Original Article

Intravascular catheter-related infections in an Indian tertiary care hospital

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Abstract

Introduction: This study had two objectives: 1) to determine the clinical and microbiological profiles of patients developing intravascular catheter-related local (localized catheter colonization and exit site) and systemic infections and their predisposing factors; 2) to study the antibiotic sensitivity patterns of the organisms isolated.

Methodology: This case-control study was conducted over 19 months involving 232 patients at a tertiary care hospital. Non-tunneled central venous catheters and midline catheters were the two types studied. Catheter tips were processed using Maki's roll plate and endoluminal flush techniques. Blood cultures were drawn under strict aseptic precautions and processed by the BacT ALERT system. A "case" was any patient with proven localized catheter colonization, exit site infection or blood-stream infection and a "control" was any patient from whom the intravascular catheter yielded no organism in semi-quantitative cultures.

Results and Conclusions: The incidence of catheter-related blood-stream infections (CRBSI) in our institute was 8.75 per 1,000 catheter days. The commonest organisms causing local infections were coagulase-negative *Staphylococci*, and those causing CRBSI were *Staphylococcus aureus*. Multidrug-resistant organisms accounted for 30.2% of the infections. Risk factors for development of catheter-related infections included an immune compromised state, duration of the catheter *in situ*, femoral venous cannulation, and triple lumen catheters. Choice of venous cannulation to minimize the risk of catheter-related infection in ascending order for risk of infection is the subclavian vein, jugular vein, basilic vein and then the femoral vein. There was no role for empirical antibiotic therapy to prevent intravascular catheter-related local or systemic infections.

Key words: central venous catheters; midline catheters; blood-stream infections; blood cultures

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Introduction

Intravascular catheters are indispensable in modern-day medical practice, particularly in intensive care units. Although such catheters provide necessary vascular access, their use puts patients at risk for local and systemic infectious complications, including local site infection, catheter-related blood-stream infections (CRBSI), septic thrombophlebitis, endocarditis, and other metastatic infections (*e.g.*, lung abscess, brain abscess, osteomyelitis, and endophthalmitis) [1].

The aims of this study were 1) to determine the clinical and microbiological profiles of patients developing intravascular catheter-related local (localized catheter colonization and exit site) infections and systemic infections and their predisposing factors; and 2) to study the antibiotic sensitivity pattern of the organisms isolated. Having these data available will help in understanding the burden of and deriving preventive measures for such infections, as well as provide insight for the correct use of antibiotics according to their sensitivity patterns in health-care settings.

Methodology

Sample collection and processing

a) Catheter tip: The skin was cleaned with 70% alcohol prior to catheter removal. The catheter was held at the proximal end and carefully removed from the patient with a sterile instrument, taking care to avoid contact with the skin. The distal end was held over a sterile tube, and the tip was cut with sterile scissors. The terminal two to three inches were collected in the tube and transported to the lab as soon as possible [2].

b) Catheter tip processing: Extraluminal Maki's roll over plate method and endoluminal catheter flush culture were used for processing [3,4].

Extraluminal Maki's roll over plate method was performed as follows: using sterile forceps, the catheter tip was removed from the transport tube and laid on a blood agar plate. The tip was rolled back and forth across the entire surface of a blood agar plate using sterile forceps and exerting slight downward pressure.

