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Interventions to Prevent Catheter-Associated Bloodstream Infections: A Multicenter Study in Korea

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Background: The purpose of this study was to determine the efficacy of infection-control interventions to decrease the incidence of catheter-associated bloodstream infections (CA-BSI) and to examine the sustainability of its effect during and after the intervention in Korea.
Materials and Methods: We conducted a prospective multi-strategy intervention in intensive care units (ICUs) at 3 university hospitals in Korea. The intervention consisted of education and on-site training for medical personnel involved in catheter care, active surveillance, and reinforcement of current intervention in each unit. After the intervention of 3 months, we identified CA-BSI cases of each hospital using the electronic database for 6 months.
Results: During the intervention, the number of CA-BSI decreased significantly compared to pre-interventional period (8.7 vs. 2.3 per 1,000 catheter days; rate ratio 0.28; 95% CI, 0.13-0.61). After the intervention, CA-BSI rate increased slightly, but was still significantly lower than that of pre-interventional period (4.3 per 1,000 catheter days; rate ratio, 0.49; 95% CI, 0.31-0.78). Reduction of gram-negative bacterial infections was noted during and after the intervention.
Conclusions: A multi-strategy approach to reduce CA-BSI could be implemented in diverse settings of medical and surgical units in Korea and decreased CA-BSI rates during the intervention.

Key Words: Catheter-associated bloodstream infections, Healthcare associated infection, Intensive care unit, Intervention

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Introduction

Primary bloodstream infections are a frequent cause of morbidity and mortality in critically ill patients. According to the report from the National Healthcare Safety Network (NHSN) of the U.S. Centers for Disease Control and Prevention (CDC), catheter-associated bloodstream infections (CA-BSI) occur at a mean rate of 2.9 per 1000 catheter-days for medical intensive care units (ICUs) in American hospitals [1]. Mortality attributable to CA-BSI has been estimated to be as high as 35%, and the length of hospital stay is increased among infected patients [2-6]. In Korea, primary bloodstream infection was the third common nosocomial infection (24%) and CA-BSI occurred at a rate of 2.58 per 1000 catheter-days in 2006 [7]. However, CA-BSI rate varied among institutions: 10 percentile 0, 90 percentile 8.38/1000 catheter days in hospitals with more than 900 beds [7]. Therefore, interventions aimed to decrease the infection rate are necessary to reduce serious public health consequences of this nosocomial infection.

Prior studies from a single hospital have shown reductions in the rates of CA-BSI by various interventional efforts, including education and surveillance [8-14]. Recent multicenter studies also showed successful sustained reductions in the rates of infection [15, 16]. However, CA-BSI rate is still high in developing countries, and their efforts to reduce CA-BSI rate have scarcely been reported [17]. In Korea, there are some reports on the interventions that was employed to reduce CA-BSI [14, 18, 19] but all have been done in a single center setting and no report on multicenter trial exist.

Therefore, we initiated a prospective multicenter study to implement a multifaceted, education-based intervention in ICUs at 3 academic medical centers in Korea. The primary purpose of this study was to assess the effect of intervention and to examine the sustainability of its effect on lowering the incidence of bloodstream infection which was associated with central venous catheters during and after the intervention.

Materials and Methods

1. Study site

The study was conducted in 6 ICUs at 3 academic tertiary care hospitals (mean size, 950.3 beds; range, 893-1,014 beds) participating in the Korean Nosocomial Infection Surveillance System (KONIS) Prevention Program. Two hospitals are located in Seoul and one is located in Gwangju city (Table 1).

Table 1. Characteristics of Hospitals which Implemented Bloodstream Infection Prevention

Hospital	ICU type	Number of beds	No. of patients during the study periods	Average catheter-days per month	Proportions of patients with catheter
A	MICU	18	6,111	168	0.33
	SICU	18	3,242	197	0.73
B	MICU	23	7,570	215	0.34
	SICU	23	7,264	257	0.43
C	MICU	14	4,824	227	0.56
	SICU	15	4,353	231	0.63

2. Description of intervention

The program was a multi-strategy approach consisting of education and on-site training for medical personnel involved in catheter care, active surveillance by infection control practitioners, and reinforcement of current intervention program in each unit over a 3-month period. The study on intervention targeted healthcare providers' use of evidence-based procedures, recommended by the U.S. CDC and identified as having the greatest impact on the rate of catheter-related bloodstream infections [20]. The recommended strategies are education and training of healthcare providers who insert and maintain catheters, hand washing, using maximal sterile barrier precautions during catheter insertion, use of a 2% chlorhexidine preparation for skin antisepsis, avoiding the femoral site if possible, and removing unnecessary catheters. It was implemented by infection control teams to reinforce correct practices for central venous catheter (CVC) insertion, manipulation, and care for 3 months.

