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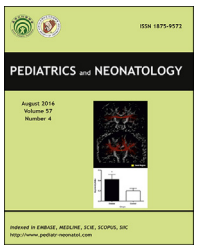

Original Article

Factors affecting the patency and complications of peripheral intravenous catheters in newborns

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Key Words
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Background: Peripheral intravenous catheters (PICs) are necessary for medication, nutrient, and fluid administration in pediatric patients. However, PICs are uneasy to access and maintain in young infants. This study identified risk factors affecting the complications and patency of PICs.

Methods: This retrospective cohort study included neonates and infants aged <4 months. All PICs inserted in the neonatal intensive care unit and intermediate care nursery were analyzed more than 5 months. The variables included gestational age, age and body weight at PIC insertion, insertion site, methods to maintain PIC patency (continuous intravenous drip [CIVD] versus intermittent flushing), fluid infusion rate and osmolarity, and ampicillin and cefotaxime concentrations. The effects of these variables on PIC complications and lifespan were assessed using binary logistic regression analysis and a general linear model, respectively.

Results: In total, 315 PICs were analyzed. The mean indwelling time was 33.8 ± 21.5 h and complication rate was 82.2%. The most frequent complications were infiltration (55.9%) and leakage (22.2%). The infusion rate and method to maintain PICs significantly impacted PIC patency. A negative correlation was noted between the infusion rate and PIC patency, with the patency decreasing by 0.9 h ($p = 0.047$) on increasing the infusion rate by 1 mL/h. Notably, compared with intermittent flushing, CIVD using a hypertonic solution significantly decreased PIC patency by 14 h ($p = 0.006$). As the patients' age increased by a month, the complication

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risk decreased by 35% ($p = 0.027$). However, as the infusion rate increased by 1 mL/h, the complication risk increased by 17% ($p = 0.018$).
Conclusions: Intermittent flushing may be preferred over CIVD to preserve PIC patency. An increased infusion rate is correlated with decreased PIC patency and increased complications. For the peripheral administration of ampicillin, we recommended preparing final concentrations below 50 mg/dL to prevent PIC complications.

1. Introduction

In pediatric hospitalization, peripheral intravenous catheters (PICs) are crucial for life support in extremely low-birth-weight preterm infants through antibiotic, nutrient, and fluid administration. Maintaining PIC patency in pediatric patients is crucial because their insertion procedure is time-consuming and associated with patient discomfort.[1] The pediatric population is more susceptible to complications than adults because of their fragile vasculature, including capillary weakness, venous network with narrow vessels, and high adiposity.[2,3] The younger the patient, the longer is the time and greater are the attempts required to successfully insert PICs.[1] Furthermore, vascular access in neonates is challenging, particularly in very-low-birth-weight (VLBW) infants and infants requiring prolonged intravenous access.[4]

PIC complications include phlebitis, infiltration, extravasation, clotting, infection, and accidental removal. In the neonatal population, the complication rate of PICs ranges from 55.6% to 86.6%, with the mean PIC lifespan being 23–84 h.[4–8] Various risk factors affect the complication rate of PICs. These include the patient characteristics (gestational age [GA], postnatal age, and body weight),[6,9] type of medication or fluid used,[4,10] concentration of medication,[10,11] osmolarity of intravenous fluid, method to maintain PIC patency (continuous intravenous drip [CIVD] versus intermittent flushing),[4,8,12] and location of PIC insertion (lower extremity).[3,9] However, few studies have assessed the effect of the volume of fluid exposure and use of a hypertonic solution in CIVD on PIC patency and complications.

As in many other countries, registered nurses are the main health-care providers in charge of inserting and maintaining PICs in Taiwan. The responsibilities of registered nurses include inserting PICs by using an aseptic technique, regularly monitoring intravenous therapy and medication administered through PICs, checking the date of PIC insertion, and replacing PICs.[3] In our hospital, the policy of PIC replacement requires changing PICs every 72 h unless there are complications or specific instructions by clinical doctors.

This study aimed to assess the incidence of complications associated with PICs and monitor the PIC lifespan in the relatively fragile pediatric population aged <4 months. Moreover, risk factors leading to complications and reducing the patency of PICs were identified.

2. Methods

2.1. Study design and setting

This retrospective cohort study included patients hospitalized in the neonatal intensive care unit (NICU) and intermediate care nursery in a regional hospital that provides neonatal intensive care in the southern Taipei area, Taiwan.

