EVALUATION OF A PROGRAM TO CONTROL CATHETER-RELATED BLOODSTREAM INFECTIONS AT A TERTIARY INSTITUTION IN MALAYSIA

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Abstract. Central venous catheters (CVCs) may increase the risk of catheter-related bloodstream infections (CRBSI). In this study, we aimed to determine the efficacy of a program to reduce CRBSI at the Universiti Sains Malaysia Hospital in Kelantan Malaysia to determine the program's potential for application to other hospitals in Malaysia. The intervention program was developed following the United States Centers for Disease Control and Prevention guidelines, and the implementation was started in January 2017. We retrospectively reviewed the medical records of all admitted patients aged ≥18 years with a CVC placed before the intervention program (admitted during April-December 2016) and after initiation of the intervention program (admitted during April-December 2017). The incidences of CRBSI, etiological organisms and antimicrobials used to treat subjects during the two study periods were compared. Prior to the intervention, 1037 patients had a CVC placed at the study institution of whom 72 (6.94%) developed a CRBSI. After the intervention, 925 patients had a CVC placed of whom 54 (5.83%) developed a CRBSI. There was no significant decrease in the incidence of CRBSI after the intervention (odds ratio = 0.83, 95% confidence interval: 0.58-1.20; $p = 0.319$). Staphylococcus aureus, including methicillin-resistant Staphylococcus aureus (MRSA), was the most common Gram-positive organism isolated during the pre-intervention (33.3%, n = 24) and post-intervention (22.2%, n = 12) periods. Klebsiella pneumoniae, including the ESBL strain, was the most common Gram-negative organism isolated during the pre-intervention (7%, n = 5) and post-intervention (9.3%, n = 5) periods. Cloxacillin was the commonest antibiotic used during the pre-intervention period and ceftazidime was the most common antibiotic used during the post-intervention period. In summary, the intervention did not significantly reduce the incidence of

CRBSI among study subjects but there appeared to be a slightly change in etiological organisms after the intervention. We conclude the intervention was not effective. Further studies are needed to determine the reason for the failure of the intervention and to determine why there appears to have been a change in the etiological organisms post-intervention.

Keywords: CRBSI, incidence rate, etiological agents, antibiotic treatment, CRBSI intervention program

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INTRODUCTION

Catheter-related bloodstream infections (CRBSI) are associated with morbidity and mortality among hospitalized patients, increasing the length of hospitalization, the frequency of broad-spectrum antibiotic use and the prevalence of bacterial resistance (Dimick *et al*, 2001). CRBSIs are defined by United States Centers for Disease Control and Prevention (US CDC) as bacteremia/fungemia in a patient with an intravascular catheter in use during the 48 hours prior to the development of the bloodstream infection with a positive blood culture, clinical manifestations of infection (*eg,* fever, chills, and/or hypotension) and no apparent source for the bloodstream infection except the catheter (Dimick *et al*, 2001; Horan *et al*, 2008; O'Grady *et al*, 2011).

CRBSI risk factors have been reported to include duration of central venous catheter (CVC) use, length of hospitalization, site of catheter insertion and presence of immunodeficiencies, such as diabetes mellitus (DM) or neutropenia (O'Grady *et al*, 2011; Pronovost *et al*, 2006; Almuneef *et al*, 2006). A randomized controlled trial comparing complications of femoral and subclavian venous catheterization in critically ill patients found that femoral catheters were associated with a higher incidence of symptoms and signs of sepsis with or without detectable bacteremia (Merrer *et al*, 2001). The CDC recommends avoiding femoral CVC for most adult patients, except hemodialysis patients; the subclavian site may be complicated by subclavian vein stenosis (CDC, 2011). The femoral vein should be avoided because the site is at higher risk for causing deep vein thrombosis and microbial colonization (Goetz *et al*, 1998; Trottier *et al*, 1995).

