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Incidence of Central Venous Catheter-Related Infection and Risk Factors in Critically Ill Post-Operative Cancer Patients: A Randomized Prospective Cohort Study

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Abstract

Background: Cancer patients are susceptive to infection. Catheter-related bloodstream infections are the first cause of nosocomial bloodstream infections in intensive care units.

Objectives: The aim of this study was to evaluate the association between the type of central intravenous catheter and bloodstream infection in post-operative cancer surgery patients at surgery intensive care units (ICU).

Methods: In a randomized, non-blind study, 66 cancer surgery patients were studied. The primary aim was rate of central venous catheter-related infection by type of catheter. The patients were enrolled in three groups: simple catheter (n = 23) (without antimicrobial), impregnated catheter in the internal part (n = 28), and AGB + catheter (n = 15) (impregnated catheter in external and internal part); all catheters were triple lumen, polyurethane (arrow, chlorhexidine and silver sulfadiazine, USA). Insertion of catheters was done in full sterile conditions based on the center for disease control (CDC) guidelines for the prevention of intravascular catheter-related infection. Catheter related infection was confirmed by positive blood culture of blood samples of central catheter. The chi square or Fisher's exact test was used to compare base values and difference in rate of colonization and bloodstream catheter-related infection. A P value of less than 0.05 was considered statistically significant.

Results: Sixty-six patients participated in this study in three groups. There was no significant difference regarding the baseline demographic and clinical characteristics of patients between groups ($P > 0.05$). Distributions of surgery types were statistically the same in the three groups ($P = 0.323$). Impregnated catheters had no significant effect on colonization ($P = 0.565$) or bloodstream infection prevention ($P = 0.490$).

Conclusions: Compared to standard catheters, impregnated catheters had no effect on colonization or bloodstream infection prevention.

Keywords: Central Venous Catheter-Related Infection, Critically Ill, Cancer Patients

1. Background

Intravascular catheters are the most common source of infection at intensive care units (ICUs). Catheter-related bloodstream infections (CRBSI) have been reported in 3% to 8% of indwelling catheters and are the most common cause of nosocomial bloodstream infections in critically ill patients (1, 2). In general, patients with cancer have 1.4 to 2.2 infections per 1000 catheter-days for central venous catheters (CVCs) (3). Catheter-related bloodstream infections cause serious morbidity and mortality and are associated with increased hospital costs and length of stay (4, 5). Attributable rate of mortality is 0% to 35%, based on the degree of control for severity of illness (1). Two main pathways have been shown for colonization of the endovascular catheter that can lead to infection: the extraluminal and the intraluminal routes (6). Skin organisms migration from the insertion site of catheter to the catheter tip colonization is the most common route of infection for short-term CVCs (1). For long-term catheters (more than 15 days), the main cause of colonization is manipulation of the venous line with organisms' migration along the internal lumen of the CVC (1).

Catheter material is an important factor that affects catheter-related infection prevention. Central venous catheter material should not be altered by prescribed IV drugs and deformable while it should be biocompatible, hemocompatible, biostable and chemically neutral. Moreover, the catheter must be flexible, resistant, as radio-opaque as possible, thin walled, resistant to sterilization and have a high ratio of internal/external diameter. Infec-

tious complications with Teflon or polyurethane catheters are less than catheters made of polyvinyl chloride or polyethylene (7, 8). Cancer patients are immunocompromised and, hence, susceptive to infection (4, 9). Infection process in cancer patients is on the quiet and its manifestations are irregular (10, 11). Many studies have investigated CRBSI in patients with cancer, yet to the best of our knowledge there are no studies that have focused on critically ill post-operative patients with cancer.

2. Objectives

We conducted the prospective observational cohort study in referral tertiary cancer surgery with the aim to determine the incidence of CRBSI in post-operative cancer surgery patients, who were admitted to the intensive care unit (ICU), based on type of CVC and important identified risk factors.

3. Methods

3.1. Study Setting and Population

This study was performed at the cancer institute of Imam Khomeini hospital complex, which is a tertiary referral center in Tehran, Iran, with medical and radiation oncology units, and special cancer surgery. After having obtained approval from the research committee, in a randomized, non-blind, prospective observational cohort study, 66 post surgery cancer patients, admitted to the cancer institute ICU, were enrolled in the study. Effect of type of CVC on catheter colonization and bloodstream infection incidence was the primary aim of the study. The patients were randomly enrolled in three groups: simple catheter (n = 23) (without antimicrobial), impregnated catheter in the internal part (n = 28) (chlorhexidine and silver sulfadiazine), AGB+ catheter (n = 15) (chlorhexidine and silver sulfadiazine, impregnated catheter in external and internal part); all of catheters were triple lumen, polyurethane (Arrow, USA). Insertion of catheter was done by one anesthesiologist under fully sterile conditions based on guidelines for the prevention of intravascular catheter-related infection (5). Sepsis was confirmed based on sepsis criteria defined by the surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock (12). The escalation of antibiotics was applied based on sepsis work-up.

