VENOUS CATHETER TIP INFECTIONS IN INTENSIVE CARE UNITS OF A TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: To determine the local and changing patterns of bacterial growth and antibiotic sensitivity for appropriate empiric treatment before culture results are available.

Study Design: Retrospective observational study.

Place and Duration of Study: This study was conducted at Khan Research Laboratories Hospital, Islamabad, Pakistan, from Jul 2014 to Dec 2016.

Material and Methods: One hundred and seventy five patients having positive cultures of venous catheter tips performed after following standard protocol were included. Age, gender, common pathogens, their sensitivity and resistance to 27 antimicrobial drugs were taken into account. Statistical Package for Social Sciences (SPSS) version 20 was used for data analysis.

Results: Total number of patients included were 175. 56.5% (n=99) were females while 43.4% (n=76) were males. Minimum age was 16 years while maximum age was 93 years. Mean age was 58.15 ± 17.94 years. 175 patients having culture positive venous catheter tips, were available for analysis. Majority of the patients were admitted in Medical ICU, 78.3% (n=137). *Staphylococcus epidermidis* (*S. Epidermidis*) was the most common isolate 24.6% (n=43) followed by *Escherichia coli* (*E. coli*) 21.7% (n=38), *Staphylococcus aureus* (*S.aureus*) 18.8% (n=33), *Klebsiella pneumonia* (*K. pneumoniae*) 14.3% (n=25), *Acinetobacter baumannii* (*A.baumannii*) 5.7% (n=10). *S. epidermidis* showed maximum sensitivity to Linezolid i.e. 100% followed by Minocyclin, 88%, Vancomycin 86%. It was resistant to Ampicillin 93%. *E. colishowed* maximum sensitivity to Amikacin i.e. 95% followed by Imipenem 87%, while being resistant to Amoxicillin/clavulanic acid (97%) and Ciprofloxacin (92%). *Staphylococcus aureus* showed maximum sensitivity to Linezolid i.e. 97% followed by Vancomycin (90%) while showing resistance to Ampicillin (100%), Ciprofloxacin (88%) and Levofloxacin (85%). *Klebsiella pneumoniae* showed decreased sensitivity to Amikacin, Imipenem, Meropenem i.e. 64% while 100% resistant to Amicillin, Amoxicillin/clavulanic acid. Acinetobacter baumannii showed maximum sensitivity to Colistin i.e. 90%. Pseudomonas aeruginosa showed maximum sensitivity to Polymyxin B (100%) and Colistin (87%), while resistant to Ceftazidime and Quinolones (37%).

Conclusion: Antibiotic pool for catheter related infections is shrinking. Commonly used as well as reserved antibiotics are no longer effective as before.

Keywords: Antimicrobial sensitivity and resistance, Catheter related blood Linezolid, Stream infections, Staphylococcus epidermidis, Staphylococcus aureus, Vancomycin.

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INTRODUCTION

The use of central venous catheters (CVCs) has permitted life-saving treatment for individuals requiring hemodynamic monitoring, total parenteral nutrition (TPN), emergency hemodialysis or chemotherapy[1]. Central venous catheters are indispensable in the treatment of intensive care unit (ICU) patients, but use of these catheters is associated with a risk of infectious complications[2]. The national nosocomial infection surveillance system (NNIS) in the United States has reported that most nosocomial blood stream infections (BSIs) in intensive care units (ICUs) are associated with indwelling intravascular devices[3]. The centers for disease control and prevention (CDC) estimated that, in 2002, 250,000 central line associated blood stream infections (CLABSIs) occurred in US hospitals, accounting for >30,000 deaths[4]. National organizations and collaborative groups have success-