A study from India reported Gram-negative bacilli caused 56% and Gram-positive cocci caused 27% of CRBSIs (Gopalakrishnan and Sureshkumar, 2010). Another study from India reported *S. aureus* caused 40%, *P. aeruginosa* caused 16%, coagulase-negative staphylococci caused 8%, *E. coli* caused 8%, *Klebsiella pneumoniae* caused 8% and *Acinetobacter baumanii* caused 4% of CRBSIs (Parameswaran *et al*, 2011). A study from Malaysia reported *Klebsiella pneumoniae* caused 38.9% and *Pseudomonas aeruginosa* caused 19.4% of CRBSIs (Tan *et al*, 2007). A study from the United States reported CRBSIs caused by *Staphylococcus aureus* and *S. epidermidis* came primarily from the patient's skin or the hands of medical personal (Hooven and Polin, 2014).

Antibiotics used to treat CRBSIs depend on the hospital, local and regional antimicrobial sensitivity patterns and national and international guidelines. CRBSIs are often difficult to treat because they become resistant to antibiotics and create a protective biofilm (Deva *et al*, 2013).

Whether a CVC should be removed or retained should be based on the duration of use, type of therapy and organism causing the CRBSI. For example, in a CRBSI caused by coagulase-negative staphylococci, it was once thought the catheter had to be removed; however, 80% of CRBSIs caused by these bacteria can be treated with glycopeptide antibiotics, such as vancomycin, without catheter removal, and there is only a 20% chance the bacteremia will recur if the CVC is not removed (Raad and Bodey, 1992). The CDC, the Infectious Disease Society of America (IDSA) and the Society for Healthcare Epidemiology in America have developed CRBSI prevention guidelines that have been reported to be effective in preventing CRBSI (CDC, 2011; Lee *et al*, 2018; Guerin *et al*, 2010; Salama *et al*, 2016). The intervention consists of implementing a CVC care program (covering CVC insertion and maintenance), an education program, a practical session (consisting of lectures, videos and posters) and strengthening surveillance for CRBSI. Strengthening surveillance of CRBSI can be done using a CVC Insertion Compliance Checklist Form and a CVC Maintenance Compliance Checklist. The attending physician is required to review the necessity of continuing the CVC daily. This is included in the CVC Maintenance Compliance Checklist Form. The completed forms are then sent to the Hospital Infection Control Unit for analysis.

The CRBSI prevention guidelines by US CDC recommend educating and training healthcare personnel on how to insert and maintain central venous catheters (CVC): using optimal sterile barriers for CVC care and using >0.5% chlorhexidine skin preparation with alcohol for antiseptic catheter maintenance (O'Grady *et al*, 2011).

Our study aimed to determine the efficacy of this CRBSI prevention program by comparing the incidence of CRBSI pre- and post-CRBSI prevention program intervention and compare the CRBSI etiological organisms pre- and post-intervention in order to determine the potential use of this intervention at other hospitals in Malaysia.

MATERIALS AND METHODS

We retrospectively reviewed the medical records of patients admitted to the study hospital who had a CVC placed before the intervention program (April-December 2016) and after initiation of the intervention program (April-December 2017). The CRBSI prevention guidelines based on CDC recommendations were implemented at our institution in January 2017. All hospitalized patients aged ≥18 years with a CVC inserted during the two study periods were included in this study. The exclusion criterion for study subjects was having some other type of central venous device than a CVC. Ethical approval for this study was obtained from the Human Research Ethics Committee of the Universiti Sains Malaysia (JEPeM; Reference number: USM/JEPeM/17010014).

Intervention

The intervention education program was conducted during January-March 2017 and the intervention was conducted immediately based on guidelines adopted by the Ministry of Health Malaysia (MOH Malaysia, 2019). Healthcare personnel performing catheter insertion were asked to perform hand hygiene and wear full protective clothing, including a mask. The patient's full body was draped and the CVC insertion site was cleaned using 2% chlorhexidine in 70% alcohol.

