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Major article

Impact of needleless connector change frequency on central line-associated bloodstream infection rate

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Background: Bloodstream infection is the most common pediatric health care-associated infection and is strongly associated with catheter use. These infections greatly increase the cost of hospital stay.
Methods: To assess the association between needleless connector (NC) change frequency and central line-associated bloodstream infection (CLABSI) rate, we modeled monthly pediatric stem cell transplant (SCT) CLABSI rate in 3 periods: baseline period during which NC were changed every 96 hours regardless of infusate (period 1); trial period in which NC were changed every 24 hours with blood or lipid infusions (period 2); and a return to NC change every 96 hours regardless of infusate (period 3). Data on potential confounders were collected retrospectively. Autocorrelated segmented regression models were used to compare SCT CLABSI rates in each period, adjusting for potential confounders. CLABSI rates were also assessed for a nonequivalent control group (oncology unit) in which NC were changed every 24 hours with blood or lipid use in periods 2 and 3.
Results: SCT CLABSI rates were 0.41, 3.56, and 0.03 per 1,000 central line-days in periods 1, 2, and 3, respectively. In multivariable analysis, the CLABSI rate was significantly higher in period 2 compared with both period 1 ($P = .01$) and period 3 ($P = .003$). In contrast, CLABSI rates on the oncology unit were not significantly different among periods.
Conclusion: In pediatric SCT patients, changing needleless connectors every 24 hours when blood or lipids are infused is associated with increased CLABSI rates. National recommendations regarding NC change frequency should be clarified.

Bloodstream infection is the most common pediatric health care-associated infection and is strongly associated with catheter use.[1] Central line-associated bloodstream infections (CLABSI) are particularly prevalent in pediatric populations.[2-6] In addition to patient suffering, CLABSI result in a profound increase in the cost of hospitalization.[7-12] Studies in pediatric intensive care unit (ICU) populations have demonstrated per-patient increases of approximately $40,000 attributable to CLABSI even after adjusting for age, severity of illness, and underlying disease.[10,11]

Interventions to improve hand hygiene, ensure sterile procedures for line insertion and use, remove lines as soon as they are no longer needed, and improve adherence to these practices have drastically decreased CLABSI incidence in adult and pediatric ICUs.[13-15] One factor that may affect CLABSI rates is the frequency with which needleless connectors (NC) on central lines are changed. A systematic review found that administration sets that do not contain lipids, blood, or blood products may be left in place up to 96 hours without increasing the incidence of infection.[16] This same review also found no evidence against changing administration sets that contain lipids every 24 hours. The Centers for

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Disease Control and Prevention (CDC) currently recommends that administration sets (tubing) used for blood or lipids be replaced within 24 hours of initiating the infusion.[17] This recommendation presumably reflects a potentially higher propensity for bloodstream infection to develop if the residue of blood or lipids, which might serve as growth media for microorganisms, remains present within the components of administration sets after infusion. The CDC recommendation for needleless components is that they be changed "at least as frequently as the administration set"; however, the recommendations also state that "there is no benefit to changing these more frequently than every 72 hours."[17] These 2 recommendations have the potential to cause confusion for providers because they are seemingly contradictory for situations in which the administration set is being changed every 24 hours. Changing the NC every 24 hours when using lipids or blood products could theoretically increase the risk of CLABSI by increasing unnecessary manipulation of the line. The impact of different NC change frequencies on CLABSI rates is poorly understood. Our objective was to assess the association between NC change frequency and CLABSI rates among hospitalized pediatric stem cell transplant (SCT) and oncology patients, a patient population with high device utilization and frequent need for blood product transfusions and parenteral nutrition (including fat emulsions). Prior research has demonstrated that receipt of these products is a risk factor for CLABSI among children in pediatric intensive care units[18,19] and hospitalized oncology patients[20]; therefore, a secondary objective was to evaluate whether the impact of NC change frequency on CLABSI rate is independent of receipt of blood products or lipids.