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fully reduced CLABSI rates with use of evidence-based recommendations to improve catheter insertion and maintenance practices[5,6]. Catheter-related bloodstream infection (CRBSI) is defined as the presence of bacteremia originating from an intravenous catheter[7]. Several interrelated factors have been proposed to participate in the pathogenesis of CRBSI. The catheter itself can be involved in 4 different pathogenic pathways like colonization of the catheter tip and cutaneous tract with skin flora; colonization of the catheter lumen caused by contamination; hematogenous seeding of the catheter from another infected site; and contami-nation of the lumen of the catheter with infusate. CRBSI means a patient with an intravascular catheter has at least one positive blood culture obtained from a peripheral vein, clinical manifestations of infections (i.e., fever, chills, and/or hypotension), and no apparent source for the BSI, except the catheter[7]. A diagnosis of CRBSI is achieved by any of the following 3 criteria: 1)same organism recovered from percu-taneous blood culture and from quantitative (>15 colony-forming units) culture of the catheter tip; 2) same organism recovered from a percutaneous and a catheter lumen blood culture, with growth detected 2 hours sooner (i.e, 2 hours less incubation) in the latter; 3) same organism recovered from a quantitative percutaneous and a catheter lumen blood culture, with 3-fold greater colony count in the latter[8]. CRBSIs are considered among the first and most "preventable" classes of nosocomial infections[8]. Risk of CRBSI can be reduced by optimizing catheter selection, insertion and maintenance, and by removing catheters when they are no longer needed[9]. Early detection and adequate treatment of causative pathogens within 24 hours of clinical suspicion of these infections (development of signs and symptoms) is critical for a favorable outcome, yet the majority of patients with suspected catheter related infection (CRI) yield negative diagnostic investigations, necessitating empiric, rather than optimal antimicrobial therapy[10]. Strict adherence to hand hygiene recommendations and the use of aseptic techniques during insertion and dressing changes remain the most important measures for the prevention of catheter-associated infections. These measures are emphasized in guidelines from the healthcare infection control practices advisory committee (HICPAC), the centers for disease control and prevention (CDC), and working groups composed of members from professional organizations representing a variety of medical disciplines[11-15]. Other preventive measures include: Choosing appropriate sites for catheter insertion, appropriate type of catheter material, barrier precautions during insertion, changing catheter administration sets at appro-priate intervals, ensuring proper catheter site care and ensuring removal of catheters when no longer essential. In general, empiric antibiotic therapy must be instituted before culture and susceptibility data are available. Subsequently therapy should be tailored to microbiology results as needed. The initial choice of antibiotics for catheter-related blood stream infection (CRBSI) depends on the clinical circumstances, including the severity of illness, the risk factors for infection, and the likely pathogens associated with the specific intravascular device. In general, coagulase-negative staphylococci are the most common cause of catheter-related infection; most isolates are resistant to methicillin[16]. Empiric therapy of CRBSI in healthcare settings should consist of vancomycin[17]. In institutions with high rates of infection due to methicillin-resistant *S. aureus* (MRSA) isolates with vanco-mycin minimum inhibitory concentration (MIC) ≥2 mcg/mL, an alternative agent such as dapto-mycin should be used[18]. Linezolid is not an appropriate agent for empiric therapy of CRBSI[19]. Additional agents with activity against coagulase-negative staphylococci and MRSA include daptomycin, tedizolid, telavancin, dalba-vancin, oritavancin, ceftaroline, and quinupristin-dalfopristin. Clinical data regarding efficacy of these agents for treatment of CRBSI are limited. The rationale this study was determine the local and changing patterns of bacterial growth and antibiotic sensitivity for appropriate empiric treatment before culture results are available.

