ORIGINAL ARTICLE

Bacterial Infection of Central Venous Catheters in Short-Term Total Parenteral Nutrition

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Summary

Fourteen severely ill ventilated patients in an intensive care unit, requiring short-term total parenteral nutrition, were examined for catheter-related infection. Microbiological analysis using Maki's SQ technique was carried out on catheter exit site, catheter hub, proximal subcutaneous segment of catheter and catheter tip. Qualitative cultures were carried out on total parenteral nutrition and peripheral blood samples.

Twenty six of 29 catheters removed (90%) were culture positive but only 7 catheters were related to positive blood cultures, giving a catheter-related bacteremia (CRB) rate of 24%. Haematogenous seeding was strongly implicated in 7/29 (24%) of catheters. Patients' skin flora appeared to be the main source of catheter-related infection.

The organisms isolated for patients with CRB included coagulase-negative staphylococci, *Acinetobacter* and *Klebsiella.*

It is suggested that to control infective complications of central venous catheters, emphasis should be focused on specialised intravenous therapy teams and the use of strict protocols for insertion and care of central lines.

Key Words: Catheter-related bacteremia, Total parenteral nutrition

Introduction

Catheter-related infections (CRI) is a recognized complication of total parenteral nutrition (TPN) therapy. Studies from Europe and America reported CRI rates of 7 to 42%.

The pathogenesis of CRI is a complex interaction of many factors. The initiating event is the entry of a microorganism into the system. Subsequent colonization and multiplication may lead to the establishment of a local and/or systemic infection. Entry to the system can occur at any point. It has been proposed that during or after catheter insertion, skin flora can invade the catheter wound and move proximally along the external surface of the catheter to reach the blood stream.

Outbreaks of CRI have been linked to the use of contaminated antiseptics for skin cleaning prior to catheter insertion. Conversely, adequate cutaneous disinfection has lowered rates of catheter-related bacteremia (CRB). Sitges-Serra showed that colonization of catheter hubs preceded catheter colonization and was predictive of bacteremia[1]. Patients with skin wounds, tracheostomies and urinary catheters, particularly those compromised with extensive burns, trauma or malignancy, tend to be colonized at these sites by nosocomiants. From these colonized sites, organisms can "seed" a catheter during a transient bacteraemia. The colonized catheter then becomes a nidus for a persistent bacteremia. Contaminated infusates have also been responsible for outbreaks of bacteremia associated with septic shock, but this route of infection is uncommon nowadays.

The epidemiology of CRB is not well studied in the tropics where the type of patients, microbial prevalence and medical and nursing practices may differ from those in western developed countries. This paper describes a study of colonization of central venous catheters (CVC) and resulting CRB in patients on short-term TPN treated in an intensive care unit in a Malaysian teaching hospital.

Methods

Study population

During a 4-month period, CVC used for TPN in critically ill patients in the Intensive Care Unit (ICU), University Hospital, Kuala Lumpur, were studied. Most of the patients received single bag TPN solutions prepared by the Hospital Pharmacy. All patients received antimicrobial therapy for sepsis throughout their stay in the ICU.

Procedures for insertion and care of catheters

All catheters studied were placed percutaneously by anaesthetic medical officers (assigned to ICU posting) wearing sterile gloves, gowns and masks. Strict aseptic protocol was followed. At the time of insertion, 10% povidone-iodine solution was the antiseptic solution used for disinfection of the insertion site and catheter sites were protected with Opsite spray and Hypafix dressing. Topical antimicrobial or antiseptic ointments were not used on any catheters in this study. If the insertion site required a change in dressing later, the area involved was cleaned with normal saline and then dressed with sterile gauze. The catheters used in the study were trilumen, cavafix and Swan-Ganz catheters made of polyurethane material and Angiocaths made of Teflon material. All catheters were non-cuffed and special in-line filters were not used. The sites for catheter insertion were mainly the internal jugular vein and the subclavian vein.

