Catheter-Related Bloodstream Infections in Children with Short Bowel Syndrome: A Single Center Retrospective Study

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Abstract

Background: Pediatric short bowel syndrome (SBS) is a devastating clinical entity that is usually managed with parenteral nutrition (PN). Catheter-related bloodstream infection (CRBSI) is a serious complication of long-term PN. The aim of this study was to evaluate the incidence and risk factors of CRBSI in SBS children.

Methods: Nineteen pediatric patients with SBS were retrospectively recruited from Shanghai Children's Hospital between August 2015 and December 2019. Clinical data, including demographics, aetiology of SBS, site and type of catheters, duration of PN, comorbidities, and microbiological data regarding CRBSI, were collected and reviewed to assess the CRBSI incidence and associated risk factors.

Results: A total of 57 catheter insertions for PN were administered in 19 SBS children. CRBSI was identified in 11 cases among 6 patients during a total catheter days of 1907. The rate of CRBSI was 5.8 per 1000 catheter days. The common manifestations of the SBS children with CRBSI were fever (6/11, 54.5%), lethargy (5/11, 45.4%), stagnation of weight (7/11, 63.6%), and increment of enterostomy fluid (7/11, 63.6%). Potential risk factors for CRBSI included an absence of ileocecal valve (p=0.046), and long duration of PN (p=0.019). The most common microorganism isolated from the blood cultures was *Klebsiella pneumoniae* (6/11, 54.55%).

Conclusions: The rate of CRBSI was 5.8 per 1000 catheter days, and *klebsiella pneumoniae* was the most common isolated pathogen of CRBSI in the studied SBS children. An absence of ileocecal valve and long duration of PN were potential risk factors of CRBSI.

Introduction

Short bowel syndrome (SBS) is a severe malabsorptive condition resulting from a reduced length of the small intestine [1]. Pediatric SBS is defined as a need for parental nutrition (PN) more than 42 days after intestinal resection or a bowel length of less than 25% as expected [2, 3]. The most common etiologies are necrotizing enterocolitis (NEC) and congenital abnormalities in pediatric SBS [4]. The children with SBS experience diarrhea, malabsorption, growth stunting, and malnutrition as a result of loss of intestinal surface area. The intestinal function is inadequate to maintain the minimum necessary for the absorption of macronutrients, fluid, and electrolytes, therefore, PN is required to keep up health and/or growth in children with SBS [2].

Intravascular catheters are integral to deliver the nutrition to the patients with SBS. However, the use of catheters is often complicated by mechanical or infectious complications, which can be life-threatening to the patients [5]. Catheter-related bloodstream infection (CRBSI) is a serious complication of long-term PN, which can lead to loss of vascular access, advancing intestinal failure-associated liver disease, sepsis, and death [6, 7]. Children with SBS are at high risk of CRBSI. Previous studies have reported that the incidence of CRBSI among children with SBS and intestinal failure ranges from 0.9 to 11.5 per 1000 catheter days [8–11]. The incidence of CRBSI in children are associated with impaired gut permeability,

altered gut microbiota, immune system dysfunction, comorbidities, the presence of an indwelling central venous catheter (CVC), and prolonged PN [12, 13].

In this study, we conducted a single-center retrospectively study to evaluate the incidence and risk factors of CRBSI in SBS children with PN.

Materials And Methods

Study population

Nineteen children with SBS from Shanghai Children's Hospital, China, between August 2015 and December 2019, were retrospectively enrolled to the study cohort. The inclusion criteria were pediatric SBS patients due to a primary intestinal disease who were received PN for more than 42 days. Patients without a suspected CRBSI were excluded. This study was in compliance with the Helsinki Declaration and was approved by the Ethical Review Board of Shanghai Children's Hospital.

Data collection

Clinical data, including demographics, aetiology of SBS, site and type of catheters, duration of PN, comorbidities, laboratory findings, and microbiological data regarding CRBSI, were collected and reviewed to assess the CRBSI incidence and associated risk factors. CRBSI was identified by positive blood culture drawn from any site in a symptomatic SBS patient receiving PN with suspected bloodstream infection [5].