MATERIAL AND METHODS

This was a retrospective observational study. It was conducted at Khan Research Laboratories Hospital, Islamabad, Pakistan. Study period was from July 2014 to December 2016. One hundred and seventy five patients having positive cultures of venous catheter tips performed after following standard protocol were included. Consecutive sampling technique was followed. Age, gender, common pathogens, their sensitivity and resistance to 27 antimicrobial drugs were taken into account. The tested antimicrobials included Imipenem, Meropenem, Cefoperazone/ Sulbactam, Pipercillin/ Tazobactam, Trimethoprim/ sulfamethoxazole (TMP/SMX), Pencillin G, Ampicillin, Amoxicillin/Clavulanic acid, Chloramphenicol, Vancomycin, Linezolid, Amikacin, Gentamycin, Nalidixic acid, Ciprofloxacin, Levofloxacin, Ofloxacin, Cefixime, Ceftriaxone, Ceftazidime,Cefoperazone, Cephradin, Tigecyclin, Doxycyclin, Colistin, Nitrofurantoin and fosfomycin. All venous lines were implanted via subclavian or femoral veins. Maximal sterile barrier precautions using sterile gloves, gown, cap, mask, and a large drape were obtained throughout the procedure. We used 10% povidone-iodine for the sterilization. All venipunctures were made with an 18-G indwelling needle after subcutaneous administ-ration of local anesthetic. For the subclavian approach, a 7-Fr 2-lumen 20 cm 0.32 inch dia. Spring-wire guide two-lumen central venous catheterization set with blue flextip was inserted over the guide wire, and the tip was placed at the level of the junction of the superior vena cava and right atrium. For femoral approach 12-Fr two-lumen central venous catheterization set with blue flextip was used.

Catheter tips were withdrawn when clinically indicated and cultured immediately onto a blood agar plate[12]. The microorganisms were identified by using standard microbiological methods. Decision of removal of catheter was taken by the Doctor in charge using the following criteria: 2 or more systemic inflammatory response syndrome (SIRS) criteria (Temperature >38.5°C or <36.0°C, Heart Rate >90 bpm, Respiratory Rate >20 bpm or $PaCO_2$ <32 mmHg or requirement for mechanical ventilation, White Blood Cells >12 000 cells/mm^3 or <4000 cells/mm^3 or presence of >10% immature neutrophils) and no other source of

Table-I: Distribution of Patients in different wards.

Patients	Medical ICU	Surgical ICU	CCU
Number	137	26	12
Percentage (%)	78.3	14.8	6.8

Table-II: Bacterial isolates.

Organism	Occurrence
Staphylococcus epidermidis	43(24.6%)
Escherichia coli	38 (21.7%)
Staphylococcus aureus	33 (18.8%)
Klebsiella pneumonia	25 (14.3%)
Acinetobacter baumannii	10 (5.7%)
Acinetobacter spp.	8 (4.6%)
Pseudomonas aeroginosa	8 (4.6%)
Enterococcus faecalis	3 (1.7%)
Enterococcus spp.	2 (1.14%)
Proteus mirabilis	2 (1.14%)
Pseudmonas spp.	1 (0.57%)
Klebsiella spp.	1 (0.57%)

sepsis evident. All catheter tips were handled under aseptic conditions and immediately, transported to the laboratory for analysis, where they were cultured. Exclusion criteria were: age <14 years, patient having catheter insertion outside hospital, patients with known malignancy and antibiotic use or admission in previous 2 weeks. Statistical package for social sciences (SPSS) version 20 was used for data analysis. The clinical data of the study patients were stated as number of patients and percentages.

RESULTS

Present study comprised of 175 patients. 56.5% (n=99) were females while 43.4% (n=76) were males. Minimum age was 16 years while maximum age was 93 years. Mean age was 58.15 ± 17.94 years. 78.3% (n=137) patients were admitted in Medical ICU. 14.8% (n=26) patients were admitted in Surgical ICU and 6.8% (n=12) patients were admitted in CCU. This is shown in table-I. Table-II illustrates frequency of microorganisms isolated. *Staphylococcus epidermidis* (*S. epidermidis*) was the most common isolate 24.6% (n=43). It was followed by *Escherichia coli (E. coli)* 21.7% (n=38), *Staphylococcus aureus* (*S.aureus*) 18.8% (n=33), *Klebsiella pneumoniae* (*K. pneumoniae*) 14.3% (n=25), *Acinetobacter baumannii* (*A. baumannii*) 5.7% (n=10). Table-III, IV & V shows antimicrobial sensitivity and resistance of the most frequent isolates.