For endoluminal catheter flush culture, the catheter lumen was flushed into a sterile vial with 1 ml of sterile normal saline with the help of sterile syringe, of which 0.01 ml was streaked onto the culture media using a 4 mm inoculating loop. The same volume of sample was also streaked onto blood agar and MacConkey agar, and incubated at 37ºC in CO_2 (performed only for quantification). Colony morphology reading, Gram staining, biochemical identification, and subculture of the organism isolated from the Maki's roll plate were performed by routine laboratory techniques. Growth upon triple sugar iron agar and mannitol motility test agar, and methyl red/Voges Proskauer, indole/H_2S detection, citrate utilization and urease tests were completed for identification of Gram-negative bacteria. Catalase and coagulase tests were performed to identify Gram-positive cocci. Antibiotic sensitivity patterns were identified using the Kirby-Bauer disk diffusion method as recommended by the Clinical Laboratory Standards Institute (CLSI) [5]. Screening for methicillin-resistant *Staphylococcus aureus* (MRSA) was performed using an oxacillin (1 µg) disk on Mueller Hinton agar. Screening for extended spectrum beta-lactamases (ESBL) was by double disc approximation or double disk synergy using amoxicillin-clavulanic acid (20/10 µg) and ceftriaxone (30 µg) at a distance of 30 mm between the centers of the two disks. American type culture collections (ATCC) were used as control strains. Multidrug resistance was defined as resistance to at least three of the four following groups: (1) imipenem or meropenem; (2) cefepime or ceftazidime; (3) piperacillin, piperacillin–tazobactam or ticarcillin–clavulanic acid; and (4) ciprofloxacin or levofloxacin [6].

c) Interpretation [2]: Agar plates were examined at 24 hours, 48 hours and 72 hours. Significant growth was defined as ≥ 15 colony forming units (CFU) by Maki's roll plate method or ≥ 100 CFU/ml by the catheter flush method.

d) Blood sampling: Blood (10 ml) was collected within 48 hours of catheter collection under aseptic precautions in a BacT bottle and analyzed using the BacT ALERT system (bioMérieux, Hazelwood, Missouri, USA).

e) Statistical analyses: Statistical analyses were performed using SPSS 16.0 for Windows (IBM Corporation, New York, USA). Chi-square was used for univariate analysis and multiple logistic regression was used for determining the predisposing risk factors. Statistical significance was determined at a 5% level of significance.

Results

Among the study subjects, 108 were cases and the remaining 124 were controls. Cases were divided into two groups: 25 had CRBSI and 83 had local catheter infections (including local catheter colonization and exit site infection).

Clinical profile of the study population

The clinical profile and catheter characteristics of the study population are depicted in Tables 1 and 2 respectively. In summary, the mean age in years among controls was 43.53 and that among patients with local catheter infections and CRBSI were 42.1 and 42.84 respectively. The commonest premorbidity among the controls and patients with CRBSI was renal failure (35.5% and 40% respectively) while that among the patients with local catheter infections was diabetes (34.9%). Local signs of inflammation such as erythema, warmth, induration, tenderness, and purulence at the exit site were seen among all patients with CRBSI and among the majority of patients with local catheter infections (96.4%).

Indication for venous cannulation

The commonest indication for central venous cannulation was for IV fluids and antibiotic administration in the controls, local catheter infections and CRBSI (57% vs. 77% vs. 64% respectively). Hemodialysis was the indication in 44% of controls and 29% and 40% in patients with local catheter infections and CRBSI respectively. Chemotherapy as an indication was observed in 3% of central venous catheters among controls and 4% of patients with local catheter infection.

Microbiological profiles of the cases

Distribution of pathogens: In our study 64% of the pathogens causing CRBSI were Gram positive and 36% were Gram negative. Furthermore, 61.3% of

Table 1. Clinical profile of study population

Clinical profile	Controls (%) n=124	Local catheter infections (%) n=83	CRBSI's (%) n=25
Gender			
Men	78 (62.9)	55 (66.3)	18 (72)
Women	46 (37.1)	28 (33.7)	7 (28)
Mean age (in years)	43.53	42.10	42.84
Mean hospital stay (in days)	22.71	29.66	28.56
Premorbidities			
Diabetes	10 (8.1)	29 (34.9)	8 (32)
Renal failure	44 (35.5)	23 (27.7)	10 (40)
AIDS	1 (0.8)	0 (0)	2 (8)
Malignancies	8 (6.5)	3 (3.6)	0 (0)
Local signs of inflammation	0 (0)	80 (96.4)	25 (100)

