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Original Article

Reducing catheter related bloodstream infection risk of infant with a prophylactic antibiotic therapy before removing peripherally inserted central catheter: A retrospective study

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Abstract *Purpose:* This study examined the efficacy of prescribing antibiotics, specifically a single dose of vancomycin, in reducing the incidence of culture-positive and culture-negative sepsis prior to the removal of peripherally inserted central catheters (PICCs).
Materials and methods: We retrospectively reviewed charts of infants who had PICCs in a tertiary level hospital during the period from 2010 to 2019. The incidence of post-catheter removal clinical sepsis between the groups with or without antibiotics was compared. The antibiotic group was defined by receiving a single dose of vancomycin or any other antibiotic prior to line removal.
Results: We enrolled 585 PICC removal episodes in 546 infants for analysis. Antibiotics were given prior to removal in 257 cases (43.9%) and not given prior to removal in 328 cases (56.1%). There were 13 episodes of post-catheter removal clinical sepsis detected within 72 h (2.2%), 2 of which were culture-positive (0.3%). A 9.3-fold decrease in the odds for clinical sepsis was observed in the antibiotic group ($p = 0.01$). The incidence of post-catheter removal

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sepsis was decreased by a single prophylactic dose of vancomycin ($p = 0.02$), whereas the use of other antibiotics showed no effect ($p = 0.35$). Logistic regression analysis demonstrated that comorbidities with gastrointestinal diseases ($p = 0.01$), PICC insertion sites in the scalp and neck ($p = 0.04$), and no vancomycin administration prior to line removal ($p = 0.02$) were independent risk factors for subsequent clinical sepsis.

Conclusion: A single prophylactic dose of vancomycin prior to PICC line removal might reduce clinical sepsis events in infants.

Introduction

A peripherally inserted central catheter (PICC) is a device inserted into a peripheral vein located in the arms, legs, or scalp and threaded into the superior vena cava or inferior vena cava for upper and lower body insertions, respectively.[1] The PICC has been widely used as a tool for administration of parenteral nutrition, vasoactive agents, or hyperosmolar medications.[2] In young infants, especially premature neonates requiring prolonged vascular access, it is not unusual to require multiple attempts at intravenous placement before successful cannulation. PICC can avoid the distress associated with multiple peripheral venipunctures and improves patient comfort.[3]

Although the use of PICC is widespread in pediatric care, it is not without risk. Its insertion and indwelling are associated with numerous complications, such as infection, bleeding, malposition, and malfunction/occlusion.[4] PICC is associated with increased risk of sepsis while the catheter is in place and even after removal.[5] It has been hypothesized that the normal bacterial skin flora migrate along the catheter at the entry site, resulting in colonization of the catheter tip.[6] Manipulation of the venous line leads to migration of these organisms along the intraluminal tract.[7] Removal of the catheter disrupts the biofilm that forms during the indwelling period, which allows the bacteria to enter the patient's bloodstream.[8] Young infants are especially vulnerable to infection because their immune defense mechanisms are immature[9]; thus, they have increased risk of post-catheter removal sepsis. In a retrospective study, clinical signs of sepsis occurred within five days after PICC removal in more than half of the cases, with peak incidence occurring within 24–72 h.[5]

Several studies have examined whether giving prophylactic antibiotics prior to the removal of central lines reduced morbidity and mortality in newborn infants, particularly in post-catheter removal-related sepsis but showed conflicting results. Three previous studies showed reduction in PICC removal-related sepsis or clinical sepsis when antibiotics were administered at the time of removal.[5,10,11] In contrast, Brooker et al.[12] and Bhargava et al.[13] did not support the use of prophylactic antibiotics prior to PICC removal. The largest study to date, conducted by Casner et al.[14] on 1,002 PICC removal cases, suggested that VLBW infants who did not receive antibiotic therapy had a 6.3-fold odds for developing culture-negative sepsis following PICC removal. In this study, we aimed to determine the effect of prescribing antibiotics prior to PICC removal, specifically a single dose of vancomycin, in reducing the incidence of clinical and culture-positive sepsis.

Methods

A retrospective review of electronic medical records was performed for patients who were admitted to the intermediate care nursery or neonatal (NICU) or pediatric intensive care units in the Taipei and Danshui branches of the MacKay Memorial Hospital between January 2010 and December 2019. Eligible patients included inborn and outborn patients aged <1 year admitted to our medical unit with a PICC line in place for at least 48 h. For patients with more than one PICC line during their hospital stay, each removal episode was analyzed as a separate event. Episodes of line removal were excluded from the analysis if the line was (1) removed because of malfunction/malposition, including occlusion or leakage, (2) still in place when the infant died or was transferred, (3) removed due to confirmed or suspected catheter-related infection, including phlebitis, (4) removed during ongoing antibiotic treatment because of a previous infection episode, (5) inserted at another hospital because that hospital may not have applied the same central line bundle during insertion, or (6) followed by replacement of a new catheter within 72 h of line removal.

