

Etiology and Epidemiology of Catheter Related Bloodstream Infections in Patients Receiving Home Parenteral Nutrition in a Gastromedical Center at a Tertiary Hospital in Denmark

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Abstract: We conducted a retrospective epidemiologic study of catheter related bloodstream infections (CRBSI) in patients receiving long-term home parenteral nutrition (HPN) from January 2002 to December 2005. Our results showed that coagulase negative staphylococci (CoNS) were the most prevalent pathogens (44.7% of all CRBSI episodes), followed by *Enterobacteriaceae* (33.2%). Prevalence for candidemia and *Enterococcus* bacteremia was relatively high (14.4% and 10.8%, respectively). Cefuroxime resistance was observed in 65.4% CoNS and 31.5% *Enterobacteriaceae*. Based on the results from the study, a new empiric antimicrobial treatment regimen was suggested.

Keywords: Etiology, epidemiology, intravascular catheter, blood stream infection, home parenteral nutrition, antimicrobial susceptibility.

INTRODUCTION

Parenteral nutrition (PN) represents a lifesaving treatment for patients with severe intestinal failure. Its use at home (HPN) was introduced in 1967 [1] and is now a commonly used procedure [2]. The most frequent HPN complication is catheter related bloodstream infection (CRBSI), which is an important factor for morbidity and hospital costs for the patients receiving HPN [3, 4]. Initial antibiotic treatment is crucial for infection outcome. Therefore, empiric treatment for CRBSI in patients receiving HPN should be guided primarily by local epidemiological data. We have surveyed the incidence of CRBSI, risk factors and predominant pathogenic organisms for CRBSI in patients receiving HPN. The efficacy of initial empirical treatment with cefuroxime, gentamicin and metronidazole was also evaluated.

MATERIAL AND METHODS

We conducted a retrospective, descriptive, observational epidemiologic study of patients receiving long-term HPN from January 2002 to December 2005 in the Department of Medical Gastroenterology at a tertiary university hospital in Denmark.

Patients: The positive blood culture data from the Department of Medical Gastroenterology between 2002 and 2005 were extracted from the microbiological database-MADS. The patients who did not receive HPN were excluded.

Information about age, gender, number of CRBSI, microbiologic characteristics, underlying disease, co-morbidity, caring methods, catheter type, complications to HPN, concurrent infections, duration of antibiotic treatment, and clinical outcome were registered for each patient after reviewing the charts. Infection parameters, total leukocyte count (LCC), C-reactive protein (CRP), were collected from the clinical biochemical department database.

Bacteremia episodes: When isolation of the same bacteria in blood culture occurred more than once in the patient within a period of 30 days, it was regarded as one episode.

The bacterial cultures were identified by automatic system VITEK II (BioMérieux) according to the manufactures instructions. When yeast is identified from the culture medium, the species identification is performed by incubating the yeast culture on chromID Candida agar (BioMérieux).

Statistical analysis: Multi-variant analysis was applied for the risk factors analysis. The examined risk factors were underlying disease, co-morbidity, HPN caring person, complications related to HPN, and concurrent infections. The statistic program used was SPSS.

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The project is approved by DataTilsynet in Denmark.

RESULTS

A total of 216 patients receiving HPN were registered in the Department of Medical Gastroenterology between 2002 and 2005. The inclusion criteria for the patient to go with parenteral support is intestinal failure, i.e. the inability to maintain sufficient fluid, electrolyte, micro- or macronutrient balance when on oral or enteral nutrition.

All patients had an uncoated one-lumen silicone rubber catheter Broviac catheter (Bard Limited, Crawley, UK).

All patients follow the standard operational procedure of the department.

There were no restrictions for the physical activities. However, most of the patients had limited physical activities and more sedentary life because of their disease. Only 20% of patients could continue their professional occupation.

The most frequent primary disease for patients receiving HPN was Crohns disease (27.8%), followed by arterial/venous mesenteric infarction (24.7%) and radiation enteritis (19.6%).

54.6 % of the patients handled the HPN by themselves, 5.2 % patients had family members to handle the HPN, while 27.8 % patients had a care assistant to handle the HPN (Table 1).