Data collection was performed between November 1, 2020, and March 31, 2021. The study was approved by the Institutional Review Board of Taipei Medical University (IRB-TMU N202108029). All 0-day- to 4-month-old patients who needed peripheral venous catheterization were included in the study. All PICs inserted in the study units were recorded from the time of insertion to the time of removal. PICs that were inserted before admission to the study units and were removed outside the units were excluded. The sample size was calculated considering 15–20 individuals per predictor in regression analysis. Eight variables, including three continuous and five categorical variables, and a total of 12 dummy variables were set in the regression model. A sample size of at least 240 PICs was considered large enough to overcome potential bias.

2.2. Outcome variables

Patient-related variables included the GA, age and weight at the time of PIC insertion, gender, and mean number of PICs inserted per patient. Catheter-related variables included the duration of PICs (time between PIC insertion and removal), reasons for PIC removal (infiltration [i.e., swelling documented on nursing records], phlebitis, leakage, occlusion, dislodgement, and end of medical need), insertion site (upper and lower extremities), type of medication, volume of fluid exposure, and method to maintain PIC patency (CIVD or intermittent flushing). The osmolarity of intravenous medication and intravenous fluid is a potential risk factor affecting the lifespan and complications of PICs. A hypotonic solution infiltrating the venous endothelial cells and blood cells may result in hemolysis, whereas a hypertonic solution may result in cell shrinkage.[13] Therefore, the intravenous fluid used to maintain PICs was categorized into hypertonic (>308 mOsm/L), isotonic (275–308 mOsm/L), and hypotonic (<275 mOsm/L). The osmolarity of the intravenous

fluid was based on Drug Instruction (Supplementary Table 1).[14–16]

Eight variables influencing the PIC lifespan and occurrence of complications were assessed. A complication was defined as an event necessitating PIC removal for reasons other than the end of medical need. The study variables included the GA (≥37, 34–36, and <34 weeks), age and body weight at PIC insertion, site of PIC insertion (upper and lower extremities), method to maintain PIC patency (CIVD with a hypertonic solution, CIVD with an isotonic solution, CIVD with a hypotonic solution, and intermittent flushing), volume of fluid exposure (expressed as the mean infusion rate, mL/min), and ampicillin and cefotaxime concentrations (≤50 and >50 mg/mL). Ampicillin and cefotaxime are frequently prescribed for early- and late-onset neonatal sepsis in patients aged <4 months. For peripheral intravenous infusion in fluid-restricted patients, the maximum concentration of ampicillin is 112 mg/mL in sterile water and that of cefotaxime is 147 mg/mL in sterile water.[14] However, concentrations exceeding 50 mg/mL of both medications will increase osmolarity beyond 500 mOsm/L, which is the higher limit for peripheral vein tolerance recommended by the Infusion Nursing Society.[17] Therefore, we set 50 mg/mL was set as the cutoff point for ampicillin and cefotaxime to examine whether intermittent exposure to high-osmolarity medications is a risk factor affecting the lifespan and complications of PICs.

2.3. Data analysis

Categorical variables are expressed as the absolute frequency and percentage. Continuous variables are expressed as the mean, standard deviation (SD), median, and interquartile range (IQR). Intergroup differences were analyzed using Student's *t* test or nonparametric analysis depending on the normality of quantitative variables. A general linear model was used to identify variables affecting the PIC lifespan. Variables that met two criteria, namely $p < 0.1$ and no evidence of collinearity, were included in the general linear model. Variables associated with a complication were identified through binary logistic regression analysis

Table 1 Catheter characteristics.