Table-III: Staphylococcus epidermidis (*S. epidermidis*) (n=43).

Sensitivity			Resistance		
Antibiotic	No.	Percentage (%)	Antibiotic	No.	Percentage (%)
Linezolid	43	100	Penicillin G	42	98
Minocyclin	38	88	Ampicillin	40	93
Vancomycin	37	86	Ciprofloxacin	32	74
Doxyclin	36	83	Levofloxacin	31	72
Amikacin	34	79	Erythromycin	29	67

Table-IV: Escherichia coli (*E. coli*) (n=38).

Sensitivity			Resistance		
Antibiotic	No.	Percentage (%)	Antibiotic	No.	Percentage (%)
Amikacin	36	95	Amoxicillin/clavulanic acid	37	97
Imipenem	33	87	Ciprofloxacin	35	92
Meropenem	32	84	Levofloxacin	35	92
Piperacillin/Tazobactum	20	53	Cefixime	34	89
Cefoperazone/Sulbactum	19	50	Ampicillin	34	89

Table-V: Staphylococcus aureus (*S. aureus*) (n=33).

Sensitivity			Resistance		
Antibiotic	No.	Percentage (%)	Antibiotic	No.	Percentage (%)
Linezolid	32	97	Ampicillin	33	100
Minocycline	31	93	Penicillin G	32	97
Vancomycin	30	90	Ciprofloxacin	29	88
Doxycyclin	29	88	Levofloxacin	28	85
Chloram-phenicol	27	82	Amoxicillin/Clavulanic acid	24	73

DISCUSSION

Intravascular catheters are indispensable in modern-day medical practice, particularly in ICUs. Although such catheters provide necessary vascular access, their use put patients at risk for local and systemic infectious complications, including site infection, CRBSIs, septic thrombophlebitis, endocarditis, and other metastatic infections (e.g., lung abscess, brain abscess, osteomyelitis, and endophthalmitis)[20]. The increase in the use of central venous catheters over the last 20 years has been associated with at least a doubling of resultant nosocomial infections[21,22]. According to the literature, 1% to 13% of central venous catheters (CVCs) develop CRBSI[23,24]. We conducted our study to determine the frequency of microorganisms associated with central line infections and their sensitivity and resistance patterns. Susceptibility pattern of pathogens has been changing over the years, implying the need for periodic monitoring in order to decrease the number of therapeutic failures and to take essential measures to decrease morbidity and mortality associated with fatal CRBSIs.

In our study *S. epidermidis* was found to be the most predominant isolated organism (24.6%), followed by *E. coli* (21.7%) and *S. aureus* (18.8%) among all the microorganisms causing catheter related infections (CRIs). In a study conducted in Rawalpindi, it was concluded that gram positive cocci were isolated in 53% cases followed by gram negative rod (42%), while 5% were fungi[32]. In a study conducted in Maharashtra, India, about Central venous catheter-related bloodstream infections in the ICU, *S. epidermidis* was found to be the most common isolate (45%)[25]. In another study conducted in United States the most commonly reported pathogens causing CLABSI remain coagulase-negative staphylococci, Staphylococcus aureus, enterococci, and Candida spp[26]. In yet another study Richet et al. found that 46.5% of the isolates were *S. epidermidis* from both central and peripheral venous catheters[27]. In a study conducted in Spain it was found that a total of 53 microorganisms were responsible for the 53 CRBSIs, of which 38 (71.70%) were Gram-positive bacteria, 12 (22.64%) were Gram-negative bacteria and 3 (5.66%) were yeasts. Isolated from the 53 microorganisms were: 23 (43.39%) coagulase-negative staphylococci; 9 (16.98%) Staphylococcus aureus; 5 (9.43%) Enterococcus faecalis; 1 (1.89%) Bacillus spp.; 8 (15.09%) *Escherichia coli*; 2 (3.77%) Enterobacter cloacae; 2 (3.77%) Pseudomonas aeruginosa; and 3 (5.66%) Candida albicans[28].