Table 2. Catheter profile of the study population

Catheter profile	Cases (%) n=108	Controls (%) n=124
Type of catheter		
Central venous catheters	82 (75.9)	107 (86.3)
Midline catheters	26 (24.1)	17 (13.7)
Number of lumens		
Single	25 (23.1)	21 (16.9)
Double	40 (37)	73 (58.9)
Triple	43 (39.8)	30 (24.2)
Site of venous cannulation		
Basilic vein	25 (23.2)	17 (13.7)
Femoral vein	36 (33.3)	20 (16.1)
Jugular vein	24 (22.2)	51 (41.1)
Subclavian vein	23 (21.3)	36 (29.1)

Table 3. Predisposing risk factors for development of catheter related infections

Variables	Adjusted Odds Ratio (95% CI)	'p' value
Immune status		
Immunocompetent	1	
Immunocompromised	2.3 (1.19, 4.45)	0.011
Duration of catheter in situ		
<12 days	1	
>12 days	2.21 (1.16, 4.20)	0.04
No. of catheter lumens		
Single	1	
Triple	35.90 (3.11, 414.26)	0.004
Site of placement		
Subclavian vein	1	
Femoral vein	20.48 (5.71, 73.37)	0.001

the pathogens causing local catheter infections were due to Gram-negative organisms and 38.7% were due to Gram-positive organisms. The commonest pathogen causing CRBSI was *S. aureus* (40%) and that among patients with local catheter infections was coagulase negative *Staphylococci*. *Candida* caused 16% of CRBSI and 10% of local catheter infections. The distribution of pathogens among the cases is shown in Figure 1.

Drug resistance patterns: MRSA accounted for 26.7% of patients with CRBSI and 16.7% of patients with local catheter infections. Additionally, 13.3% of the isolates among CRBSIs and 4.2% among patients with local catheter infections were extended spectrum beta-lactamase (ESBL) producing organisms. Multidrug resistant (MDR) strains were isolated from 6.7% of patients with CRBSI and 37.5% of patients with local catheter infections. Overall, the antibiotic sensitivity profiles showed that 6.3% were ESBL producing organisms, 30.2% were multidrug resistant (MDR) and among the *Staphylococci* isolated, 31% were MRSA and 69% were methicillin sensitive (MSSA).

Antibiotic sensitivity: In patients with local catheter infections, both the MRSA and methicillin resistant coagulase negative *Staphylococci* (MRCONS) isolated were 100% sensitive to vancomycin, teicoplanin and linezolid; the *Pseudomonas aeruginosa* isolates were sensitive to cefoperazone-sulbactum, piperacillin-tazobactum, ticarcillin-clavulanic acid (85.7% for each antibiotic) and meropenem (78.6%); the *Escherichia coli* were sensitive to cefuroxime and meropenem (88.9% for each antibiotic); and the *Klebsiella pneumoniae* were sensitive to amikacin (12.5%) and meropenem (50%) (The percentages within parenthesis express the number of strains sensitive to a particular antibiotic of the total organisms isolated). Among patients with CRBSI, all *P. aeruginosa* isolates were sensitive to ciprofloxacin, cefepime, cefoperazone-sulbactum, piperacillin-tazobactam, ticarcillin-clavulanic acid and meropenem, all *E. coli* were sensitive to meropenem, and all *K. pneumoniae* were sensitive to gentamicin, netilmicin, amikacin and meropenem. Only one strain of *Acinetobacter baumannii* isolated from a patient with CRBSI was resistant to all routine and reserved drugs.