Item	N	%	PIC duration (hr)		P-value
	N = 315		Median	IQR	
Ward of IC insertion					0.379
NICU	81	25.7%	25.3	23.0	
Intermediate care nursery	234	74.3%	29.9	25.5	
Sex					0.561
Female	122	38.7%	28.0	29.1	
Male	193	61.3%	29.6	24.2	
Age at catheter insertion					0.896
<30 days	239	75.9%	29.4	24.3	
1–4 months	76	24.1%	29.2	30.7	
Weight at catheter insertion					0.424
<1000 g	5	1.6%	46	42.6	
1000–1499 g	7	2.2%	32.2	21.5	
1500–2499 g	58	18.4%	32.2	28.6	
2500–3999 g	175	55.6%	28.1	23.9	
>4 kg	70	22.2%	29.5	26.6	
Methods to maintain catheter					0.001
Hypertonic CIVD	197	62.5%	25.3	23.0	
Isotonic CIVD	87	27.6%	34.2	30.8	
Intermittent flush	31	9.8%	38.4	31.4	
Insertion site					0.179
Dorsum of the hand	175	55.6%	26.2	25.3	
Forearm	84	26.7%	31.1	26.5	
Ankle	41	13.0%	34.3	23.7	
Dorsum pedis	12	3.8%	26.4	18.9	
Calf	3	1.0%	16.9		
Reason for catheter removal					0.019
End of medical need	56	17.8%	38.7	37.1	
Infiltration	176	55.9%	25.8	22.2	
Leaking	70	22.2%	31.7	24.0	
Occlusion	12	3.8%	41.0	49.3	
Dislodgement	1	0.3%			

CIVD: continuous intravenous drip; IQR: interquartile range; NICU: neonate intensive care unit.

using the forward likelihood ratio method ($p < 0.1$ was the cutoff point). All statistical analyses were performed using SPSS 20 (SPSS Inc., Chicago, IL, USA), and $p < 0.05$ was considered statistically significant.

3. Results

3.1. Patient demography

In total, 103 patients with 315 PICs were included in this study. The patients' mean age was 0.66 ± 0.94 months, and 73% were neonates. Moreover, 60% of the patients were male. The mean GA was 37 ± 3 weeks (range, 28–41 weeks), with the GA being ≥37 weeks in 76.7% of the patients. The patients' mean weight was 3.36 ± 1.16 kg (range, 0.69–6.91 kg), and 75% of them weighed more than 2.5 kg. On average, three PICs were inserted into a hospitalized patient per course (SD, 1.88; range, 1–11).

3.2. PIC characteristics

In total, 315 PICs were included in this study (Table 1). The size of all PICs was 24 gauge (Introcan Safety® IV Catheter 24 Ga × 0.75 in., PUR, Straight). Their mean indwelling time was 33.8 ± 21.5 h (range, 1–149.7 h). Most PICs (259 PICs, 82.2%) were removed because of complications, including infiltration, leakage, occlusion, and dislodgement. The most common complication was infiltration (176 PICs, 55.9%), followed by leakage (70 PICs, 22.2%), occlusion (12 PICs, 3.8%), and dislodgement (1 PIC, 0.3%). Only 56 PICs (17.8%) were removed without any complication (i.e., the end of medical need). PICs without complications had a longer lifespan than those with complications (41.6 ± 28.5 h versus 32.1 ± 19.3 h). In total, 300 PICs (95%) were inserted for administering antibiotics and other medications. On average, 1.7 ± 0.7 medications (range, 0–4) were administered per PIC. The most frequently administered medication was ampicillin (76.8%), followed by gentamicin (56.2%) and cefotaxime (17.1%). Moreover, 82% of PICs were inserted in the upper extremity and 90% of PICs were maintained using CIVD. Most PICs (62.5%) were maintained using CIVD with a hypertonic solution, while no PIC was maintained using CIVD with a hypotonic solution. CIVD with a hypertonic solution (4.1 ± 2.7 mL/h; range, 2–18 mL/h) had a similar infusion rate to CIVD with an isotonic solution (4.8 ± 3.3 mL/h; range, 2–20 mL/h). Only 10% of PICs (31 PICs) were maintained using intermittent flushing. Intermittent flushing maintained a longer PIC lifespan than CIVD with hypertonic and isotonic solutions (intermittent flushing, 46.4 ± 30.5 h; CIVD with an isotonic solution, 38.2 ± 23.6 h; CIVD with a hypertonic solution, 29.9 ± 17.4 h).

3.3. Risks factors affecting PIC lifespan

Univariate analysis revealed that the PIC lifespan was influenced by the patients' age, infusion rate, method used to maintain PICs, and cefotaxime concentration. As the patients' age increased by a month, the PIC lifespan increased by 2.5 h ($p = 0.048$). However, as the infusion rate increased by 1 mL/h, the PIC lifespan decreased by 0.9 h ($p = 0.020$). The mean PIC lifespan using both CIVD methods was 8 h lower than that using the intermittent flushing method (CIVD with a hypertonic solution, −8.31 h, $p = 0.002$; CIVD with an isotonic solution, −8.149 h, $p = 0.062$). The patients' body weight, PIC insertion site, and ampicillin concentration did not affect the PIC lifespan (Table 2).

