Risk factors for central venous catheter-related bloodstream infections

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SUMMARY

Our study aimed to identify the risk factors playing a role in central venous catheter-related bloodstream infections (CR-BSI) in a tertiary large volume university hospital. The current prospective clinical trial was conducted in a university hospital with 1400 beds. All demographic data, length of hospital stay, coexisting diseases, features of catheters used, invasive diagnostic and therapeutic procedures and all antibiotics used in patients with CVCs were recorded. A total of 356 CVCs inserted in 281 patients were followed up for 5667 catheter days. The mean duration of catheterization was recorded as 15.9±12.7days. CR-BSI was detected in 46 (12.9%) patients. The incidence of CR-BSI was found to be 8.12 in 1000 catheter days. Advanced age and longer duration of catheterization were found to be independent risk factors for the development of CR-BSI in multivariate analysis. Coagulase-negative staphylococci (15.2%), *Candida* spp (13%) and *Klebsiella pneumoniae* (13%) were the agents most frequently isolated.

Keywords: central venous catheter, infection, risk factor, catheterization.

INTRODUCTION

Central venous catheters among are becoming increasingly more frequently used for requirements such as hemodynamic monitoring, fluid and electrolyte replacement, infusion blood or blood products, chemotherapy and parenteral nutrition [1]. The incidence of catheter related bloodstream infections (CR-BSI) vary according to volume of the hospital, intensive care conditions and the type of the CVC used. According to 2012 data of National Hospital Infections Surveillance Network (UHESA), the incidence of CR-BSI has been reported as between 1.8 and 9.4 in 1000 catheter days and this value varies according to services in the hospital. Despite the decreased incidence thanks to developments in infection control measures and the bundle care CR-BSI still remain the 3rd most frequent hospital-associated infection after ventilator-associated pneumonia (VAP) and catheter-associated urinary tract infections (CAUTI) [2]. Mortality rates of CR-BSI are reported as 12-25% and CR-BSI is defined as one of the most fatal types of health-care related infections and carries high morbidity and mortality risk. In addition, CR-BSI requires longer hospital stay and higher cost [3, 4]. A variety of risk factors related with host, healthcare workers, catheter, and environmental conditions of hospital, responsible for the development of CR-BSI have been described by authors in the literature [5-8]. Although there are study reports on CR-BSI from our country, studies conducted after the foundation of UHESA and the establishment of the healthcare transformation program are limited in number [9-11].

The aim of our study is to identify the risk factors

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likely to be responsible for the development of CR-BSI and to estimate the incidence of this condition, as well as establishing the infection prevention packages, suggesting the empiric therapy protocols and to enlighten the further investigations.

PATIENTS AND METHODS

The study protocol was approved by Dicle University Medical Faculty, Non-Interventional Clinical Studies Ethics Committee (Session Nr: 371-25.03.2013) and informed consents were obtained from all participants. Our study was conducted in the largest tertiary referral university hospital of south-eastern Turkey. Between March 2013 and January 2014, central venous catheterized adult patients over the age of 18 years treated in internal medicine, general surgery, cardiovascular surgery, cardiac and neuro-intensive care, infectious diseases, haematology and nephrology wards were included in the study.

Patients hospitalised for 48 hours or shorter, and patients catheterised outside our hospital were excluded from the study. Temporary catheters were inserted by resident physicians while tunnelled catheters and catheters with port systems were inserted by experienced cardiovascular surgeons under aseptic conditions. The insertion point of the CVC was aseptically cleaned with povidone-iodine. After the catheter was inserted, the insertion point was covered with sterile gauze. The dressing was lifted every 48 hours for the observation of the insertion point and it was replaced after cleaning with povidone-iodine.

From the patients with suspicious of CR-BSI, simultaneous catheter blood cultures and at least one peripheral blood culture were obtained. From the catheter removed patients, catheter tip cultures and at least one peripheral blood culture was obtained. Before the blood cultures were sampled, the skin was cleaned with povidone-iodine and 7-10 mL of blood was drawn into blood culture vials to be incubated in BACTEC 9240 or BACTEC 9120 (Becton Dickinson, ABD) automatic blood culture devices. Positive blood cultures were inoculated to 5% of sheep blood and eosin methylene blue agar (EMB).

