

# Central line bundle including split-septum device and single use prefilled flushing syringes for prevention of port associated bloodstream infections: A cost and resource utilization analysis

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## Research article

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# Abstract

**Background:** Central line bundle programs were found to be effective in decreasing central line-associated bloodstream infection rates in pediatric cancer patients with ports. However cost-effectiveness studies of central line bundle programs in pediatric cancer patients are limited and most available data are from intensive care unit or adult studies.

**Methods:** In this 6 years cross-sectional study, comprehensive assessment of total health care costs attributable to CLABSI's associated with ports between two periods including 3 years of pre-bundle period and bundle period.

**Results:** This cross-sectional study was carried out in the pediatric hematology-oncology ward of Dr. Behçet Uz Children's Hospital from 1 August November 2011 to 31 July 2017. The CLABSI rates decreased significantly from 8,31 CLABSIs to 3.04 per 1000 central line days (  $p < 0.0001$ ). In the prebundle period, total attributable costs spent for of patients with CLABSI were \$130661,68 and in the bundle period, total attributable costs spent for patients with CLABSI were \$116579,05. Within bundle implantation, 71 potential CLABSI were prevented which saved an additional \$208977,81. In other words, for one dollar spent for bundle program, \$ 6,54 was saved by decreasing the expected CLABSI.

**Conclusion:** our study shows that central line bundles decreases not only the CLABSI rate, but also decreases attributable costs due to CLABSI. Expenses spent for bundle elements, were covered by savings by preventing CLABSI with higher costs

## Background

Totally implantable venous access devices (TIVADs, ports) are one of the essential elements of cancer treatment which improve the quality of life significantly (1). In a recent study from United States, Central Line Associated Blood Stream Infections (CLABSI) associated with ports were reported to change 0.16 to 1.48 port days which was lower compared to tunneled externalized catheters (2). However when occurs, they increase morbidity and mortality significantly (3,4). Moreover CLABSI, cause additional costs to the patient and health care system. Previous studies from United States and Germany reported that CLABSI caused an additional expense per case as \$69, 332 and \$6970 consecutively (5,6). Previous studies focusing on CLABSI in pediatric-hematology patients, had reported attributable additional length of stay as 12 to 21.2 days which also increased the hospital costs significantly (5,6).

Central line bundles (CLBs) for prevention of infections, including chlorhexidine gluconate skin preparations and complying with maximal sterile barriers during insertion, preferring the subclavian or internal jugular vein instead of the femoral vein, strict hand hygiene, and daily review of necessity of central line had been reported to prevent CLABSI especially in intensive care units (7–11). However; studies including CLBs for long-term CLABSI's in pediatric cancer patients and bone marrow transplant patients were limited (12–16). Moreover cost-effectiveness studies of CLB applications in pediatric cancer patients are limited and most available data are from intensive care unit or adult patient studies.

In this 6 years cross-sectional study, we performed a comprehensive assessment of total health care costs attributable to CLABSIs associated with TIVADs in pediatric cancer patients in two periods including 3 years of pre-bundle period and bundle period.

## Methods

### Setting:

This cross-sectional study was carried out in the pediatric hematology-oncology ward of Dr. Behçet Uz Children's Hospital from 1 August November 2011 to 31 July 2017. Dr. Behçet Uz Children's Hospital, is a 400-bed pediatric teaching hospital. At the time of the study, the oncology-hematology department had 28 beds and received 60 newly diagnosed hematologic and oncologic patients per year.

The study included 2 time periods: the 3-years baseline period before the initiation of the CLB (1 Aug 2011 to 31 July 2014) and the 3 years of CLB period (1 Aug 2014 to 31 July 2017). The data were evaluated and recorded by 3 investigators and the other investigators were blinded to the patients' information to protect patient confidentiality.

According to our infection control committee policy, ports were the preferred route for vascular access for the pediatric hematology-oncology patients and inserted was before starting induction chemotherapy, under sterile conditions in the operating room.

### Microbiology and definitions:

In our center, two central venous blood culture samples for aerobic and anaerobic culture were taken from patients with fever (under aseptic conditions and after disinfection of the central venous access device hub in addition to blood culture sample from peripheral veins. Fever was defined as body temperature  $>38.5^{\circ}\text{C}$  for at least 4h or once  $>39^{\circ}\text{C}$ . Neutropenia was defined as a total number of granulocytes  $<0.5 \times 10^9/\text{L}$  or a total number of leukocytes  $<1.0 \times 10^9/\text{L}$  without differential counts available (17).

Each blood culture bottle (taken from blood or ports) was placed in the BacT/ALERT 9240 automated system (bioMérieux, Marcy l'Etoile, France) (18). The microorganisms were identified with VITEK-2 compact system (bioMérieux). Identification and antibiotic susceptibility tests of Gram-positive bacteria were performed using the automated VITEK-2 system with Gram-positive identification card ASTP592, a supplementary Etest (bioMérieux, Durham, NC, USA), and a disk diffusion test according to the manufacturer's instructions(19). This system was also used for identification and antibiotic susceptibility tests of Gram-negative bacteria with Gram-negative identification card AST-N325, AST-N326, and AST-N327(20). Yeast identification was performed using API 20°C AUX (bioMérieux)(21).

