



Original/*Pediatría*

## Reorganization of nutritional therapy can markedly reduce the rate of catheter-related blood stream infections in pediatric patients receiving parenteral nutrition – a 7-year prospective follow-up study

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### Abstract

**Background:** Implementation of hygienic measures and simple changes in the structure of medical team may considerably reduce the rate of catheter-related bloodstream infections (CRBSIs) in parenterally nourished patients.

**Aim:** To analyze the effects of organizational changes in parenteral nutrition services on the CRBSI rates in pediatric patients.

**Methods:** We compared the CRBSI rates documented prior to, during and after the implementation of the organizational changes (introduction of a nutritional support team and related procedures, medical staff training).

**Findings:** A total of 260 courses of parenteral nutrition were offered to 141 pediatric patients during the analyzed period. Thirty CRBSIs were documented during this period. The most frequent etiological factors were staphylococci (21/30), followed by *Klebsiella pneumoniae*, *Escherichia coli* and *Candida albicans* (2/30 each). The reorganization was reflected by more than 8-fold reduction of the CRBSI incidence rate: from the initial value of 10.14 to 6.89 per 1000 catheter days and 1.17 per 1000 catheter days during and after the reorganization, respectively.

**Conclusion:** Introduction of a nutritional support team, accompanied by extensive training of medical staff,

### CAMBIO DE LA ORGANIZACIÓN DEL TRATAMIENTO NUTRICIONAL PUEDE REDUCIR CONSIDERABLEMENTE LA TASA DE BACTERIEMIA ASOCIADA AL CATÉTER (BAC) EN PACIENTES PEDIÁTRICOS QUE RECIBEN NUTRICIÓN PARENTERAL, UN ESTUDIO PROSPECTIVO DE SEGUIMIENTO DE 7 AÑOS DE DURACIÓN

### Resumen

**Antecedentes:** La implementación de medidas higiénicas y cambios sencillos en la estructura del personal médico puede reducir considerablemente la tasa de bacteriemia asociada al catéter (BAC) en pacientes que reciben nutrición parenteral.

**Objetivo:** Analizar el impacto de los cambios organizacionales dentro de los servicios de nutrición parenteral sobre las tasas de BAC en pacientes pediátricos.

**Métodos:** Hemos comparado las tasas de BAC documentadas antes, durante y después de la implementación de los cambios organizacionales (introducción de un grupo de apoyo nutricional y los procedimientos relacionados, formación del personal médico).

**Descubrimientos:** Un total de 260 series de nutrición parenteral fueron ofrecidos a 141 pacientes pediátricos durante el periodo analizado. Se documentaron treinta BAC durante este periodo. Los factores etiológicos más frecuentes eran staphylococci (21/30), seguidos por *Klebsiella pneumoniae*, *Escherichia coli* y *Candida albicans* (2/30 cada uno). Los cambios organizacionales fueron reflejados en una reducción de la incidencia de BAC en más de 8 veces: el valor inicial disminuyó desde 10.14 hasta 6.89 por 1000 días-catéter y hasta 1.17 por 1000 días-catéter durante y después de la reorganización, respectivamente.

**Conclusión:** La introducción de un grupo de apoyo nutricional, acompañada de una extensa formación del personal médico puede resultar en una reducción considera-

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can result in a marked reduction of CRBSI rate in pediatric patients nourished parenterally in a hospital setting.

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Key words: *Catheter-related blood stream infection. Nutritional support team. Parenteral nutrition. Pediatric gastroenterology.*

## Introduction

Parenteral nutrition is an option of treatment of both acute and chronic intestinal failure. Although beneficial, it is associated with a relatively wide range of complications, such as central catheter thrombosis, catheter occlusion, mechanical problems, liver disease and infections<sup>1,2</sup>. Catheter-related blood stream infections (CRBSIs) are the most common complication observed in patients receiving parenteral nutrition<sup>3</sup>. The infection may originate from two sources: extraluminal –when microbes migrate from the skin to the catheter insertion site, and intraluminal– with the catheter hub, infusion set connectors or nutritional admixture as a portal of entry<sup>4</sup>.

Connector-related infections result from manipulations associated with drawing blood, exchanging sets and drug administration. Furthermore, improper management of catheter insertion site can lead to its colonization with microorganisms and further microbial migration along the catheters' wall into the lumen of a blood vessel<sup>5,6</sup>.