As the semiquantitative culture, the central venous catheter was removed under sterile conditions, a 5 cm distal section of the catheter was cut using sterile scissors and sent to the microbiology laboratory in a sterile Petri dish [12]. The section of the catheter was inoculated on the 5% sheep blood and EMB agar by rolling 4-5 times with the help of a sterile forceps.

The demographic characteristics, date of admission and the diagnosis, comorbid conditions, features of the catheter used, the diagnostic and therapeutic interventions, the antibiotics used and the Sepsis-related Organ Failure Assessment (SOFA) score for the patients treated in ICU were recorded in the patient follow-up form.

Definitions

The diagnosis of CR-BSI was based on the diagnostic criteria by the Centers for Disease Control and Prevention (CDC) [13]. In the patients with a CVC, CR-BSI was diagnosed when the clinical findings of infection (fever, shivering and/or hypotension) were accompanied by bacteremia or fungemia proven with at least one positive culture obtained from the peripheral vein blood while there was no other foci of infection other than the catheter in the presence of one of the conditions mentioned below:

– growth of the same microorganism in the semiquantitative culture obtained from the peripheral blood culture and catheter segment (>15 cfu in every catheter segment);

or

– growth of the same microorganism in the automated blood culture system at least two hours before the peripheral blood culture in the simultaneously obtained catheter blood culture;

or

– no blood or catheter tip cultures.

Statistical analysis

The risk factors likely to be responsible for the development of CR-BSI in patients with CVC were evaluated. Patients with CVC were compared with each other in terms of the presence of CR-BSI. The SPSS for Windows version 18 (SPSS Inc., Chicago, IL) was used for statistical analysis. Comparisons of continuous variables were made by using Kruskal Vallis and Mann Whitney U test. Pearson's chi-square test was used for categorical variables. All P values <0.05 were accepted as significant. The significant data from the univariate analysis were evaluated by using the logistic regression analysis.

RESULTS

A 281 catheterized patients with 356 CVC were evaluated in our study. There were 149 (53%) male and 132 (47%) female patients. The patients' ages ranged from 18 to 94 years and mean age was 58.1±19.9 years. The mean duration of catheterisation was 15.9±12.7 days, and total number of catheter days was found as 5667. About 304 (85.3%) patients were treated in the internal medicine clinic, 52 (14.7%) patients were in the surgical clinic and 213 (59.8%) patients were in ICU for different periods. Mean SOFA scores of patients in the ICU were noted as 6.4±3.4 whereas were noted as 6.8±2.7 in patients with CR-BSI in the ICU. The primary diagnosis of the catheterised patients were renal diseases in 199 (55.9%) patients, cerebrovascular disease in 39 (11%), surgical interventions in 38 (10.7%), hematologic diseases in 29 (8.1%) cardiopulmonary diseases in 21 (5.9%) and others in 30 (8.4%). İmpairment of renal functions was the most frequently encountered coexisting problem and observed in 246 (69.1%) patients and followed diabetes mellitus in 84 (23.6%), congestive heart failure in 34 (9.5%) and chronic obstructive pulmonary disease in 34 (9.5%) respectively.

Comorbidities were scored by using the Charlson comorbidity index and classified as mild, moderate, severe and very severe according to the result [14]. The types of catheters used in catheterisation were detailed as double-lumen CVC in 320 (89.9%) cases, triple-lumen CVC in 34 (9.6%) and single-lumen CVC in 2 (0.6%). According to anatomic localization, catheters were inserted into subclavian vein in 195 (54.8%) cases, jugular vein in 136 (38.2%) and femoral vein in 25 (7%).