### Prebundle and bundle periods:

The prebundle period included a 3 years period before the implementation of CLB. During this period, povidone iodine at 10% was used for disinfection, three-way stop-cocks were the choice of connection. In this period, flushing was performed using 5 or 10 mL of 0.9% NaCl which was manually filled from the common polyvinyl chloride bags.

The 3 years of CL bundle period comprised the following elements, including steps of the needle insertion in the ports and management). The insertion of needle in the ports included strict hand hygiene, chlorhexidine skin antiseptis (>0.5% chlorhexidine in alcohol solution), complying maximal barrier precautions. The maintenance steps included daily inspection of the catheter sites and cap connection, disinfection of the hub with > 0.5% chlorhexidine in alcohol solution, use of needless connectors (BD Q-Syte; BD, Sandy, UT), use of sterile gauze or transparent semi-permeable membrane and using single-use prefilled saline syringes (BD PosiFlush SP, BD, NJ) for flushing.

Employees were informed about bundle implementations and feedback has been made on bundle adjustment rates and CLABSI rates in addition to educational programs. The education program was provided on weekly in the first 6 months and at monthly base by bundle team. During the study period, prospective and active, surveillance for CLABSI rates and the monitoring of compliance with the bundle components were performed by the bundle team weekly.

Employees were informed about bundle applications and feedback has been made on bundle adjustment rates and CLABSI rates in addition to educational programs. Compliance to the bundle was observed by supervisor nurses and recorded in the checklist forms.

## **Cost-analysis and statistics:**

Demographic and clinical features with hospital costs and length of stay were reviewed from the medical files and computerized system of the hospital retrospectively. Attributable length of stay for hospital admission was considered as the span of days for treatment of CLABSI. Attributable costs of CLABSI for hospitalization were based on charged amounts and included charges for inpatient costs, laboratory costs, imaging, antimicrobial costs and other medications, operation costs for port removal if required. All costs were calculated in Turkish Lira (TL) and were converted to USD (\$), regarding the average TL to USD currency between 1 August November 2011 to 31 July 2017. (TL1 = 0,4484 \$) (22)

Analysis of the data was carried out by using IBM SPSS Statistics 17.0 program (IBM Corporation, Armonk, NY, USA).

Numbers of CLABSI per day was calculated for each group and rate of infections with the Poisson 95% confidence interval in each bundle group and the relative risk reduction between groups were calculated and given as percentages. The relative risk ratio was also calculated to compare the risks for each two groups with 95% confidence interval for the incidence rate. The Statistical analysis was performed using Medcalc v 11.6 (Ostend Belgium).

This study was approved by the local ethical committee and institutional review board of Dr. Behçet Uz Children's Training and Research Hospital.

## Results

During the 6 years of study period, the total catheter line days were 18,672 days (Table 1). Total CL days were 5,175 in the prebundle period, and 13,497 days in the bundle period. During the prebundle period, there were 43 CLABSIs in 5,175 CL-days with an overall rate of 8,31 CLABSIs per 1000 CL-days. After implantation of the central line bundles, there were 41 CLABSIs in 13,497 CL-days, which counts for an overall rate of 3.04 CLABSIs per 1000 CL-days (Table 1). The incidence rate difference with these two groups was 0.005271, indicating a relative risk reduction of 59% ( $p < 0.0001$ ; Table 1).

Among the 84 CLABSI, 8 infections were poly-microbial (9,5%). Among the 92 isolations, 59 isolations were gram negative bacteria (64.1%), followed by gram positive bacteria (18.4%) and fungal infections (17,3%). The most common isolated microorganisms in the whole 6 years period was *Klebsiella pneumoniae* (21.7%), *Candida* species (16.3%) and *Escherichia coli* (14.1%). Infections due to *coagulase negative Staphylococcus* and *S.aureus* was 8.6% and 3.2%, consecutively. The other microorganisms were reviewed in table-2.

## Economic analysis and projection

In the prebundle period, total attributable costs spent for of patients with CLABSI were \$13,0661,68 and in the bundle period, total attributable costs spent for patients with CLABSI were \$11,6579,05 (Table-2). The costs spent for items used for bundle including needless connectors, transparent semi-permeable membrane and using single-use prefilled saline syringes for three years were \$31,944,10. The majority of the costs were drugs in the both of prebundle and bundle period were \$73,231,89 and \$ 48169. The attributable cost of one CLABSI including both prebundle and bundle period was \$2,943,35.

Before intervention (bundle), CLABSI rate was 8,31 CLABSIs per 1000 CL-days. In our projection, if no intervention (bundle) was performed, we estimated that for additional 13,497 CL days, we would expect to see additional 112 CLABSI. However within bundle implantation, we had observed 41 CLABSI and 71 potential CLABSI was prevented. The total money saved within the implantation of the bundle was \$20,8977,81 (calculated by cost per one CLABSI X number of prevented CLABSIs by bundle). In other words, for one dollar spent for bundle, \$ 6,54 was saved by decreasing the expected CLABSI.