Due to a relatively high probability for the development of central catheter-related infection during parenteral nutrition, numerous previous studies have investigated the potential risk factors for this complication. The risk for infection was found to increase proportionally to the duration of catheterization, frequency of catheter-associated manipulations and catheter use for parenteral nutrition administration<sup>7,8</sup>. Furthermore, bloodstream infections were more likely to develop in *Staphylococcus aureus* carriers<sup>9</sup>.

Appropriate management of the catheter insertion site is vital for the prevention of CRBSIs. Chlorhexidine proved to be the most effective of all disinfectants used in the prevention of catheter-related infections<sup>10,11</sup>. Also octenidine, used for disinfection of the skin prior to the insertion, and for insertion-site care, was found to reduce the risk of catheter-related colonization in a recently published randomized trial<sup>12</sup>. The strategies to prevent infectious catheter complications were studied extensively during last years. Antibiotic, 70% alcohol and tauridine locks were shown to reduce the CRBSI rates<sup>13-17</sup>.

Nevertheless, it is sterility during catheter-related manipulations which plays a vital role in CRBSI prevention<sup>4,18</sup>. Although further studies of novel protective modalities are still required, introduction of simple changes in the structure of the medical team, as well as implementation of hygienic measures, e.g. wearing sterile gloves, masks and coats during central catheter insertion and manipulation, disinfecting patient's skin with chlor-

ble de la tasa de BAC en pacientes pediátricos que reciben nutrición parenteral en un entorno hospitalario.

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**Palabras clave:** *Bacteriemia asociada al catéter. Grupo de apoyo nutricional. Nutrición parenteral. Gastroenterología pediátrica.*

hexidine and avoiding the femoral catheter placement, can considerably reduce the infection rates<sup>19</sup>.

In pediatric parenteral nutrition, CRBSI rate is a sensitive marker of the quality of care. According to the ESPGHAN/ESPEN/ESPR guidelines, the incidence of infectious complications in hospitalized patients should not exceed 0.45 to 1.00 per year<sup>20</sup>. In our previous study, we showed that the number of CRBSIs associated with parenteral nutrition may decrease considerably shortly after implementation of simple organizational changes<sup>21</sup>. The aim of this study was to analyze the long-term effects of the changes implemented at our clinic; we compared the CRBSIs rates in children receiving parenteral nutrition throughout a 7-year follow-up period prior to, during and after the reorganization.

## Material and Methods

### *Organizational changes*

Beginning in 2007, we started to reorganize nutritional therapy services offered at our pediatric gastroenterology department. The reorganization program was based on: 1) creating a nutritional support team comprised of pediatricians, nutrition nurse specialists and pharmacists, 2) providing training for team members at a reference center (Nutritional Ward of the Pediatric Clinic, The Children's Memorial Health Institute in Warsaw), 3) implementation of nutritional therapy and central catheter placement procedures, 4) documentation of all central catheterizations, 5) limiting central-catheter-associated manipulations to a necessary minimum, 6) authorization of staff involved in central catheter manipulation, 7) providing education and motivation to medical personnel, and 8) monitoring complications associated with nutritional therapy. Our program of nutritional therapy reorganization followed current recommendations and standards of care<sup>20-23</sup>.

### *Study design*

This analysis included three periods: 1) prior to the reorganization, i.e. between April 1<sup>st</sup>, 2005 and December 31<sup>st</sup>, 2006, 2) during the reorganization, i.e. between January 1<sup>st</sup> 2007 and September 30<sup>th</sup>, 2007, and 3) after the reorganization, i.e. between October 1<sup>st</sup>, 2007 and September 30<sup>th</sup>, 2014. In the case of period 1, a retrospective analysis of medical documentation was

conducted, whereas the data concerning periods 2 and 3 were examined prospectively.

We analyzed the rates of CRBSIs documented during these three periods in patients nourished parenterally at our clinic. The inclusion criteria were as follows: patient's age between 2 and 48 months of life, at least four consecutive days of parenteral nutrition, and infusion of nutritional admixture through the central catheter.

The protocol of this study was approved by the Local Ethics Committee of the Medical University in Gdansk.