Temporary (without tunnel) catheters were inserted in 343 (96.3%) cases whereas permanent or semi-permanent with tunnel catheters were used in 13 (3.7%) central vein catheterisation. Duration of catheterization was longer than seven days in 270 (75.8%) of the patients whereas seven day or shorter in 86 (24%) patients. The indication of CVC insertion was central venous measurement in 343 patients, fluid and electrolyte replacement in 315(88.5%), haemodialysis in 183 (51.4%), infusion of blood and blood products in 45 (12.6%) and total parenteral nutrition in 19 (5.3%). During the catheterization period, 168 (47.2%) of all patients received β-lactam antibiotics, 112 (31.5%) of were treated with carbanepem, 60 (16.8%) of them received glycopeptide and 5 (1.4%) of received quinolones of all patients with CR-BSI, 24 (52.2%) were male and 22 (47.8%) were female. Catheter exit site infections were noted in 5 (1.4%) patients. The incidence of CVC-related infection was found as 8.12 in 1000 catheter days while the frequency of CVC insertion was noted as 0.50. About 30 (65.2%) of patients with CR-BSI were treated without removing the catheter whereas catheter had to be removed in 16 (34.8%) patients. Mortal-

Table 1 - Microorganisms isolated from cultures of the patients with CR-BSI.

Type of microorganisms	*Total*		*ICU*		*Wards*	
	n	%	*n*	%	*n*	%
Gram positive	20	43.5	12	35.3	8	66.7
Coagulase-negative staphylococci	7	15.2	2	5.9	5	41.7
Staphylococcus aureus	5	10.9	3	8.8	2	16.7
Enterococcus spp.	5	10.9	5	14.7	0	0
Corynebacterium	3	6.5	2	5.9	1	8.3
Gram negative	20	43.5	16	47.0	4	33.3
Klebsiella pneumoniae	6	13.0	5	14.7	1	8.3
Acinetobacter baumannii	5	10.9	5	14.7	0	0
Escherichia coli	4	8.7	3	8.8	1	8.3
Pseudomonas aeruginosa	3	6.5	3	8.8	0	0
Enterobacter spp.	2	4.4	0	0	2	16.7
Candida spp.	6	13.0	6	17.7	0	0

ity due to CR-BSI was observed in 22 (47.8%) patients treated in ICU. The diagnosis of CR-BSI was confirmed by the culture results after death in 9 (19.6%) patients. Gram-positive bacteria was the most common agent isolated from the culture of the patients with CR-BSI treated in wards whereas gram-negative agents were more common in the cultures of the patients with CR-BSI treated in ICU. The most commonly isolated agents were coagulase-negative staphylococci (15.2%), *Candida* spp (13%) and *Klebsiella pneumoniae* (13%), respectively. Isolated agents from the cultures of the patients treated in wards or ICU were summarized in Table 1.

Risk factors

When the comorbid conditions were assessed in the univariate analysis, staying at ICU (p=0.037) and antibiotic treatment during catheterisation (p=0.005) were noted significantly more common in the patients with CR-BSI compared to the control group. The incidence of renal disease in the patients with CR-BSI was found significantly lower (p=0.033) than that of control group

Table 2 - Risk factors for the development of CR-BSI in univariate analysis.

Risk factors	*Proportion of CR-BSI*	*%*	*Proportion of control cases*	*%*	*OR*	*CI (%95)*	*p values*
Indications of CVC							
Advanced age							.001
Haemodialysis	18/46	39.1	165/310	53.2	0.56	0.30-1.06	.074
Blood product infusion	7/46	15.2	38/310	12.2	1.28	0.53-3.07	.573
Total parenteral nutrition	5/46	10.9	14/310	4.5	2.57	0.88-7.50	.084
Catheter types							
Double lumen	40/46	87.0	280/310	90.3	0.71	0.28-1.82	.439
Triple lumen	6/46	13.0	28/310	9.0	1.51	0.58-3.87	.418
Catheter location							
Subclavian vein	27/46	58.7	168/310	54.2	1.20	0.64-2.25	.567
Jugular vein	16/46	34.8	120/310	38.7	0.84	0.44-1.61	.609
Femoral vein	3/46	6.5	22/310	7.0	0.91	0.26-3.18	.592
Experience of applier							
Beginner resident	10/46	21.7	92/310	29.7	0.65	0.31-1.38	.266
Senior resident	32/46	69.6	200/310	64.5	1.25	0.64-2.45	.502
Teaching staff	4/46	8.7	18/310	5.8	1.54	0.49-4.78	.506
Emergency indication for catheter insertion	10/46	21.7	92/310	29.7	0.65	0.31-1.38	.266
Asepsis compliance	36/46	78.3	225/310	72.6	1.36	0.64-2.86	.416
Renal diseases	19/46	41.3	180/310	58.0	0.50	0.27-0.95	.033
Hematologic problems	2/46	4.3	26/310	8.4	0.49	0.11-2.16	.556
Monitorisation at ICU	34/46	73.9	179/310	57.7	2.07	1.03-4.15	.037
Diabetes mellitus	10/46	21.7	72/310	23.2	0.91	0.43-1.94	.823
Charlson comorbidity index score ≥5	5/46	10.9	36/310	11.6	0.92	0.34-2.50	.883
Surgical intervention	11/46	23.9	81/310	26.1	0.88	0.43-1.83	.749
Antibiotic treatment during catheterisation	44/46	95.6	241/310	77.7	6.29	1.48-26.64	.005
Glycopeptide usage	12/46	26.0	48/310	15.5	1.92	0.93-3.98	.073

