J Infect Chemother xxx (2013) 1–6

Contents lists available at ScienceDirect

Journal of Infection and Chemotherapy

journal homepage: http://www.elsevier.com/locate/jic

Original article

Incidence, risk factors and microbiology of central vascular catheter-related bloodstream infection in an intensive care unit

Zied Hajjej*, Mourad Nasri, Walid Sellami, Hedi Gharsallah, Iheb Labben, Mustapha Ferjani

Intensive Care Unit, Military Hospital of Tunis, 1008 Montfleury, Tunis, Tunisia

ARTICLE INFO

Article history:
Received 13 June 2013
Received in revised form
25 August 2013
Accepted 30 August 2013

Keywords:
Central vascular catheters
Incidence
Infection
Risk factors
Microbiology
Intensive care unit

ABSTRACT

Although there are many studies about catheter related infection in industrialized countries, very few have analyzed it in emerging countries. The aim of our study was to determine the incidence, microbiological profile and risk factors for catheter-related bloodstream infection (CRBSI) in a Tunisian medical intensive care unit. Over eight months (1 January 2012–30 August 2012) a prospective, observational study was performed in an 18-bed medical surgical intensive care unit at Tunis military hospital. Patients who required central venous catheter (CVC) placement for a duration greater than 48 h were included in the study. Two hundred sixty patients, with a total of 482 CVCs were enrolled. The mean duration of catheterization was 9.6 ± 6.2 days. The incidence for CRBSI and catheter colonization (CC) was 2.4 and 9.3 per 1000 catheter days, respectively. Risk factors independently associated with CRBSI were diabetes mellitus, long duration of catheterization, sepsis at insertion and administration of one or more antibiotics before insertion. The mortality rate among the CRBSI group was 21.8%. The predominant microorganisms isolated from CRBSI and CC episodes were Gram negative bacilli. All Gram negative organisms isolated among dead patients in CRBSI group were Extensive Drug Resistant (XDR). In our study the mortality rate among patients with CRBSI was high despite a low incidence of CRBSI. This high rate can be explained by the high-virulent status of Gram negative bacteria involved in CRBSI.

© 2013, Japanese Society of Chemotherapy and The Japanese Association for Infectious Diseases. Published by Elsevier Ltd. All rights reserved.

1. Introduction

Central venous catheters (CVCs) are commonly used in the intensive care unit (ICU). Indeed, up to 80% of critically ill patients may require central venous catheterization [1]. However, use of CVCs can lead to bloodstream infection, frequently referred to as catheter-related bloodstream infection (CRBSI). Such infections are associated with serious morbidity and mortality and with increased health care costs [2]. Despite the large number of published studies on Catheter-related infections (CRI), the data from intensive care units of emerging countries are few. Limited resources in these countries impose strict monitoring of nosocomial infections, in particular CRI. The aim of our study was to determine the incidence, microbiological profile and risk factors for CRBSI in a Tunisian medical intensive care unit.

2. Materials and methods

2.1. Patients and data collection

Over eight months (1 January 2012–30 August 2012) a prospective, observational study was performed in an 18-bed medical surgical intensive care unit at Tunis military hospital. The approval of the ethics committee was not necessary given the strictly observational nature of the study.

Patients who required central venous catheter (CVC) placement for a duration greater than 48 h were included in the study. If a patient had more than one CVC inserted during the ICU stay, each CVC inserted that met the inclusion criteria was enrolled.

The catheters used were multi-lumen, made of polyurethane and not antibiotic-impregnated.

The placement and maintenance of catheters were performed according to the following protocol. The catheters were inserted by physicians with sterile-barrier precautions: use of sterile full body drapes around the insertion site, surgical antiseptic hand wash, and sterile gown, gloves, mask and cap. The skin insertion site was disinfected with 10% povidone–iodine. The catheters were percutaneously inserted using the Seldinger technique and were fixed to

* Corresponding author. Tel.: +216 71 391 133; fax: +216 71 391 099.
E-mail addresses: hajjej_zied@hotmail.com (Z. Hajjej), nasrimourad80@yahoo.fr (M. Nasri), drsellamiwalid@yahoo.fr (W. Sellami), gharsallahhedi@yahoo.fr (H. Gharsallah), iheb1labbene@yahoo.fr (I. Labben), mustapha.ferjani@planet.tn (M. Ferjani).

1341-321X/$ – see front matter © 2013, Japanese Society of Chemotherapy and The Japanese Association for Infectious Diseases. Published by Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.jiac.2013.08.001

Please cite this article in press as: Hajjej Z, et al., Incidence, risk factors and microbiology of central vascular catheter-related bloodstream infection in an intensive care unit, J Infect Chemother (2013), http://dx.doi.org/10.1016/j.jiac.2013.08.001

the skin with silk suture. After the line insertion, the site was covered by a dry sterile gauze occlusive dressing for 24 h then changed by a sterile, transparent, semipermeable dressing. No topical antibiotic ointment or creams on insertion sites were used.