METHODS

We performed a quasiexperimental study at Boston Children's Hospital. Prior to August 2010, our institutional policy called for NC on central lines to be changed every 96 hours, regardless of infusate. After clarification of the intention of the CDC recommendation, from August 2010 to June 2011, we altered our policy and changed NC every 24 hours when blood or lipids were being infused. We noted an apparent increase in CLABSI rates on our SCT unit during this period. Therefore, in July 2011 we decided to return to our previous policy of every 96-hour NC changes regardless of infusate. No other changes in CLABSI prevention strategies occurred during these periods. For this study, we therefore evaluated 3 distinct time periods: November 2009 to July 2010 (period 1), August 2010 to June 2011 (period 2), and July 2011 to January 2012 (period 3). This structure allowed us to perform an interrupted time-series analysis with treatment removal ("treatment" being conversion to an NC change frequency of every 24 hours for blood or lipid use, and "treatment removal" being the reversion to the original policy of every 96 hours).

We also evaluated CLABSI rates on our oncology unit, a nonequivalent control group. Inclusion of a control group in interrupted time-series analyses strengthens the inference that any changes in the intervention group are related to the intervention of interest.[21] In our case, the oncology unit had the "treatment" but not the "treatment removal" because they continued to change NC every 24 hours for blood and lipids even after the SCT unit had reverted back to 96-hour NC changes. During the study period, the specific NC used for patients on both the SCT and oncology units was MaxPlus (CareFusion, San Diego, CA), a positive displacement NC. Hospital practice was for NC to be scrubbed for 15 seconds with 70% isopropyl alcohol prior to line entry on both units throughout the study period.

CLABSI rate was expressed as number of infections per 1,000 central venous line (CVL)-days. CLABSI were defined using standard National Healthcare Safety Network surveillance definitions[22] and were identified prospectively throughout the study period by infection preventionists working in conjunction with a unit-based nurse from the oncology program. Patient-days and central line-days (stratified as permanent or temporary lines) were also recorded. Unit-level hand hygiene compliance (defined as number of compliant hand hygiene events divided by number of opportunities observed) during the study period was measured using unannounced direct observation of practices by trained nurses. We also prospectively collected data for compliance with our central line access bundle (which included 2 components: hand hygiene and self-reported disinfection of the NC for at least 15 seconds with alcohol for all central line entries; both components were required for the measure to be scored as compliant). For this analysis, we retrospectively collected monthly unit-level data on other potential risk factors for CLABSI, including transfusion of red blood cells (RBC), platelets, or fresh frozen plasma or cryoprecipitate (each expressed as number of transfusions per month), use of parenteral lipids (expressed as number of "begin bag" events), use of liposomal amphotericin B (milligrams administered), SCT type (for SCT patients, classified as allogeneic or autologous), and underlying oncologic diagnosis (for oncology unit patients, classified as hematologic malignancy or solid tumor). Kruskal-Wallis tests were used to compare median monthly rates of the risk factors across the 3 time periods. We modeled mean monthly CLABSI rates in the 3 periods on the SCT and oncology units using autocorrelated segmented regression models, adjusting for the potential confounders outlined above. To ensure that any observed association between NC change frequency and CLABSI rate was not being driven by the use of blood products and lipids, we also performed a secondary analysis in which we included only CLABSI cases that had exposure to blood products or lipids prior to the CLABSI and normalized CLABSI rate to the monthly number of infusions of these products, as a better measure of opportunity for infection than CVL-days. Two-sided *P* values less than .05 indicated statistical significance. All analyses were performed using SAS version 9.3 (SAS Institute, Inc, Cary, NC). The Boston Children's Hospital Committee on Clinical Investigation approved the study protocol.

Table 1
Microbiology of CLABSI on pediatric stem cell transplant and oncology units

Organism	SCT unit, n (%)*	Oncology unit, n (%)*
Enterococci	4 (20)	12 (41)
Oral or enteric gram negative bacteria	5 (25)	8 (28)
Oral gram-positive cocci	4 (20)	1 (3)
Candida species	3 (15)	1 (3)
Staphylococcus aureus	2 (10)	2 (7)
Nonenteric gram-negative rods	1 (5)	1 (3)
Coagulase-negative staphylococci	1 (5)	1 (3)
Streptococcus pneumoniae	0	1 (3)
Gram-positive rods	0	2 (7)

SCT, stem cell transplant.
*Percentage is expressed out of total number of organisms recovered (n = 20 for SCT and n = 29 for oncology). Totals may not sum to 100% because of rounding.