Education sessions and small-group meetings of staffs with or without two-weeks-campaign for appropriate hand-washing were carried out in three hospitals. The education included the principles concerning catheter care as follows: skin preparation, preferred site of CVC insertion, CVC insertion technique, the use of maximum barrier precaution, the use of antimicrobial impregnated CVC, dressing type, dressing interval, manipulation of hub and line, and CVC replacement. Small group education sessions were held with residents from medical and surgical departments who would potentially insert the CVC. Seperate education classes included nurses who worked in each ICU.

Observation and on-site training of CVC care were performed by infection control staffs and nurses in ICUs in each hospital. Two kinds of checklists were used: one for the insertion of CVCs, and the other for the maintenance of CVC in ICUs. The checklist for CVC insertion included hand-washing before procedure, skin preparation, site of insertion, use of maximum barrier precaution, and replacement. The other checklist for CVC dressing and manipulation was used once the patients with CVC had been admitted to ICUs or a CVC was inserted to patients in the ICUs. On-site training was performed during surveillance. When wrongdoing of catheter care was noticed, immediate correction was implemented. If central catheter was judged to be unnecessary, catheter removal was recommended.

3. Data collection

Baseline data collection to identify ICU-acquired, catheter-associated bloodstream infections was initiated in July 2007, 3 months before the intervention. All patients with CVC for more than 24 hours and admitted to ICUs were directly enrolled during both baseline and intervention periods. Study personnel collected the data on the total number of patient-days and the total number of catheter-days per month per ICU. Additional information obtained included patients' demographics, anatomic location of catheters (i.e., in the femoral, subclavian, or internal jugular veins), date and place of catheter insertion (i.e., in the ICU, operating room, emergency room, general ward, or other hospitals), and survival of patients. Each hospital's infection control team reviewed the results of all blood cultures that were carried out in the study units or within 48 hours after discharge from the unit. After the intervention, we monthly identified patient-days, catheter-days, CA-BSI cases, and their microbiological characteristics of each hospital from the KONIS electronic database from January to June 2008.

All of the data were presented on the basis of time when the intervention was implemented: at baseline (3 months), during the intervention (3 months), or after the intervention (6 months). A bloodstream infection was considered to be ICU-related if it occurred 48 hours after admission to or within 48 hours after discharge from the ICUs. We adopted the definitions of laboratory-confirmed CA-BSI, proposed by the CDC [21]. Laboratory-confirmed CA-BSI was defined as the detection of a pathogen isolated from one or more blood cultures and not related to other site infections.

4. Statistical analysis

The incidence rate of CA-BSIs per 1,000 catheter-days was calculated for each hospital and in aggregate. Comparisons of the incidence rates of CA-BSIs during and after the intervention with that of the baseline were analyzed by Poisson regression and 95% confidence intervals (CIs) were also presented. A multivariate logistic regression analysis was performed to estimate the simultaneous effects of multiple variables on the CA-BSI with the data directly collected during baseline and the intervention periods.

All data were analyzed using SPSS for Windows software (version 13.0; SPSS Inc, Chicago, IL, USA). $P<0.05$ was considered statistically significant.

Results

1. Baseline characteristics

The six study units had a mean of 18.5 ICU beds (range, 14-23 beds). We evaluated a total of 15,532 catheter-days (3,898 at baseline, 3,063 during the intervention, and 8,571 after the intervention) during 33,364 patient-days (7,943 at baseline, 8,319 during the intervention, and 18,568 after the intervention). The overall proportion of catheter-days to patient-days was not different significantly among 3 periods: 0.49, 0.45, and 0.46 catheter-days per patient-days, respectively.

2. CA-BSI rates and causative organisms

Thirty-four primary bloodstream infections occurred in 3,898 catheter-days at baseline, i.e. during 3 months before the intervention (Table 2). During the intervention period when education and active surveillance were implemented, the number of CA-BSI dropped to 7 in 3,063 catheter-days (8.7 vs. 2.3 per 1,000 catheter days; rate ratio, 0.28; 95% CI=0.13-0.61). After the intervention, the number of CA-BSI slightly increased to 37 in 8,571 catheter-days (4.3 per 1,000 catheter days; rate ratio, 0.49; 95% CI=0.31-0.78). This CA-BSI rate was still significantly lower than that of baseline. However, in the subgroup analysis, CA-BSI rates in each center, except for the center C, did not differ significantly during and after the intervention compared with that of baseline (Table 2).