Hand hygiene procedures, either by washing hands with conventional soap and water or with alcohol-based hand rubs (ABHR), were performed before and after palpating catheter insertion sites as well as before and after accessing, repairing, or dressing catheters.

The percutaneous entry sites were examined on a daily basis for presence of local inflammation and purulence by the ICU nurse in charge of the patient and the doctors on their daily round. Catheter dressings were changed every 48 h, or sooner if the dressing was contaminated. The administration sets were changed every 48 h in patients not receiving blood, blood products or fat emulsions. Tubing used to administer blood, blood products, or fat emulsions were replaced within 24 h of initiating the infusion.

In handling venous lines and when changing the dressing on catheters, health care professionals wore clean gloves. All injection ports of the CVC were cleaned with a pre-packed alcohol wipe before accessing the system.

Catheters were removed when they were no longer needed or if a systemic or local complication occurred and when the patient was transferred from the unit. Otherwise, a scheduled catheter replacement was made every 7 days in accordance with a local unit protocol. The catheters were removed using a sterile technique by physicians. For the new catheter, the insertion site was always changed.

Data collected from the medical charts of the patients and from the treating physicians included gender, age, Acute Physiology and Chronic Health Evaluation (APACHE)II score, reasons for hospitalization, CVC insertion site, insertion and removal dates, total duration of catheterization, cause of CVC removal, CVC maintenance details (insertion site dressings, change of connecting lines),use of total parenteral nutrition (TPN), total duration of hospitalization, site of infection, species identification and antimicrobial susceptibility of the pathogen, mechanical ventilation, any antimicrobial therapy administered up to 30 days prior to recovery of the isolate, and final outcome. In addition, the following comorbid conditions were documented: heart disease (coronary disease, arrhythmias and hypertensive cardiopathy), respiratory disease (chronic obstructive pulmonary disease -COPD, asthma and pneumonia), solid organ neoplasm, diabetes mellitus, renal insufficiency (requiring dialysis).

Exclusion criteria were burn or dermatitis at the insertion site, or when catheter was used as vascular access for hemodialysis.

2.2. Microbiological procedures

The following specimens for culture were obtained from all patients:

1) The distal 4–5 cm of the tip after CVC removal.
2) Tow blood samples, drawn from the catheter and a peripheral vein.
3) If a blood sample cannot be drawn from a peripheral vein, 2 blood samples were drawn through different catheter lumens.

The definitions of catheter colonization (CC) and CRBSI published by IDSA were used [3].

CC was defined as the growth of $\geq$15 colony forming units (CFUs) in cultures of catheter tips prepared by the semi-quantitative roll-plate method or $\geq$1000 CFU by the quantitative culture. Criteria for the diagnosis of CRBSI were defined as the presence of either one of the following situations in a patient with accompanying clinical signs and symptoms of bloodstream infection without any other apparent source:

1) The isolation of the same organism from the colonized catheter and at least 1 peripheral blood culture.
2) When the culture of 2 blood samples, one from a catheter hub and the other from a peripheral vein, meet the CRBSI criterion for quantitative blood cultures: a colony count of microbes grown from blood obtained through the catheter hub that is at least 3-fold greater than the colony count from blood obtained from a peripheral vein. Differential time to positivity (DTP), defined by growth of microbes from a blood sample drawn from a catheter hub at least 2 h before microbial growth in a blood sample obtained from a peripheral vein, is not being used routinely in our hospital.
3) When 2 quantitative blood cultures of samples obtained through 2 catheter lumens in which the colony count for the blood sample drawn through one lumen is at least 3-fold greater than the colony count for the blood sample obtained from the second lumen.

When blood cultures were plated out to measure 3-fold difference in colony counts they are done at the same time in agreement with the microbiologist.

All microorganisms recovered from the cultures were identified by standard microbiological procedures. Antibiotic susceptibility testing, depending on species identification, was performed using the disk-agar diffusion method according to the European Union Committee on Antimicrobial Susceptibility Testing (EUCAST) [4]. The antimicrobial agents tested were as follows: Ampicillin, Ticarcillin, Piperacillin ticarcillin–clavulanate (Tic–Clv), Piperacillin–Tazobactam(Pip–Taz), Cefazolin, Cefotaxime Ceftazidime, Imipenem,Ciprofloxacin, Amikacin, Tobramycin, Gentamicin, Colistin, Tigecyclin and trimethoprim–sulfamethoxazole (TMP–SMX). All susceptibility results were evaluated according to the EUCAST criteria.

