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Research Report

CATHETER DURATION AND THE RISK OF SEPSIS IN PREMATURE BABIES WITH UMBILICAL VEIN CATHETERS

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ABSTRACT

Umbilical catheters are frequently required in the management of severely ill premature babies. The risk of complications may increase with duration of UVC use. ***Objective:*** *To determine whether the risk of central line-associated bloodstream infections (CLA-BSIs) and sepsis remained constant over the duration of umbilical vein catheters (UVCs) in high-risk premature neonates.* ***Methods:*** *retrospective analysis. The data were collected from the medical record of high risk premature neonates who had a UVC placed in neonatal care unit of Husada Utama Hospital between April 1st 2008 to April 30th 2011 with purposive sampling. Catheter duration was observed before and after 14 days on placement. Blood and UVC culture was performed to establish the risk of CLA-BSIs and sepsis. Chi-square and logistic regression analysis were performed in the laboratorium data.* ***Result:*** *A total 44 high risk premature babies with UVCs were enrolled (sepsis group: n = 23 and non sepsis group: n = 21). Baseline demographics were similar between the groups. 15 babies in sepsis group have UVCs duration > 14 days, and 8 babies have UVCs < 14 days (p = 0.533). Days of UVC < 14 days show UVCs culture performance in 11 babies with positive evidence, blood culture performance shows negative in 21 babies (p = 0.516). Days of UVC >14 days show blood culture performance in 11 babies with positive evidence, UVCs culture performance is negative in 18 babies (p = 0.456). Burkholderia cepacia and Klebsiella pneumonia mostly appeared in blood culture performance. 25% of UVC culture performance shows Pseudomonas aeroginosa.* ***Conclusions:*** *The catheter duration have no significant difference in risk of sepsis in premature babies with Umbilical Vein Catheters.*

Key words: *Premature babies - Sepsis – days of UVC – CLA-BSIs*

INTRODUCTION

Umbilical catheters are frequently required in the management of severely ill neonates.[1.2] Umbilical-vein catheters (UVCs) can be used for intravenous administration of parenteral nutrition, hypertonic solutions, blood products, and medication. Umbilical-artery catheters (UACs) can be used for blood sampling and continuous monitoring of blood pressure. However, the advantages of umbilical catheters must be carefully balanced against the potential risks. Several life threatening complications have been associated with the use of umbilical catheters including catheter-related infections, intestinal necrosis, thrombosis, cardiac arrhythmias, myocardial perforation, as well as pleural and pericardial effusion.[1.2.3] According to the literature, mechanical adverse events occur in 5 to 19% of patients with a UVC, infectious adverse events in 5 to 26% and thrombosis in 2 to 26%.[4.5]

The incidence of neonatal sepsis is approximately 1 to 10 cases per 1000 live births and 1 per 250 live premature births. The incidence rates of neonatal infection in several referral hospitals in Indonesia is approximately 8.76%–30.29% with the mortality rate is 11.56%–49.9%. The incidence rates of neonatal sepsis in several referrals hospital in Indonesia is 1.5%–3.72% with the mortality rate is 37.09%–80%.[6]

Because the risk of complications may increase with duration of use, UVCs are often removed after relatively short periods and replaced with percutaneous central venous catheters (PCVCs) for maintenance of long-term fluid and nutritional status.[2.7] On the basis of these limited data, the Centers for Disease Control and Prevention

currently recommend use of UVCs be limited to 14 days. In a retrospective review of 230 infants with birth weights 1251 g who were admitted to our NICU and required a UVC and/or PCVC, the apparent proportion of catheters remaining infection free at 20 days (the time at which the last UVC was removed) was 89% for UVCs and 73% for PCVCs.[8]

UVCs comprise a large proportion of central lines inserted in the NICU. Central line–associated bloodstream infections (CLA-BSIs) can complicate PICCs. An estimated 80 000 CLA-BSIs occur in the United States every year. The mortality rate for these CLA-BSIs remains unclear, but recent studies demonstrated a range of 4% to 20%. CLA-BSI extends patient length of stay by an average of 7 days, and the attributable cost is $3700 to $29 000 per infection.[3.5.8]

In this study, we prospectively examined catheter-related bacteremia and associated sepsis complications in long-term use of UVCs.