RESULTS

During the entire study period, there were 20 CLABSI caused by 20 organisms on the SCT unit and 24 CLABSI caused by 29 organisms (3 blood cultures grew 2 organisms and 1 grew 3 organisms) on the oncology unit. The microbiology of these infections is outlined in Table 1. CLABSI rates are displayed in Figure 1. On the SCT unit, the mean CLABSI rate per 1,000 CVL-days increased significantly from period 1 to period 2 (0.41 [95% confidence

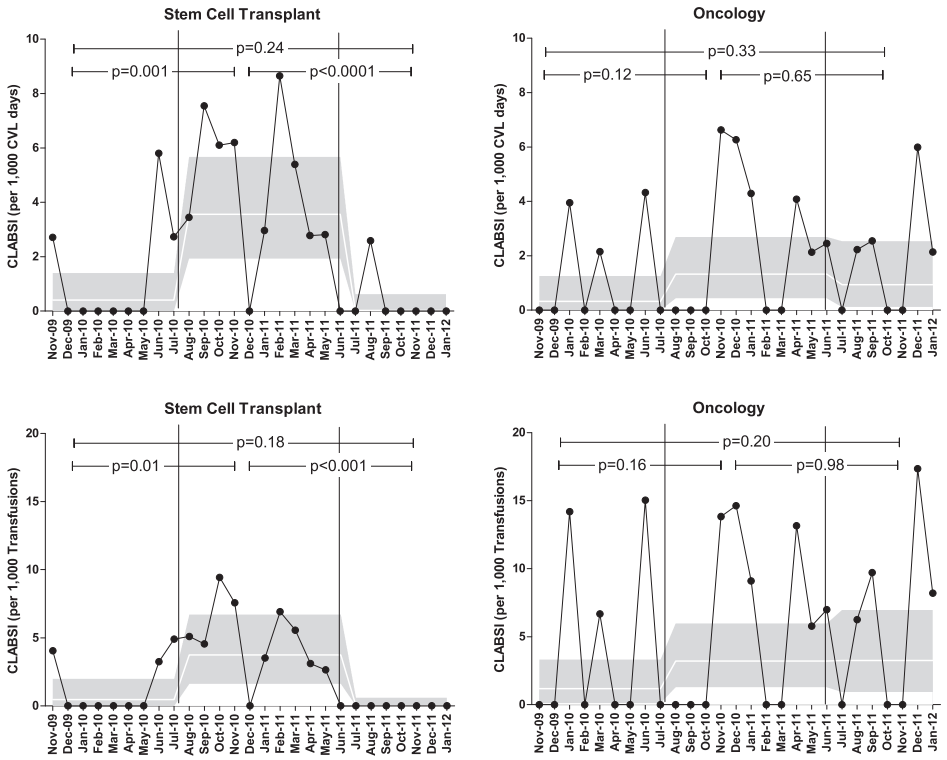

Fig 1. Central line-associated bloodstream infection rates. Vertical lines indicate divisions between study periods. Shading represents 95% confidence intervals for the mean.

interval (CI): 0.01-1.40] vs 3.56 [95% CI: 1.93-5.67], $P = .001$) and then decreased significantly in period 3 to 0.03 (95% CI: 0.001-0.63, $P < .0001$). The rates in periods 1 and 3 were not statistically different. In contrast, there was a nonsignificant trend toward a higher CLABSI rate on the oncology unit from periods 1 to 2 (0.33 [95% CI: 0.001-1.26] to 1.33 [95% CI: 0.44-2.69], $P = .12$), with no significant change in rate in period 3 (0.94 [95% CI: 0.12-2.54], $P = .65$ vs period 2).