2.3. Statistical analysis

Statistical analysis was performed using SPSS 20.0 statistical software. Patients with CRBSI were designated as group A, patients with CC were designated as group B and patients without CC or CRBSI were designated as group C. Continuous variables are expressed as mean $\pm$ standard deviation, while categorical variables are expressed with absolute and relative frequencies. The normality assumption of continuous variables was evaluated using the Kolmogorov–Smirnov criterion. For the comparison of continuous variables between the three groups one-way analysis of variance (ANOVA) was performed. Data were modeled using multiple logistic regression analysis. Odds ratios and 95% confidence intervals were computed from the results of logistic regression analysis. Two multiple logistic regression analyses were performed with dependent variables those defined from groups B/C and A/C, using stepwise backward elimination with a significance level for removal of $P = 0.10$ in order to find the best model fitting our data. All reported P values are two-tailed. Statistical significance was set at $P < 0.05$.

3. Results

Among 363 patients admitted in the ICU during the study period, 282 have required CVC insertion for a duration greater than 48 h. Of the 282 eligible patients, only 260 were included because data in twenty-two patients were incomplete. The number of CVCs was 482 and the global duration of days of catheterization was 4670. The ratio of exposure to CVC was 77% and the mean duration of catheterization was 9.6 $\pm$ 6.2 days. CVC insertion sites included the subclavian (58%), the internal jugular (33%) or the femoral vein (9%). Overall, 32 (12.3%) patients were classified as having CRBSI (group A, with a total of 54 CVCs), 108 (41.5%) patients as having CC

Please cite this article in press as: Hajjej Z, et al., Incidence, risk factors and microbiology of central vascular catheter-related bloodstream infection in an intensive care unit, J Infect Chemother (2013), http://dx.doi.org/10.1016/j.jiac.2013.08.001

(group B, with a total of 210 CVCs) and 120 (46.2%) patients neither had CC nor CRBSI (group C, with a total of 218 CVCs). CRBSI incidence was 2.4 per 1000 catheter days, whereas CC incidence was 9.3 per 1000 catheter days. Descriptive statistics and univariate analysis among the three groups are presented in Table 1.

The most common comorbid conditions were surgical intervention (16.5%), heart disease.

(18%), respiratory diseases (26.3%), renal failure not dialyzed (11.4%), hematological malignancy (2.6%) and solid organ neoplasm (9.2%).

The mortality rate among group A patients was 21.8% (three patients with *Pseudomonas aeruginosa*, two patients with *Acinetobacter baumannii*, one patient with *Staphylococcus aureus* and one patient with *Candida* spp.). Among group B patients the mortality rate was 11.1% and it was 8.3% among group C.

The placement and maintenance protocol were rigorously observed in all catheters but this was not the same for manipulation. Indeed, in 48 (10%) catheters, performing hand hygiene procedures, in accordance with the protocol, was missing.

The mean duration of catheterization (CD) was 9.6 ± 6.2 days. Patients with longer CD were more likely to have CRBSI or CC (22 ± 7 or 19 ± 7 vs 12 ± 8, $p < 0.001$).

Table 1
Characteristics of patients and univariate analysis of data.

Variable	Patient group[a]			Comparison between groups, *P*		
	A *n*(%)	B *n*(%)	C *n*(%)	A/C	B/C	A/B
Age (mean ± SD, years)	56 ± 4	52 ± 6	51 ± 3	0.684	0.781	0.752
Males	15(46)	52(48.1)	60(50)	0.059	0.084	0.816
APACHE II[b] at admission (mean ± SD)	28 ± 9	19 ± 6	14 ± 2	0.003*	0.421	0.218
Main reason for ICU admission						
Septic shock	10(31.2)	23(21.3)	17(14.2)	0.006*	0.26	0.14
Other etiologies of shock	3(9.3)	14(12.9)	13(10.8)	0.562	0.471	0.254
CAP[c]	6(18.7)	15(13.8)	17(14.2)	0.061	0.123	0.054
Exacerbations of COPD[d]	5(15.6)	19(17.5)	24(20)	0.063	0.098	0.438
Coma	4(12.5)	22(20.3)	22(18.4)	0.038*	0.357	0.023*
Trauma	4(12.5)	15(13.8)	27(22.5)	0.089	0.197	1
Length of stay in ICU (mean ± SD, days)	29 ± 8	30 ± 4	27 ± 2	0.079	0.067	0.089
Duration of catheterization (mean ± SD, days)	22 ± 7	19 ± 7	12 ± 8	<0.001*	<0.001*	0.869
Comorbidities						
Diabetes mellitus	8(25)	26(24)	15(12.5)	0.043*	0.018*	0.989
Solid tumor	4(12.5)	12(11.1)	8(6.6)	0.052	0.053	0.716
Hematological malignancy	1(3.1)	3(2.7)	3(2.5)	0.061	0.624	0.482
Mechanical ventilation	12(37.5)	46 (42.6)	52 (43.3)	0.126	0.064	0.051
Sepsis at insertion	14(43.7)	26 (24)	20 (16.6)	0.001*	0.29	0.004*
One or more Antibiotics before insertion	12(37.5)	22(20.3)	14(11.6)	0.002*	0.003*	0.002*
Catheter site						
Subclavian	30(55.5)	130(61.9)	118(54.1)	0.692	0.057	0.581
Internal jugular	14(25.9)	62(29.5)	86(39.4)	0.041*	0.048*	0.687
Femoral	10(18.5)	18(8.5)	14(6.4)	0.002*	0.241	0.053
Parenteralnutrition	8(14.8)	48(22.8)	25(11.4)	0.741	0.029*	0.053
Insertion context						
Emergency	24(44.4)	101(48.1)	98(45)	0.796	0.681	0.672
Programmed	30(55.6)	109(51.9)	120(55)	0.846	0.801	0.735
Mortality	7(21.8)	12(11.1)	10(8.3)	0.009*	0.63	0.055