During CVC maintenance, the practitioner was required to perform the hand hygiene specified by the program each time before manipulating the CVC system or changing the CVC site dressing. Each time it was used, the CVC hub was cleaned with an alcohol wipe and let dry for 15 seconds prior to use. A daily review of line necessity was conducted and the CVC was removed promptly when no longer needed. A reminder to do this was placed on the patient chart.

A CVC kit was prepared and used for placing the CVC. This kit consisted of a CVC checklist, a surgical face mask, a cap, sterile gloves, site preparation solution composed of 2% chlorhexidine in 70% alcohol, a blade, suture, a 3-way connector, gauze (op-site), a catheter lumen, a syringe, a needle and a sterile gown.

An education program was conducted at the time of initiation of the intervention. This program consisted of education regarding correct CVC insertion and CVC care. A practical part of this program consisted of demonstration on a mannequin. CVC placement and care followed a checklist to avoid missing steps.

Criteria for diagnosis of CRBSIs in the laboratory

A CRBSI was defined as having two positive blood cultures obtained at least 48 hours after placing a CVC where one culture was obtained from the peripheral blood and the other from the CVC and a difference in the time to positivity (DTP) using the Bactec system (Becton Dickinson Microbiology Systems, Sparks, MD) of >2 hours between the sample obtained from the peripheral blood and the sample obtained from the CVC (Manian, 2009).

Data collection and analysis

Subject demographics, history of co-morbid illnesses, the clinical manifestations of the CRBSI and the results of clinical laboratory testing were recorded. The incidences of CRBSI among study subjects were calculated pre- and post-intervention. Odds ratios (OR) and 95% confidence intervals (CI) were calculated. The incidences pre- and post-intervention were compared using two-sample Poisson rate analysis. The etiological organisms and antibiotics used to treat the subjects for their CRBSI pre- and post-intervention were also recorded.

All data were analyzed using RStudio version 1.4.1717 (https://www.R-project.org/ and http://www.rstudio.com/) and the Statistical Package for the Social Sciences (SPSS), version 24 (IBM Corp, Armonk, NY).

Numerical variables were described using means and standard deviations (SD) and categorical variables were described using frequencies and percentages. Pre- and post-intervention study subject characteristics were compared using independent sample t-test or Mann Whitney U test for numerical variables, and Chi square test of association or Fisher Exact test for categorical variables. A *p*-value <0.05 was considered statistically significant.

RESULTS

There were no significant differences in age, sex, ward admitted to, catheter days and catheter site between the pre- and post-intervention study subjects (Table 1).

Prior to the intervention, 1,037 patients had a CVC placed at the study institution of whom 72 (6.94%) developed a CRBSI. After the intervention 925 patients had a CVC placed, of whom 54 (5.83%) developed a CRBSI. There was no significant decrease in the incidence of CRBSI after the intervention (odds ratio = 0.83, 95% confidence interval: 0.58-1.20; p = 0.319) (Tables 2 and 3).

During the pre-intervention period, more Gram-positive organisms (62.5%) were isolated than Gram-negative organisms (30.6%). The etiological organisms isolated were: *Staphylococcus aureus*, including methicillin-resistant *Staphylococcus aureus* (MRSA), (33.3%,

n = 24), methicillin-resistant coagulase-negative staphylococci (MRCONS) (8.3%, n = 6), *Enterococcus fecalis* (8.3%, n = 6), *Klebsiella pneumoniae*, including the ESBL strain (6.9%, n = 5), *Burkholderia cepacia* (4.2%, n = 3), *Candida tropicalis* (2.8%, n = 2) and *Candida albicans* (1.4%, n = 1) (Table 4).