Observed hand hygiene compliance on the SCT unit was high throughout the 3 study periods (period 1, 97.3% [181/186]; period 2, 95.9% [307/320]; period 3, 97.8% [176/180]). Reported compliance with the central line access bundle (hand hygiene and disinfection of the NC for at least 15 seconds with alcohol prior to line entry) was also high throughout the 3 study periods (period 1, 96.8% [452/467]; period 2, 99.8% [406/407]; period 3, 100% [242/242]). Unit-level patient characteristics and interventions by study period are displayed in Table 2. There were no statistically significant differences in any of these risk factors across study periods. In multivariable analyses, RBC transfusion and time period were independently associated with CLABSI rates. CLABSI rate on the SCT unit remained significantly higher in period 2 compared with both period 1 ($P = .01$) and period 3 ($P = .003$) after adjusting for RBC usage.

In our secondary analysis of CLABSI rates per 1,000 transfusions (of RBC, platelets, plasma/cryoprecipitate, and lipids), 3 cases were excluded because of a lack of exposure to blood and lipids prior to the CLABSI. Among the remainder, the mean CLABSI rate per 1,000 transfusions on the SCT unit was 0.46 (95% CI: 0-1.99) in period 1, which increased significantly to 3.73 (95% CI: 1.63-6.71, $P = .01$) in period 2 and then decreased to 0.004 (95% CI: 0.001-0.61, $P < .001$) in period 3. On the oncology unit, the rates per 1,000 transfusions were 1.19 (95% CI: 0.13-3.32), 3.21 (95% CI: 1.29-5.98), and 3.25 (95% CI: 0.93-6.97) in periods 1, 2, and 3 respectively, with none of the changes reaching statistical significance.

DISCUSSION

In this quasiexperimental study, we found that changing NC every 24 hours when blood products or lipids are infused was associated with significantly higher CLABSI rates in hospitalized pediatric SCT patients. Although central line insertion practices are an important part of CLABSI prevention, evidence suggests that daily line maintenance care contributes more strongly to CLABSI risk among hospitalized children.[15] Current central line maintenance bundles typically contain several components, including scrubbing the NC with a disinfectant prior to line entry, regular dressing changes, and daily discussions about whether the line can be removed. There are many other potential adjunctive line maintenance practices that could influence the risk of CLABSI, such as antimicrobial locks, antiseptic-impregnated sponges or dressings, and chlorhexidine bathing, but these strategies are associated with additional cost.[23] Survey data suggest variable uptake of these adjunctive practices in pediatric hospitals, likely reflecting the lack of high-quality evidence in children to support each individual measure.[24]

NC change frequency is another factor that may impact CLABSI risk but has been poorly studied. Whereas changing these devices more frequently might reduce the burden of contamination that could lead to bloodstream infection (particularly if the NC is not disinfected adequately),[25] it is also possible that more frequent manipulation of the line for NC changes could increase the risk of infection. In one observational study of increased CLABSI rates in a pediatric ICU, exposure to a new NC that was changed every 6 days was associated with a higher CLABSI rate, which decreased to baseline when the device was replaced every 24 hours.[26] However, in that study the ICU had also changed from an NC with a rubber endpiece that was left uncovered to a different NC covered by an endcap, making it difficult to know the relative contribution of the change frequency to the infection rate.