Statistical analysis

Statistical analysis was performed by SPSS 20.0 software. Descriptive analyses were performed to catalog the characteristics of the patients and catheters as number with percentage. Quantitative data were summarized as medians and interquartile range (IQR 25th-75th), and compared using the t test or χ^2 test. A p value of <0.05 was considered to be statistically significance.

Results

As shown in Table 1, 19 children with SBS met the inclusion criteria were included in the study, 14 were boys (14/19, 73.7%). The median gestational age at birth was 36 (IQR, 32, 38) weeks, with a median birth weight of 2.44 (IQR, 1.57, 3.39) kg. The etiology of SBS was intestinal atresia (4/19, 21.1%), NEC (4/19, 22.1%), volvulus (5/19, 26.3%), congenital megacolon (3/19, 15.8%), Gastrointestinal perforation (2/19, 10.5%), and incarcerated hernia (1/19, 5.3%). Mean length of residual small bowel prior to the first time of PN was 60 (IQR, 40, 70) cm, and most of the patients (14/19, 73.7%) retained the ileocecal valve (73.7%).

Table 1
Characteristics of SBS children with PN

Characteristics	Value
Sex, n /total (%)	
Male	14/19 (73.7)
Female	5/19 (26.3)
Gestational age at birth, weeks, median (IQR)	36 (32, 38)
Birth weight, kg, median (IQR)	2.44 (1.57, 3.39)
Etiology of SBS, n/total (%)	
Intestinal atresia	4/19 (21.1)
Necrotizing enterocolitis	4/19 (21.1)
Volvulus	5/19 (26.3)
Congenital megacolon	3/19 (15.8)
Gastrointestinal perforation	2/19 (10.5)
Incarcerated hernia	1/19 (5.3)
Residual small bowel length, cm[a]	60 (40, 70)
Ileocecal valve, n (%)	14 (73.7)
Catheter type (n = 57)	
CVC	26/57 (45.6)
PICC	26/57 (45.6)
PORT	5/57 (8.8)
Insertion site (n = 57)	
Jugular vein	33/57 (57.9)
Femoral vein	21/57 (36.8)
Axillary vein	2/57 (3.5)
Umbilical vein	1/57 (1.8)
Total catheter days per patient (total = 1907)	55 (32, 100)

SBS, short bowel syndrome; IQR, interquartile ranges; CVC, central vascular catheter; PICC, peripherally inserted central catheter; PORT, totally implantable venous access port; PN, parenteral nutrition

[a]Length of residual small bowel prior to the first time of PN

Characteristics	Value
Total PN days per patient	112 (60, 138)
No. of positive cultures, n/total (%)	
All negative	13/19 (68.4)
1 positive culture	4/19 (21.1)
2 positive cultures	1/19 (5.3)
5 positive cultures	1/19 (5.3)
SBS, short bowel syndrome; IQR, interquartile ranges; CVC, central vascular catheter; PICC, peripherally inserted central catheter; PORT, totally implantable venous access port; PN, parenteral nutrition	
[a]Length of residual small bowel prior to the first time of PN	

During the study period, a total of 57 catheter insertions for PN were administered in 19 SBS children. The catheterization methods were central vascular catheter (CVC, 26/57, 45.6%), peripherally inserted central catheter (PICC, 26/57, 45.6%), and totally implantable venous access port (PORT, 5/57, 3.5%). The catheterization sites were internal jugular vein (33/57, 57.9%), femoral vein (21/57, 45.6%), axillary vein (2/57, 3.5%), and umbilical vein (1/57, 1.8%).

Total catheter days per patient were 55 (IQR, 32, 100) days. CRBSI was identified in 11 cases among 6 patients during a total catheter days of 1907. The rate of CRBSI was 5.8 per 1000 catheter days. Among 6 (6/19, 31.6%) patients experienced CRBSI, 4 had 1 CRBSI, 2 had 2 CRBSI, and 1 had 5 CRBSI. The common manifestations of the SBS children with CRBSI were fever (6/11, 54.5%), lethargy (5/11, 45.4%), stagnation of weight (7/11, 63.6%), and increment of enterostomy fluid (7/11, 63.6%).