Table 1. Demographical and Clinical Characteristics for the 97 Patients with CRBSI in the Period 2002-2005

Characteristics	Cohort
Sex, number of patients	
Male: female	38:59
Age, years	
Mean (range)	54.2 (18-87)
Primary disease, number (%)	
Chrohn's disease	27 (27.8)
Colitis ulcerosa	8 (8,3)
Arteial/venous mesenteric infarction	24 (24.7)
Radiation enteritis	19 (19,6)
Miscellaneous	19 (19,6)
Co-morbidity, number (%)	
Diabetes mellitus	10 (4,4)
Immunosuppression ^a	10 (4,4)
Others	15 (16,5)
HPN caring, number (%)	
Patient self	53 (54,6)
Patient's family	27 (27,8)
Caregiver	5 (5,2)
Patient self and caregiver/family member	12(12,4)

^aPatients who had received chemotherapy or radiation therapy in the past one month, and/or if the total leukocyte count is less than 1.5 million/ml were considered as immunosuppressed.

225 ICRB episodes from 97 patients were identified by the microbiological database-MADS and the patients clinical chart. The incidence of CRBSI was 44.9%.

Fifty out of 97 patients (51%) had more than one CRBSI episode. Polymicrobial infections were registered in thirty-seven out of 225 episodes (16.4%). CRBSI occurred after 30 days of catheter installation in 92.9% of episodes, while CRBSI occurred after one year of catheter installation comprised 61.4% of the patients. Fifteen patients died during the observation period, while no death related to CRBSI among the patients on HPN was observed.

The catheters were preserved as long as it is functional. When CRBSI occurs, preservation of the catheter will be attempted with relevant antimicrobial therapy. Recurrent infections and sepsis related to CRBSI are two of the indications for the removal of a catheter.

The distribution of the predominant microorganism based on infection episodes were:

Coagulase negative *Staphylococci* (CoNS) appeared in 44.7 % CRBSI episodes (43 patients). *Enterobacteriaceae* appeared in 33.2% (47 patients), *Candida* spp. in 14.4% (18 patients), *Enterococcus* spp. in 10.8% (13 patients), and *S. aureus* in 9.2% (15 patients). Anaerobic bacteria were found only in 1.3% (3 patients). Among *Candida* spp., 38.6% (13 patients) had *C. albicans*, 31.8% (9 patients) had *C. glabrata*, while in 5 patients both *Candida* spp. were found. It was not possible to evaluate the infections were nosocomial or community acquired, since the patients were in the hospital surroundings very often. The distribution of predominant microorganisms for each year is shown in Table 2.

Antimicrobial susceptibility:

Among CoNS, 65.4% were methicillin resistant, and 31.6% were resistant to both methicillin and gentamicin. All *S. aureus* isolates were sensitive to methicillin and gentamicin. No MRSA was observed in the period. Among *Enterococcus* spp., 37.8% isolates were resistant to carbapenems. All *Staphylococcus* and *Enterococcus* isolates were susceptible to vancomycin. Among *Enterobacteriaceae*, 9.2% were ciprofloxacin resistant, 10.6% were gentamicin resistant, 31.5% were cefuroxime resistant, and 11.4% were resistant to ceftriaxon. Only 4% were resistant to both cefuroxime and gentamicin. The presence of extended β -lactamase was not investigated since it was not part of the routine procedure. All *Enterobacteriaceae* isolates were susceptible to carbapenem.

Combination of intravenous cefuroxime, gentamicin and metronidazole was the standard empirical antimicrobial therapy regimen in this department and this combination was used as initial treatment for 61.1% of the CRBSI episodes. Cefuroxime, ciprofloxacin and metronidazole was the initial treatment in 12.4 % episodes. All patients received antibiotic treatment at duration of 6-14 days. None of the examined risk factors were associated with higher risk for relapse or recurrent infections or any specific microorganism based on multi-variant analysis (SPSS).