During the post-intervention period, more Gram-negative organisms (48.2%) were isolated than Gram positive organism (40.7%). The etiological organisms isolated were: *Staphylococcus aureus*, including methicillin-resistant *Staphylococcus aureus* (MRSA) (22.2%, n = 12), *Enterococcus fecalis* (7.4%, n = 4), methicillin-resistant coagulase-negative staphylococci (MRCONS) (5.6%, n = 3), *Klebsiella pneumonaie*, including the ESBL strain (9.3%, n = 5), *Pseudomonas aeruginosa* (7.4%, n = 4),

Table 1

Comparison of study subject characteristics between pre- and post-intervention groups

Variables	Pre-intervention group (N = 72)	Post-intervention group (N = 54)	p-value
Age in years, mean ± SD	55.53 ± 15.50	54.61 ± 14.94	0.738
Sex, n (%)			
Male	36 (50.0)	26 (48.1)	0.837
Female	36 (50.0)	28 (51.9)	
Ward, n (%)			
Medical	42 (58.3)	35 (57.4)	0.051
Surgical	25 (34.7)	16 (26.2)	
Intensive Care Unit	3 (4.2)	10 (16.4)	
Others	2 (2.8)	0 (0.0)	
Mean (IQR) catheter days	13.5 (21.0)	11.0 (9.0)	0.085
Catheter site			
Internal jugular	35 (48.6)	24 (44.4)	0.719
Femoral	37 (51.4)	30 (55.5)	
Subclavian	0 (0.0)	0 (0.0)	

IQR: interquartile range

Table 2

Odds of having a CRBSI in pre- and post-intervention groups

Group	Total patients with a CVC	Subjects with a CRBSI	Odds of CRBSI	OR (95% CI)	*p*-value
Pre-intervention	1037	72	0.075		
Post-intervention	925	54	0.062	0.83 (0.58-1.20)	0.319

CRBSI: catheter-related blood stream infections; CVC: central venous catheter; CI: confidence interval; OR: odds ratio

Table 3

Incidence of CRBSI in pre- and post-intervention groups

Group	Total patients with a CVC	Subjects with a CRBSI	Incidence	Incidence difference (95% CI)	*p*-value
Pre-intervention	1037	72	6.94%		
Post-intervention	925	54	5.83%	-1.11 (-1.13 to 3.34%)	0.332

CRBSI: catheter-related blood stream infections; CVC: central venous catheter; CI: confidence interval

Escherichia coli, including the ESBL strain (5.6%, *n* = 3) *Candida tropicalis* (3.7%, *n* = 2), *Candida parapsilosis* (3.7%, *n* = 2) and *Candida haemulonii* (1.9%, *n* = 1) (Table 4).

Pre-intervention the antimicrobials used to treat study subjects were: cloxacillin (20.8% *n* = 15), piperacillin-tazobactam (12.5%, *n* = 9), meropenem (9.7%, *n* = 7), ceftazidime, (6.9%, *n* = 5), vancomycin (6.9%, *n* = 5), tigecycline (1.4%, *n* = 1) and fluconazole (1.4%, *n* = 1). Post-intervention the antimicrobials used to treat study subjects were: ceftazidime (24.1%, *n* = 13), cloxacillin (20.4%, *n* = 11), piperacillin-tazobactam

Table 4

Etiologies of catheter related blood stream infections among study subjects

Causative organisms	Pre-intervention (N = 72) *n* (%)	Post-intervention (N = 54) *n* (%)
Gram-positive	45 (62.5)	22(40.7)
Staphyloccus aureus	23 (31.9)	11 (20.4)
CONS	1 (1.4)	0 (0.0)
MR-CONS	6 (8.3)	3 (5.6)
MRSA	1 (1.4)	1 (1.9)
Enterococcus faecalis	6 (8.3)	4 (7.4)
Enterococcus faecium	1 (1.4)	0 (0.0)
Corynebacterium amycolatum	3 (4.2)	0 (0.0)
Bacillus spp	3 (4.2)	2 (3.7)
Corynebacterium jeikeium	1 (1.4)	0 (0.0)
Propionibacterium acnes	0 (0.0)	1 (1.9)
Gram-negative	22 (30.6)	26 (48.2)
Pseudomonas aeruginosa	2 (2.8)	4 (7.4)
Klebsiella pneumoniae	2 (2.8)	3 (5.6)
Klebsiella pneumoniae (ESBL)	3 (4.2)	2 (3.7)
Achromobacter xylosoxidans	2 (2.8)	0 (0.0)

