Peripherally inserted central catheters and the incidence of candidal sepsis in VLBW and ELBW infants: is sepsis increased?

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Original article

Background: **Peripherally inserted central catheters (PICCs) have been widely used in neonatal clinics. However, the complications such as infection after PICC treatment are also confronting neonatologists especially in developing countries. This study was undertaken to investigate whether PICCs is a safe treatment for very low birth weight (VLBW) infants and extremely low birth weight (ELBW) infants.**

Methods: **Fifty-nine VLBW and ELBW infants receiving PICCs and 89 VLBW and ELBW infants receiving peripheral intravenous catheters (PIVCs) were included in this study. The incidence of sepsis and mortality were compared retrospectively between the two groups.**

Results: **There was no difference in the total sepsis incidence and mortality between the PICCs and PIVCs groups (*P*=0.11 and *P*=0.61 respectively). However, the candidal sepsis incidence was higher in the PICCs group than in the PIVCs group [6/59 (10.2%) vs 2/89 (2.2%); *P*=0.044 (Exat Sig. 1-sided), OR=4.93, 95% CI 0.96-25.3].**

Conclusion: **Placement and indwelling of PICCs are a potential risk factor for candidal sepsis among VLBW and ELBW infants.**

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Key words: **candidal sepsis;**
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Introduction

Peripherally inserted central catheters (PICCs) have been used in neonates who need a long-term intravenous access since the 1980s.[1,2] PICCs are more effective than peripheral intravenous catheters (PIVCs) in reducing needle punctures, improving patients' satisfaction, and assuring drug and fluid administration. Furthermore, the practice of placing PICCs was found to be safer and more feasible than surgically placed central venous catheters, percutaneous subclavian vein catheters, and umbilical venous catheters.[3-5]

One of the issues regarding use of PICCs is how to protect the infants from infection, especially the preterm infants (gestational age <37 weeks). Preterm infants, particularly very low birth weight (VLBW, birth weight <1500 g) and extremely low birth weight (ELBW, birth weight <1000 g) infants, hospitalized in the neonatal intensive care units (NICUs), have a high rate of infection with nosocomial sepsis.[6,7] Among all kinds of nosocomial sepsis, catheter-related bloodstream infections (CRBSIs) are one of the leading causes of morbidity in NICUs.[8,9] At present, candidal sepsis has become an increasingly important part of nosocomial infections in VLBW and ELBW infants.[10,11] Although there are many risk factors associated with neonatal nosocomial sepsis, some studies reported intravenous catheters indwelling as well as the parental nutrition and lipid emulsion that the catheters deliver are the most common causes.[12-14]

In this retrospective study, we will compare the infections and mortality and morbidity among VLBW and ELBW infants who received PICCs and PIVCs respectively in our NICU.

Methods

Patients

Of 148 VLBW and ELBW infants enrolled in this retrospective study, 59 received PICCs and the remaining 89 received PIVCs. All of the infants were admitted to the NICU of West China Second University

Hospital, Sichuan University between April 2006 and August 2008. This study was approved by the Ethics Committee of the West China Second University Hospital, Sichuan University and was in accordance with the ethical standards of the *Helsinki Declaration* of 1975 (and its revision in 2000). Informed consent was obtained from all the parents of the patients.

Study designs

In the PICCs group, 59 VLBW and ELBW infants (VLBW vs ELBW = 44:15) who needed long-term transfusion and parental nutrition received PICC [26G (1.9FR), Becton Dickinson Infusion Therapy Systems Inc, USA] treatment with agreement of their parents. The preferred puncture sites for PICC were the basilic vein or cephalic vein. The axillary vein was the second choice. After placement of a PICC, chest X-ray was performed to identify the location of the catheter tip. The ingredients administered through the PICC included antibiotics and parental nutrition containing intravenous lipid emulsion. The PICC was kept for 19-62 days. The catheter was replaced in 6 infants for 2-3 times due to catheter occlusion or phlebitis, and 40 infants were treated with third-generation cephalosporins for 15.58±9.18 days.

In the PIVCs group, 89 VLBW and ELBW infants (VLBW vs ELBW = 69:20) who needed long-term transfusion and parental nutrition but whose parents did not agree to use PICCs received PIVCs (Becton Dickinson Medical Devices Co., Ltd, China) as the regular treatment. Fluids transfused through PIVCs included parental nutrition, antibiotics and other medicines. Most PIVCs were indwelled less than 3 days each time for mechanical complications such as catheter occlusion or leak. In this group, 61 infants were treated with third-generation cephalosporins for 15.36±7.57 days.

Statistical analysis

Data were expressed as means ± SD and analyzed using the Chi-square test, Student's *t* test, and Fisher's exact test. Analysis was made with SPSS statistical software 11.0 version.

Results

General condition of patients in both PICCs and PIVCs groups

The gestational age, birth weight, sex, drugs administration, and hospital stay were not significantly different between the PICCs and PIVCs groups (Table 1).

Data collection

Infections

The sepsis was identified by a blood culture showing Candida or another bacterium growing. The results of blood culture in both groups are illustrated in Table 2. In the PICCs group, PICC line tips were cultured after PICC treatment. *Candida albicans* were found in 2 infants and coagulase-negative *Staphylococci* in 1 infant by the cultures of PICC line tips.

