The risk of central line-associated bloodstream infections with different types of central vascular catheters in a multidisciplinary neonatal and pediatric intensive care unit

MAJA PAVCNIK-ARNOL (✉)
Department of Paediatric Surgery
and Intensive Care
University Medical Centre Ljubljana
Bohoriceva 20, 1525 Ljubljana, Slovenia
Phone: +386-1-522-48-29
Fax: +386-1-522-11-09
E-mail: maja.pavcnik@kclj.si

MAJA PAVCNIK-ARNOL

ABSTRACT

Objective. Central line-associated bloodstream infections (CLABSIs) are a significant cause of morbidity in critically ill neonates and children. The objective of this study was to compare CLABSI rate associated with different types of central vascular catheters (CVCs) in a multidisciplinary neonatal and pediatric intensive care unit (ICU).

Methods. A prospective cohort study was conducted in a multidisciplinary neonatal and pediatric ICU. All patients, admitted between January 1st 2011 and February 29th 2012, requiring a CVC were included and monitored for CLABSI (defined by CDC/NHSN criteria). CLABSI rates were calculated for each type of CVC as CLABSI episodes/1000 catheter-days. CLABSI rates were compared between patients with single and multiple CVCs.

Results. Of the 557 patients admitted, 362 (65%) required insertion of a CVC (4259 patient-days, 3225 catheter-days, CVC utilization ratio 0.76). There were 14 episodes of CLABSI. CLABSI rate was lowest for umbilical catheters (0/1000 catheter-days), followed by short-term noncuffed and nontunneled CVCs (3.1/1000 catheter-days) and peripherally inserted CVCs (8.8/1000 catheter-days). Higher rates were observed with long-term cuffed and tunneled CVCs (15.9/1000 catheter days) and noncuffed, nontunneled CVCs for temporary renal replacement therapy (RRT) (20.0/1000 catheter days). CLABSI rate expressed per 1000 catheter-days was 3.0 and 19.7 for patients with single or multiple CVCs at the same time, respectively.

Conclusion. The use of noncuffed, nontunneled CVCs for temporary RRT and the presence of multiple CVCs at the same time are associated with a significant increase in the rate and risk of developing CLABSI in a multidisciplinary neonatal and pediatric ICU population.

Key words: central line-associated bloodstream infections, nosocomial infections, central vascular catheter, bloodstream infections, pediatric intensive care unit, neonate, child

Introduction

During the last few decades, the development of new techniques to provide central vascular access has been a revolutionary step in the care of critically ill neonates and children. Unfortunately, the use of central vascular catheters (CVCs) is associated with the risk of central line-associated bloodstream infections (CLABSIs), caused by micro-organisms that colonize the implanted device or contaminate the fluid pathway. (1) CLABSIs are the single most important cause of health care-associated infections in neonatal (NICU) and pediatric intensive care units (PICU) (2-7) and are associated with increased morbidity, hospital lenght of stay, and health care costs. (8)

Several factors have been reported in critically ill neonates and children as being associated with an increased CLABSI rate, including the presence of multiple CVCs, (4) the total duration of CVC use, (4,6) administration of parenteral nutrition, packed red blood cell transfusions, (5,6) and the use of

extracorporeal membrane oxygenation (ECMO). (4) Patient-related factors have also been reported to increase the risk for CLABSI, including age (neonates), birthweight, gastrointestinal diagnoses, oncologic diagnoses, and cardiac surgery. (2,6,7,9)

The various types of CVCs are associated with different risks of CLABSI in adults. (10) Although it is generally acknowledged that the same principle applies for pediatric population, the magnitude of variability in CLABSI rate with different types of CVCs in critically ill neonates and children is largely unknown. Recently, a study of CLABSI rates in all children under care in a children's hospital (intensive care, general wards, out-patient setting) identified the highest risk of CLABSI in neonates with peripherally inserted central venous catheters (PICCs) and the lowest risk in children with totally implanted CVCs (Porth-a-cath). (11) However, most of these patients were not critically ill. Patients being cared for in a multidisciplinary neonatal and pediatric ICU probably have a different CLABSI risk profile. Few data exist regarding CLABSI rates with different types of CVCs in multidisciplinary PICUs. (4)

The goal of this study was therefore to prospectively assess the current burden of CLABSI in our multidisciplinary neonatal and pediatric ICU and to identify the CLABSI rate associated with different types of CVCs.