### *Diagnostic criteria of CRBSI*

CRBSI was diagnosed whenever clinical symptoms of infection (poor general condition and body temperature above 38.5°C) co-existed with elevated levels of inflammatory markers (CRP and peripheral leukocyte count) and leukocyte left shift. Furthermore, the criteria required that the same microorganism was isolated simultaneously from the blood obtained from the catheter and from peripheral blood, in absence of other sites of infection<sup>18,20,24</sup>.

### *Microbiological verification*

Catheter and peripheral blood samples (2-5 ml) were analyzed using the automated incubation system BacT/Alert (BioMerieux, France). Initially, the blood was cultured in the PediBacT medium (i.e. non-selective growth medium for aerobic microflora isolated from pediatric patients). If the culture was positive, the samples were passaged onto specific media for testing bacterial and fungal growth (BioMerieux, France). The material was incubated at 35°C under aerobic conditions or 5-10% CO<sub>2</sub>. Species identification was performed by means of routine microbiological methods and with an aid of VITEK2 system (BioMerieux, France). Antibiotic susceptibility of isolates was tested with disk-diffusion method in Mueller-Hinton II medium in accordance with the CLSI standards and with an aid of VITEK2 system.

### *Statistical analysis*

Normal distribution of continuous variables (patients' age and the duration of nutritional therapy) was verified with the Kolmogorow-Smirnov test. The results were presented as arithmetic means and their standard deviations (SD) and compared with ANOVA and Tukey post-hoc test. The distributions of categorical variables were compared with the Pearson's chi-square test or Fischer's exact test. All calculations were performed using Statistica 10 (StatSoft®, Tulsa OK, USA) software, and statistical significance was defined as  $p \leq 0.05$ .

## **Results**

A total of 260 courses of parenteral nutrition lasting at least 4 consecutive days were offered to 141 patients during the period covered by this study (Table I). This corresponded to 7 715 procedures of parenteral nutrition (one procedure defined as one day of parenteral nutrition offered to a single patient). Mean age of patients who received parenteral nutrition prior to and during the reorganization was significantly lower than the age of patients treated nutritionally after the reorganization ( $p=0.028$ ). Also mean duration of parenteral nutrition decreased significantly, from 76 days per course prior to the reorganization to 20 days per course thereafter ( $p<0.001$ ).

Short bowel syndrome was the main indication for parenteral nutrition in the vast majority of cases. Nevertheless, the frequency of this indication decreased gradually with time: from 68% during period 1, to 59% and 55% during periods 2 and 3, respectively. However, this tendency did not prove significant on statistical analysis.

A total number of 30 CRBSIs were documented throughout the analyzed period. The reorganization was reflected by more than 8-fold reduction in the CRBSI incidence rate: from initial value of 10.14 to 6.89 per 1000 catheter days and 1.17 per 1000 catheter days during and after the reorganization, respectively (Table II). Staphylococci: *S. aureus* (n=4) and *S. epidermidis* (n=17) were identified as etiological factor of infection in 21 out of the 30 cases. The remaining CRBSIs resulted from infection with *Enterococcus fecalis* (n=1), Gram-negative bacteria (n=6) and *Candida albicans* (n=2).

## **Discussion**

Parenteral nutrition is associated with a number of complications<sup>1,2</sup>, and the rate of infectious complications constitutes a sensitive quality marker of nutritional therapy<sup>20</sup>. Therefore, the aim of this study was to verify if simple organizational changes implemented at our department exerted sustained effect on the CRBSI rate. Organization of a nutritional support team and reorganization of nutritional therapy was shown to result in more than 8-fold reduction of the CRBSI rate (from 10.14 to 1.17 per 1000 catheter days) throughout a 7-year follow-up period. As a result, the incidence of infections approximated the safety limit stated in the ESPGHAN/ESPEN/ESPR guidelines<sup>20</sup>. Majority of previous studies dealing with the problem in question analyzed only the short-term effects of organizational changes on the CRBSI rates. A number of these studies confirmed that organization of nutritional support is reflected by lower number of catheter-related infections. Pronovost *et al.*<sup>19</sup> observed a dramatic decrease in the mean CRBSI rate, from 7.7 at baseline to 1.4 per 1000 catheter days at 16-18 months after implementation of organizational changes similar to those proposed in our study. Also other authors documented marked reduction of infection rates, resulting from implementation of training programs and

