54.6 (26.7)</td>
</tr>
<tr>
<td>PN dependent</td>
<td>11 (17)</td>
<td>27.3 (14.9)</td>
</tr>
<tr>
<td>Died</td>
<td>8 (13)</td>
<td>27.8 (10.0)</td>
</tr>
<tr>
<td>Underwent transplant</td>
<td>4 (6)</td>
<td>34.9 (25.0)</td>
</tr>
</tbody>
</table>

Abbreviations: IQR, interquartile range; PN, parenteral nutrition.
probability of weaning based on the percentage of predicted small intestinal length. With 50% of predicted length, the predicted probability of weaning was 0.95 (0.76, 0.99) and increased to 0.99, 0.99, and 1.00 with 70%, 80%, and 90% of predicted length, respectively. Of the 40 who were weaned, 9 patients (23%) continued to receive maintenance hydration fluid for a variable number of days per week and an overall length of time, although none of these patients resumed PN for the remainder of the study period.

The median PN duration was 6.5 (3.8, 14.7 [range, 0.5-57.1]) months in weaned patients, 50.5 (43.2, 61.7 [range, 35.8-86.0]) months in PN-dependent patients, 11.1 (8.4, 15.0 [range, 6.2-18.6]) months in patients who underwent transplant, and 9.8 (5.0, 13.4 [range, 2.3-19.8]) months in patients who died. Residual small intestinal length at a CGA of no more than 30 days was found to correlate with duration of PN in patients who were weaned (Spearman rank correlation, −0.57 [P < .001]). The cumulative probability of wean over time, stratified by intestinal length (<50 and ≥50 cm) and percentage of predicted intestinal length (<50% and ≥50%) is represented in Figure 3. For patients with small intestine of at least 50 cm, the cumulative probability of weaning from PN was 88% after 12 months and 96% after 24 months. Patients with small intestine of less than 50 cm had a cumulative probability of weaning of 23% after 12 months and 28% after 24 months. The cumulative probability of weaning in this latter group of patients reached 71% after 57 months. Among the patients with citrulline levels of less than 15 μmol/L (22 of 23 with <50% predicted small intestinal length), the cumulative probability of wean was 22% after 12 months of PN and 40% after 24 months.

Exact logistic regression was used to identify predictors of wean. Patients who underwent transplant and those who died were excluded from the analysis. Small intestinal length was found to be the primary predictor of PN wean. Patients who were weaned had a mean intestinal length of 54.6 (26.7) cm compared with PN-dependent patients with a mean length of 27.3 (14.9) cm (P = .002). After adjusting for small intestinal length remaining, the number of major abdominal procedures (ie, exploratory laparotomy) was associated with failure to wean (P = .009). Procedures including intestinal anastomosis (n = 41), tapering enteroplasty (n = 8), intestinal lengthening (n = 7), and strictureplasty (n = 5) were the individual candidate predictors evaluated. Peritoneal drain placement (n = 10), ileocecal valve resection (n = 23), and open liver biopsy (n = 24) were evaluated as procedural components. For the analysis, exploratory laparotomy and intestinal resection were omitted, as the majority of patients underwent these procedures. Intestinal lengthening was found to be a significant independent predictor after adjustment for small intestinal length. Among those who underwent this procedure, 2 of 7 patients (29%) were weaned compared with 38 of 44 patients (86%) who did not undergo the procedure (P = .003) with the probability of wean dependent on remaining intestinal length. In addition, nonsurgical predictors, including demographics, diagnoses, nutritional information, and bloodstream infections were evaluated. Fewer infections and earlier GA were found to be significant independent predictors that increased the probability of wean (P = .04 and P = .05, respectively, after adjustment for small intestinal length). In the multivariate analysis, the best fitting model consisted of small intestinal length (P = .009) and intestinal lengthening procedure (P = .04) (Figure 2C). No other predictor, when added to the model, was significant.