The results of the univariate analysis showed that there were no significant differences in catheter site, catheter type, or the catheter repair or placement in past 7 days between children with CRBSI and those without CRBSI (Table 2). We found that an absence of ileocecal valve ($p = 0.046$), and long-term duration of PN prior to CRBSI ($p = 0.019$) was positively associated with an increase risk of CRBSI, respectively. Furthermore, use of antibiotics, use of antacids at least 1 day that month of catheterization, percentage of calories from carbohydrate (CHO), fat, or protein was not associated with CRBSI (Table 2). However, multivariate analysis did not determine an absence of ileocecal valve, and long-term duration of PN as independent risk factors for CRBSI in our study cohort (Table 3).

Table 2
Univariate analysis of factors associated with CRBSI

Variable	CRBSI (N = 11)	No CRBSI (N = 46)	Z/F	*p*
Catheter site, n (%)				
Jugular vein	8/11 (72.7)	25/46 (54.3)	1.547	0.672
Femoral vein	3/11 (27.3)	18/46 (39.1)		
Axillary vein	0/11 (0)	2/46 (4.4)		
Umbilical vein	0/11 (0)	1/46 (2.2)		
Catheter type, n (%)				
CVC	5/11 (45.4)	21/46 (45.7)	1.603	0.449
PICC	4/11 (36.4)	22/46 (47.8)		
PORT	2/11 (18.2)	3/46 (6.5)		
Absence of ileocecal valve, n (%)	8/11 (72.7)	18/46 (39.1)	-1.922	**0.046**
Duration of PN ≥ 120 days, n (%)[a]	7/11 (63.64)	12/46 (26.1)	-2.352	**0.019**
Catheter replaced in past 7 days, n (%)	6/11 (54.5)	15/46 (32.6)	-1.343	0.179
Use of antibiotics at least 1 day that month, n (%)	11/11 (100)	39/46 (84.8)	-1.369	0.171
Use of antacids at least 1 day that month, n (%)	6/11 (54.5)	18/46 (39.1)	-0.922	0.357
% of estimated caloric requirements from PN calories that month, median (IQR)				
% PN calories from CHO	55.8 (52.5, 61.1)	56.4 (53.6, 60.7)	0.361	0.550
% PN calories from fat	29.8 (25.5, 35.9)	28.7 (24.8, 32.9)	-0.293	0.769
% PN calories from protein	14.5 (13.1, 17.0)	14.6 (14.1, 16.2)	-0.384	0.701

CRBSI, catheter-related bloodstream infections; CVC, central vascular catheter; PICC, peripherally inserted central catheter; PORT, totally implantable venous access port; PN, parenteral nutrition; IQR, interquartile ranges; CHO, carbohydrate

[a]Total days of PN prior to CRBSI

Table 3
Multivariate analysis of factors associated with CRBSI

Variable	*p*	OR	95% CI
Absence of ileocecal valve	0.286	2.429	0.476–12.399
Duration of PN ≥ 120	0.128	3.333	0.708–15.696

CRBSI, catheter-related bloodstream infections; OR, odds ratio; CI, confidence interval; PN, parenteral nutrition

As shown in Table 4, a total of 11 microorganisms grew in the harvested blood cultures, including 2 gram-positive bacterial species (18.2%), 1 gram-negative bacterial species in 6 cases (54.5%), 1 fungal species in 2 cases (18.2%), and 1 case (9.1%) of co-infection with *Staphylococcus aureus* and *Klebsiella pneumoniae*. The most common microorganism cultured was *Klebsiella pneumoniae* (6/11, 54.55%). The catheters in patients with CRBSI were removed, and the patients were treated with antimicrobial therapy to clear the microorganisms.

Table 4
Pathogens isolated in CRBSI in SBS children

Microorganism (N = 11)	No (%)
Gram-positive bacteria	2/11 (18.2)
Propionibacterium acnes	1/11 (9.1)
Enterococcus faecalis	1/11 (9.1)
Gram-negative bacteria	6/11 (54.5)
Klebsiella pneumoniae	6/11 (54.5)
Fungus	2/11 (18.2)
Candida albicans	2/11 (18.2)
Polymicrobial	1/11 (9.1)
Staphylococcus aureus + Klebsiella pneumoniae	1/11 (9.1)

SBS, short bowel syndrome; CRBSI, catheter-related bloodstream infections

Discussion

Children with SBS suffer from strikingly high rates of morbidity and mortality, due in part to their susceptibility to life-threatening microbial infections [4, 14]. SBS children are at high risk for CRBSI and associated complications for their initial surgical management, malabsorption, immune system dysfunction, intestinal microecological changes, and their need for PN [12, 13, 15]. In this study, the rate of CRBSI in SBS children with long-term PN was 5.8 per 1000 catheter days, which was comparable with

several previous studies [9, 11, 16]. The rate of CRBSI was 4.6 per 1000 catheter days in a study enrolled 16 children with intestinal failure for a total follow up of 233 months [16]. In another study from China, the incidence of CRBSI was 5.85 per 1000 catheter days in a group of infants with intestinal failure with PICC [9].