Table 2
Monthly unit-level patient characteristics and interventions by period

	Unit	Period 1 (NC change every 96 hours)	Period 2 (NC change every 24 hours with blood/lipids)	Period 3 (NC change every 96 hours)	*P* value
Number of months		9	11	7	
Allogeneic stem cell transplant (% of patient-days/month)	SCT	78 (71, 93)	83 (46, 95)	79 (72, 96)	.85
Hematologic malignancy diagnosis (% of patient-days/month)	Oncology	63 (56, 67)	70 (53, 73)	64 (54, 75)	.36
CVL-days (per month)	SCT	364 (286, 383)	328 (265, 371)	354 (294, 399)	.51
	Oncology	467 (431, 507)	464 (407, 490)	450 (361, 506)	.16
Red blood cell transfusions (number/month)	SCT	36 (24, 45)	38 (29, 60)	25 (20, 42)	.07
	Oncology	63 (53, 69)	65 (49, 98)	52 (35, 69)	.07
Platelet transfusions (number/month)	SCT	77 (58, 107)	92 (62, 178)	72 (21, 123)	.16
	Oncology	54 (28, 73)	63 (36, 97)	47 (27, 66)	.16
Plasma or cryoprecipitate transfusions (number/month)	SCT	1 (0, 8)	3 (0, 11)	1 (0, 37)	.64
	Oncology	3 (0, 13)	6 (0, 33)	2 (1, 13)	.61
Lipids (bags started/month)	SCT	153 (108, 211)	124 (58, 254)	158 (74, 268)	.51
	Oncology	19 (11, 67)	19 (12, 41)	31 (0, 70)	.47
Begin bag events (/month)*	SCT	257 (196, 333)	264 (190, 434)	305 (119, 392)	.95
	Oncology	136 (101, 193)	145 (119, 220)	123 (89, 173)	.63
Liposomal amphotericin (milligrams administered/100 CVL-days/month)	SCT	1,666 (971, 3,943)	1,827 (718, 4,913)	1,262 (49, 3,849)	.26
	Oncology	677 (310, 1,214)	703 (0, 1,706)	515 (43, 1,136)	.85

CVL, central venous line; *NC*, needleless connector, *SCT*, stem cell transplant.
NOTE. Values are expressed median (minimum, maximum) of the monthly values within the time period.
*Begin bag events represents the total number of transfusions of red blood cells, platelets, plasma/cryoprecipitate, and lipids.

The 2011 CDC guideline for the prevention of catheter-related infections recommends that needleless components be changed at least as frequently as administration sets but not more frequently than every 72 hours.[17] If hospitals are replacing the tubing used to administer blood products or fat emulsions every 24 hours, as is also recommended in the guideline, then it may be unclear whether the NC should be changed every 24 hours to match the tubing change or whether to wait at least 72 hours before changing the NC. Our data suggest that, at least for pediatric SCT patients, changing more frequently when blood and lipids are used is associated with higher infection rates. It is possible that NC change frequencies may impart different risks in different patient populations, as suggested by our data from the oncology unit, where no difference was seen in CLABSI rates when the NC were changed more often. Additional studies in specific high-risk groups are needed to further assess this possibility. Whether different NC types (eg, neutral displacement devices) might alter the association between NC change frequency and CLABSI rates is also unknown.

To our knowledge, this study is the first to use a quasiexperimental design to evaluate the impact of NC change frequency on CLABSI rates. A strength of this study is the use of an interrupted time-series analysis with a control group, a design that provides more confidence that the effect on CLABSI rates was related to the intervention of interest. The fact that the CLABSI rate increased after the intervention and then decreased when it was removed (in the absence of other changes) is suggestive that the association is real. We also adjusted for other risk factors that are known to be associated with CLABSI, allowing us to demonstrate that the contribution of NC change frequency to CLABSI rates is independent of several known confounders. It is possible that other unmeasured confounders of this association (eg, number of line entries) were not included in the analyses; however, we have no reason to believe such confounders would have differed during the 3 time periods of this study, and there were no other institutional changes in CLABSI prevention strategies at our hospital across the time periods. Our data on compliance with disinfection of the NC for line entries is limited by being self-reported by nurses rather than directly observed, but we have no reason to believe that reporting would have differed across study periods. Our secondary analysis provides further confidence that the observed association between NC change frequency and CLABSI rate was not driven by use of blood products and lipids because the association persisted when we excluded CLABSI cases with no blood or lipid exposure and normalized the CLABSI rate to the number of blood product and lipid infusions. Given that each study period comprised a different set of calendar months, it is possible that maturation effects of some clinical providers could have differentially impacted care practices across periods. Because these data are from hospitalized pediatric SCT and oncology patients, the findings may not be generalizable to other patient populations, and further studies should be performed to evaluate this question in different contexts. Until additional research is available, we believe that national recommendations regarding NC change frequency should be revisited and clarified. Pediatric SCT units that have been unable to reduce CLABSI rates using standard infection prevention strategies should consider a trial of changing NC less frequently than every 24 hours when blood products or lipids are being infused.

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