METHODS

Subjects

The study was retrospectively done at NICU of Husada Utama hospital, conducted for 3 years (April 1st 2008 until April 30th 2011). The premature infants with birth weights less than 2000 g who had a UVC placed on NICU admission were eligible for the study. Infants who required a UVC for exchange transfusion, infants with gastrointestinal abnormalities including gastroschisis and omphalocele, or infants with congenital heart disease with intra cardiac shunting were excluded. The parents or legal guardians of the patients gave informed consent before enrollment.

Umbilical Catheterization

Placement of a UVC was attempted in infants < 2000 g on admission to the NICU. Either a single or double lumen catheter (3.5F diameter, Polyurethane 1270 Catheter; Vygon Healthcare, Gloucestershire, UK) was inserted under sterile conditions. A double-lumen UVC was used if it was technically possible to place one. Care of the catheters was standardized. Catheters were attached to transducers, was changed every 24 hours if the infused concentration of dextrose was >12.5 g/L and every 72 hours for concentrations of dextrose <12.5 g/L. All UVCs had continuous infusion of solutions in the main port. Both infusion and flush solutions contained heparin (1.0 IU/mL for infants >1000 g and 0.5 IU/mL for infants <1000 g or on total parenteral nutrition). All catheter connections were checked hourly to guard against any disconnection.

Catheter placement was confirmed with a chest and abdominal radiograph. The catheter placement was adjusted to place the catheter tip at the inferior vena cava/right atrial junction. We had confirmed the depth of catheter tips using antero-posterior chest X-rays. Ideal position of the UVC was defined as the catheter tip being visible between the 9th and 10th thoracic vertebrae on a chest X-rays. Catheters were sutured in place into the umbilical cord, and tape was then used to secure the catheter to the infant's abdomen.

Blood and tips UVC tips Cultures

Blood culture test was performed in premature babies with suspected sepsis based on clinical symptoms, complete blood test and CRP using VITEX method. Whole blood (0.3–1.0 mL) was placed in sterile Isolator tubes and transported to the microbiology laboratory. Blood was streaked onto blood and chocolate agar plates and then incubated for 5 days under aerobic conditions. UVC tips Cultures were placed in an automated reader (Bact-alert; Biomerieux). Any positive or potentially positive cultures were Gram-stained, streaked on to blood and/or chocolate agar plates (depending on the likely pathogen), and incubated under aerobic conditions. Organisms were isolated by either culture system identified with standard microbiologic techniques.

Definitions

Clinical Sepsis

The definition of infection included symptomatology (eg, temperature instability, increased ventilator settings, increased apnea, bradycardia or desaturations, feeding intolerance, lethargy, or blood pressure instability) and either a single positive blood culture for prospectively defined definite pathogens or multiple positive cultures (≥ 2 within 48 hours) for other organisms from usually sterile site(s) (blood, catheter tip, urine, or cerebrospinal fluid, with at least 1 positive culture from the blood).[1.9.10]

CRBSI

Bacteremia/fungemia in a patient with an intravascular catheter with at least 1 positive blood culture obtained from a peripheral vein, clinical manifestations of infections (fever, chills, and/or hypotension), and no apparent source for the BSI except the catheter. One of the following should be present: a positive semi quantitative (>15 CFU/catheter segment) or quantitative (>103 CFU/catheter segment catheter) culture whereby the same organism (species and antibiogram) is isolated from the catheter segment and peripheral blood; simultaneous quantitative blood cultures with a >5:1 ratio CVC versus peripheral; differential period of CVC culture versus peripheral blood culture positivity of >2 hours.[8.11.12]

Statistical Analysis

Data are presented in distribution tabulation and data analysis was performed with a computer assisted statistical package (SPSS ver. 12.0). Descriptive analysis of catheter duration and risk of sepsis, UVCs and blood culture of the patient were calculated. Chi-square analysis and logistic regression were performed in the laboratorium data.

RESULTS

Data from April 1st 2008 until April 30th 2011 revealed the premature babies with UVCs were 44 samples. All of them were eligible for analysis, 23 in sepsis group and 21 in no sepsis group. The characteristics of the sample are listed in table 1.