After taking all variables into account, the infusion rate and method to maintain PICs were found to affect the PIC lifespan. A negative correlation was noted between the infusion rate and PIC lifespan, with a 0.9-h decrease in PIC lifespan being observed on increasing the infusion rate by 1 mL/h ($p = 0.047$). Compared with intermittent flushing, CIVD with a hypertonic solution significantly decreased the PIC lifespan by 14 h ($p = 0.006$), while CIVD with an isotonic solution no significantly decreased the patency of PICs by 7 h ($p = 0.212$). Moreover, ampicillin concentrations >50 mg/mL no significantly reduced the patency of PICs by 3.5 h in comparison with concentrations ≤50 mg/dL ($p = 0.264$; Table 2).

3.4. Risk factors affecting PIC complications

Univariate analysis revealed that younger age, the use of the CIVD method to maintain PICs, and the use of ampicillin contributed to PIC complications. As the patients' age increased by a month, the complication risk decreased by 28% ($p = 0.019$). CIVD with a hypertonic solution had the highest complication rate (86.3%), followed by CIVD with an isotonic solution (79.3%) and intermittent flushing (64.5%). Compared with intermittent flushing, CIVD with a hypertonic solution led to a 3.4-fold increase in the complication risk ($p = 0.004$). Moreover, compared with ampicillin concentrations ≤50 mg/mL, ampicillin concentrations >50 mg/dL tended to increase the complication risk (odds ratio [OR], 1.148; $p = 0.736$). However, compared with the absence of ampicillin, higher concentrations of ampicillin led to higher risks of complications (ampicillin concentrations of 50.1–100 mg/mL: OR, 3.527; $p = 0.003$; ampicillin concentrations ≤50 mg/mL: OR, 3.072; $p = 0.001$). The patients' body weight, infusion rate, GA, insertion site, and cefotaxime concentration did not affect the incidence of PIC complications (Table 3).

After taking all variables into account, the patients' age, infusion rate, and ampicillin concentration (50.1–100 mg/mL) were found to affect the complication risk. Age had a positive impact on the complication risk. As the patients' age increased by a month, the complication risk decreased by 35% ($p = 0.027$). By contrast, the infusion rate had a negative impact on the complication risk. As the infusion rate increased by 1 mL/h, the complication risk increased by 17% ($p = 0.018$). High ampicillin concentrations (>50 mg/mL) non-significantly increased the complication risk (1.5-fold increase) in comparison with low ampicillin concentrations (≤50 mg/mL, $p = 0.265$). However, compared with the absence of ampicillin, high ampicillin concentrations significantly increased the complication risk (threefold increase, $p = 0.008$). Low ampicillin concentrations also led to an increased risk, but with a wide confidence interval (CI) (95% CI, 0.859–4.115).

Table 2 Factors influencing lifespan of peripheral intravenous catheters.

Item	N	%	IC patency (hr)		Simple regression			Multiple regression		
			Mean	SD	β	95%CI	P value	β	95% CI	P value
Age at catheter insertion (months)	315	100%	33.8	21.5	2.537	(0.021, 5.053)	0.048	3.439	(−0.557, 7.435)	0.091
Weight at catheter insertion (kg)	315	100%	33.8	21.5	−0.182	(−2.249, 1.855)	0.863			
Infusion rate (mL/hr)	315	100%	33.8	21.5	−0.910	(−1.678, −0.143)	0.020	−0.900	(−1.788, −0.013)	0.047
Gestational age							0.058			0.463
GA <34 weeks	34	10.8%	42.1	27.2						
GA 34−36 weeks	26	8.3%	33.1	25.7	−9.042	(−19.992, 1.907)	0.105	−1.523	(−13.250, 10.205)	0.799
GA ≧37 weeks	255	81.0%	32.8	20.0	−9.309	(−16.982, −1.636)	0.018	−4.738	(−13.674, 4.198)	0.298
Insertion site							0.538			
Upper extremity	259	82.2%	33.5	22.2						
Lower extremity	56	17.8%	35.4	17.7	1.955	(−4.282, 8.191)				
Methods to maintain catheter							0.000			0.012
Intermittent flush	31	9.8%	46.4	30.5						
CIVD isotonic fluid	87	27.6%	38.2	23.6	−8.149	(−16.722, 0.425)	0.062	−7.030	(−18.101, 4.042)	0.212
CIVD hypertonic fluid	197	62.5%	29.9	17.4	−8.310	(−13.586, −3.033)	0.002	−14.302	(−24.469, −4.134)	0.006
Ampicillin							0.061			0.001
≦50 mg/mL	160	50.8%	33.3	20.9						
50.1−100 mg/mL	82	26.0%	38.1	25.6	4.824	(−0.884, 10.533)	0.097	−3.545	(−9.779, 2.690)	0.264
No ampicillin	73	23.2%	30.1	16.6	−3.217	(−9.154, 2.720)	0.287	−13.324	(−20.234, −6.415)	0.000
Cefotaxime							0.022			0.086
≦50 mg/mL	40	12.7%	34.6	19.0						
50.1−125 mg/mL	14	4.4%	49.1	37.4	14.501	(1.491, 27.511)	0.029	13.613	(0.277, 26.949)	0.045
No cefotaxime	261	82.9%	32.9	20.5	−1.695	(−8.809, 5.419)	0.640	0.587	(−6.527, 7.700)	0.871