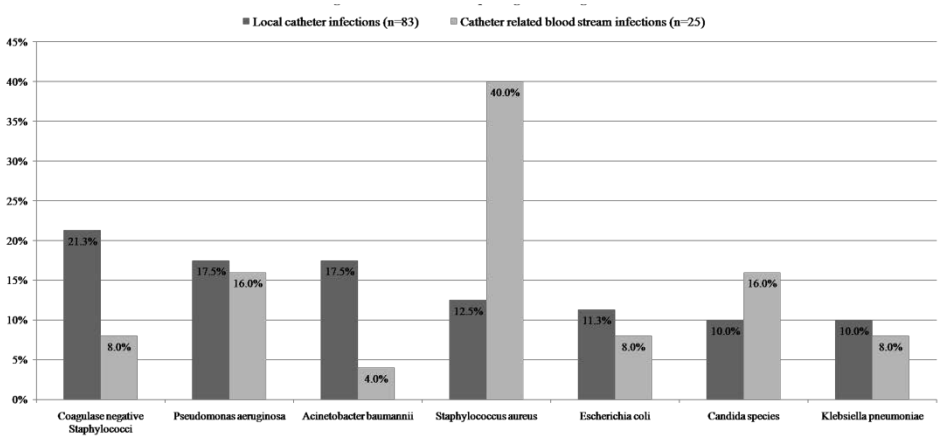
Predisposing risk factors

A number of variables were compared between the cases and controls. Using logistic regression, the odds ratio was calculated for each of the below-mentioned variables and this data is presented in Table 3.

Immune status: 61.1% of the cases were immune compromised and the remainder (38.9%) were immune competent. Immune status is an important predisposing risk factor for development of catheter-related infections with a statistically significant *P* value of 0.011.

Duration of catheter *in-situ*: Duration of the catheter *in situ* is a predisposing risk factor ($P = 0.04$) for development of catheter-related infections. The mean duration of catheter *in situ* (in days) was higher among cases than controls (14.06 vs. 10.96).

Figure 1. Distribution of pathogens



Number of catheter lumens: The incidence of developing catheter-related infections was highest with triple lumen catheters (39.8%) followed by double lumen and single lumen catheters (37% vs. 23.1%) indicating that the risk of infection is higher with multi-lumen central venous catheters (P = 0.004).

Site of catheter placement: Femoral venous catheters accounted for 33.3% of infections followed by midline and jugular catheters (23.1% vs. 22.2%). The lowest risk was observed with subclavian venous catheters (21.3%). The site of venous cannulation is a risk factor for development of catheter related infections (P = 0.001).

Discussion

This study analyzed the incidence density, clinical and microbiological profiles, and risk factors for the development of catheter-related infections in a tertiary care hospital. Four similar studies have previously analyzed catheter-related infection in detail [7-10], but the numbers of catheters used in these (300, 499, 2,595 and 1,314 respectively) were higher than the number in the current study (n = 232). This study has three limitations. First, different catheter insertion sites were not randomly assigned. No randomized trials, however, have compared infection rates for central venous catheters (CVCs) placed in three different sites, and patients were randomly assigned to undergo central venous cannulation at the femoral or subclavian sites only in the study by Merrer *et al*. [11]. Secondly, not every vascular catheter inserted during the study period was sampled; and thirdly, patients with local catheter infections were not defined into exit site infections (or) localized catheter colonization as the numbers were too small for the latter subset. The CRBSI incidence density at our hospital is 8.75 per 1,000 catheter days. This is comparable to that of the National Nosocomial Infections Surveillance (NNIS) System Report (2 to 11.3 per 1,000 catheter days) and a study by Pawar *et al*. (4.01 per 1,000 catheter days) [10].

Several variables have been quoted as contributing to catheter-related infections. These include the number of catheter lumens, cannulation site, duration of catheterization, and immune status of the patient.

Which cannulation site is associated with the highest risk of infection remains controversial. Several studies have analyzed the catheter tip colonization (CTC) incidence according to different CVC sites. Our study showed the highest incidence of local catheter infection at the femoral venous site (30.1). Merrer *et al*. [11] observed a higher incidence of infection-related complications at the femoral venous site in comparison with the subclavian venous site (19.8% vs. 4.5%). Goetz *et al*. [8] also reported an increased risk for infection with femoral catheters, and with those that were inserted as an emergency, as well as for post transplant patients. Probable reasons for an increased incidence of such complications at femoral venous sites are (1) femoral access is often used in emergency situations, during which adequate procedures cannot be always fully respected, and (2) the femoral site is usually chosen for patients with a contraindication to a cervicothoracic insertion. Because these patients are more seriously ill, they might be at a greater risk for infectious complications. Presence of a higher density of local

skin flora in the groin area is also postulated to be a reason for more infections at the femoral site [12].