*Significant difference.
[a] Group A: patients with catheter related bloodstream infection (CRBSI), Group B: patients with catheter colonization (CC), Group C: patients without CRBSI or CC.
[b] APACHE II: acute physiology and chronic health evaluation.
[c] CAP: Community-acquired pneumonia.
[d] COPD: chronic obstructive pulmonary disease.

Table 2
Risk factors associated with catheter related bloodstream infection (CRBSI): multivariate analysis.

Variable	Patients with CRBSI (%)	Patients without CRB or CC[a] (%)	OR (95% CI)[b]	*P*
Diabetes mellitus				
Yes	25	12.5	2.43 (1.09–5.7)	0.027*
No	75	87.5		
Duration of catheterization (mean ± SD, days)	22 ± 7	12 ± 8	1.95 (1.21–2.13)	<0.001*
Sepsis at insertion				
Yes	43.7	16.6	3.80(1.91–7.87)	<0.001*
No	56.3	83.4		
One or more antibiotics before insertion				
Yes	37.5	11.6	4.46(2.08–10.1)	<0.001*
No	62.5	88.4		

*Significant difference.
[a] CC: Catheter colonization.
[b] Odds ratio (95% confidence interval).

Univariate analysis (Table 1) revealed that CRBSI and CC were significantly associated with increased CD, diabetes mellitus, use of one or more antibiotics before insertion and CVC insertion site. In addition, sepsis at insertion was significantly associated with CRBSI but not with CC and parenteral nutrition was significantly associated with CC but not with CRBSI.

Multivariate analysis revealed that CD was independently associated with CRBSI .In addition, patients with diabetes mellitus, with sepsis at insertion and having received one or more antibiotics before insertion, had greater odds for having CRBSI (Table 2).

Multivariate analysis showed also that CD was independently associated with CC. Patients with diabetes mellitus and having received parenteral nutrition were more likely to have CC (Table 3).

In our study, 74% of the pathogens causing CRBSI were Gram negative and 18.5% were Gram positive. Furthermore, 78% of the pathogens causing CC were due to Gram negative organisms and 17% were due to Gram positive organisms.

The commonest pathogen causing CRBSI and CC was *Pseudomonas aeruginosa* with a rate of 22.2% and 28.5% respectively. *Coagulase negative Staphylococci* was in the third position after *A. baumannii* causing both CRBSI and CC. *Candida* caused 7.5% of CRBSI and 5% of CC. The distribution of pathogens among the cases is shown in Fig. 1.

Antimicrobial resistance levels for the most common Gram negative organisms frequently isolated from the study population are shown in Table 4.

A relatively high proportion of *Escherichia coli* isolates displayed resistance to ampicillin, piperacillin, and piperacillin–

Table 3
Risk factors associated with catheter colonization (CC): multivariate analysis.

Variable	Patients with CC (%)	Patients without CRBSI[a] or CC (%)	OR (95% CI)[b]	*P*
Diabetes mellitus				
Yes	24	12.5	2.30 (1.02–5.42)	0.041*
No	76	87.5		
Duration of catheterization (mean ± SD, days)	19 ± 7	12 ± 8	1.55 (1.11–1.93)	<0.001*
Parenteralnutrition				
Yes	22.8	11.4	2.40(1.04–5.84)	0.037*
No	77.2	88.6		

*Significant difference.
[a] CRBSI: catheter related bloodstream infection.
[b] Odds ratio (95% confidence interval).

