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Major Article

Clinical impact and cost-effectiveness of a central line bundle including split-septum and single-use prefilled flushing devices on central line–associated bloodstream infection rates in a pediatric intensive care unit

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Background: Central line–associated bloodstream infections (CLABSIs) are among the most frequent health care–associated infections. Central line bundle (CLB) programs are useful for reducing CLABSIs.
Methods: A retrospective study was designed to compare 2 periods: the prebundle and bundle periods. We evaluated the impact of a CLB including implementation of split-septum (SS) devices and single-use prefilled flushing (SUF) devices in critically ill children.
Results: During the prebundle period, the overall rate was 24.5 CLABSIs per 1,000 central line (CL) days, whereas after the initiation of the CLB, the CLABSIs per 1,000 CL days dropped to 14.29. In the prebundle period, the daily cost per patient with CL and CLABSI were $232.13 and $254.83 consecutively. In the bundle period, the daily cost per patient with CL and CLABSI were $226.62 and $194.28 consecutively. Compared with the period with no CLB, the CLB period, which included SUF and SS devices, resulted in more costs saving by lowering the daily total costs of patients and indirectly lowering total drug costs by decreasing antibacterial and more significantly antifungal drugs.
Conclusions: CLB programs including SS and SUF devices were found to be effective in decreasing the CLABSI rate and decreasing the daily hospital costs and antimicrobial drug expenditures in children.

Central line–associated bloodstream infections (CLABSIs) are among the most frequent health care–associated infections and are reported to be associated with increased number of inpatient days, higher cost, and attributable mortality rates,[1-6] not sparing high-income or limited-resource countries.[1,2]

Prevention practices, including the use of chlorhexidine gluconate skin preparations and maximal sterile barriers during insertion, use of the subclavian or internal jugular vein instead of the femoral vein, hand hygiene, and daily review of line necessity, have been developed for preventing CLABSIs.[7-10] Increased adherence to central line bundles (CLBs) has been reported to result in a 70% reduction of CLABSIs rates.[7] Moreover, in developing countries, it is reported that CLABSI rates can be reduced by >50% by implanting multidimensional prevention strategies.[11-16]

In our center, we started a CLB program in which needleless split-septum (SS) devices (BD Q-Syte; BD, Sandy, UT) and single-use prefilled flushing (SUF) devices (BD PosiFlush Pre-filled Saline Syringe; BD) were adopted to other standard precautions to reduce CLABSIs in the pediatric intensive care unit (PICU). The aim of this study was to evaluate the cost-effectiveness and clinical impact of the CLB by comparing baseline (6 months before the initiation of the CLB) with 6 months after the initiation of the CLB in the PICU. Because there are limited information in comparison with adult studies, this study provides the important data of cost-effectiveness of the CLB in children.

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METHODS

Background

Dr. Behçet Uz Children's Hospital, Izmir, Turkey is a 400-bed pediatric teaching hospital with 2015 annual outpatient visits of >565,000 patients and approximately 21,000 hospitalizations per year. The PICU of Dr. Behçet Uz Children's Hospital is a 24-bed unit where annual admission is approximately 600 patients per year. The incidence of CLABSI episodes per 1,000 patient days in our PICU was 24.35, and the infection control committee decided to implant the CLB program to reduce CLABSI rates.

Setting

The study was carried out in the PICU of Dr. Behçet Uz Children's Hospital. The study included 2 time periods: the 6-month baseline period before the initiation of the CLB (December 1, 2013-May 31, 2014) and the 6 months of the CLB initiation period (June 1, 2014-November 30, 2014). The study was approved by the local ethical committee and institutional review board. The data were evaluated and recorded by 2 investigators (N.Y. and Y.O.), and the other investigators only saw the recoded data, to protect patient confidentiality.

Subject and design

In this study, the clinical impact and cost-effectiveness of the CLB program for reducing the incidence of CLABSI were evaluated. All patients who had been hospitalized in the PICU during the study period and patients who had central lines (CLs) were included in further analysis.