Table 1. Characteristic of High Risk Premature Neonates Who had a UVC Placed in NICU

Parameters	Sepsis	No Sepsis	P
	n = 23 (%)	n = 21 (%)	
Gender			.121
Female	7 (38.9)	11 (61.1)	
Male	16 (61.5)	10 (38.5)	
Birth weight (g)	1428.3 (SD 324.33)	1450.0 (SD 321.71)	.52
Gestational age			.467
< 30 week's	9 (50.3)	7 (43.8)	
> 30 week's	14 (50)	14 (50)	
Apgar score			.322
≤ 6	8 (61.5)	5 (38.5)	
> 6	15(48.4)	16 (51.6)	
Mechanical ventilator			.068
Yes	18 (62.1)	11 (37.9)	
No (n-CPAP)	5 (33.3)	10 (66.7)	

Table 1 shows that the results have no significant difference based on the gender, birth weight, gestational age, apgar score in premature babies with sepsis risk treated in NICU Husada Utama hospital. However baby with mechanical ventilator shows to have higher risk compared with n-CPAP. In this case: 18 premature babies with mechanical ventilator and 5 with n-CPAP affected by sepsis. Babies with apgar score less than 6 during the labor have higher risk affected by sepsis, on the other hand apgar score more than 6 shows lower risk.

Table 2. Catheter Duration and The Risk of Sepsis in Premature Babies

Days of UVC	Sepsis	
	Positive n(%)	Negative n(%)
< 14 days	15 (53.6)	13 (46.4)
> 14 days	8 (50)	8 (50)

Chi Square X^2test p = 0.533

Table 2 shows that days of UVC have no significant difference in the risk of sepsis in premature babies treated in NICU Husada Utama hospital. In this study 15 babies with days of UVC less than 14 days were in the risk of sepsis. 8 babies with days of UVC more than 14 days were in the risk of sepsis.

Table 3. Catheter Duration and The Risk of CLA-BSIs

Days of UVC	UVC Culture		Blood Culture	
	+	–	+	–
< 14 days	11 (68.8)	5 (31.2)	7 (25)	21 (75)
> 14 days	10 (35.7)	18 (64.3)	11 (68.8)	5 (31.2)

Chi Square X^2 test p = 0.516; p = 0.456

Table 3 shows that days of UVC have no significant difference in UVC and blood culture result in premature babies treated in NICU Husada Utama hospital. Days of UVC less than 14 days show UVC culture performance in 11 babies suspected sepsis is positive, in fact blood culture performance shows negative in 21 babies. Days of UVC more than 14 days show blood culture performance in 11 babies with blood culture positive evidence, even though UVC culture performance is negative in 18 babies.

Table 4. Pathogens that Caused CLA-BSI in Neonates with UVCs in Premature Babies

Microorganisms	Blood Culture		UVC Culture	
	n	%	N	%
Acinetobacter baumanii	1	2.3	5	11.4
Burkholderia cepacia	4	9.1	4	9.1
Candida albicans	1	2.3	0	0
Enterobacter asburie	1	2.3	0	0
Klebsiella pneumoniae	4	9.1	3	6.8
Escherichia coli	0	0	4	9.1
Pseudomonas aeroginosa	0	0	11	25
Enterobacter cloacae	0	0	2	14.5
Stenotrophomonas maltophila	1	2.3	0	0
No organism growth	12	27.3	15	34.1

Table 4 shows the types of microorganism appeared in blood and UVC culture in 44 premature babies treated in NICU Husada Utama hospital. *Burkholderia cepacia* and *Klebsiella pneumonia* mostly appeared in blood culture performance. 25% of UVC culture performance shows *Pseudomonas aeroginosa*. Of 23 babies suspected sepsis 12 babies show no organism growth on blood culture performance while 15 babies show no organism growth on UVC culture performance.

DISCUSSION

CLA-BSIs are a common cause of morbidity and mortality among neonates.[1,3,6,10] Several factors have been

shown to contribute to the pathogenesis of nosocomial CLA-BSI. Host-related risk factors include age, immunologic immaturity, and severity of underlying disease.[12.13] In this study shows that gestational age < 30 weeks and mechanical ventilator have contributed the risk of CLA-BSI.

The risk profiles of a long term UVC to a long-term PCVC have seldom been compared. On the basis of these limited data, the Centers for Disease Control and Prevention currently recommend use of UVCs be limited to 14 days. However, a survey of nursery directors revealed that some NICUs leave UVCs in place for a longer period of time.[7.14.15] The limited data available after 14 days in this study suggest the possibility of increased infection. Duration of catheter > 14 days show 11 babies with blood culture positive evidence, although not statistically significant, would have potential clinical significance if it were to be substantiated.