CIVD: continuous intravenous drip; NICU: neonate intensive care unit; hr: hour.

Table 3 Factors influencing complication of peripheral intravenous catheters.

Item	Complication		No complication		Univariate analysis			Multivariate analysis		
	N	%	N	%	OR	95%CI	P value	OR	95%CI	P value
Age at catheter insertion (months)	259	82.2%	56	17.8%	0.720	(0.548, 0.946)	0.019	0.648	(0.441, 0.953)	0.027
Weight at catheter insertion (kg)	259	82.2%	56	17.8%	0.901	(0.705, 1.152)	0.405			
Infusion rate (mL/hr)	259	82.2%	56	17.8%	1.112	(0.991, 1.248)	0.070	1.169	(1.027, 1.330)	0.018
Gestational age							0.118			
GA <34 weeks	24	70.6%	10	29.4%						
GA 34–36 weeks	20	76.9%	6	23.1%	1.389	(0.430, 4.490)	0.583			
GA ≧37 weeks	215	84.3%	40	15.7%	2.240	(0.995, 5.041)	0.051			
Insertion site							0.432			
Upper extremity	215	83.0%	44	17.0%						
Lower extremity	44	78.6%	12	21.4%	0.750	(0.367, 1.535)				
Methods to maintain catheter							0.012			
Intermittent flush	20	64.5%	11	35.5%						
CIVD Isotonic fluid	69	79.3%	18	20.7%	2.108	(0.857, 5.187)	0.104			
CIVD hypertonic fluid	170	86.3%	27	13.7%	3.463	(1.494, 8.024)	0.004			
Ampicillin							0.001			0.027
≦50 mg/mL	215	83.0%	44	17.0%						
50.1–100 mg/mL	44	78.6%	12	21.4%	1.148	(0.516, 2.554)	0.736	1.591	(0.688, 3.899)	0.265
No ampicillin	49	67.1%	24	32.9%	0.325	(0.168, 0.632)	0.001	0.555	(0.241, 1.164)	0.114
Cefotaxime							0.624			
≦50 mg/mL	35	87.5%	5	12.5%						
50.1–125 mg/mL	11	78.6%	3	21.4%	0.524	(0.108, 2.552)	0.424			
No cefotaxime	213	81.6%	48	18.4%	0.634	(0.236, 1.703)	0.366			

CIVD: continuous intravenous drip; GA: gestational age; kg: kilogram.

4. Discussion

4.1. PIC lifespan and risks factors

Our findings revealed that PICs without complications had a longer lifespan (41.6 ± 28.5 h) than PICs with complications (32.1 ± 19.3 h). Previous studies have also revealed longer patency in PICs without complications.[4,18] The mean PIC lifespan in our study was 33.8 ± 21.5 h. The PICs included in our study were predominantly inserted in newborns (73%). In studies focusing on neonates, the mean catheter lifespan ranged from 23 to 84 h; the PIC lifespan in our study was comparable to previous findings.[4,6–9,12,18]