The CLABSI incidence was compared between 2 periods (pre-CLB and CLB periods). Consumable costs included the price of the catheters, the price of components of the CLB, total diagnosis costs, total hospital costs, antimicrobial (antibacterial/antifungal therapy) treatment costs, total bed costs, total laboratory costs, and total patient costs for each patient. All data were collected from the medical files of the patients and prepared forms, including a checklist for the CLB. The efficacy of the CLB in daily practice was measured with the forms prepared by the infection control nurse.

The CLB was comprised of the following elements: selection of catheters with minimal lumen and optimal insertion site, use of optimal hand hygiene, chlorhexidine skin antisepsis, maximal barrier precautions for catheter insertion, daily inspection of the catheter sites, use of SS and SUF devices, prompt catheter removal, kits containing all the equipment recommended for catheter insertion, use of optimal hand hygiene and use of aseptic techniques, and use of transparent dressings. Implementation included programs to educate staff about clinical leadership and infection risks and bundle methods, in addition to surveillance and feedback to health care personnel in the PICU on CLABSI rates and performance. In the pre-bundle period, when available, mechanical valves (MV) or 3-way stopcocks (3WSC) were used in the PICU.

Statistical analysis

Statistical analysis was performed using SPSS version 15.0 (IBM SPSS, Chicago, Illinois). Quantitative data were shown as the mean ± SD or the median with interquartile ranges (quartile 1-quartile 3). Qualitative variables were expressed as absolute and relative frequencies. Univariate comparisons were performed using the appropriate tests—χ^2 test with Fisher exact correction where required for discrete variables and Student *t* test for parametric and Wilcoxon rank-sum test for nonparametric continuous variables. Significance was set at $P = .05$. For cost-benefit analysis, total costs of the program were calculated as subsequently detailed.

Cost-effectiveness analysis

Cost-effectiveness analysis was performed both on health care payer perspective and on hospital costs. The cost of screening cultures was calculated as converting the price that had been billed to the Republic of Turkey Social Security Institution per culture to the U.S. dollar exchange rate. For each patient with a CL, daily cost of hospitalization (determined by healthcare payer) and actual daily cost of hospitalization, including laboratory tests, antimicrobial drugs, drugs other than antimicrobial drugs, and total item expenditures, were calculated. Cost of the CLB was calculated for every patient with a CL in the bundle group. The cost of the SS device was $2.85, and the cost of the SUF device was $0.52. The cost of the total CLB was calculated for each patient because total intravenous infusions may change according to the patient's clinical status and underlying disease. Because we had higher rates of fungal-related CLABSIs in our center (because of the properties of our population, including hemato-oncological malignancies and primary immunodeficiencies), one of the breakpoints for this study is the cost of antifungal drugs.

RESULTS

Clinical analysis

During the study period, a total of 554 patients were hospitalized in the PICU during 8,262 bed days, and 90 of the 554 patients (16.2%) required CLs, with a total of 3,034 CL days. During the prebundle period, there were 33 CLABSIs for an overall rate of 24.5 CLABSIs per 1,000 CL days. After the initiation of the CLB, there were 24 CLABSIs, which count for an overall rate of 14.29 CLABSIs per 1,000 CL days, which was lower than the prebundle period (Table 1). One of the breakpoints of the study was to decrease *Candida*-associated CLABSIs, and the overall rate of *Candida*-associated CLABSIs per 1,000 CL days decreased to 6.55 (bundle period) from 14.02 (prebundle period) (Table 1).

Microbiologic results

The microorganism profile was reviewed in Figure 1, including comparison of the prebundle and bundle periods. The major organism responsible for CLABSIs in the prebundle period was *Candida parapsilosis* (57.5%), followed by coagulase-negative staphylococci (9.09%). Despite lower rates compared with the prebundle period, *C parapsilosis* was still the predominant causative agent in the bundle period (45.8%) (Fig. 1). In our center, coagulase-negative staphylococci and other rare microorganisms, including *Ralstonia pickettii*, *Achromobacter* spp, *Burkholderia cepacia*, *Moraxella catarrhalis*, and *Saccharomyces cerevisiae*, have been found to cause CLABSIs. Although

Table 1
CLABSI rates in the bundle and prebundle periods

Variable	Prebundle period	Bundle period
Patients, n	354	204
Total patient days, n	4,046	4,216
Patient number with CL	45	45
CL days	1,355	1,679
CLABSIs, n	33	24
CLABSI rate per 1,000 CL days, n	24.35	14.29
Candida-associated CLABSI rate per 1,000 CL days	14.02	6.55

CL, central line; *CLABSI*, central line–associated bloodstream infection.