Table 3 shows that the most common pathogens identified at baseline were *Candida* species, followed by *Staphylococcus aureus* and coagulase-negative staphylococci. During the intervention period, the number of isolates decreased from 36 to 7, with a decrease in the percentage of gram-negative bacterial isolates and a relative increase of gram-positive bacterial isolates. This phenomenon persisted until the period after the intervention, except for the increase of CA-BSI by *Acinetobacter*

Table 2. Catheter-associated Bloodstream Infection Rates and Incidence Rate-Ratios According to the Period of Implementation of the Intervention

	No. of CA-BSIs (No. per 1,000 catheter-days)			Incidence rate ratio (95% confidence interval)		
	Baseline	During intervention	After intervention	Baseline	During intervention	After intervention
Hospital A	8 (6.7)	3 (2.8)	5 (2.4)	1.00	0.46 (0.13-1.59)	0.37 (0.13-1.07)
Hospital B	9 (6.8)	0 (0.0)	13 (3.9)	1.00	0.07 (0.00-1.19)	0.56 (0.24-1.28)
Hospital C	17 (12.3)	4 (4.1)	19 (6.1)	1.00	0.36 (0.13-1.02)	0.50[a] (0.26-0.94)
Total	34 (8.7)	7 (2.3)	37 (4.3)	1.00	0.28[a] (0.13-0.61)	0.49[a] (0.31-0.78)

Rates of catheter-related bloodstream infection during and after implementation of the study intervention were compared with baseline (preimplementation) values by Poisson regression.
[a]$P<0.05$. CA-BSI rates in each center, except for the center C, did not differ significantly during and after the intervention compared with the baseline period.

Table 3. Microorganisms Isolated from Catheter-Associated Bloodstream Infection Cases during the Study Periods

Organisms	No. (%)		
	Baseline	During intervention	After intervention
Gram (+) organisms			
Staphylococcus aureus	7 (19.4)	2 (28.6)	7 (20.6)
Coagulase-negative staphylococci	6 (17.7)	1 (14.3)	9 (26.5)
Enterococcus species	2 (5.6)	1 (14.3)	4 (11.8)
Gram (–) organisms			
Escherichia coli			1 (2.9)
Acinetobacter spp.	5 (13.9)		6 (17.6)
Acromobacter xylosoxidans	1 (2.8)		
Klebsiella pneumoniae	1 (2.8)	1 (14.3)	
Pseudomonas aeruginosa	2 (5.6)		1 (2.9)
Serratia marcescence	1 (2.8)		1 (2.9)
Stenotrophomonas maltophilia	1 (2.8)		
Candida species	10 (27.8)	2 (28.6)	5 (14.7)
Total	36	7	34

Table 4. Multiple Logistic Regression Analysis Assessing the Risk Factors Associated with Catheter-Associated Bloodstream Infection

	Odds Ratio (95.0% confidence interval)	*P* value
Age	1.029 (1.003 -1.055)	0.029
Duration of hospital admission	1.009 (1.005-1.014)	<0.001
Duration of catheter placement	1.008 (0.985-1.031)	0.517
Places where catheter were inserted		
ICU	1.000	
Emergency room	1.039 (0.436 -2.475)	0.932
Operating room	0.000	0.995
Ward	1.186 (0.376-3.746)	0.771
Other hospital	0.000	0.998
Arterial line	0.536 (0.210-1.372)	0.194
Study hospital		
A	1.000	
B	0.452 (0.143-1.436)	0.178
C	1.016 (0.369-2.797)	0.976
Study period		
Baseline	1.000	
Intervention	0.395 (0.167-0.938)	0.035

species.

3. Effect of the intervention on CA-BSI rates

In the univariate analysis, CA-BSI occurred more frequently in patients who were older, whose duration of admission in the ICU or hospital was longer, whose duration of catheter placement was longer, and to whom catheter was inserted in the ICU (data not shown). Therefore, multiple logistic regression analysis was performed to confirm the effect of the intervention after adjusting for these risk factors. Table 4 indicates that intervention (OR=0.395, 95% CI=0.167-0.938) significantly reduced the CA-BSI rate after adjusting for centers, patients' age, duration of catheter placement, and sites of catheter insertion. Old age of patients and longer duration of hospital admission were significant risk factors for CA-BSI.