The most common symptoms at the time of diagnosis of CRBSI in children are fever, chills, and lethargy [16–18]. In the current study, not all SBS children had fever during CRBSI, which was different from previous study [17]. Some patients presented increasing enterostomy fluid or stagnation of weight without fever when CRBSI happened. Therefore, early CRBSI should not be evaluated simply by fever. The change of enterostomy fluid and stagnation of weight may be identified as indicators of CRBSI with a large cohort.

Potential risk factors for CRBSI in the current study included an absence of ileocecal valve, and long-term duration of PN. However, multivariate analysis did not determine an absence of ileocecal valve, or long-term duration of PN as independent risk factors for CRBSI. A previous study showed that use of double-lumen tunneled CVCs, jugular placement of CVC, higher doses of lipid emulsion, and use of antacids were potential risk factors for CRBSI in children with intestinal failure [16]. A recent study found that lower white blood cells (WBC) and platelet count, as defined by age- and sex-specific reference ranges, were highly associated with risk of CRBSI [19]. Furthermore, age less than 1 year, high level of absolute neutrophil count and C-reactive protein (CRP) were associated with an increase risk of CRBSI [20, 21]. In addition, a study of adult found a higher incidence of CRBSI in patient with a residual small bowel less than 50 cm, which may due to the loss of lymphoid tissue with gut resection [22]. Similarly, high rate of CRBSI was identified in children with less than 50 cm or less than 50% of normal length of small bowel for age [16]. Unfortunately, we did not confirm those risk factors for CRBSI due to lack of the data or small size of enrolled subjects. For example, the length of small bowel was not measured prior to each time of PN.

Gram-negative bacteria *klebsiella pneumoniae* (54.5%, 6/11) was the most common isolated microorganism of CRBSI in our SBS children, which was similar to several previous studies [16, 19, 21]. However, other studies showed that Gram-positive bacteria were the major pathogens of CRBSI in pediatric patients [15, 20]. A study focused on CRBSI in children of intestinal failure with home PN found that Gram-positive bacteria were the most isolated microorganisms, such as coagulase-negative staphylococci (CONS), and *Enterococcus spp* [20]. In addition, Gram-positive bacteria were the most common microorganisms growing in blood cultures in a group of infants with intestinal failure with PICC [15]. Nevertheless, this difference may be caused by the different study population.

Conclusions

In summary, the rate of CRBSI was 5.8 per 1000 catheter days, and *klebsiella pneumoniae* was the most common isolated pathogen of CRBSI in the studied SBS children. An absence of ileocecal valve and long

duration of PN were potential risk factors of CRBSI. However, the results need to be further confirmed by a multi-centre study with a large cohort.

Abbreviations

SBS, short bowel syndrome; PN; parental nutrition; CRBSI, catheter-related bloodstream infection; NEC, necrotizing enterocolitis; CVC, central venous catheter; IQR, interquartile range; PICC, peripherally inserted central catheter; WBC, white blood cells; CONS, coagulase-negative staphylococci; CRP, C-reactive protien

Declarations

Ethics approval and consent to participate

Written informed consent was obtained from the parents of the patients for the genetic study and publication of this study. The study was approved by the Regional Ethical Review Board in Shanghai Children's Hospital.

Consent for publication

All authors have read and approved the content, and they agree to submit it for consideration for publication in the journal.

Availability of data and material

The raw data supporting the conclusions of this manuscript will be made available by the authors without undue reservation to any qualified researcher.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

YW and TZ designed the study. CY, XL and YW drafted the manuscript. CY, XL, HH, DL, and MX acquired, analyzed, and interpreted the data. YW and TZ edited the manuscript. All authors agreed to be accountable for all aspects of the work.

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