Some studies show a higher incidence of infection with jugular catheters [7,13,14]. The exact reason for this observation was not clear but Richet *et al*. [7] explained that it could be related to the presence of hair in this area, contamination with oropharyngeal secretions, the insertion technique, or the fact that jugular-site dressings are often loose. A few studies compared only jugular versus subclavian access, finding a higher incidence in the former [15-17]. Sadoyama *et al*. [16] asserted that jugular catheters are also associated with longer ICU stays, hospitalization, and a higher mortality.

Multi-lumen lines have been associated with a higher incidence of CRBSI [18-20]. In the present study, the incidence of catheter-related infection was highest with triple lumen catheters (39.8%, OR = 35.9, p = 0.002). Pemberton *et al*. [18] observed an incidence of 19% among triple lumen and only 3% among single lumen subclavian catheters used for total parenteral nutrition. McCarthy *et al*. [20] also had similar observations in a study in which they compared triple lumen with single lumen catheters (12.8% vs. 0%) for administering parenteral nutrition. Higher rates of infection in triple lumen catheters were attributed to frequent handling of such catheters by health-care providers and the possibility of contamination during such procedures.

The duration of catheterization was a significant factor that determined the development of catheter-related infections. Although previous studies have confirmed that central venous catheterization longer than five to seven days was associated with a higher risk of catheter-related infection [7,14,21,22], the mean duration of catheterization in our study was 12.32 days and no attempts were made to replace catheters as the CDC guidelines of 1996 [23] and 2002 [1] recommend against routinely replacing CVCs to prevent catheter-related infections. The risk of infection for catheters placed for more than 12 days was 2.21 times that of those *in situ* for less than 12 days (P = 0.016). Moro *et al*. [17] showed age, transparent dressing, jugular insertion, male gender, duration of catheterization, and hub colonization were independent risk factors for skin colonization.

The commonest isolates among the patients with local catheter infections were Gram negative (61.3%), while Gram-positive organisms (64%) caused the majority of the CRBSI. Overall, in the entire study, *S. aureus* was the commonest pathogen isolated, accounting for 19%, followed by coagulase negative *Staphylococcus* species (CONS) (18.1%), *P. aeruginosa* (17.1%), *A. baumannii* (14.3%), *E. coli* (10.5%) and *K. pneumoniae* (9.5%). In the prospective analysis from the SCOPE database of 24,179 nosocomial BSIs occurring in 49 hospitals in the United States between 1995 and 2002, Wisplinghoff *et al*. [24] showed that the commonest isolates were CONS (31%) and *S. aureus* (20%). Subba Rao *et al.* [25] also showed that the commonest isolates in ICU patients were CONS (32.4%), *Pseudomonas* and *Enterobacter* species. CONS and *S. aureus* commonly originate from the skin surface and track along the external surface of the catheter. In comparison, the hands of health-care workers often introduce Gram-negative organisms during the manipulation of catheters or intravenous tubing [26].

In this study, *Candida* species was isolated from 11.4% of the study population and specifically accounted for 16% of blood-stream infections. Pawar *et al*. [10] showed that 11.4% of CRBSI was caused by *Candida* species in cardiothoracic surgical ICUs and Subba Rao *et al*. [25] demonstrated that 20% of catheter-related infections occurred in pediatric ICUs. Evidence suggests that the actual burden of nosocomial candidemia in Indian hospitals is under-recognized [27].

Conclusion

Central venous catheters are increasingly used in the inpatient and outpatient setting to provide long-term venous access. However, infection of CVCs remains a major problem. Early diagnosis and treatment are vital to reduce the morbidity and mortality involved. This study demonstrates the risk factors and the pathogens isolated from patients defined to have such infections in an Indian tertiary hospital. Despite advances in management, this common clinical problem could still benefit from future breakthroughs.

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