Discussion

This study is the first multicenter study in Korea which showed that an active multidisciplinary intervention could reduce the incidence of catheter-related bloodstream infection. The maximal reduction of CA-BSI rates in our study occurred during the 3 months of intervention and was sustained after an active intervention. However, the effect declined shortly after finishing intervention. The result of infection rate surveillance in the post-intervention period showed slight increase of CA-BSI rate. Three months of intervention might be too short to achieve a maximum decrease of infection rate. According to a multicenter intervention by Warren et al., it took approximately 7-12 months to change practice pattern of nurses and physicians, thereby getting a maximum reduction of infection rate [15]. In another multicenter study including more than 100 ICUs which had low infection rate (2.7 per 1000 catheter-days) before the intervention [16], the median rate of infection reached 0 within 3 months after implementation of intervention to decrease CA-BSIs, and continued throughout 15 months of follow-up. In the baseline period of this study, the CA-BSI rates of each hospital were higher than 75 percentile of CA-BSI rates from medical or surgical ICUs in the National Healthcare Safety Network of the USA (4.2 or 4.4 case per 1,000 catheter days) [1], but lower than mean rate obtained in 8 developing countries (12.5 case per 1,000 catheter days) [17], It is, therefore, warranted to compare the efficacies of 3-month intervention and that of longer-period intervention in order to determine whether longer period of intervention is needed to achieve a maximal reduction of infection and sustain this reduction in hospitals with high CA-BSI rate.

Industrialized countries such as the USA and UK have established standards for institutional surveillance and control of healthcare-associated infection [1, 22]. Most studies related to healthcare-associated infection have been conducted in developed countries and demonstrated the efficacy of surveillance and its significant contribution to minimizing morbidity, mortality, and medical cost [2, 3, 8-10, 12, 13, 15, 16, 23]. On the other hand, only a few studies on healthcare-associated infection using standardized definitions and intervention are available in developing countries, especially in Asia [24, 25]. As suggested earlier, studies from developing countries showed higher rates of device-associated infection and this could be due to the lack of guidlines mandating healthcare-associated infection control programs, variable hand hygiene standards, scarce funds and resource - especially lower nurse-to-patient staffing ratios in ICUs - for infection control, and limited use of outdated technology for prevention [17]. A higher baseline infection rate together with these limitations seemed to work against maintaining sustained improvement after the active intervention in the current study. Surveillance of healthcare-associated infections appears to be truly the first step toward reducing the risk of infection in vulnerable hospitalized patients. Our experiences, however, indicate that continued efforts of active intervention are needed to sustain the reduced infection rate after the surveillance.

In this study, 3 university hospitals harboring similar number of ICU beds were enrolled, but the infection rate and outcome of intervention were different in each hospital. The reason can be partly because of several differences in catheter-practices and clinical characteristics of the patients in each hospital (data not shown). For example, subclavian vein insertion rate was practiced in 28.6%, 67% or 76% in each hospital patients, respectively ($P<0.001$), and the places where catheter was inserted were significantly different (ICU, ER or OR): 33%, 23% or 30% vs. 79%, 7% or 8% vs. 28%, 34% or 29% in each hospital, respectively ($P<0.001$). Mean age of the patients, severity score of baseline diseases, and duration of admission were also different. Therefore, to decrease the CA-BSI, careful observation and understanding the problems in catheter-practice in each institution are necessary.

It is noted in this study that infection by gram-negative bacteria was dramatically decreased during and after the intervention. Bacteremia due to these organisms emerges usually from non-catheter-related sources, such as nosocomial urinary tract infection or nosocomial pneumonia. During the intervention period, one-time use of sterile 3-way cap of infusion hub and cleaning of injection port with 70% alcohol before accessing the infusion system were recommended to reduce hub-originated catheter infection in this study. In one report, surveillance hub culture predicted the pathogen of CA-BSI especially when gram-negative organisms were identified [26] and in another report, hub contamination control reduced CA-BSI caused by gram-negative organisms, although statistical significance was not found [27]. Therefore we thought that those interventions might reduce bacteremia due to gram-negative bacteria in this study. When CVC is no longer necessary, immediate removal would also contribute to the reduction of infection.

This study has several limitations. The study design, a preintervention-postintervention comparison, diminished the ability to make a causal relation between the intervention and reduction in CA-BSI rates. However, since randomized controlled assignment of the intervention in an ICU setting was not feasible, several intervention studies adopted pre-postintervention design [15, 16]. Second, CA-BSI rates varied among three hospitals involved, suggesting substantial differences in severity of illness, efficiency of surveillance, and availability of institutional resources for prevention between the hospitals. This variation is likely to have occurred, because bloodstream infections are rare and the presence of small number of cases or outbreaks substantially affects the infection rate. Third, because of the same reason as mentioned above, each center did not show significant reduction in CA-BSI rates both during and after the intervention, in spite of the reduction in overall CA-BSI rate. Last, we included only three medical centers that voluntarily participated in the intervention, thus limiting the ability to generalize the findings.

Both in the developing and the developed countries, catheter-associated bloodstream infections are a huge threat to the safety of patients. This study demonstrated that a multi-strategy approach to reduce CA-BSI can be implemented in a diverse setting of medical and surgical units in Korea and can decrease CA-BSI rates during the intervention. Future interventional effort is urgently needed to prolong the effect of intervention which includes diverse strategy for a longer period of time, depending on each center's demand.

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