Materials and methods

This was a prospective study in a level III multidisciplinary 14-bed neonatal and pediatric PICU of Department of Paediatric Surgery and Intensive care at University Medical Center Ljubljana, Slovenia. It is a combined medical and surgical PICU that provides critical care for children from newborn through 18 years old. The study was approved by the National Medical Ethics Committee.

Participants for this study were all patients admitted to the PICU between January 1st 2011 and February 29th 2012 who required a CVC. Patients were monitored for the development of CLABSI from the day of PICU admission until 48 hours after PICU discharge. Denominator data consisting of patient-days and central vascular catheter-days (catheter days) were collected daily, at the same time each day, using standardized Center for Disease Control/National Healthcare Safety Network (CDC/NHSN) methods and definitions. (9) Data were separately collected and analyzed for the following CVC subgroups: 1. short-term noncuffed and nontunneled CVCs; 2. umbilical catheters (arterial and venous); 3. long-term cuffed, tunneled CVCs; 4. noncuffed, nontunneled CVCs for temporary renal replacement therapy (RRT) (RRT CVCs); and 5. peripherally inserted central venous catheters (PICCs). A subgroup of short-term noncuffed and nontunneled CVCs was used as a reference group for comparison of CLABSI risk between different types of CVCs. Patients with ≥ 2 CVCs in place at the same time were defined as having multiple CVCs.

CLABSI was defined according to CDC/NHSN surveillance definitions as laboratory-confirmed bloodstream infection that is not secondary to an infection meeting CDC/NHSN criteria at another body site and a CVC was in place at the time of, or within 48 hours before, onset of the event (for additional information about these criteria refer to Horan et al. (12) According to the changed CDC CLABSI definition (beginning in January 2008) 1 positive blood culture yielding a normal skin contaminant (eg, coagulase-negative staphylococci) did not fulfill the case definition and two or more positive blood cultures drawn on separate occasions were required. (12)

Data-analysis. Descriptive analyses were performed to characterize the patient population, reporting mean/median values with ranges and percentages. The CLABSI rate per 1000 catheter-days was calculated separately for different types of CVCs by dividing the number of CLABSI by the number of catheter-days and multiplying the result by 1000. Chi-square test for equal proportions was used for bivariate comparisons of the risk and crude rates of CLABSI associated with the different types and numbers of CVCs. A p value of < 0.05 was considered statistically significant. SPSS for Windows (Version 16.0; SPSS, Chicago, IL, USA) was used in the statistical analysis.

Results

A total of 557 admissions to the PICU were identified during the 14-month study period from January 1st 2011 to February 29th 2012, of whom 258 were medical and 299 were surgical. A total of 362 admissions (65 %) involved the use of 1 or more CVCs. The mean age of the population was 2.7 years (range few hours – 18 years). A total of 457 (82 %) admissions required mechanical ventilation and 161 (29 %) required vasopressor/inotropic support. During the study period 26 (4.7 %) patients died, of whom 11 were medical and 15 surgical patients.

We identified a total of 4259 patient-days, 3225 catheter-days (CVC utilization ratio 0.76) and 14 episodes of CLABSI with an overall CLABSI rate of 4.3/1000 catheter-days in our PICU. The use and duration of use for different types of CVCs is shown in table 1. The crude risk for development of CLABSI, risk ratio for CLABSI and CLABSI rate per 1000 catheter-days by different types of CVCs are shown in table 2. We did not detect any episode of CLABSI associated with use of umbilical catheters. We used short-term noncuffed and nontunneled CVCs as a reference group for bivariate associations between the use of different types of CVCs and the risk of CLABSI. Patients that required RRT CVCs had 12.9-fold increased risk for developing CLABSI compared with the reference group of patients (p<0.001, Pearson's chi-square test). Patients with long-term cuffed, tunneled CVCs and PICCs had 1.8- and 1.9-fold increased risk, respectively, for developing CLABSI as compared with the reference group of patients, but this increased risk was not statistically significant.