In our study *S. epidermidis* showed greater sensitivity to Linezolid (100%) as compared to Vancomycin (86%) and Amikacin (79%), whereas being resistant to Penicillin G (98%), Ampicillin (93%) and Ciprofloxacin (74%). According to a study conducted in India it was shown that *S. epidermidis* showed maximum susceptibility to amikacin, doxycycline and amoxicillin/ clavulanic acid and was susceptible to vancomycin (100%)[25]. In our study *S. aureus* also showed greater sensitivity to Linezolid (97%), Vancomycin (90%) and Chlorampenicol (81%), while resistant to Ciprofloxacin (88%) and Amoxicillin/clavulanic acid (73%). Khanna et al. found that all resistant Staphylococcus (MRSA) isolated from CRBSI were 100% sensitive to co-trimoxazole and chloramphenicol among routine antibiotic and 100% sensitive to vancomycin, teicoplanin, and linezolid among reserved antibiotics. All methicillin sensitive Staphylococci were 100% resistant to Ciprofloxacin[20]. For all common pathogens causing CLABSIs, anti-microbial resistance is a problem, particularly in ICUs. Although methicillin-resistant Staphylococcus aureus (MRSA) now account for more than 50% of all Staphylococcus aureus isolates obtained in ICUs, the incidence of MRSA CLABSIs has decreased in recent years, perhaps as a result of prevention efforts[29]. The second most common causative organism of CRIs in our study was *E. coli* (21.7%). It showed maximum sensitivity to Amikacin (95%), Imipenem (87%) and Meropenam (84%) while only 53% and 50% to Piperacillin/ Tazobactum and Cefoperazon/Sulbactum respectively. Of particular interest is resistance to Amoxicillin/calvulanic acid (97%), Ciprofloxacin and Levofloxacin (92%). A study conducted in India showed that the most sensitive routine antibiotic for *E. coli* isolated in catheter related local infections (CRLI) was cefuroxime (88.9%) and the most sensitive reserved antibiotic was meropenem (88.9%)[20].

K. pneumoniae showed reduced sensitivity to almost all antibiotics. This is because of the emergence of multidrug resistance strains. Sensitivity to Amikacin, Imipenem and Meropenem stood at 64%, while showing alarming resistance to Ampicillin, Amoxicillin/ Clavulanic acid (100%) and Cefixime and Ceftriaxone (96%). Gaynes et al, reported that for gram negative rods, antimicrobial resistance to third generation cephalosporins among *K. pneumoniae* and *E. coli* has increased significantly[30]. Given their multidrug resistance, therapeutic options are limited and should be reevaluated and optimized. A. baumannii showed sensitivity to Colistin (90%), Tigecyclin (80%), Cefoperazone/ Sulbactum (30%) and Amikacin (20%) while shows 100% resistance to Ampicillin, Ceftriaxone, Cefixime, Amoxicillin/ Clavulanic acid and 90% to Ciprofloxacin. A study conducted in University of Edinburg showed that the incidence of infections with carbapenem-resistant Gram-negative bacteria is increasing, especially for Acinetobacter spp[31]. Another study reported that the most sensitive routine antibiotic for *A. baumannii* isolated in CRLI was amikacin (35.7% sensitive) and cefoperazone-salbactum in reser-ved antibiotic (35.7% sensitive)[20]. In our study *P. aeruginosa* showed sensitivity to Polymyxin B (100%), Colistin (87%), Piperacillin/ Tazabactum (87%), Amikacin (75%) and Imipenem (63%), while resistance to Ceftazidine and Ciprofloxacin (37%). Studies have shown that *P. aeruginosa* has increasing resistance to imipenem and cefta-zidime[30].

CONCLUSION

Antibiotic pool for catheter related infections is shrinking. Commonly used as well as reserved antibiotics are no longer effective as before.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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