Data Collection

The anaesthesiologist in charge of the study followed each patient from catheter insertion to removal and collected data on patient profile (age, sex and diagnosis) and data related to TPN courses (duration, site, catheter type and outcome).

An episode of catheterization was defined as the time from insertion of the CVC in a specific site to its removal. A new catheter was always inserted at a different site.

Inspection of insertion site was carried out daily by the same anaesthesiologist. Peripheral blood cultures were taken from patients on the day of CVC removal. Catheters were removed aseptically and cultures were obtained. Swabs were taken immediately from the catheter insertion site and from the hub.

Line violations were recorded. The following were considered as line violations during the administration of TPN:

a) extraction of clot from the CVC
b) using the line for central venous pressure measurement intermittently
c) administration of medication through the line
d) administration of blood and blood products
e) flushing of line with sterile water

Microbiological Methods

Prior to the catheter removal, the skin around the exit site was examined for signs of inflammation and then a 20cm^2 area swabbed for culture on blood agar. The catheter was removed with sterile forceps, without touching the patient's skin. Two segments were cut off ; an intravascular segment from the tip to 3 cm up the catheter and a 3 cm long subcutaneous segment beginning just a few mm below the skin-catheter interface. Each segment was rolled back and forth at least 4 times on the surface on a blood agar plate. The catheter hub was sampled with a sterile premoistened swab and inoculated onto a blood agar plate. Semi-quantitative bacterial counts were carried out for all specimens. Two ml of the TPN solution in use were collected and cultured in broth which was subcultured onto blood agar after overnight incubation. In addition two sets of blood cultures were taken from peripheral veins on the day of CVC removal. Blood cultures were collected in aerobic (NR 16A) and anaerobic (NR 17A) media and processed using the Bactec NR 730 System (Beckton Dickinson) over a 5 day cycle.

Only qualitative cultures were carried out on the TPN and blood culture samples.

In the laboratory, all inoculated plates were incubated at 37°C for 18-24 hours after which all colony types appearing on the agar were counted, identified according to standard laboratory procedures and tested for susceptibility to antibiotics. Isolates from TPN broth cultures were similarly identified by standard methods.

Skin culture was considered positive if >200 colonies were present in skin swab cultures[2], catheter tip or subcutaneous segment cultures were positive if >15 cfu were isolated from the samples[3] and catheter hub cultures were positive if >100 cfu were isolated from the swab taken from the hub[4].

Definitions

Catheter-related infections were defined as follows[5]:

1. localized infection of the catheter site
   - isolation of a significant number of bacteria with or without inflammation at catheter site or
   - the presence of purulent discharge at vascular site
2. catheter-related bacteremia
   - isolation of significant number of bacteria from the catheter and isolation of the same organism from blood cultures drawn by separate venepuncture
   - and no other obvious source of bacteremia.

Identification of the potential source of catheter-related infections[5]

The following criteria were used:
The skin at catheter insertion site was considered as the potential source if the same organism was isolated from the skin and catheter tip. Hub-related infections were defined as isolation of the same organism from the catheter hub and the catheter tip. Both the skin and hub were considered as sources of infection if the same organism was isolated from the catheter tip, the skin and the hub. Infusate-related infection was said to occur if the same organism was isolated from the TPN solution and the catheter tip. Haematogenous seeding of the catheter was thought to have taken place when the same organism was cultured from the catheter tip, blood and a distant source of infection.

Results

A total of 29 CVCs used on 14 patients were examined. There were 4 female and 10 male and the mean age was 45 years (range 16 -71 years). The average duration of catheter insertion was 6.6 days (range 4-14 days). Seven patients succumbed to their illness in the ICU.

Twenty-six of the 29 catheters removed (89.7%) were culture-positive (Table I). The proximal segment and catheter tip cultures correlated very well (97%) in the organisms isolated as well as the bacterial counts. Hence, they are discussed as a single unit (catheter tip).