**Table I**  
Clinical characteristics of patients receiving parenteral nutrition during the period of this study

Parameter	Prior to the reorganization (1)	During the reorganization (2)	After the reorganization (3)	p-value		
				1 vs. 2	2 vs. 3	1 vs. 3
Patients (n)	8	10	123	-	-	-
Patients' gender (F/M)	5/3	5/5	55/68		0.600*	
Patients' age in months (mean±SD)	7.2±4.4	11.9±6.0	21.4±31.0	0.590	0.138	0.028
Parenteral nutrition courses (n)	22	22	216	-	-	-
Total days of parenteral nutrition (n)	1675	1162	4278	-	-	-
Days per course of nutrition (mean±SD)	76±108	53±75	20±28	0.092	0.001	<0.001
Indications to parenteral nutrition (n)						
Short bowel syndrome:	15/22	13/22	120/216		0.754*	
- agangliosis	2	1	14		-	
- intestinal atresia	4	3	35		-	
- ileus	6	4	1		-	
- NEC	1	1	30		-	
- gastroschisis	1	1	33		-	
- others	1	3	7		-	
Mitochondrial cytopathy	0	0	3/216		-	
Crohn disease	0	0	6/216		-	
Motility disorders	6/22	9/22	41/216	0.526	0.026	0.250
Severe malnutrition	1/22	0/22	13/216		0.484*	
Other	0/22	0/22	33/216	-	0.036	0.036

\*no post-hoc testing.

**Table II**  
Characteristics of catheter-related blood stream infections (CRBSIs) documented in parenterally nourished patients during the period of this study

Parameter	Total (4)	Prior to the reorganization (5)	During the reorganization (6)	After the reorganization (7)	p-value		
					5 vs. 6	6 vs. 7	5 vs. 7
Number of CRBSIs	30/7115	17/1675	8/1162	5/4278	-	-	-
CRBSI rate per 1000 catheter days	4.2	10.14	6.89	1.17	0.043	<0.001	<0.001
Etiological factor (n)							
<i>Staphylococcus aureus</i>	4/30	0	3	1	0.028	0.196	-
<i>Staph. epidermidis</i>	17/30	12	2	3	0.032	0.086	0.662
<i>Enterococcus faecalis</i>	1/30	0	1	0		0.257*	
<i>Klebsiella pneumoniae</i>	2/30	2	0	0		0.418*	
<i>Escherichia coli</i>	2/30	2	0	0		0.418*	
<i>Haemophilus influenzae</i>	1/30	0	1	0		0.257*	
<i>Pseudomonas aeruginosa</i>	1/30	0	0	1		0.083*	
<i>Candida albicans</i>	2/30	1	1	0		0.680*	

\*no post-hoc testing.

organizing nutritional support teams. However, the reduced rates were not as low as in our study. Costello *et al.*<sup>25</sup> reported more than a three-fold decrease in the infection rate of children hospitalized at intensive care units (from 7.8 to 2.3 per 1000 days), resulting from organization of central catheter team and a system for monitoring and analyzing all CRBSI cases. In turn, Warren *et al.*<sup>26,27</sup> analyzed the effectiveness of the obligatory training of

medical personnel, and showed that this approach resulted in more than two-fold decrease in the infection rate. Also, Coopersmith *et al.*<sup>28</sup> revealed similar effectiveness of the training program for medical personnel (a decrease in the incidence of septic complications from 11.6 to 2.4 per 1000 days of parenteral nutrition).

Contrary to the studies mentioned above, the principal aim of our research was to analyze the long-term effects

of organizational changes on the incidence of catheter-related infections. To the best of our knowledge, only few similar long-term observations have been published to date. The authors of one of these studies analyzed two 18-month periods after the implementation of CRBSI prevention program at intensive care units. They showed that the initial reduction of CRBSI rate observed during the first period sustained for another 18 months, and thus concluded that the program was integrated well into routine clinical practice<sup>29</sup>. In another study, the CRBSI rate at an intensive care unit decreased from 3.38 to 0.46 per 1 000 catheter days during a 4-year follow-up period after reorganization<sup>30</sup>. The sustained reduction of CRBSI rate was also documented in a multicenter study conducted at another intensive care unit<sup>31</sup>, as well as in a 6-year follow-up one-center study including all units using central venous catheters<sup>32</sup>. In our study, we documented sustained reduction of CRBSI rate at the pediatric gastroenterology unit of a tertiary hospital, thus showing that a relatively simple reorganization accompanied by educational activities may efficiently improve the quality of care. Our findings are consistent with the results of another study conducted at non-intensive care units of a tertiary hospital, which showed that educational intervention among nurses may reduce the risk for peripheral venous catheter infections<sup>33</sup>.