Table 4 (cont)

Causative organisms	Pre-intervention (N = 72) *n* (%)	Post-intervention (N = 54) *n* (%)
Escherichia coli	1 (1.4)	1 (1.9)
Escherichia coli (ESBL)	0 (0.0)	2 (3.7)
Burkholderia. cepacia	3 (4.2)	2 (3.7)
Enterebacter cloacae	2 (2.8)	1 (1.9)
Acinetobacter baumannii	2 (2.8)	2 (3.7)
Salmonella spp	1 (1.4)	0 (0.0)
Stenotrophomonas maltophilia	2 (2.8)	2 (3.7)
Aeromonas hydrophila	1 (1.4)	0 (0.0)
Proteus mirabilis	1 (1.4)	1 (1.9)
Pantoea spp	0 (0.0)	1 (1.9)
Ralstonia mannitolilytica	0 (0.0)	2 (3.7)
Serratia marcescens	0 (0.0)	1 (1.9)
Acinetobacter baumannii (MDR)	0 (0.0)	1 (1.9)
Enterococcus cloacae (CRE)	0 (0.0)	1(1.9)
Enterococcus faecalis and Achromobacter xylosoxidans	1 (1.4)	1 (1.9)
Enterococcus. faecium and Klebsiella pneumoniae	1 (1.4)	0 (0.0)
Fungi	3 (4.2)	5 (9.3)
Candida tropicalis	2 (2.8)	2 (3.7)
Candida albicans	1 (1.4)	0 (0.0)
Candida parapsilosis	0 (0.0)	2 (3.7)
Candida haemulonii	0 (0.0)	1 (1.9)

CONS: coagulase negative staphylococci; CRE: Carbapenem resistant enterobacteriaciae; ESBL: extended spectrum β-lactamases; MDR: Multidrug resistant organism where resistant to one or more classes of antibiotics; MR-CONS: Methicillin resistant coagulase negative staphylococci; MRSA: Methicillin resistant *Staphylococcus aureus*

(16.7%, *n* = 9), meropenem (9.3%, *n* = 5), fluconazole (7.4%, *n* = 4) vancomycin (5.6%, *n* = 3) and sulperzone (5.6%, *n* = 3). Pre-intervention 40.3% of subjects (*n* = 29) were treated with a combination of antimicrobials and post-intervention 11.1% (*n* = 6) were treated with a combination of antimicrobials (Table 5).

DISCUSSION

Previous meta-analyses have reported implementation of a CRBSI prevention program resulted in a significant reduction in CRBSI in adults, pediatric patients and neonates (Ista *et al*, 2016; Apisarnthanarak *et al*, 2010, Lavallée *et al*, 2017). However, a randomized control study reported no significant reduction in CRBSI with implementation of the prevention program (Anthony *et al*, 2011) as was seen in our study.

One possible reason for this lack of significant improvement in CRBSI in our study after intervention was the short duration of evaluation post-intervention of 9 months. Other studies that did find a significant reduction were conducted for longer periods of time (Jeong *et al*, 2013; Ista *et al*, 2016).