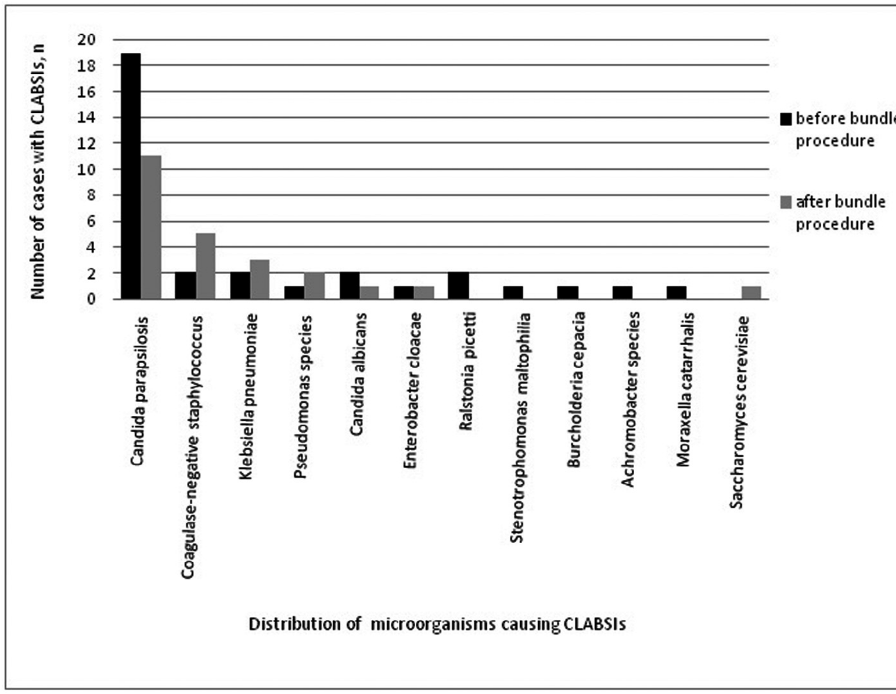

Fig 1. Comparison of the microorganisms responsible for central line–associated bloodstream infections (CLABSIs) during the prebundle and bundle periods.

those microorganisms are well-known contaminants, CLABSIs were diagnosed in these patients following Centers for Disease Control and Prevention criteria, and at least 2 positive cultures taken at different times in patients who had fever and hypotension were required for the diagnosis. Moreover, no other etiologic agents of infections except reported microorganisms were found in these patients.

Cost-effectiveness

In the prebundle period, daily costs of patients with CLABSI were $254.83 per patient day. In the bundle period, daily costs of patients with CLABSI were $194.28 (Table 2). In the prebundle period total costs of antifungal and antibacterial drugs were $84,504.75 and $29,514.95, respectively, whereas in the bundle period total costs of antifungal and antimicrobial drugs were $19,684.34 and $25,233.3, respectively. Our findings show that the CLB, including the use of SUF and SS devices, is more costs saving than the period in which no CLB was used, by lowering the daily total costs of patients and indirectly lowering total drug costs by decreasing antibacterial and more significantly antifungal drugs.

Table 2
Total and daily hospitalization costs and total drug costs, including antifungal and antibacterial therapy costs

Hospital costs of patients	Prebundle period	CLB period
Patients with CLs*		
Total costs	493,990.44	523,049.52
Total drug costs	194,289.32	140,206.80
Total antibacterial drug costs	29,514.95	25,233.33
Total antifungal drug costs	84,504.75	19,684.34
Total item expenditure costs	69,097.57	86,836.10
Total costs for laboratory investigations	125,216.88	181,705.68
Daily hospitalization costs†	232.13	226.62
Patients with CLABSIs		
Total costs	345,295.37	326,201.76
Total drug costs	153,617.05	83,396.52
Total antimicrobial drug costs	21,594.38	16,050.35
Total antifungal drug costs	72,912.77	7,570.99
Total item expenditure costs	42,999.57	55,769.04
Total costs for laboratory investigations	80,930.17	114,335.24
Daily hospitalization costs	254.38	194.28

CL, central line; *CLB*, central line bundle; *CLABSI*, central line–associated bloodstream infection.
*All costs are in U.S. dollars.
†Daily hospitalization cost was calculated as total costs/total patient days.