The PIC lifespan was clearly affected by the method used to maintain PICs and the osmolarity of CIVD solution after adjustment for all the included variables. The intermittent flushing method maintained a longer PIC lifespan than the two CIVD methods (intermittent flushing, 46.4 ± 30.5 h; CIVD with an isotonic solution, 38.2 ± 23.6 h; CIVD with a hypertonic solution, 29.9 ± 17.4 h). Similarly, Perez et al. and Hoff et al. found that intermittent flushing maintained a longer PIC lifespan than CIVD (Perez et al.: 92.8 versus 62.1 h, $p = 0.01$; Hoff et al.: 47.1 versus 35.4 h, $p = 0.041$).[8,19] However, Stock et al. found that the PIC lifespan was similar between intermittent flushing and CIVD methods (55.42 versus 57.48 h, $p = 0.797$).[12] In their study, many catheters were removed at approximately 48 h because of antibiotic discontinuation. This short duration could have disguised the actual effects on the statistics of PIC patency.

Assessment of the effect of osmolarity revealed that compared with intermittent flushing, CIVD with a hypertonic solution reduced the PIC lifespan by 14 h. Of the 197 PICs that used a hypertonic solution in our study, 194 PICs used a solution in which the osmolarity was over the 500 mOsm/L limit defined by the Infusion Nursing Society.[17] Abdelaziz et al. also found that a high-osmolarity solution could reduce catheter lifespan (10% dextrose solution, 556 mOsm/L: 49.95 h versus normal saline, 308 mOsm/L: 96.67 h; $p = 0.003$).[10] We considered the effects of ampicillin and cefotaxime concentrations >50 mg/mL; however, osmolarity >500 mOsm/L may be risky. We could not prove this assumption in our multiple regression analysis. Hoff et al. revealed that antibiotic use did not affect catheter lifespan.[19] Gupta et al. found that cefotaxime reduced catheter lifespan, whereas ampicillin did not.[4] Few studies have examined the effect of osmolarity or concentration of intravenous medication on catheter lifespan. Further research is warranted to answer this question.

Our findings revealed that CIVD with a hypertonic solution clearly reduced the PIC lifespan. Moreover, the PIC lifespan was negatively correlated with the infusion rate. As the infusion rate increased by 1 mL/h, the PIC lifespan decreased by 0.9 h ($p = 0.047$). This could be attributed to the larger volume of fluid exposed to blood vessels, higher pressure, or irritation of the capillary vasculature.

The body weight, gestational age (GA), and insertion site had no impact on the PIC lifespan in our study, similar to the findings of Gupta et al.[4] Hoff et al. demonstrated that the body weight and insertion site did not affect the lifespan of catheters. However, they found that extremely preterm neonates had a significantly longer catheter lifespan.[19] In our study, less than 3% of PICs were inserted in extremely preterm neonates; therefore, the data were insufficient to examine the effect on extremely preterm neonates.

4.2. PIC complications and risk factors

The complication rate of PICs was high (82.2%) in our study, and the most frequent complication was infiltration (55.9%). Several studies focusing on neonates have also reported a high complication rate of PICs (range, 55%–86%) and high susceptibility of this population to infiltration/extravasation (range, 37%–68%).[4,6–8,18,19] In our study, treatment completion was achieved to a greater extent using the intermittent flushing method (35.5%) and by not administrating ampicillin (32.9%). Among all the variables studied, CIVD with a hypertonic solution had the lowest treatment completion rate (17.3%). Univariate analysis revealed that CIVD with a hypertonic solution led to a 3.5-fold higher complication risk than intermittent flushing. CIVD with an isotonic solution also increased the complication risk, but with a wide CI. Compared with the CIVD method, Stock et al.[12] reported a lower complication rate and Hoff et al.[19] reported a lower extravasation rate when the intermittent flushing method was used. Although Perez et al. reported no difference in complications between the two methods, they noted an increase in the PIC lifespan when the CIVD method was used in neonates.[8] Our findings were similar to these previous findings. In contrast to our findings, Jacinto et al. found that the intermittent flushing method led to a higher occurrence of phlebitis than the CIVD method in older children with a median age of 7–8 years.[20] The divergent results between our study and that of Jacinto et al. may be attributed to population differences. Our study population consisted of patients aged <4 months. Most of them were neonates who were physically more fragile and were administered fluid more carefully than the older pediatric population in the study of Jacinto et al.