Please cite this article in press as: Hajjej Z, et al., Incidence, risk factors and microbiology of central vascular catheter-related bloodstream infection in an intensive care unit, J Infect Chemother (2013), http://dx.doi.org/10.1016/j.jiac.2013.08.001

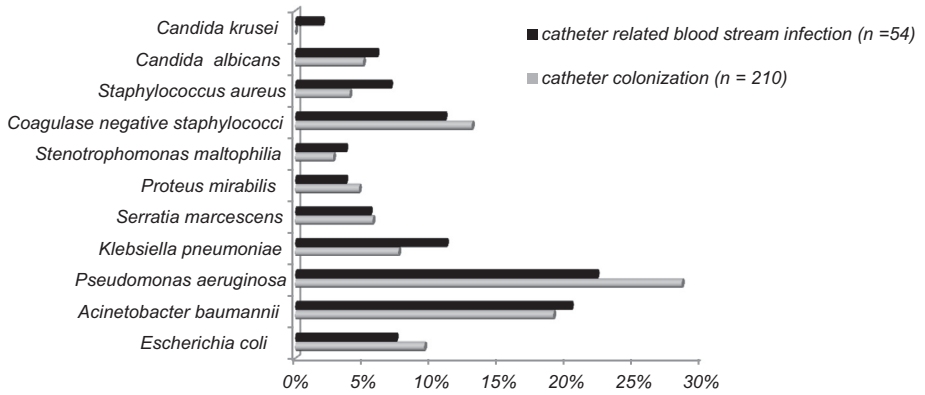

Fig. 1. Distribution of pathogens.

tazobactam (64.1%, 51.3%, and 42.3% respectively). Third-generation cephalosporins, aminoglycosides, and ciprofloxacin displayed activity against most isolates, as did imipenem (≤25% of isolates were resistant). Of the *A. baumannii* isolates, 93.9%, 82.8% and 56.6%, were resistant to piperacillin, ceftazidime, and imipenem, respectively. No resistance to Colistin and Tigecyclin were detected. 89.1% and 1.3% of *pseudomonas aeruginosa* isolates were resistant to ceftazidime and Colistin, respectively. Resistance to ciprofloxacin was seen in 32.1% of tested isolates. For *Klebsiella pneumoniae* isolates, third-generation cephalosporins, amikacin, ciprofloxacin, and imipenem were active against more than 50% of isolates tested. For *Stenotrophomonas maltophilia*, ticarcillin–clavulanate, trimethoprim–sulfamethoxazole and ciprofloxacin displayed activity against most isolates (≤10% of isolates were resistant, no resistance to trimethoprim–sulfamethoxazole was detected). The proportion of *coagulase negative staphylococci* and *staphylococcus aureus* isolates with methicillin resistance was 79.2% and 41.3%, respectively.

Note that all Gram negative organisms isolated among dead patients in CRBSI group (group A) were Extensive Drug Resistant (XDR) as defined by an international expert proposal for interim standard definitions for acquired resistance [5].

4. Discussion

The epidemiology of CRBSI is dependent on the type of intensive care unit considered (medical, surgical…) and on the socioeconomic level of the country studied. Industrialized countries, albeit with some differences, have a CRBSI incidence significantly lower than in emerging countries or otherwise called limited-resources countries [6]. Among industrialized countries, France presented the lowest density incidence of CRBSI. Indeed, according to the 2007 data of the Warning Network, investigation and surveillance of nosocomial infections, density incidence of CRBSI was about 0.9 per 1000 catheter days which is less than what has been found in our study (2.4 per 1000 catheter days) [7]. In terms of emerging countries, studies are limited. One of the most was a multicentric study, published in 2006, including eight countries. In this study, the density incidence of CRBSI was significantly higher than ours, on the order of 12 per 1000 catheter days [8]. This result has been updated recently in a multicentric study including 36 countries published by the International Nosocomial Infection Control Consortium in 2012. The density incidence of CRBSI was in decrease: about 6 per 1000 catheter days [9].

Compared to other emerging countries, this low incidence in our study (all misconducts leading to underestimate the real incidence

Table 4
Rates of antimicrobial resistance among Gram-negative organisms most frequently isolated from study population.

Antimicrobial drug	Escherichia coli ($n = 24$)	Acinetobacter baumannii ($n = 51$)	Pseudomonas aeruginosa ($n = 72$)	Klebsiella pneumoniae ($n = 22$)	Stenotrophomonas maltophilia ($n = 8$)
	Rate of resistant (%)	Rate of resistant (%)	Rate of resistant (%)	Rate of resistant (%)	Rate of resistant (%)
Ampicillin	64.1	99.2	86	100	100
Ticarcillin	53.1	92.1	61.8	100	86.4
Piperacillin	51.3	93.9	68.4	79.8	94.3
Tic–Clv[a]	46	87	56	53.4	9.1
Pip–Taz[b]	42.3	86.6	46.2	69.4	84.2
Cefazolin	45.2	100	92	95.2	99.5
Cefotaxime	24.1	98	89.1	46.3	99.6
Ceftazidime	19.2	82.8	54.6	49.3	68.1
Imipenem	12.1	56.6	36	9	89.4
Ciprofloxacin	22.3	72	32.1	34.9	2.4
Amikacin	19.4	76.4	24.6	26.8	100
Tobramycin	ND[d]	35.3	ND	ND	ND
Gentamicin	31.4	69.2	76	52	100
Colistin	0	0	1.3	0	69.1
Tigecyclin	ND	0	0	ND	ND
TMP–SMX[c]	44.2	78.4	100	58.3	0

[a] Tic–Clv:ticarcillin–clavulanate.
[b] Pip–Taz: Piperacillin–Tazobactam.
[c] TMP–SMX: trimethoprim–sulfamethoxazole.
[d] ND: not done.