Haematogenous seeding was deemed to have occurred in 7 catheters. Five of these were used on 2 patients who were bacteremic despite antibiotic cover, before their catheter insertions (one patient had a gangrenous bowel which was the most likely source for his repeated *Klebsiella* infections and the other had Acinetobacter in his tracheal secretion and blood 12 days and 7 days respectively, before catheter insertion). The sixth catheter was probably seeded from a pneumonia and the seventh was presumed to be seeded from blood although no distant focus of infection was noted because the catheter tip isolate was found only in the blood and not on the hub or the patient's skin.

Only 7 of the positive blood cultures were apparently catheter-related, giving a CRB rate of 24%.

Organisms recovered from the catheter tips were found on the skin, hub and in the blood on 21, 14 and 14 occasions respectively (Table II). The patient's skin flora appeared to be the main source of CRI.

There were obvious signs of inflammation around 13 of the catheter wounds at the time of catheter removal.

There were 14 culture-positive catheter hubs; four of these occurred in catheters with haematogenous seeding and the remaining were associated with positive skin cultures and hub contamination probably occurring during nursing procedures. It was not possible to confirm hub-related bacteremia except on 2 occasions when the catheter and blood cultures both yielded a mixture of 2 organisms, 1 of which was also recovered

from the skin and the other from the hub. In these 2 instances, it could be said that both skin-related and hub-related bacteremia occurred.

The 7 episodes of CRB occurred in 5 patients who were infected by a *Klebsiella* species, 3 strains of *Acinetobacter* and 4 of coagulase-negative staphylococci (with mixed Acinetobacter and staphylococcal infection in 1 patient). Three of these patients died compared with 2 deaths among 5 patients without bacteremia.

Table I
Results of 29 catheter cultures

	No. of catheters	Bacterial count (no. cfu) >15	<15
Culture negative	3	0	3
Culture positive with:			
haematogenous seeding	7	7	0
negative blood culture	12	12	0
positive blood culture	7	7	0
Total 29	26	3	

cfu : colony forming units

Table III shows the type of organisms involved in CRI during the 29 episodes of catheter changes in 14 patients. All TPN solutions cultured negative.

Line violations were noted in 10 of the 29 catheter insertions and these consisted mainly of flushing of the line and using the line for intermittent central venous pressure measurement.

Discussion

ICU patients are at particular risk of infection; many require long term TPN and multiple venous access.

The increased susceptibility of the immunocompromised patient to infection is further aggravated by lapses of aseptic techniques often occurring during emergency procedures.

The accurate diagnosis of CRI is important for patient management but often this is difficult as the only signs are those of systemic sepsis. With the presence of a CVC, the sudden onset of high fever with or without shock, absence of a focus of infection, fever unresponsive to antimicrobial therapy, the presence of local infection and the development of endocarditis, vertebral osteomyelitis and other metastatic infections acquired in the hospital are strongly suggestive of CRB.

Removal of the catheter removes the entry port of

Table II
Sources of catheter colonization

Sites of positive culture				No.	
Catheter tip	Skin	Hub	Blood	TPN	positive
+	+	+	+	–	4
+	+	–	+	–	4
+	–	+	+	–	4
+	–	–	+	–	2
+	+	+	–	–	5
+	+	–	–	–	7

+ = positive culture with the same isolates appearing in the different catheter parts, skin and blood

Table III
Microorganisms isolated from Skin/hub and blood

Organism	Skin/hub/ catheter tip	Blood	CRB(%)
Coagulase-negative staphylococcus	15	5	4 (27)
Acinetobacter calcoaceticus	10	6	3 (30)
Streptococcus B	1	0	0
Klebsiella pneumonia	6	3	1 (17)
Pseudomonas aeroginosa	1	2	0
Strptococcus faecalis	1	0	0
Staphylococcus aureus	4	1	0
Diphteroids	3	0	0
Torulopsis famata	1	0	0
Candida krusei	1	0	0
Flavobacterium species	0	1	0