We identified a total of 27 patients and 254 catheter-days with multiple (≥ 2) CVCs in place at one time. Five of 14

Table 1. The use of different types of central vascular catheters (CVCs).

Type of central vascular catheter	Number of patients	Catheter days	Duration of catheter use in days, median (range)
Short-term noncuffed and nontunneled CVCs	217	2248	5 (1-45)
Umbilical vascular catheters	75	524	4 (1-11)
Long-term cuffed and tunneled CVCs	46	189	12 (1-120)
Noncuffed, nontunneled CVCs for temporary renal replacement therapy	8	150	8 (1-32)
Peripherally inserted CVC	16	114	4 (1-55)

Table 2. Crude risk for development of central line-associated bloodstream infection (CLABSI), risk ratio (RR) and CLABSI rate per 1000 catheter-days by different types of central vascular catheters (CVCs).

Type of central intravascular catheter	Number of CLABSI	Crude CLABSI risk (%)	RR (95% CI)	CLABSI rate per 1000 catheter days*
Short-term noncuffed and nontunneled CVCs	7	7/217 (3.2)	reference group	3.1
Umbilical vascular catheters	0	0	NA	0.0
Long-term cuffed and tunneled CVCs	3	3/46 (6.5)	1.8 (0.7-4.8)	15.9
Noncuffed, nontunneled CVCs for temporary renal replacement therapy	3	3/8 (37.5)	12.9 (3.6-46.1)[†]	20.0
Peripherally inserted CVC	1	1/16 (6.3)	1.9 (0.6-6.6)	8.8

CI, confidence interval; NA, non-applicable; RR, risk ratio.

*Number of CLABSI/Number of catheter-days x 1000

[†]p < 0.05 compared to short-term noncuffed and nontunneled central venous catheters

children (35 %) with CLABSI had multiple CVCs in place at the time of CLABSI. The use of multiple CVCs at the same time was associated with a crude risk for CLABSI of 18.5% and with a 5.7-fold increase in the risk of developing CLABSI compared with the reference group of patients with only one CVC in place at one time (95% confidence interval (CI): 1.5-24.0). This increased risk was statistically significant (p<0.001, Pearson's chi-square test). CLABSI rate expressed per 1000 catheter-days was 19.7 and 3.0 in association with the use of multiple CVCs or single CVC at the same time, respectively.

Discussion

In this study, CLABSI rate of 4.3 per 1000 catheter-days was established in our multidisciplinary neonatal and pediatric ICU. This overall CLABSI rate compares favourably with some studies in PICUs that reported rates up to 20.6 per 1000 catheter-days, (13-15) but is high-

er than the pooled mean rate of 3.0 per 1000 catheter-days for medical/surgical PICUs reporting to the CDC/NHSN system. (9) The higher CLABSI rate in our study could be attributable to the large proportion of neonates, including extremely premature neonates, in our PICU that are known to be at highest risk for CLABSI. (9) Furthermore, a high percentage of our patients are neonates and children undergoing complex cardiac surgery that are also known to have higher CLABSI rates, partly because of extensive use of invasive devices. (9,16) Accordingly, in a multicenter study that included multidisciplinary as well as dedicated cardiac PICUs, CLABSI rate was the same as in our study. (17)