Please cite this article in press as: Hajjej Z, et al., Incidence, risk factors and microbiology of central vascular catheter-related bloodstream infection in an intensive care unit, J Infect Chemother (2013), http://dx.doi.org/10.1016/j.jiac.2013.08.001

were prevented) could be due to strict adherence to Guidelines for the Prevention of Intravascular Catheter-Related Infections at insertion and care [10].

The mortality rate among patients with CRBSI was 21.8% in our study, higher than previously reported rates [11,12], which could be explained by the fact that all Gram negative organisms isolated among dead patients in CRBSI group (group A) were Extensive Drug Resistant (XDR). Considering the severity of the clinical status of the study groups, attested by the level of APACHE II score at admission, there was a significant difference only between group A and group C (Table 1). But if we consider dead patients in each group, there was no significant difference between groups: group A vs group B (22 ± 4 vs 18 ± 5, $p = 0.314$), group A vs group C (22 ± 4 vs 13 ± 3, $p = 0.054$) and group B vs group C (18 ± 5 vs 13 ± 3, $p = 0.422$). Therefore it was most likely that the mortality in CRBSI group was due to CRBSI.

Duration of catheterization is a well-known risk factor for CRBSI [13–16]. The present study showed that for every one-day increase in duration, the likelihood of CRBSI increased by 13%. For this reason, CVCs should not be kept more than absolutely necessary.

Multivariate analysis revealed that from all the comorbid factors examined, diabetes mellitus was independently associated with CRBSI and CC. This observation is in line with a previous study indicating that all conditions leading to immunosuppression with CVCs were statistically more likely to have a CRBSI episode [17].

A systemic antibiotic therapy administered before insertion of CVC is a protective factor found in some studies and no rational explication could be advanced [18,19]. Paradoxically, in our study patients with sepsis at insertion and having received one or more antibiotics before insertion had greater odds for having CRBSI but not for CC. We must insist on the fact that to administer systemic antimicrobial prophylaxis routinely before insertion or during use of an intravascular catheter to prevent catheter colonization or CRBSI is not recommended [10].

The site of CVC insertion is a recognized risk factor, and jugular vein catheters are considered more prone to cause CRBSI [20–22]. Accordingly, in the present study, placing the catheter in the jugular, but also in the femoral vein, was associated with a higher incidence of CRBSI and CC in comparison with the subclavian site. This result was not confirmed in multivariate analysis. Note that it is recommended that using the femoral vein for central venous access in adult patients should be avoided and a subclavian site should be used rather than a jugular site [10].

The most commonly reported causative pathogens of CRBSI and CC remain Gram positive organisms with a rate ranging from 40 to 65% depending on the studies. Gram negative bacilli accounted for 19% and 21% of CRBSI reported to Centers for Disease Control and Prevention (CDC) and the Surveillance and Control of Pathogens of Epidemiological Importance (SCOPE) database, respectively [7,23,24].

Our study, on the contrary, showed that Gram negative rods were more commonly the causative micro-organisms with *Pseudomonas aeruginosa* being the commonest either in CRBSI (22.2%) or CC (28.5%).

These microbiological differences are difficult to explain and are probably multifactorial: variations related to local ecology, impact of the use of broad spectrum antibiotics on resistance development. The predominance of Gram negative organisms in CRBSI and CC is probably related to a mechanism of cross-transmission by the medical and paramedical staff during handling venous lines. Indeed hand hygiene was missing in 10% of cases during catheters manipulation and that influenced, probably, the ecology but not the incidence of CRI.

The rate of hand hygiene missing could be explained by a low nurse-to-patient ratio. In our unit the ratio was1:3 which can increase workload and decrease the vigilance of nurses.

A recent study had investigated the association between nursing workload and mortality of ICU patients. Although no statistically significant differences were detected, these may offer a new perspective on detecting associations between nurse understaffing and ICU patient's mortality by indicating the importance of considering individual care demands of patients [25]. In another study the relationship between nurse staffing and ICU patient's mortality was significant. Indeed, in Korean secondary hospitals, every additional patient per nurse was associated with a 9% increase in the odds of dying (OR = 1.09, 95% CI = 1.04–1.14) [26].

Candida species involved in CRBSI and CC were poorly represented (5–7%) in our study. This is comparable to what is found in the literature [7,23,24].