Predictors of time to wean were evaluated using Cox regression analysis for the entire group of 63 subjects. Stepwise proportional hazards regression resulted in a model contain-
ing the following 3 statistically significant predictors of time to wean: amount of small intestine remaining (hazard ratio, 1.94 [95% CI, 1.45-2.58] per 20 cm of intestine; \( P < .001 \)), whether the entire care was within our institution (3.27 [1.59-6.72]; \( P = .001 \)), and whether an intestinal lengthening procedure was performed (0.19 [0.04-0.84]; \( P = .03 \)). Ileocecal valve resection and the resultant duration of PN were evaluated and found to be statistically insignificant (0.52 [0.26-1.03]; \( P = .06 \)). These hazard rates were independent of all other predictors evaluated, and no other predictor added to this model, including other procedures and procedural components, was statistically significant.

Excluding patients who underwent transplant and those who died, 8 PN-dependent patients (73%) were boys with a median GA of 34 (28, 36) weeks and birth weight of 1910 (1150, 2750) g. The most common diagnoses in the PN-dependent group were necrotizing enterocolitis (36%) and jejunal atresia (36%), followed by gastrochisis (27%). Administration of PN was started on median day of life 3 (2, 14), and 100% of patients received the fish oil–based lipid emulsion for the management of PN-associated liver disease. Among these factors, the only significant difference between patients who were weaned and who remained PN dependent was the frequency of gastrochisis (3% vs 27% \( P = .03 \)).

There was no difference in demographics, initiation of PN, use of the fish oil–based lipid emulsion, or transfer status between patients who died (n = 8) and those who did not (n = 55). Patients who died had a median GA of 34 (27, 35) weeks with a birth weight of 1420 (800, 2860) g and were equally distributed by sex (4 boys and 4 girls). The most frequent diagnosis was necrotizing enterocolitis (4 patients [50%]), followed by gastrochisis (3 [38%]) and jejunal atresia (2 [25%]). Administration of PN was initiated within the first week of life for 5 of these 8 neonates (63%), and 7 neonates (88%) received a fish oil–based lipid emulsion. For the 8 patients who died, the median uncorrected age at time of death was 10.0 (6.0, 13.4) months, with cardiac arrest, multisystem organ failure, sepsis, shock, intracerebral hemorrhage, and withdrawal of care secondary to severe periventricular leukomalacia listed as the causes of death. One patient who died had been transferred to our institution.

Discussion

Short bowel syndrome is a condition that requires supplemental PN to sustain growth and development. The duration of PN has been shown to correlate directly with morbidity, and long-term use is associated with potential serious complications. Mortality has historically been related to residual intestinal length, absence of the ileocecal valve, incidence of sepsis, and liver failure. In particular, sepsis and cholestasis are well-known contributors to the high mortality rates. Although residual intestinal length has been correlated with survival, the introduction of hepatoprotective strategies in PN administration, advances in neonatal care, and an improved understanding of PN-associated liver disease has contributed to enhanced survival in neonates with SBS.

The results of the current study demonstrate that the majority of patients with SBS will wean from PN despite short intestinal length. Excluding patients who underwent transplant and those who died, 78% of patients achieved enteral autonomy, as defined by the absence of PN for at least 1 year. Even patients with extremely short small intestinal length weaned over time. Of the 40 patients who weaned, 29% had small intestinal length of no more than 30 cm. Furthermore, with 50% of predicted small intestinal length, the probability of wean was 0.95 (0.76, 0.99). The cumulative probability of wean in patients with small intestine of less than 50 cm was 23% after 12 months, 38% after 24 months, and 71% when continued to 57 months. These results support continuation of PN even with short intestinal length, despite intestinal transplant and comfort measures only being other available treatment options. The continuation of enteral autonomy over time has previously been demonstrated by Squires et al with 31%, 40%, and 47% of infants (independent of intestinal length) weaned from PN at 12, 24, and 60 months, respectively; however, autonomy was defined as the discontinuation of PN for more than 3 consecutive months, and the majority of data were collected before the introduction of fish oil–based lipid emulsions.