Migration of skin organisms at the insertion site into the umbilical catheter tract with colonization of the catheter tip is the most common route of infection for centrally inserted, shortterm catheters.[4.8.9] Contamination of the catheter hub contributes substantially to intraluminal colonization of long-term catheters. Occasionally, catheters might become hematogenously seeded from another focus of infection. Rarely, infusate contamination leads to CRBSI.[1.16]

Important pathogenic determinants of catheter-related infection are 1) the material of which the device is made and 2) the intrinsic virulence factors of the infecting organism.[8.9.11] In vitro studies demonstrate that catheters made of polyvinyl chloride or polyethylene are likely less resistant to the adherence of microorganisms than are catheters made of Teflon, silicone elastomer, or polyurethane.[9.13.15] Some catheter materials also have surface irregularities that enhance the microbial adherence of certain species (eg, coagulase-negative staphylococci, *Acinetobacter calcoaceticus*, and *Pseudomonas aeruginosa*); catheters made of these materials are especially vulnerable to microbial colonization and subsequent infection.[4.7.8] Additionally, certain catheter materials are more thrombogenic than others, a characteristic that also might predispose to catheter colonization and catheter-related infection. This association has led to emphasis on preventing catheter-related thrombus as an additional mechanism for reducing CRBSI.[17]

One study reports that the incident rate of PICC related sepsis is between 2 and 21%. This study suggests that the lower incidence of infection in PICCs, when compared to other UVCs, might be related to the low concentration of bacteria in peripheral areas (50 to 100 colonies of bacteria per cm^2 of skin) when compared to the thorax (1,000 to 10,000 colonies of bacteria per cm2 of skin).[18]

The literature shows that there are microorganisms more prevalent in catheter-related primary sepsis. The gram-positive cocci are responsible for 65% of infections, while the most prevalent are the *Staphylococcus epidermidis* (31%) and the *Staphylococcus aureus* (14%). The gram-negative bacilli account for 30% of infections and the most prevalent are the *Pseudomonas sp* (7%) and the *Escherichia coli* (6%). Infection by *Candida SP* is responsible for the remaining 5% of catheter-related infections.[1.2.19] Coagulase negative staphylococcus was the dominant infection (55.6%) within the first 2 weeks, whereas Gram negative bacteria were dominant pathogens (58.3%) after the first 2 weeks.[20.21] However, the most frequent microorganism isolated in cultures in this study was the *Pseudomonas aeroginosa.*

To avoid contaminating central venous catheters, several measures should be implemented in their insertion and maintenance.[10.11] Central catheter insertion, whether it is a PICC or a UVC, should be aseptic and include measures of barrier precaution such as wearing a cap, mask, sterile gown, sterile gloves and drapes. It is recommended to wash hands with chlorhexidine detergent or alcohol gel before and after contacting with the catheter during UVC maintenance. The dressing has to be changed every seven days or when it is wet or for other reasons taken off, change taps, equipment and extensions every 72 hours and the equipment for parenteral nutrition should be changed every 24 hours, always swabbing the connections and taps of the catheter with 10% concentration of alcohol before handling them.[2.6.11.15]

Adverse events in central catheters were frequent in neonatal populations, both for PICCs and in UVCs. The most prevalent adverse event in PICCs was catheter occlusion, while clinical sepsis prevailed in UVCs.[8.21] PICCs presented a higher frequency of mechanical adverse events, especially catheter occlusion and rupture. However, its use presented very low rates of catheter-related infections; these rates are similar or less than those reported in the literature.[20] Therefore, we assert that PICC is a safe means for parenteral administration in the neonatal population due to the low risk of infection found in this study and in the literature. The use of UVCs resulted in a lower rate of mechanical adverse events: occlusions or ruptures were not found in this catheter in this study. However, the rates of infectious adverse events related to this catheter are the most prevalent.[20.21]

Several limitations should be considered when interpreting our data. We conducted the study on a large cohort of patients over a 3-year period, because our unit has low incidence of CLA-BSI. Several confounding factors still persist in this study. Underlying disease, duration of mechanical ventilator, nosocomial infection were the risk of sepsis in premature babies with UVCs.

CONCLUSIONS

The catheter duration have no significant difference in risk of sepsis in premature babies with Umbilical Vein Catheters. *Burkholderia cepacia* and *Klebsiella pneumonia* mostly appeared in blood culture performance. 25% of UVC culture performance shows *Pseudomonas aeroginosa*.

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