Table 3 - Risk factors for the development of CR-BSI in multivariate analysis.

Risk factors	*p value*	*OR*	*% 95 CI*
Renal diseases	0.255	1.56	0.72-3.37
Staying at ICU	0.941	1.03	0.43-2.47
Antibiotic usage	0.055	4.26	0.96-18.8
Advanced age	0.018	1.02	1.00-1.04
Duration of catheterisation	0.010	1.03	1.00-1.06

patients. When the catheter-related risk factors were evaluated through the univariate analysis, there was no significant difference between the patients with CR-BSI and control group patients (Table 2).

Variables seemed to be significant in the univariate analysis were added to the model formed for the multivariate analysis. The logistic regression analysis showed that advanced age and longer duration of catheterisation were significant risk factors for the development of CR-BSI (Table 3).

DISCUSSION

Surveillance data obtained from nosocomial infections are considered as the indicator of the quality of the patient care. Thus it is very important to identify the risk factors likely to be responsible for the development of CR-BSI and necessary to infection control particularly in ICU. Taking the measures to control the infection can be possible only knowing these factors. Despite the advances infection control packages, CR-BSI continues to be challenging problem particularly in ICU. In the literature a variety of factors including the type of the catheter, area of catheterisation, frequency of catheter manipulation, duration of catheterisation, parenteral nutrition, admittance to ICU, renal disease, antibiotic treatment, use of glycopeptides, duration of mechanical ventilation, catheterisation under emergency conditions, and poor hand hygiene have been reported as responsible for the development of CR-BSI [7-11, 15, 16].

In our study, we have found advanced age and longer duration of catheterisation as independent risk factors for the development of CR-BSI in the multivariate analysis.

According to the National Nosocomial Infections Surveillance (NNIS) reports, the rate of CR-BSI in the ICUs in USA was found as 1.8-5.2 in 1000 catheter-days. A meta-analysis performed without distinguishing between the ICU and the wards reported this rate as 2.5 in 1000 catheter days, while another meta-analysis including only ICUs found it as 5 in 1000 catheter-days [17-19]. In a recent multi-center study conducted by Leblebicioglu et al. in 13 centers in our country, the rate of CR-BSI was found as 12.3 in 1000 catheter-days [20]. In a prospective study conducted in our hospital by Hosoglu et al., the incidence of CR-BSI was reported as 9.2 in 1000 catheter-days [10]. Although the rate of 8.12 in 1000 catheter-days observed in our study is rather high compared to the NNIS data, it is consistent with the local epidemiological data from our hospital and country in general. Studies have shown that the incidence of CR-BSI may be reduced to a reasonable level through the adoption of infection control measures especially in the ICU [20]. The volume of the patients admitted to ICUs are limited compared to those of admitted to clinics.

In the study conducted on 1071 patients by Yoshida et al., both univariate and multivariate analyses have shown that admission to the ICU was a significant risk factor for the development of CR-BSI [7]. In the study of Wittekamp et al. conducted on ICU patients, the univariate analysis showed that the duration of ICU stay was found significantly longer in patients with CR-BSI compared to the patients without CR-BSI [21]. The duration of ICU stay seemed to be as a significant factor for CR-BSI in the univariate analysis whereas it was not an independent risk factor for CR-BSI in the multivariate analysis. This could be explained by the fact that the presence of CR-BSI requires longer hospitalization in ICU, viceversa longer stay in ICU may be a triggering factor for the patient.