DISCUSSION

In this retrospective study, the CLABSI incidence rate significantly decreased with implementation of the CLB. There was decline in daily hospital costs and antifungal drug expenditures as well, despite increased CL days in the bundle period. The implementation of CLBs have been reported to decrease CLABSIs with different ratios.[17-24] In a previous study, including 29 PICUs, CLABSI rates were reported to decrease by 56% with the insertion of the CLB over 36 months, supporting our findings.[15] To our knowledge, this is the first study conducted in children where SS and SUF devices were implemented in the CLB program.

In this study, important elements of the CLB were the SS and SUF devices, instead of MVs, which had been routinely used in our PICU before the bundle. A recent randomized clinical trial by Rosenthal et al reported that the use of SS plus SUF devices was associated with significantly lower CLABSI rates than the use of 3-way stopcocks,[25] supporting the major impact of SS and SUF devices in clinical practice. Because CLBs consist of multiple steps as previously mentioned, the decrease in CLABSIs was not totally attributable to usage of SS plus SUF devices. However, because MVs had been widely used in the prebundle period, implementation of the SS and SUF devices into the bundle program was thought to have a major impact on reducing CLABSI rates. Salgado et al reported that CLABSI rates were significantly higher during the needleless MV device period than during the needleless SS device period, supporting our findings with SS plus SUF devices.[26]

The microorganisms' profile in our study was somehow different from previous studies. In a recent study by Rosenthal et al, the prominent bacteria were *Enterococcus* spp (37.5%) in the SS plus SUF devices group and *Klebsiella* spp (36.4%) in the 3-way stopcock group.[25] Salgado et al also reported the same profile as *Enterococcus* spp (25.0%) in the SS plus SUF devices group and *Klebsiella* spp (20.0%) in the 3WSC group.[26] However, in our study, *Candida* spp, mostly *C parapsilosis*, had been the dominant microorganism in both the prebundle and bundle periods, which was different from previous studies with SS and SUF devices. Although *Candida* spp lead as the causative agent, implementation of the CLB resulted in a decrease in the rate of *Candida*-associated CLABSIs per 1,000 CL days by 50%.

In this study, implementation of the CLB in the PICU had not only lowered CLABSI rates, but it also decreased the daily cost of the patients, mainly by decreasing the antimicrobial and antifungal drug costs by increasing infection-free catheter days. In our study, total laboratory costs and total item expenditures were higher in the bundle period. Higher costs in bundle period could be caused by high total patient days and catheter days compared with the prebundle period. Moreover, because this study was not a randomized study, the patients' primary diseases, underlying diseases, and complications other than infections were not under control while analyzing and therefore might affect laboratory and item expenditures. The dramatic decrease in antimicrobial and antifungal drug costs saved $60 per patient day, which is approximately one-fifth of the daily cost of hospitalization determined by the health care payer. The economic impact of CLABSIs has been well demonstrated before in both PICUs and adult intensive care units. A study in a neonatal intensive care unit in Belgium reported a 24 day longer hospital stay with an additional cost of €12,000 in patients with hospital acquired infections.[27] Another study from United States reported that the presence of CLABSIs extended the entire hospital length of stay by 6.5 days in the PICU and resulted in an additional hospital costs by $33,039, due to the increase in length of stay days.[28] Therefore, it is not surprising that implementation of a CLB in our center decreased the hospital costs per day, suggesting the CLB would be an appropriate strategy for lowering CLABSIs and therefore daily hospital costs.

In this study, CLB programs including SS and SUF devices was found to be effective in decreasing CLABSI rates and decreasing the daily hospital costs and antimicrobial drug expenditures in children.

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