Short-term noncuffed and nontunneled CVCs are the most prevalent type of CVC used in our unit (70% of catheter-days) and therefore accounted for the majority of CLABSIs (50%) in our study. However, when CLABSI rate

was expressed per 1000 catheter-days, short-term noncuffed and nontunneled CVCs had a CLABSI rate of 3.1, which was lower than the rate for long-term cuffed, tunneled CVCs, RRT CVCs and PICCs, but considerably higher than the CLABSI rate for umbilical catheters. We observed the highest CLABSI rate of 20.0 per 1000-catheter days in RRT CVCs. Patients that required RRT CVC had a 12.9-fold increased risk for developing CLABSI compared to patients with short-term noncuffed and nontunneled CVCs. Our results are consistent with the study by Odetola et al. that also observed an increased risk of developing CLABSI in PICU patients requiring RRT CVC. (4) The observed increase in CLABSI risk in neonates and children requiring RRT has a number of intuitive pathophysiologic explanations. First, these patients are exposed to immunosuppressive effects of extracorporeal circulation. The initial response is mainly proinflammatory, followed by an anti-

nflammatory response. (18) If the anti-nflammatory response is pronounced or prolonged, the host becomes immunosuppressed, susceptible to secondary infections (19) and less tolerant of microcontamination that an immune competent host could effectively mitigate. (7) Second, increased susceptibility for CLABSI is exacerbated by the need to routinely access RRT CVCs for blood-sampling and treatment in these patients. (20) A greater number of CVC interruptions are known to predispose PICU patients to CLABSI. (21) Thirdly, neonates and children with RRT CVCs often have multiple other CVCs. The increased risk of CLABSI in this population warrants further study to better understand the nature of this risk and to develop specific prevention interventions. In adults with acute renal failure, noncuffed, nontunneled hemodialysis CVCs are associated with a substantially higher risk of CLABSI compared to cuffed and tunneled hemodialysis CVCs, (10,22) so one intervention to reduce CLABSI rate in this high risk PICU population could be the use of short-term cuffed and tunneled RRT CVCs for temporary RRT.

In our study, long-term cuffed, tunneled CVCs were the subgroup of CVCs with the second highest CLABSI rate per 1000 catheter-days (15.9) and were associated with a 1.8-fold increased risk of developing CLABSI as compared with the short-term noncuffed and nontunneled CVCs. Similar to the study by Odetola et al., this increase did not reach statistical significance. (4) The high CLABSI rate in long-term cuffed, tunneled CVCs was unexpected as these CVCs are generaly associated with a low prevalence of CLABSI, a characteristic thought to be related to the use of a subcutaneous tunnel and cuff before entering the vein. (23) However, all patients with long-term cuffed, tunneled CVCs complicated by CLABSI in our study were high risk premature infants with surgical intestinal diseases and long-term need for total parenteral nutrition. Surgical neonates with long-term tunneled CVCs were previously reported to have high CLABSI rates of

24% (compared to 6.5% in our study). (24) Several other explanations exist for the high CLABSI rate in our population with long-term cuffed, tunneled CVCs. First, total parenteral nutrition, prematurity and low birth-weight are recognized risk factors for CLABSI. (25,26) Second, patients with gastrointestinal diseases have an increased risk for CLABSI. (7,27) Furthermore, bacterial translocation across the intestinal mucosa is also more frequent in patients with gastrointestinal diseases and may be attributed by default to a CVC when using the current CDC/NHSN surveillance definition for CLABSI. (7) For long-term central venous access, cuffed and tunneled CVCs are associated with a higher risk for CLABSI than totally implanted devices (Porth-a-cath). (10,11,28). However, if the patient needs continuous access for many days or intermittent access day after day, a cuffed and tunneled CVC is preferable to a totally implanted device. (10) According to this, switching to Porth-a-cath CVCs would not be appropriate for long-term central venous access in our population of neonates with complex surgical intestinal diseases that currently receive long-term cuffed, tunneled CVCs.

In our study PICCs, with a CLABSI rate of 8.8 per 1000 catheter-days, posed a 1.9-fold increased risk for CLABSI compared to short-term noncuffed and nontunneled CVCs. As PICCs are used exclusively in neonates in our unit, we looked at other studies of PICCs in critically ill neonates. The incidence of CLABSI in neonates with PICC lines ranges from 0 to 18.2 episodes per 1000 catheter-days, with the higher rates occuring in neonates weighing less than 1500 g. (29-32) Njere et al. recently reported PICC CLABSI rate of 18.2 per 1000 catheter-days in medical neonates and 15.8 per 1000-days in surgical neonates in NICU. (29) Comparing these results with data in children outside ICU (PICC CLABSI rate of 2.58 per 1000 catheter-days), (33) emphasizes the fact that neonates and children in ICU have a different risk profile for CLABSI compared to neonates and children on general wards. There-

fore, comparing studies of CLABSI from different settings is challenging and should be adjusted for different hospital locations, types of illness and degrees of illness severity.