Gender, mean age, length of ICU stay, rate of infection, result of blood culture, indwelling site and use duration of CVC, Acute physiologic and chronic health evaluation (APACHE) II score on admission day and kind of surgery were recorded. No patient had neutropenia.

3.2. Definitions

Catheter-related bloodstream infection was determined by clinical manifestations and positive culture of CVC blood sample or positive blood culture of peripheral vein and CVC with the same organism with growth of microbe in a CVC blood sample at least two hours earlier than the blood sample of peripheral vein (positivity criteria of differential time) (5, 13, 14). After confirming CRBSI, the tip of CVC was sent for culture. Enteral feeding (oral or tube feeding) was started on the second day and parenteral nutrition (TPN) was initiated on the third day of ICU admission in cases with contraindication of gastrointestinal feeding. Incidence of CRBSI was considered as the number of CRBSIs divided by the number of central line-days in the study period per 1000 individuals.

3.3. Statistical Analysis

Data are presented as mean $\pm$ standard deviation. Independent sample t-test was used to compare quantitative variables between the groups. We aimed to detect the rate of infection induced by CVC type between groups with a two-sided type I error protection of 0.05. A P value of less than 0.05 was conceived statistically significant. Chi square and Fisher's exact test was used for comparing primary outcome (catheter colonization and bloodstream infection) and categorical variables between the groups, and the association was presented as relative risk (rr). statistical analyses were applied by the SPSS 16 application (SPSS Inc., Chicago).

4. Results

Sixty-six patients were enrolled in the study in three groups. There was no significant difference regarding the demographic and clinical characteristics of patients in the three groups (Table 1). Some patients were intubated or received a vasopressor but there was no statistically significant difference between the three groups (P = 0.912, P = 0. 453, respectively) (Table 1). Distribution of surgery types was statistically the same in the three groups (P = 0.323) (Table 1). Minimum and maximum duration of CVC stay was four and 29 day, respectively (mean = 15.6, median = 15.5 day).

There was no significant association between result of peripheral cultures or CVC blood sample, tip of CVC and type of CVC (P = 0.454, P = 0.648, P = 0.440, respectively) (Table 2).

Compared to simple catheters (n = 23), impregnated AGB+ catheters (n = 15) had no significant effect on colonization (P = 0.480, RR: 0.47 [95% CI: 0.04 - 5.06]) or bloodstream infection prevention (P = 0.503, RR: 0.51 [95% CI:

Table 1. Distribution of Basic Variables in the Two Groups[a]

Variable	Simple	Impregnated Internal Part Catheter	AGB+	P Value
Gender				0.600
Male	19 (82.6)	24 (85.7)	11 (61.1)	
Female	4 (27.4)	4 (14.3)	4 (38.9)	
Age, mean ± SD	39.4 ± 13.7	43.9 ± 13.6	41.3 ± 15	0.502
APACHE II score, mean ± SD	14.4 ± 2.9	15.8 ± 3.8	14 ± 3.7	0.275
GCS, mean ± SD	10.2 ± 3.8	11.2 ± 3.2	11.8 ± 1.3	0.409
Intubation				0.912
Yes	16 (69.6)	18 (62.1)	5 (62.5)	
No	7 (30.4)	11 (37.9)	3 (37.5)	
Vasopressor				0.453
Yes	7 (30.4)	10 (35.7)	1 (12.5)	
No	16 (69.6)	18 (64.3)	7 (87.5)	
Kind of surgery, No.				N/S
Breast	3	0	0	
GI	12	13	3	
H and N	6	10	5	
Liver	1	2	0	
Others	1	3	0	

Abbreiations: APACHE, acute physiologic and chronic health evaluation; GCS, glasgow coma scale; GI, gastrointestinal; H and N, head and neck; N/S, not stated.
[a]Values are expressed as No. (%) unless otherwise indicated.

0.05 - 5.22]). Also, antimicrobial catheters (impregnated catheter (n = 43) vs. simple catheter (n = 23)) had no statistically significant effect on colonization (P = 0. 333, RR: 0.32 [95% CI: 0.05 - 2.10]) or bloodstream infection prevention (P = 0.300, RR: 0.47 [95% CI: 0.12 - 1.85]).

5. Discussion

Catheter-Related Bloodstream Infection is one of the most serious nosocomial infections in the ICU (1). The risk of catheter-related infection correlates with the patient's age, weight, underlying diseases, immune system status and type of fluid injection (15, 16). Several preventive techniques have been shown, which can reduce the incidence of infections including: adequate knowledge, insertion and keeping of catheter only in necessary situations, hygiene, use of appropriate solutions (alcoholic-chlorhexidine) for skin disinfection, care protocol implementation, CVC insertion under ultrasound guidance, preference of subclavian line instead of other sites, change of dressings (no more than seven days), and avoiding antibiotic prophylaxis (1, 17-20). The most important principle of prevention is personnel training for catheter care and observing the principles of sterilization (15, 21).