## Discussion

In this study, significant differences in CLABSI incidence rate and significant saving with CLB including SS and SUF were observed. The CLABSI rate decreased from 8,31 CLABSIs to 3,04 per 1000 CL-days within implantation of the CLB and \$208977,81 was saved due to preventing possible CLABSIs. This

study is one of the few studies giving economical view of the CLBs for ports in pediatric malignancy patients.

Rinke et al reported a decrease from 2.25 to 1.79 CLABSIs per 1000 central line days in the pediatric hematology patients including a high CL days of 14 059(13). In another study from Germany in which CLB for ready-to-use sterile Na Cl 0.9% syringes were used, a decrease in BSI were observed, however in this study, Broviac catheters were inserted instead of ports(17). In another study from Turkey, CLB including needless connectors and using single-use prefilled saline syringes significantly decreased CLABSI rates from 14.5 to 2.63 per 1000 CL-days. In this study; the total CL days was 3831 days and the study duration was approximately two years (16). These studies in addition to our study had showed the clinical efficiency of CLB programs for prevention of CLABSIs in TIVADs (13,16,17).

Up to our knowledge, this is the first study that has been designed for evaluating the economic aspect of a CLB including needless connectors and using single-use prefilled saline syringes for prevention of CLABSI in pediatric malignancy patients. The CLABSI numbers decreased from 43 to 41 during prebundle period, while catheter days had nearly tripled the reflecting the device utilization rate (5175 CL-days versus 13497 CL-days). In our study, more complicated CLB was performed and according to our projection, 71 CLABSI had been prevented with the implantation of CLB if the same CLABSI rates were observed. The money spent for CLB program in our institute including needless connectors, single-use prefilled saline syringes and transparent semi-permeable membrane was \$31944,10 for the three years. Comparing the prebundle and bundle period, for one dollar spent for bundle, \$ 6,54 could be saved by decreasing the expected CLABSI. Rosenthal et al had compared cost-effectiveness of needless connectors and using single-use prefilled saline syringes versus 3-way stopcocks in a randomized clinical trial. The use of needless connectors and using single-use prefilled saline syringes in the adult intensive care units had saved \$402.88 and \$124 for each extra dollar invested in the CLB (23). Despite the difference of the patient characteristics, clinical settings and design, these two studies had demonstrated the cost-effectiveness of the CLB including needless connectors and using single-use prefilled saline syringes.

The cost calculations in our study were attributed to drugs, biochemical tests, blood culture and radiological investigations to check if they were directly or indirectly linked to treatment of CLABSI. Thus it reflected the clear and most correct attributable costs of CLABSI. Most of the cost distribution in the total period was drug costs (mostly antimicrobial costs) in the both of the period, which had decreased during the bundle period, while laboratory costs had also decreased in the second period. However, the saving was more significant when we did the analysis adding central line days. As the central line days increase, the risk of developing infection would increase too if no precaution has not been taken. Victor et al had also calculated quality adjusted-life years and found an increase of quality-adjusted life years of 0.0008 per patient (23). In our study, we did not had focused on quality of life measures. However, previous study from our clinic focusing on pediatric cancer patients, had reported that patients quality of life were improved by preventing port removal due to infections by 90%(16).

This study has limitations due to its design. First of all, data including costs were collected retrospectively from the medical files, hospital accounting and data system and attributable costs were reviewed by two clinicians which could result in bias. Moreover current study had mainly focused on measurable costs of CLABSI, and some other benefits and indirect savings of prevention of CLABSI could not be measured. For example the time of delay in the treatment of the primary disease due to the infection was not measured. In the bundle period, flushing with SUF device which was a 4 step process compared to flushing using multi dose vials which was a 10 step process was preferred and the time saved by the nursing staff was not also calculated.

## **Conclusion**

The CLB programs including needless connectors and using single-use prefilled saline syringes devices, was associated with a significantly lower CLABSI rate and found to be cost effective and money saving by preventing CLABSI. Central line bundle programs should be used more widely, since they had advantages for all the stakeholders including patients, health care staff and hospital management.

## **Declarations**

Ethical approval: This study was approved by the local ethical committee and institutional review board of Dr. Behçet Uz Children's Training and Research Hospital.

The data used for this study was retrospectively collected and included no personal information which could harm patient's privacy and personal rights.

Consent for publication: Not Applicable

Availability of data and material: The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Competing interests: The authors have no any financial and non-financial competing interests to disclose

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Authors' contributions: ID involved in protocol development, data analysis and manuscript writing and will act as guarantor for the paper. MTO, involved in data collection. IC, involved in data collection. YO, involved in data collection, and microbiological investigations. ND, involved in data collection, and microbiological investigations NT, involved in protocol development, data collection. NB, involved in protocol development, data collection. CV, involved in protocol development, data analysis and manuscript writing

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## **Abbreviations**

CLABSI: Central Line Associated Blood Stream Infections

TIVAD: Totally implantable venous access devices

CLB: Central line bundle

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## Tables

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