There was no significant difference in the incidence of septicemia between the PICCs and PIVCs groups [14/59 (23.7%) vs 12/89 (13.5%); *P*=0.11, OR=1.99, 95% confidence interval (CI) 0.85-4.69] or incidence of bacterial sepsis [8/59 (13.6%) vs 10/89 (11.2%); *P*=0.67, OR=1.24, 95% CI 0.46-3.35]. However, there is difference in the incidence of *Candida albicans* infection between the two groups [PICCs vs PIVCs: 6/59 (10.2%) vs 2/89 (2.2%); *P*=0.044 (Exat Sig. 1-sided), *P*=0.059 (Exat Sig. 2-sided), OR=4.93, 95% CI 0.96-25.3].

In this study, infants with *Candida albicans* sepsis were found between 12 to 31 days after PICC placement. *Candida albicans* sepsis was diagnosed in 2 infants with placement of PIVC on day 17 and day 25 respectively after hospitalization.

Mortality

Fourteen of the 59 infants died in the PICCs group, including 6 infants with sepsis. Eighteen of the 89 infants died in the PIVCs group, and in the 18 infants,

Table 1. Comparison of the patients' characteristics in the peripherally inserted central catheters (PICCs) group and peripheral intravenous catheters (PIVCs) group

Variables	PICCs group (*n*=59) (means ± SD)	PIVCs group (*n*=89) (means ± SD)
Gestational age (wk)	30.7±1.9 (26.2-34.0)	30.3±1.2 (26.5-34.1)
Birth weight (g)	1173.1±187.9 (730-1490)	1208.4±127.7 (750-1490)
Male	27 (45.8%)	40 (44.9%)
Female	32 (54.2%)	49 (55.1%)
Ventilation (tracheal intubation)	25 (42.4%)	34 (38.2%)
Pulmonary surfactant	26 (44.1%)	36 (40.4%)
Length of hospital stay (d)	31.5±11.7 (20-79)	28.6±10.1 (20-80)

Table 2. Comparison of blood culture results between the peripherally inserted central catheters (PICCs) group and peripheral intravenous catheters (PIVCs) group

Organisms	PICCs group (*n*=59)	PIVCs group (*n*=89)
Candida albicans	6*	2
Coagulase-negative *staphylococci*	4	5
Klebsiella pneumonia	2	2
Escherichia coli	1	2
Streptococcus faecalis	1	1

*: *P*=0.044 (Exat Sig. 1-sided), *P*=0.059 (Exat Sig. 2-sided), OR=4.93, 95% CI 0.96-25.3, compared with the PIVCs group.

Table 3. Comparison of the mortality caused by sepsis between the peripherally inserted central catheters (PICCs) group and peripheral intravenous catheters (PIVCs) group

Causes of death	PICCs group *n*=59 (%)	PIVCs group *n*=89 (%)
Candida	2 (3.4)	0 (0.0)
Coagulase-negative *staphylococci*	2 (3.4)	2 (2.2)
Klebsiella pneumonia	1 (1.7)	2 (2.2)
Streptococcus faecalis	1 (1.7)	1 (1.1)
Escherichia coli	0 (0.0)	2 (2.2)
Total	6 (10.2)*	7 (7.9)

*: *P*=0.85, compared with the PIVCs group.

7 were due to sepsis. Besides sepsis, intraventricular hemorrhage, necrotizing enterocolitis, and pulmonary hemorrhage were also the causes of death (Table 3). There was no significant difference in the total mortality or in the mortality caused directly by sepsis between the PICCs and PIVCs groups.

Discussion

PICCs provide a prolonged stable venous access assuring administration of all kinds of medications and assuring better parental nutrition to VLBW and ELBW infants who are unable to tolerate enteral feedings. However, PICC treatment has been involved with potential risks such as catheter mechanical complications and nosocomial sepsis in VLBW and ELBW infants. Candidal sepsis has become an increasingly frequent problem in all kinds of nosocomial sepsis.[15,16] The reported incidence of candidemia was 1.2% among all infants surviving for more than 3 days, but it increased to 2.6%-12.9% among VLBW infants, and 5.5%-20% among ELBW infants.[17-19] Among VLBW infants, *Candida albicans* has become the third most frequent organism causing late-onset sepsis.[20,21]

Evidence has shown that there are many risk factors for candidal sepsis in VLBW and ELBW infants, such as long stay in NICU, prolonged use of antibiotics, mechanical ventilation, use of systemic corticosteroids, invasive fungal dermatitis and central venous catheters indwelling and delayed removal of a catheter.[22] In this study, although we did not find an absolute statistical difference in candidal sepsis between PICC and PIVC treatment, PICC is a potential risk factor for candidal sepsis among VLBW and ELBW infants. Our findings are in agreement with previous studies.[23] To reduce the risk, an aggressive strategy has been reported to improve the sterility and decrease the duration of central venous catheters in intensive care units.[24]

It is a challenge to reduce the incidence of neonatal candidal sepsis in NICU. Healy et al[25] reported that prophylactic fluconazole can decrease the incidence of invasive candidiasis and invasive candidiasis-associated mortality rates in ELBW infants, indicating a promising prevention for preterm candidal sepsis in VLBW and ELBW infants.

In our series, we identified that placement of PICC may predispose neonates to a higher incidence of fungal infections but not total nosocomial sepsis.

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Competing interest: There is no conflict of interest with other organizations or persons.

Contributors: Bin X wrote the first draft of this paper. All authors contributed to the intellectual content and approved the final version. Tang J is the guarantor.

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