One study (22) showed that catheters coated with antimicrobial or antiseptic agents decrease microorganism adhesion and biofilm production, and, hence, the risk of catheter-related infection. Despite the additional expense, use of the antimicrobial/antiseptic-coated catheter is cost-effective and, hence, may decrease hospital cost. Nevertheless, the routine use of antimicrobial CVCs is not recommended considering ecological impact and costs (23, 24). The 2002 healthcare infection control practices advisory committee of the centers for disease control and prevention reserved the use of antimicrobial-impregnated CVCs only for conditions with an incidence of blood stream infection $\geq$ 3.3 per 1000 CVC-days, such as in ICUs (25).

Ramritu's study (25) compared this method with the standard catheter; the first generation coated catheters (extra luminal side coated with chlorhexidine/silver sulfadiazine) could decrease the colonization and bloodstream infection of catheters significantly, yet bloodstream infection with second-generation catheters (external and internal surfaces coated) was statistically the same.

Crnich et al. (24) showed that antimicrobial impregnated CVCs were associated with a 46% and 40% reduc-

Table 2. Colonization and Bloodstream Infection Rate Between Groups[a]

Variable	Catheter Type			P Value
	Simple	Impregnated Internal Part	AGB+	
CVCBC				0.830
No	20 (86.9)	25 (89.3)	14 (93.3)	
Yes	3 (13.1)	3 (10.7)	1 (6.7)	
P-BC				0.454
No	18 (78.3)	24 (85.7)	14 (93.3)	
Yes	5 (21.7)	4 (14.3)	1 (6.7)	
Colonization				0.217
No	19 (83.3)	27 (96.4)	14 (93.3)	
Yes	4 (16.7)	1 (3.6)	1 (6.7)	
CRBSI				0.363
No	20 (86.9)	25 (89.3)	15 (93.3)	
Yes	3 (13.1)	3 (10.7)	1 (6.7)	
Microorganism of CRBSI				N/S
S. aureus	1	0	0	
Klebsiella	1	1	0	
Acinetobacter	1	1	1	
P. aeruginosa	0	1	0	
Insertion site				0.148
Subclavian	12 (52.3)	16 (57.1)	4 (26.7)	
Jugular	11 (47.7)	12 (42.9)	11 (73.3)	
Nutrition				0.747
EN	11 (47.7)	14 (50)	9 (60)	
TPN	12 (52.3)	14 (50)	6 (40)	
Length of CVC use, d (mean ± SD)	15.7 ± 6.5	15.4 ± 6	17 ± 5.6	0.811
Length of CVC use, d				0.936
≤ 10	4 (17.4)	5 (17.9)	1 (12.5)	
> 10	19 (82.6)	23(82.1)	7 (87.5)	
Length of ICU stay, d (mean ± SD)	13.9 ± 6.2	11.7 ± 6.3	8.2 ± 4.7	0.070

Abbreviations: CVCBC, central venous catheter blood culture; CRBSI, catheter related bloodstream infection; P-BC: peripheral blood culture; EN, enteral feeding; TPN, total parenteral nutrition; CVC, central venous catheter; N/S, not stated.
[a]Values are expressed as No. (%) unless otherwise indicated.

tion in the number of colonized and blood stream infections, respectively, when compared with control non-impregnated CVCs.

Catheter-Related Bloodstream Infection has been reported in 3 to 8% of insertion catheters (1, 2); and 1.1 to 7.9 infections per 1000 catheter-days for CVCs in patients with cancer (3, 26). In this study, total positive result of blood culture (CVC or peripheral blood sample) was 22.7% (15 of 66 cases) and rate of CRBSI was 9.1% or 5.8 infections per 1000 catheter-days for CVCs.

Hematologic and oncologic patients are often immune compromised with high burden of comorbidities, and, hence, they are at risk of serious infection and high mortality (27). Rate of CRBSI at our center was the same as previous studies. Gram-negative bacilli (e.g., *Acinetobacter* spp. and *Pseudomonas* spp.) were the most common cause of CRBSI in our study, similar to the studies of Schiffer (3) and Hentrich (26).

In our study, despite reduction of CBRSI rate in impregnated CVC compared with the standard type (10% vs. 13.1), this difference was not statistically significant (Table 2). This result may be induced from low sample size of our study. However, Ramritu (25) also did not find a difference between standard and second generation impregnated CVC regarding rate of CRBSI.

In the near future, mainly because of resistance of pathogenic microorganisms against antibiotics, CVC-related infection could become a serious problem (28). Although certain studies (1, 6, 25) showed that coated CVCs were the most effective way for reduction of CRBSI, yet limited evidence suggests that antimicrobial CVCs did not succeed in significant reduction of sepsis outcome or mortality (29).

5.1. Conclusions

The use of impregnated CVCs should be limited in special situations such as for critically ill and immune compromised patients and their routine use should be avoided. Also, we need new methods for diminish rate of catheter related infection in special patients such as cancer patients and intensive care situations. For these reasons, we should implement prophylaxis infection control protocols.

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