Another possible reason for lack of a significant reduction in CRBSI post-intervention in our study could be health care worker's compliance with

Table 5

Antibiotics used to treat catheter related blood stream infections among study subjects

Antibiotics	Pre-intervention (N = 72) *n* (%)	Post-intervention (N = 54) *n* (%)
Cloxacillin	15 (20.8)	11 (20.4)
Ceftazidime	5 (6.9)	13 (24.1)
Meropenem	5 (9.7)	5 (9.3)
Vancomycin	5 (6.9)	3 (5.6)
Piperacillin-tazobactam	5 (12.5)	9 (16.7)
Tigecycline	5 (1.4)	0(0.0)
Sulperazone	0(0.0)	3 (5.6)
Fluconazole	1 (1.4)	4 (7.4)
Combination therapy*	29 (40.3)	6 (11.1)

*Combination therapy: ceftazidime and cloxacillin, cloxacillin and piperacillin-tazobactam and meropenem and vancomycin all the components of the intervention. The attitudes and practices of health care workers are vital to infection control. A previous study reported changing health behaviors is complex and involves multiple factors that are interrelated (Craig *et al*, 2008).

Another possible reason for the lack of a significant reduction in CRBSI post-intervention in our study could be the education program was inadequate to result in behavioral change. An effective, locally appropriate education program needs to be created, conducted and tested to determine how best to educate the healthcare workers at the study institution. After an effective program has been proven, it is necessary to determine how often the program needs to be repeated to maintain this a significant reduction in CRBSI. A previous study conducted by the National Health Service in the United Kingdom found it is necessary to give health care workers evidence-based strategies to reduce CRBSI (NHS, 2014).

Failing to take into account the psychology of the participants in a program can also impact the efficacy of that program (Michie *et al*, 2005).

Another reason for our study results could be the health care workers were short-staffed or over-worked which can compromise good practices, such as hand hygiene.

In our study, prior to the intervention, Gram positive bacteria, which were primarily Gram-positive cocci, were the leading cause of CRBSI and after the intervention, Gram negative organisms, all of which were Gram-negative bacilli, were the leading cause of CRBSI. A similar finding was also previously reported in another study (Rodríguez-Créixems *et al*, 2013). Other studies have reported Gram-negative bacilli are now the leading cause of CRBSIs and the incidence has been increasing (Marcos *et al*, 2011; Lin *et al*, 2017).

There are several possible reasons for this change from Gram-positive cocci to Gram negative bacilli, including: patient premorbid illness, having neutropenia, older patient age and antibiotic prescription practices. One study reported neutropenia and older patient age were associated with the change to Gram-negative bacilli being the major cause of CRBSI (Calò *et al*, 2020). The reason for this change at our institution is unclear and requires further investigation.

In our study, *Staphylococcus aureus* was the most common Gram-positive cocci isolated both before and after the intervention and *Klebsiella* spp and *Pseudomonas* spp were the most common Gram-negative bacilli isolated both before and after the intervention. Similar findings have been reported by other studies (Marcos *et al*, 2011; Mermel *et al*, 2009).

Lower extremity CVC insertion sites are associated with higher risk of infection than upper extremity sites (Mermel *et al*, 2009; Oliver *et al*, 2000). However, the World Health Organization does not specify CVC insertion site change as a measure to reduce CRBSI. It is possible the femoral site was selected for catheter insertion because it is easier or because the staff have less experience in inserting an internal jugular catheter and little or no experience in inserting a subclavian catheter. This suggests a need to educate and train the staff who insert CVC in how to inset at a lower risk site.

In our study the median lengths of time a CVC was in place pre- and post-intervention were not significantly different from each other. Our finding is similar to the results of a previous study (Salama *et al*, 2016). This possibly indicates the minimum length of time a catheter was in place prior to the intervention was already as short as possible and it was not possible to significantly reduce this number further.

A limitation of our study was we had missing data for study subject in the pre-intervention group regarding the number of days catheterization. Another limitation was the retrospective nature of our study so we could not control for all confounding factors.

In summary, the intervention did not significantly reduce the incidence of CRBSI among study subjects but there appeared to be a slightly change in etiological organisms after the intervention. We conclude the intervention was ineffective and a new education program needs to be developed and tested to determine if it is possible to further reduce CRBSI at the study institution.

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