Undoubtedly, one potential limitation of this study stems from the combined retrospective/prospective character of our analysis. During the period covered by this study, the status of our clinic was changed to a reference center for nutritional therapy. Continuous increase in the experience of our medical team was reflected by changes in patients' profile, as shown by greater number of children qualified to parenteral nutrition therapy at the clinic<sup>34</sup>. Moreover, mean age of patients who received parenteral nutrition prior to and during the reorganization was significantly lower than the age of children treated nutritionally after the reorganization ( $p=0.028$ ). Also this phenomenon may be explained by greater heterogeneity of patients referred for nutritional therapy at a reference center. Importantly, the reorganization resulted in a significant decrease in the mean duration of nutritional therapy, from initial 76 days to no more than 20 days ( $p<0.001$ ). Also this might contribute to the lower CRBSI rates. Event taking a potential confounding effect of the abovementioned factors into account, our study confirmed that implementation of simple organizational changes may be reflected by a considerable decrease in the incidence of catheter-related infections. It is noteworthy that the changes implemented at our clinic generated relatively low costs (mostly associated with training of the personnel) and considerable financial savings (data not shown), inherent to lower CRBSI rates<sup>35,36</sup>. The most frequent etiological factors of CRBSIs documented in parenterally nourished children treated at our clinic were staphylococci (21/30), followed by *Klebsiella pneumoniae*, *Escherichia coli* and *Candida albicans* (2/30 each). This distribution of etiological factors of CRBSIs is similar to those reported previously<sup>9,37</sup>.

Aside from the risk for infection, parenteral nutrition may also result in mechanical and metabolic complications, and nutritional disorders. According to literature, the risk for mechanical complications, such as pneumothorax, air embolism or displacement of a catheter inside the vessel, is markedly lower in centers having nutritional support teams<sup>38</sup>. Some authors suggested that organization of the nutritional support team may be reflected by 3.6% to 24% reduction of mechanical complication rates<sup>39,40</sup>, and Png *et al.*<sup>41</sup> claimed even on a complete elimination thereof. However, the period covered by the latter study (initial 6 months after nutritional support team implementation) seems too short for such radical conclusion. Nevertheless, parenterally nourished patients supervised by a nutritional support team were shown to be characterized by lower incidence of metabolic disorders, such as hyper- or hypoglycemia, abnormal levels of sodium, phosphorus and magnesium ions<sup>39,40,42</sup>. Also, energy and protein deficiencies are less frequently reported from patients receiving parenteral nutrition at centers having dedicated nutritional support teams<sup>39,40,43</sup>.

Appropriate qualification to nutritional therapy represents a crucial task of the nutritional support team. According to literature, the fraction of patients qualified to nutritional treatment by such teams is markedly lower than the fraction qualified by regular medical personnel. Png *et al.*<sup>41</sup> showed that as many as 41% of patients who were initially prescribed parenteral nutrition, were re-qualified to enteral nutrition following a consultation with nutritional support team, and this switch was associated with marked reduction in morbidity rates. Also, Gurgueira *et al.*<sup>44</sup> reported that the nutritional support team introduced to an intensive care unit qualified patients to enteral feeding rather than to parenteral nutrition. As a result, the fraction of patients receiving enteral nutrition increased from 25% to 67% following the introduction of nutritional support team<sup>44</sup>. This is consistent with Saalwachter *et al.*'s<sup>45</sup> findings; these authors observed that the nutritional support team may reduce the fraction of patients who were inappropriately qualified to parenteral nutrition from 32% to 7.9%.

According to modern standards, efficient parenteral nutrition requires multidisciplinary approach and involvement of various medical specialists. This goal can be achieved by the introduction of nutritional support teams. Our study confirmed that such reorganization, supported by extensive training and education of medical staff, may result in sustained reduction of CRBSI rates of pediatric patients nourished parenterally in a hospital setting. This leads to the conclusion that even relatively simple and inexpensive changes may constitute a key for marked improvement of medical care.

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