After taking all variables into account, we found that the complications of PICs were affected by the patients' age, infusion rate, and ampicillin concentration. Age was negatively correlated with the complications of PICs in our study. Foster et al. found that neonates were 5.5 times more likely to have some degree of phlebitis than populations older than neonates.[21] However, Abdelaziz et al. and Sulinan et al. found that age was not a predictor of complications.[3,10] Therefore, age is still an equivocal factor in PIC complications. We found that the infusion rate was positively correlated with PIC complications. Few studies have discussed the relationship between the infusion rate and catheter complications in the pediatric population. Hecker and Mentin et al. found that a higher infusion rate and an infusion volume larger than 2000 mL/day, respectively, increased the incidence of catheter complications in adult patients.[22,23] In the case of ampicillin, compared with no ampicillin administration, the administration of ampicillin at concentrations >50 mg/mL with osmolarity >500 mOsm/L conferred a clear complication risk (OR, 3.093; $p = 0.008$). Similarly, Jacinto et al. found that risk solutions or medications had a sevenfold higher chance of leading to complications.[20] They defined risk solutions and medications as those with pH less than 5 or greater than 9 or with osmolarity above 350 mOsm/L.[20] In our study, compared with the absence of ampicillin, ampicillin concentrations ≤50 mg/mL led to a 1.9-fold increase in the complication risk ($p = 0.114$). Of the 215 PICs administering ampicillin at concentrations of ≤50 mg/mL in our study, 210 used ampicillin at a concentration of 50 mg/mL. Preparing ampicillin at a concentration of 50 mg/mL by using normal saline as a diluent provides an osmolarity of 493 mOsm/kg, which is close to the risk concentration mentioned above. This may explain why ampicillin concentrations ≤50 mg/mL led to a 1.9-fold increase in the complication risk in our study ($p = 0.114$). The sample size of the high cefotaxime concentration group (>50 mg/dL, $n = 14$) was not sufficient to prove the effect of high osmolarity (osmolarity >500 mOsm/L) on the complication risk. Further studies are required to examine the effect of cefotaxime concentration on the complication risk.

The body weight, GA, and insertion site did not affect the complication risk in our study. Similarly, Yuningsih et al. found that GA did not affect the risk of phlebitis.[9] However, as per the findings of Danski et al., the lower the weight of the newborn on the puncture day, the greater was the complication risk (risk ratio of 1, 1.25, and 1.29 for body weight >2500 g, between 1500 and 2400 g, and <1500 g, respectively; $p = 0.0093$).[6] Moreover, Yuningsih et al. found that VLBW infants (1000–1499 g) had a fivefold greater risk of developing phlebitis than low-birth-weight (LBW) infants (1500–2499 g).[9] In contrast to our findings, Abdelaziz et al. found that the insertion site did not affect the complication risk.[10] However, Yuningsih et al. and Suliman et al. found that the lower extremities were linked to an increased incidence of phlebitis.[3,9] Further studies are required to assess the effects of these factors on PIC complications.

4.3. Strength

This is the first cohort study to explore factors leading to complications and reducing the PIC lifespan in the Asian pediatric population. Our results provide pilot data for improving the maintenance of PICs in patients aged <4 months in clinical practice. Although studies have assessed whether CIVD or intermittent flushing is a better method for preserving PICs, these studies have used a small infusion rate (range, 0.5–2 mL/h).[8,12,19] However, our study assessed the effects of a wide range of continuous infusion rates (range, 2–20 mL/min) on the complications and patency of PICs in the pediatric population.

4.4. Limitations

Our study has some limitations. First, the major population of our study consisted of neonates with body weight >1500 g. Only 5% of the patients were VLBW and LBW

infants; therefore, our results could not be extrapolated to very and extremely preterm babies with body weight <1500 g. Second, because of limited data accessibility, we could not include all variables that may influence the PIC lifespan and incidence of complications. These variables include the PIC fixation method, effect of other medication or blood transfusion, and procedure time of catheter insertion.[3,7,9,24] Finally, the lowest continuous infusion rate used to maintain PICs was above 2 mL/h. We could not examine whether using a small continuous infusion rate (less than 2 mL/h) could improve the patency of PICs and reduce complications in comparison with that by using the intermittent flushing method.

5. Conclusion

Based on our findings, we recommend using the intermittent flushing method and intravenous medication with osmolarity <500 mOsm/L to maintain PICs. If continuous intravenous fluid is indicated, we recommend using an isotonic solution with the lowest infusion rate that can satisfy patients' needs.

Declaration of Competing Interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pedneo.2022.07.011.