No CLABSI episode associated with the use of umbilical catheters was detected during the study period. Our results are better than the reported pooled mean umbilical catheter-associated CLABSI rate of 0.9-3.9 per 1000 catheter-days for level III NICUs in the USA. (9) Other than the type of catheter, a very important extrinsic risk factor for CLABSI is duration of catheterization. (32,33) The median duration of umbilical catheter use in our study was 4 days (range 1-11 days), which was less than for other types of CVCs and could be a very important factor in zero CLABSI rate. This is further emphasized by a recent randomized trial that evaluated whether long-term umbilical venous catheterization (up to 28 days) would result in the same or fewer CLABSIs when compared with neonates who were randomized to short-term umbilical venous catheterization for 7-10 days followed by PICCs. CLABSI rate was higher (20%) among long-term catheterized neonates when compared with short-term catheterized neonates (13%). (34) It is therefore very important to continually reassess the need for all types of CVCs and promptly remove unnecessary CVCs, particularly during the second week of catheterization and thereafter. (7)

Our data confirm previous findings (3,6) that the presence of multiple CVCs at the same time is associated with an increased risk for CLABSI. In our study, the presence of multiple CVCs was associated with a 5.7-fold increased risk for CLABSI compared with the presence of a single CVC. CLABSI occurred in 2.7% of children with a single and 18.5 % of children with multiple CVCs. CLABSI rate expressed per 1000 catheter-days was 3.0 and 19.7 in association with the use of a single CVC or multiple CVCs at the same time, respectively.

Several limitations should be considered when interpreting our findings. First, this is a small cohort, single-institution

study and our findings may not be generalizable to other settings. Secondly, we were underpowered to perform multivariate logistic regression analysis. Further, the data analyzed in this study did not contain detailed information on some patient care practices (eg, severity of illness score, total parenteral nutrition, lipid solutions, blood products); consequently, we were unable to assess the effect of these factors on the risk of CLABSI with different types of CVCs. Finally, confounding effect could also be caused by the current CDC/NHSN definition. (12) This definition has limitations in both specificity (eg, inclusive of gut translocation) and exposure adjustment (eg, a central catheter-day may be exposure to more than 1 central catheter) and is limited in attribution to a specific CVC type when there are multiple CVCs (especially for patients that almost always have coexisting CVCs, such as with ECMO and RRT). (7,35) The problem of an inadequate definition of CLABSI was recently addressed by several authors. (7,35,36)

Despite these limitations, our study provides useful data that define the risk of CLABSI with the various types of CVCs in use in a multidisciplinary neonatal and pediatric ICU, at the present time. Our data suggest that all types of CVCs pose significant but widely differing risk of CLABSI and that all CLABSI studies should include types of CVCs utilized. We have identified that the use of RRT CVCs and multiple CVCs at the same time are associated with the highest risk for CLABSI in a multidisciplinary neonatal and pediatric ICU. Larger future studies will need to validate these predictors for CLABSI, controlling also for severity of illness and to determine how prevention strategies can target this high risk group of patients. One such intervention could be the use of a cuffed tunneled RRT CVC instead of noncuffed, nontunneled RRT CVC in critically ill neonates and children with acute renal failure. Although our center-specific CLABSI rates in general compared well to publish data, measures to further decrease the observed CLABSI rates should be achieved with strict adherence to CVC insertion and maintenance bundles. (37) Hopefully, these efforts will improve the safety and quality of care for critically ill neonates and children in our and other PICUs.