Intestinal length was found to be the primary predictor of wean from PN. Similar to previous reports, longer small intestinal length correlated with PN wean. In the present study, patients who weaned had a mean small intestinal length of 54.6 (26.7) cm compared with 27.3 (14.9) cm in PN-dependent patients. Collectively, these patients were similar with the exception of the frequency of gastrochisis, which was 3% in weaned vs 27% in PN-dependent patients. The overall incidence of gastrochisis was 13%, which included 3 patients who died. Nonetheless, this motility disorder could affect the ability to wean. Apart from small intestinal length, fewer abdominal procedures while on PN significantly increased the probability of wean. As previously suggested by Arsenault et al, the timing of operative intervention for PN-dependent patients with PN-associated liver disease may be important in the preservation of liver function. However, findings from Andorsky et al suggested that early restoration of intestinal continuity may ameliorate the development of PN-associated liver disease. Additional research is needed to further elucidate the optimal timing of surgical intervention among PN-dependent neonates in nonemergent settings. As a procedural component, resection of the ileocecal valve (41% of patients) was not shown to affect the probability of wean or duration of PN. Prior studies have demonstrated that the presence of an ileocecal valve shortens the duration of PN and hence contributes to wean, although these findings and other previously published studies found no such relationship. Intestinal lengthening was the only procedure found to significantly lower the probability of wean, with 29% of patients weaned compared with 86% who did not undergo the procedure. In addition, intestinal lengthening was shown to prolong the duration of PN. The present data caution against lengthening, as overall 78% of patients achieved enteral autonomy, including approximately one-third with a small intestinal length of no more than 30 cm. Despite the small sample size, the results of the current study demonstrate that the majority of patients with SBS will wean from PN despite short intestinal length. Excluding patients who underwent transplant and those who died, 78% of patients achieved enteral autonomy, as defined by the absence of PN for at least 1 year.
size, increasing length surgically does not appear to enhance or expedite wean.

Nonsurgical independent predictors of PN wean included fewer infections and earlier GA. Central venous catheter sepsis is a well-known serious and potentially virulent complication that can contribute to morbidity and mortality in PN-dependent patients. Proper catheter care and ethanol locks have likely reduced infection rates, although sepsis remains a significant problem in this population. An additional finding that has been used historically to predict PN independence is plasma citrulline level. The present data found that the cumulative probability of wean in patients with citrulline levels of less than 15 μmol/L was 22% after 12 months and 40% after 24 months. Although not all patients had citrulline levels measured, 22 of the 23 patients (96%) who did had less than 50% of predicted intestine length. Citrulline levels have been proposed as surrogate markers for intestinal length and function, with low levels predictive of PN dependence, although the present results demonstrate patients can be weaned from PN with levels as low as 3 μmol/L. Nonetheless, further studies are needed to more thoroughly evaluate citrulline concentrations in this setting.

One potential explanation for the high wean and low mortality rates may result from the introduction of hepatoprotective strategies, mainly lipid minimization and administration of a fish oil-based lipid emulsion compared with the traditional soybean oil-based lipid emulsion. From prior studies, an elevated direct bilirubin level resulted in significant mortality, especially in association with sepsis in PN-dependent patients. One study reported mortality approaching 90% in cholestatic infants receiving PN for longer than 1 year. Although the exact mechanism remains unknown, exposure to fish oil allows for the time necessary for intestinal growth and promotes adaptation with eventual achievement of enteral autonomy while avoiding cholestasis and progression to end-stage liver disease. Apart from the administration of fish oil to 81% of the cohort, management at an academic center with expertise in SBS and intestinal rehabilitation could have contributed to the study outcomes. The importance of a multidisciplinary management team within an institution has been shown previously to be beneficial and specifically correlated with improved survival. The present data are further supportive, as transfer status was a significant predictor that prolonged time to wean.

Conclusions

These results are encouraging, as it appears the majority of patients will achieve enteral autonomy. Although intestinal length is predictive of wean, even patients with intestinal length of less than 30 cm weaned over time. Despite the prolonged duration of PN, overall, 78% of patients weaned (excluding those who underwent transplant and those who died). Since the end of the study, 1 additional patient has been weaned from PN for longer than 1 year. These data should ultimately help to guide clinicians in counseling parents of PN-dependent neonates and provide hope that enteral autonomy should be achievable for the majority of patients. The present findings argue for persistence in the continuation of PN, implementation of hepatoprotective strategies, operative intervention only when necessary while on PN, caution when considering intestinal lengthening, and proper central venous catheter care. Management at an academic facility with expertise in neonatal SBS, management of long-term PN, and multidisciplinary care is recommended.

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Correction: This article was corrected on May 29, 2014, to fix the subtitle.

REFERENCES