% = number causing CRB divided by number isolated from skin/hub/catheter tip

microorganisms and a possible focus of on-going sepsis but catheter replacement is not without problems. Empirical diagnosis of possible CRB in a compromised host not responding to appropriate antibiotic therapy may result in the removal of many catheters which eventually are shown not to be the cause of bacteremia. Furthermore, microbiology findings may be confounded by the use of antibiotics in the ICU setting or by low grade bacteremia resulting in falsely negative results.

Maki's SQ technique is most commonly used to differentiate between infection and contamination; the method is standardized, quick, cheap and simple and is suitable for the culture of short-term CVC[6]. A positive tip culture in combination with positive blood cultures with the same organism is highly suggestive of CRB in the absence of other foci of infection[7].

The organisms associated with CRI in our setting are similar to those from other studies where coagulase-negative staphylococci predominate followed by Gram-negative bacilli, *S. aureus* and other skin commensals. Infection with yeasts occurred infrequently. A high incidence of CRI *Acinetobacter* species and *Klebsiella* species and this was in keeping with the bacteria flora of the ICU in our setting. Although 90% of the catheters used were infected, the rate of CRB was 24%. It has been said that isolation of coagulase-negative staphylococci is not highly predictive of systemic infection, but isolation of *S. aureus, P. aeruginosa* or Candida species from the tip carries a 31-57% chance of CRB[3,6].

Catheter tip culture is more predictive of CRB than exit site swabs.

The frequency with which types of microorganisms caused CRB to some extent reflected the frequency with which these flora were found in the skin, hub or catheter tip of the patient with coagulase-negative staphylococcal, *Acinetobacter* and *Klebsiella* being the organisms isolated from patients with CRB.

Although *S. aureus* caused 4 CRI, CRB did not occur with this pathogen.

The culture of catheter hub allows detection of infection as a result of the migration of pathogens down the internal surface of the catheter. This

contributed to at least 2 CRB in this study. Skin flora found on patients were most likely transferred to the hub during nursing procedures.

SQ culture of the proximal segment helps to identify external surface migration from the skin. The almost complete concurrence of catheter tip and proximal segment cultures in this study indicated most of the infections were skin-related rather than hub-related, even in the presence of positive hub cultures.

Skin signs were present on 13/26 (50%) occasions with positive catheter culture, that is, 50% catheter positive patients had no skin signs.

There were 12/26 catheters with >15 CFU unassociated with bacteremia compared with 14/26 catheters (54%) with >15 CFU associated with bacteremia but 7 were most likely to be from haematogenous seeding. The positive predictive value was better than the average 30% PPV reported in literature[7].

Negative catheter cultures may be the result of antibiotic cover. This probably explained 3 culture negative episodes in this study.

The high CRB rate (24%) in this study (usual risk of 2-9% from literature[2,8]) was probably contributed by several factors, such as the use of hyperalimentation fluids and hypertonic solutions, placement of triple lumen catheters (20/29) and presence of line violations. Other predisposing factors included compromised status of ICU patients, use of antibiotics, seeding from distant colonization and presence of local wound infections.

In order to reduce the infective complications of CVC, it is suggested that specialized intravenous teams, the use of strict protocols for the insertion and care of central lines and the intensive training of medical and nursing staff, are necessary.

Conclusion

Colonization of central venous catheters for short-term TPN is inevitable in critically ill patients in ICU. Antibiotic prophylaxis is not effective and CRB still occurs in patients covered with multiple powerful antbiotics. Significant CRB is difficult to conclude in such patients. Although increased mortality is present among many critically ill patients in ICU with or without CRB, many physicians still would remove catheters with significant numbers of microorganisms especially when supported by positive blood cultures and clinical signs. A continuous audit of CRI would contribute to rational management in ICU.

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