Data from the Extended Prevalence of Infection in Intensive Care (EPIC II) study, which comprised 75 countries, found that mortality was higher among ICU patients with infections due to Gram negative organisms [27].In our study, mortality was higher among patients with CRBSI due to Candida species (25%). Mortality among CRBSI due to Gram negative bacteria was 12.5% and among CRBSI due to Gram positive bacteria was 10%.

The rates of antimicrobial resistance identified among our study population were higher than those identified in northern Europe [28] and north America [23,29] but lower than rates reported in other series from emerging countries [30].

Our study includes three limitations. First, its observational design. Indeed different insertion sites were not randomly assigned. Second, it was a monocentric study and reflects only the reality of one hospital structure in one city in Tunisia, so results cannot be extrapolated. And third is the catheter colonization day's definition we have used. Indeed the approach overestimates the true catheter colonization days.

5. Conclusion

This study disclosed the incidence of CRBSI and CC among the patients of an intensive care unit in Tunis, Tunisia, and revealed risk factors for CRBSI and CC, factors related to patients' own conditions, but also to medical personnel practice that needs to be improved. It was a step that allowed us to have an idea about the epidemiology of CRI in our unit.

The incidence of CRBSI in our ICU was 2.4 per 1000 catheter days which is low compared to other emerging countries. The mortality rate among patients with CRBSI was 21.8%, higher than previously reported rates. The predominant microorganisms isolated from CRBSI and CC episodes were Gram negative bacilli.

All Gram negative organisms isolated among dead patients in CRBSI group were Extensive Drug Resistant (XDR), which could explain the high mortality rate among this group.

The high rates of antibiotic resistance, as well as local patterns of species distribution and drug susceptibilities, should guide empirical therapy of nosocomial bloodstream infections.

The continuous surveillance of the epidemiology of CRBSI is essential in taking active measures for infection prevention and control, such as education of medical personnel, strict hygiene practice and a higher nurse-to-patient ratio.

Declaration of conflict of interest

The author(s) declare that they have no competing interests.

Acknowledgments

We are indebted to the doctors and nurses with the Intensive Care Unit who provided care for the patients included in the study.

Please cite this article in press as: Hajjej Z, et al., Incidence, risk factors and microbiology of central vascular catheter-related bloodstream infection in an intensive care unit, J Infect Chemother (2013), http://dx.doi.org/10.1016/j.jiac.2013.08.001