REFERENCES

1. Safdar N, Maki DG. The pathogenesis of catheter-related bloodstream infection with noncuffed short-term central venous catheters. Intensive Care Med 2004;30:62-7.

2. Aly H, Herson V, Duncan A, Herr J, Bender J, Patel K, et al. Is bloodstream infection preventable among premature infants? A tale of two cities. Pediatrics 2005;115:1513-8.

3. Yogaraj JS, Elward AM, Fraser VJ. Rate, risk factors, and outcomes of nosocomial primary bloodstream infection in pediatric intensive care unit patients. Pediatrics 2002;110:481-5.

4. Odetola FO, Moler FW, Dechert RE, van der Elzen K, Chenoweth C. Nosocomial catheter-related bloodstream infections in a pediatric intensive care unit: Risk and rates associated with various intravascular technologies. Pediatr Crit Care Med 2003;4:432-6.

5. Elward AM, Fraser VJ. Risk factors for nosocomial primary bloodstream infection in pediatric intensive care unit patients: a 2-year prospective cohort study. Infect Control Hosp Epidemiol 2006;27:553-60.

6. Costello JM, Graham DA, Morrow DF, Potter-Bynoe G, Sandora TJ, Laussen PC. Risk factors for central line-associated bloodstream infection in a pediatric cardiac intensive care unit. Pediatr Crit Care Med 2009;10:453-9.

7. Niedner MF, Huskins WC, Colantuoni E, Muschelli J, Harris II JM, Rice TB, et al. Epidemiology of central line-associated bloodstream infections in the pediatric intensive care unit. Infect Control Hosp Epidemiol 2011;32(12):1200-8.

8. Nowak JE, Brilli RJ, Lake MR, Sparling KW, Butcher J, Schulte M, Wheeler DS. Reducing catheter-associated bloodstream infections in the pediatric intensive care unit: Business case for quality improvement. Pediatr Crit Care Med 2010;11:579-87.

9. Edwards JR, Peterson KD, Mu Y, Banerjee S, Allen-Bridson K, Morrell G, et al. National Healthcare Safety Network (NHSN) report: Data summary for 2006 through 2008, issued December 2009. Am J Infect Control 2009;37:783-805.

10. Maki DG, Kluger DM, Crnich CJ. The risk of bloodstream infection in adults with different intravascular devices: a systematic review of 200 published prospective studies. Mayo Clin Proc 2006;81:1159-71.

11. Wagner M, Bonhoeffer J, Erb TO, Glanzmann R, Hacker FM, Paulussen M, et al. Prospective study on central venous line associated bloodstream infections. Arch Dis Child 2011;96:827-31.

12. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. Am J Infect Control 2008;36:309-32.

13. Almuneef MA, Memish ZA, Balkhy HH, Hijazi O, Cunningham G, Francis C. Rate, risk factors and outcomes of catheter-related bloodstream infection in a paediatric intensive care unit in Saudi Arabia. J Hosp Infect 2006;62:207-13.

14. Becerra MR, Tantalean JA, Suarez VJ, Alvarado MC, Candela JL, Urcia FC. Epidemiologic surveillance of nosocomial infections in a pediatric intensive care unit of a developing country. BMC Pediatrics 2010;10:66.

15. Rey C, Alvarez, De-La-Rua V, Concha A, Medina A, Diaz JJ, et al. Intervention to reduce catheter-related bloodstream infections in a pediatric intensive care unit. Intensive Care Med 2011;37:678-85.

16. Costello JM, Forbes Morrow D, Graham DA, Potter-Bynoe G, Sandora TJ, Laussen PC. Systematic intervention to reduce central line-associated bloodstream infection rates in a pediatric cardiac intensive care unit. Pediatrics 2008;121:915-23.

17. Jeffries HE, Mason W, Brewer M, Oakes KL, Munoz EI, Gornick W, et al. Prevention of central venous catheter-associated bloodstream infections in pediatric intensive care units: a performance improvement collaborative. Infect Control Hosp Epidemiol 2009;30:645-51.