Recent studies have shown that advanced age was a risk factor for the development of CR-BSI in multivariate analysis [22, 23]. Coexisting diseases and low immunity are frequently encountered problems in elderly critical patients. Catheters with larger diameter are required to ensure hemodynamic stabilization and intravenous medication in these group patients. As a result, the risk of development CR-BSI is high in elderly critical patients [23]. Mean age of our patients with CR-BSI was found significantly high compared with

the ones of the study previously conducted in our hospital. Advanced age was found as a significant risk factor for the development of CR-BSI in multivariate analysis [10]. Longer duration of catheterisation is known as a risk factor for the development of CR-BSI [24]. According to many authors, seven day is a reasonable period for CVC, but the duration of the catheterisation longer than seven days is a significant risk factor for the development of CR-BSI [9, 23]. In the literature, a part of comparative studies have not indicated any limitation for an acceptable duration of catheterisation. However they reported that the duration of catheterisation plays a role in the development of CR-BSI [8, 25].

In the multivariate analysis, we have found longer duration of catheterisation as an independent risk factor for the development of CR-BSI in our study. There are many studies reporting also the presence of correlation between the impairment of renal function and the development of CR-BSI. Although previous studies have demonstrated that impairment of the renal function was an independent risk factor for the development of CR-BSI [10], In our study, the results of univariate analysis indicated that impairment of renal functions were significantly more common in patients without CR-BSI. This result could be explained by the fact that the majority of the patients with impaired renal function were followed up outside ICU and that their mean duration of hospital stay and catheterisation were shorter than that of the patients without renal impairment.

Although there are reports claiming that the prophylactic use of glycopeptides before or during catheterisation prevents the development of CR-BSI, prophylactic antibiotic use is not routinely recommended in the guidelines [9, 26, 27]. Studies have demonstrated that the prophylactic use of glycopeptides before catheterisation does not prevent CR-BSI due to gram-positive bacteria and may even increase the tendency to CR-BSI [10, 28]. In our study, it has been shown that the use of antibiotics during catheterisation increased the incidence of CR-BSI in the univariate analysis while it seemed not to be an independent risk factor for CR-BSI in the multivariate analysis.

The univariate analysis has showed that the use of antibiotics during catheterisation increased the incidence of CR-BSI and the multivariate analysis has not shown it to be an independent risk factor. Gram-positive bacteria are known as the predominant bacteria type in the skin flora and plays an important role in the aetiology of CR-BSI [9, 10, 29]. Seber et al. have reported that skin is an important reservoir of microorganisms associated with CR-BSI and there was a significant correlation between the high counts of staphylococci and catheter tip contamination at the insertion site infections [30]. However many authors reported that increasing in the incidence of gram-negative bacteria, particularly in the ICU, even surpassed the gram-positive bacteria in the recent studies [20,23,31]. Cases of CR-BSI due to gram-negative bacteria were more common in our ICU patients. These findings were consistent with the findings in recent literature. This change in the aetiologic agents of CR-BSI could be explained by being tertiary stage of our ICUs. Coexisting problems were more frequently encountered in our ICU patients previously treated with wide spectrum antibiotics and also mean age of these patients were found higher than that of the other group patients. It has been reported that renal impairment, glycopeptides treatment, quinolone treatment and catheterisation due to haemodialysis were significant risk factors in the univariate analysis for the development of CR-BSI in another retrospective surveillance study conducted in our hospital 12 years ago. On the contrary, surgical intervention has not been found as a significant factor for CR-BSI.

In our study, only renal impairment was found as an independent risk factor for CR-BSI in the multivariate analysis and the incidence of CR-BSI was found as 9.2 in 1000 catheter-days [10]. Although an infection control regulation was implemented and a national surveillance network has been established by the Ministry of Health in the last 12 years, no significant reduction was observed in the CR-BSI rate and preventable risk factors still play a role in the development of CR-BSI.

In conclusion, factors such as advanced age and longer duration of catheterisation were found as significant for the development of CR-BSI in our study. We also think that it is very important to be aware of preventable risk factors for CR-BSI for all health personnel.

Disclosure

Authors have no conflict of interests.

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