References

[1] Vincent JL, Bihari DJ, Suter PM, Bruining HA, White J, Nicolas-Chanoin MH, et al., The EPIC International Advisory Committee. The prevalence of nosocomial infection in intensive care units in Europe. Results of the European Prevalence of Infection in Intensive Care (EPIC) study. JAMA 1995;274(8):639–44.
[2] Worth LJ, Brett J, Bull AL, McBryde ES, Russo PL, Richards MJ. Impact of revising the National Nosocomial Infection Surveillance System definition for catheter-related bloodstream infection in ICU: reproducibility of the National Healthcare Safety Network case definition in an Australian cohort of infection control professionals. Am J Infect Control 2009;37:643–8.
[3] Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009. Update by the Infectious Diseases Society of America. Clin Infect Dis 2009;49(1):1–45.
[4] Kahlmeter G, Brown DF, Goldstein FW, MacGowan AP, Mouton JW, Odenholt I, et al. European Committee on Antimicrobial Susceptibility Testing (EUCAST) technical notes on antimicrobial susceptibility testing. Clin Microbiol Infect 2006;12(6):501–3.
[5] Magiorakos AP, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clin Microbiol Infect 2012;18:268–81.
[6] Edwards JR, Peterson KD, Andrus ML, Tolson JS, Goulding JS, Dudeck MA, et al. NHSN facilities: National Healthcare Safety Network (NHSN) report, data summary for 2006, issued June 2007. Am J Infect Control 2007;35:290–301.
[7] Warning network, investigation and surveillance of nosocomial infections-Nosocomial infections in adult intensive care unit. France, results, http://cclin-sudest.chu-lyon.fr/; 2007 [accessed 10.04.13].
[8] Rosenthal VD, Maki DG, Salomao R, Moreno CA, Mehta Y, Higuera F, et al. Device-associated nosocomial infections in 55 intensive care units of 8 developing countries for the International Nosocomial Infection Control Consortium (INIC). Ann Intern Med 2006;145:582–91.
[9] Rosenthal VD, Bijie H, Maki DG, Leblebicioglu H, Fisher D, Álvarez-Moreno C, et al. International Nosocomial Infection Control Consortium (INICC) report, data summary of 36 countries, for 2004-2009. Am J Infect Control 2012;40(5):396–407.
[10] O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections. Clin Infect Dis 2011;52(9):e162–93.
[11] JARVIS WR. Selected aspects of the socioeconomic impact of nosocomial infections: morbidity, mortality, cost, and prevention. Infect Control Hosp Epidemiol 1996;17:552–7.
[12] Klevens RM, Edwards JR, Richards CL, Horan TC, Gaynes RP, Pollock DA, et al. Estimating health care-associated infections and deaths in U.S. hospitals, 2002. Public Health Rep 2007;122(2):160–6.
[13] Reed CR, Sessler CN, Glauser FL, Phelan BA. Central venous catheter infections: concepts and controversies. Intensive Care Med 1995;21:117–83.
[14] Tacconelli E, Tumbarello M, Pittiruti M, Leone F, Lucia MB, Cauda R, et al. Central venous catheter related sepsis in a cohort of 366 hospitalized patients. Eur J Clin Microbiol Infect Dis 1997;16(3):203–9.
[15] Arruda E, Marinho IS, Rodrigues E, Basso M, Vilela IS, Gobara S, et al. Central venous catheter-related infections in intensive care units. Braz J Infect Dis 1997;1(4):182–5.
[16] Yoshida J, Ishimaru T, Kikuchi T, Matsubara N, Asano I. Association between risk of bloodstream infection and duration of use of totally implantable access ports and central lines: a 24-month study. Am J Infect Control 2011;39(7):e39–43.
[17] Raad I, Hachem R, Hanna H, Bahna P, Chatzinikolaou I, Fang X, et al. Sources and outcome of bloodstream infections in cancer patients: the role of central venous catheters. Eur J Clin Microbiol Infect Dis 2007;26:549–56.
[18] Safdar N, Kluger DM, Maki DG. A review of risk factors for catheter-related bloodstream infection caused by percutaneously inserted noncuffed central venous catheters implications for preventive strategies. Medicine 2002;81:466–79.
[19] Zingg W, Sax H, Inan C, Cartier V, Diby M, Clergue F, et al. Hospital-wide surveillance of catheter-related bloodstream infection: from the expected to the unexpected. J Hosp Infect 2009;73:41–6.
[20] Merrer J, De Jonghe B, Golliot F, Lefrant JY, Raffy B, Barre E, et al., French Catheter Study Group in Intensive Care. Complications of femoral and subclavian venous catheterization in critically ill patients: a randomized controlled trial. JAMA 2001;286(6):700–7.
[21] Lorente L, Henry C, Martín MM, Jiménez A, Mora ML. Central venous catheter-related infection in a prospective and observational study of 2,595 catheters. Crit Care 2005;9:R631–5.
[22] Nagashima G, Kikuchi T, Tsuyuzaki H, Kawano R, Tanaka H, Nemoto H, et al. To reduce catheter-related bloodstream infections: is the subclavian route better than the jugular route for central venous catheterization? J Infect Chemother 2006;12:363–5.
[23] Wisplinghoff H, Bischoff T, Tallent SM, Seifert H, Wenzel RP, Edmond MB, et al. Nosocomial bloodstream infections in US hospitals: analysis of 24,179 cases from a prospective nationwide surveillance study. Clin Infect Dis 2004;39:309–17.
[24] Gaynes R, Edwards JR, The National Nosocomial Infections Surveillance System. Overview of nosocomial infections caused by gram-negative bacilli. Clin Infect Dis 2005;41:848–54.
[25] Kiekkas P, Sakellaropoulos GC, Brokalaki H, Manolis E, Samios A, Skartsani C, et al. Association between nursing workload and mortality of intensive care unit patients. J Nurs Scholarsh 2008;40(4):385–90.
[26] Cho SH, Hwang JH, Kim J. Nurse staffing and patient mortality in intensive care units. Nurs Res 2008 Sep–Oct;57(5):322–30.
[27] Vincent JL, Rello J, Marshall J, Silva E, Anzueto A, Martin CD, et al. International study of the prevalence and outcomes of infection in intensive care units. JAMA 2009;302:2323–9.
[28] Kresken M, Hafner D, The Study Group Bacterial Resistance of the Paul-Ehrlich- Society for Chemotherapy. Drug resistance among clinical isolates of frequently encountered bacterial species in central Europe during 1975–1995. Infection 1999;27(Suppl. 2):S2–8.
[29] Diekema DJ, Pfaller MA, Jones RN. Age-related trends in pathogen frequency and antimicrobial susceptibility of bloodstream isolates in North America. SENTRY Antimicrobial Surveillance Program, 1997–2000. Int J Antimicrob Agents 2002;20:412–8.
[30] Aissaoui Y, Chouaib N, Chouikh C, Rafa M, Azendour H, Balkhi H, et al. Central venous catheter-related bacteraemia: prospective study in a Moroccan medical intensive care unit. Annales Françaises d'Anesthésie et de Reanimation 2010;29:897–901.

Please cite this article in press as: Hajjej Z, et al., Incidence, risk factors and microbiology of central vascular catheter-related bloodstream infection in an intensive care unit, J Infect Chemother (2013), http://dx.doi.org/10.1016/j.jiac.2013.08.001