18. Bhatia M, He M, Zhang H, Moochhala S. Sepsis as a model of SIRS. Front Biosci 2009;14:4703-11.

19. Ward NS, Casserly B, Ayala A. The compensatory anti-inflammatory response syndrome (CARS) in critically ill patients. Clin Chest Med 2008;29:617-25.

20. Klevens RM, Edwards JR, Andrus ML, Peterson KD, Dudeck MA, Horan TC, et al. Dialysis surveillance report: National Healthcare Safety Network (NHSN)-Data Summary for 2006. Seminars in Dialysis 2008;21:24-8.

21. Hatler C, Buckwald L, Salas-Allison Z, Murphy-Taylor C. Evaluating central venous catheter care in a pediatric intensive care unit. Am J Crit Care 2009;18:514-21.

22. National Kidney Foundation. III. NKF-K/DOQI Clinical Practice Guidelines for Vascular Access:update 2000. Am J Kidney Dis 2001;37:S137-81.

23. Shapiro ED, Wald ER, Nelson KA. Broviac catheter-related bacteremia in oncology patients. Am J Dis Child 1982;136:679-81.

24. Klein MD, Rood K, Graham P. Central venous catheter sepsis in surgical newborns. Pediatr Surg Int 2003;19:529-32.

25. Hentschel J, Brungger B, Studi K. Catheter duration and risk of CLA-BSI in neonates with PICCs. Pediatrics 2010;125:648-53.

26. Hoang V, Sills J, Chandler M, Busalani E, Clifton-Koeppel R, Modanlou HD. Percutaneously inserted central catheter for total parenteral nutrition in neonates: complications rates related to upper versus lower extremity insertion. Pediatrics 2008;121:e1152-9.

27. Wylie MC, Graham DA, Potter-Bynoe G. Risk factors for central line-associated bloodstream infection in pediatric intensive care units. Infect Control Hosp Epidemiol 2010;31:1049-56.

28. Alexander N. Question 3. Do Portacaths or Hickman lines have a higher risk of catheter-related bloodstream infections in children with leukemia? Arch Dis Child 2010;95:239-41.

29. Njere I, Islam S, Parish D, Kuna J, Keshtgar AS. Outcome of peripherally inserted central venous catheters in surgical and medical neonates. J Pediatr Surg 2011;46:946-50.

30. Chien L, Macnab Y, Aziz K. The Canadian Neonatal Network. Variations in central venous catheter-related infection risks among Canadian neonatal intensive care units. Pediatr Infect Dis J 2002;21:505-11.

31. Golombek SG, Rohan AJ, Parvez B. Proactive management of percutaneously inserted central catheters results in decreased incidence of infection in the ELBW population. J Perinatol 2002;22:209-13.

32. Sengupta A, Lehmann C, Diener-West M, Perl TM, Milstone AM. Catheter duration and risk of CLA-BSI in neonates with PICCs. Pediatrics 2010;125:648-53.

33. Advani S, Reich NG, Sengupta A, Gosey L, Milstone AM. Central line-associated bloodstream infection in hospitalized children with peripherally inserted central venous catheters: extending risk analyses outside the intensive care unit. Clin Infect Dis 2011;52:1108-15.

34. Butler-O'Hara M, Buzzard CJ, Reubens L, McDermott MP, DiGrazio W, D'Angio CT. A randomized trial comparing long-term and short-term use of umbilical venous catheters in premature infants with birth weights of less than 1251 grams. Pediatrics 2006;118:e25-35.

35. Sexton DJ, Chen LF, Anderson DJ. Current definitions of central line-associated bloodstream infection: is the emperor wearing clothes) Infect Control Hosp Epidemiol 2010;31:1286-9.

36. Miller MR, Griswold M, Harris II JM, Yenokyan G, Huskins C, Moss M, et al. Decreasing PICU catheter-associated bloodstream infections: NACHRI's quality transformation efforts. Pediatrics 2010;125:206-13.

37. O'Grady N, Alexander M, Burns LA, Dllinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections. Clin Infec Dis 2011;52:e162-93.