DISCUSSIONS

The incidence of CRBSI varies from studies to studies [5-7]. In this study, 44.9% of all patients receiving HPN in

Table 2. Epidemiology of Microorganisms Causing Catheter-related Bloodstream Infections in Patients Receiving Home Parenteral Nutrition (HPN) from Year 2002 to 2005 (Some of the Episodes were Multi-microbial)

Pathogenes	Episodes with Certain Pathogen in Number (%)			
	2002	2003	2004	2005
<i>S. aureus</i>	5 (12.1)	6 (13.0)	2 (4.4)	5 (5.4)
CoNS	8 (19.5)	12 (25.5)	21 (46.7)	41 (44.6)
<i>Enterobacteriaceae</i>	17 (41.4)	19 (40)	12 (24.4)	29 (31.5)
<i>Enterococcus</i> spp.	2 (4.9)	5 (10.6)	3 (6.7)	12 (13.0)
<i>Candida albicans</i>	1 (2.4)	2 (4.2)	1 (2.2)	5 (5.4)
<i>Candida non albicans</i>	5 (12.1)	2 (4.2)	2 (4.4)	8 (8.7)
Total CRBSI episodes (number)	41	47	45	92

the period 2001-2005 had CRBSI. Though the rate of CRBSI is relatively high, the mortality related to CRBSI was zero during the period year 2002 to 2005.

This study shows that the first infections occurred after 30 days of catheter installation in 92.9% of cases. Besides, we could not identify any of the risk factors registered for relapse/recurrent infections, which indicated that the prolonged use of catheter is probably the only predisposing factor for CRBSI in this population. This can only be clarified by a prospective or a case-control study.

The most predominant microorganisms found in this population were CoNS, comprising 44.7% of the CRBSI episodes. This is in agreement with the earlier published studies [5, 6, 8]. 31.6% of CoNS were resistant to both methicillin and gentamicin, leading to 13.8% of all CRBSI episodes. There was an increase of CoNS CRBSI from 2002 (19.6%) to 2005 (44.6%), while *Enterobacteriaceae* and *S. aureus* became less dominant (Table 2). Apparently, the empirical antibiotic therapy played important role on the population of microorganisms.

The number of blood cultures increased from 2002 to 2004 annually at about 13%, while from 2004 to 2005 increased at 50 %. This probably had contributed partly to the significant increase in the number of CRBSI episodes in 2005 (Table 2). The number of new patients per year with CRBSI was relatively constant, approximately 25 patients/year.

Candida spp. had been involved in 14.4% CRBSI episodes. Among these episodes, 61.4 % had non-albicans species involved, which demand treatment with broad-spectrum anti-fungal drugs. The high prevalence of candidemia was also shown from earlier studies [5, 8], which is a reflection of the long-term use of intravascular catheter. It has been reported that the incidence of candidemia has increased in various parts of the world over the last decades and some species are not fully susceptible to fluconazole [9, 10]. This implies that empiric treatment for *Candida* in CRBSI should be with echinocandins, liposomal amphotericin or new generation azoles.

The empirical antibiotic therapy was cefuroxime, gentamicin and metronidazol in the period 2001-2005. The cur-

rent antibiotic therapy regiment for this patient group is changed to cefuroxime and ciprofloxacin. The removal of metronidazol from the empirical antibiotic therapy was guided by the fact that only 1.3 % of all CRBSI episodes were caused by anaerobic bacteria. Both antibiotic regiments are able to treat most of the serious bacterial infections, such as *S. aureus* and *Enterobacteriaceae*. However, these regiments are not able to cover 95% of the predominant etiology, leaving especially a great part of the CoNS (13.8 % of all infection episodes), *Enterococcus* spp. (10.4 %), and *Candida* spp. (14.4 %) untreated. Consequently, we suggest that vancomycin and an effective anti-fungal drug, such as echinocandin, could be considered into the empirical therapy.

According to the results from this study, we strongly believe that the empiric antibiotic treatment regiment should be based on the local epidemiology data. Regular monitoring of the predominant pathogenic organisms for CRBSI in patients receiving HPN is important for adjusting the empiric treatment strategy.

CONFLICT OF INTEREST

All authors report no conflicts of interest relevant to this article.

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None declared.

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