Patients were divided into two groups by the presence or absence of antibiotics 12 h before PICC removal. The antibiotic group received a single dose of vancomycin 2 h prior to line removal or any other antibiotics as part of the planned antibiotic course. The single dose of prophylactic vancomycin (10 mg/kg) was infused through the PICC line over 60 min. The decision to administer a single dose of vancomycin as prophylactic antibiotic therapy was made by the attending physician based on the patient's clinical condition and physician's preference.

The indications and contraindications for a PICC line were evaluated in each patient. The PICC lines were inserted according to the standard protocol of MacKay Memorial Hospital. The procedure was conducted with using sterile gowns, caps, masks, and appropriate hand hygiene. Silicone (Bard Access Systems. Inc, Salt Lake City, Utah, United States) or polyurethane (Vygon, GmbH & Co. KG, Aachen, Germany) PICCs were used. The PICC lines were preferably inserted in the upper (antecubital veins) or lower (greater saphenous veins) extremities, and in the scalp (temporal

veins) or neck (external jugular veins) only when required. The insertion sites were covered with a transparent adhesive dressing and kept sealed until PICC removal. If the fixation length was changed, usually to adjust the catheter tip, then the dressing was changed at insertion sites every seven days with povidone-iodine (for infants with body weight >1000 gm) or normal saline (for infants with body weight <1000 gm). Radiographs were taken to confirm the position of the PICC tip. No intravenous antibiotic prophylaxis was administered prior to PICC placement.

Demographic and clinical data were collected including gestational age, postnatal age, sex, birth weight, comorbidities during PICC in use, number of attempts for PICC line insertion, PICC line position, length of the PICC line in use, number of times the PICC line required adjustment, length of total parenteral nutrition (TPN), type and number of days antibiotic therapy was administered, duration of patients under invasive mechanical ventilation, number of infectious events occurring while the catheter was indwelled, number of operations performed while the PICC line was in use, reasons for line removal, whether a single dose of vancomycin was administered prior to PICC removal, whether any other antibiotic was administered within 12 h of catheter removal, and PICC tip cultures, if collected.

Collected outcome data included (1) whether any clinical sepsis event developed after 72 h of catheter removal; (2) results of blood cultures obtained within 72 h after removal; and (3) treatment course duration if post-catheter removal-related sepsis was recognized.

Clinical sepsis is defined by the Centers for Disease Control and other previous literature which are based on clinical symptoms of systemic illness, such as fever, increased frequency of apnea, bradycardia, respiratory distress, hypotension, feeding problems, abdominal distension, and decreased activity, with initiation of antibiotic therapy but without a positive blood culture.[15,16] A workup for sepsis includes complete blood count with differential count, blood, cerebrospinal fluid, and urine cultures; C-reactive protein level measurement performed within 72 h of PICC line removal; and administration of antibiotics for at least 48 h. The duration for evaluating clinical sepsis was based on published literature on PICC line removal-related sepsis.[5,10]

In our study, PICC tip cultures were collected immediately after line removal. When post-catheter removal-related sepsis was suspected in the following 72 h, the PICC tip culture growth guided empiric antibiotic therapy, especially for the infants who did not receive antibiotics within 12 h prior to catheter removal.

Requirement for informed consent was waived. The study was approved by the Institutional Review Board of the MacKay Memorial Hospital (IRB number: 20MMHIS179e).

Statistical analysis

Student's t-test was performed to compare the characteristics between the two groups. Fisher's exact test was performed for dichotomous or ordinal variables, as appropriate, to analyze the incidence of post-catheter removal-related sepsis. Multivariate logistic regression analysis was performed to determine the risk factors for clinical sepsis following line removal; sex, gestational age, birth weight, age at PICC insertion, PICC indwelling time, PICC insertion site, PICC fixation adjustment, PICC insertion attempts, TPN administration, operations, and length of intubation with PICC in use, comorbidities with GI diseases, and single-dosage vancomycin administration were analyzed. Data were presented as mean ± standard deviation. A p-value of <0.05 was considered statistically significant.

Results

We reviewed a total of 740 patients. Among them, 585 PICC removal episodes from 546 infants met our study criteria. The flow chart for how PICC removal episodes were selected, grouped, and analyzed is presented in Fig. 1. There were 35 patients with 2 PICC line removal episodes; 2

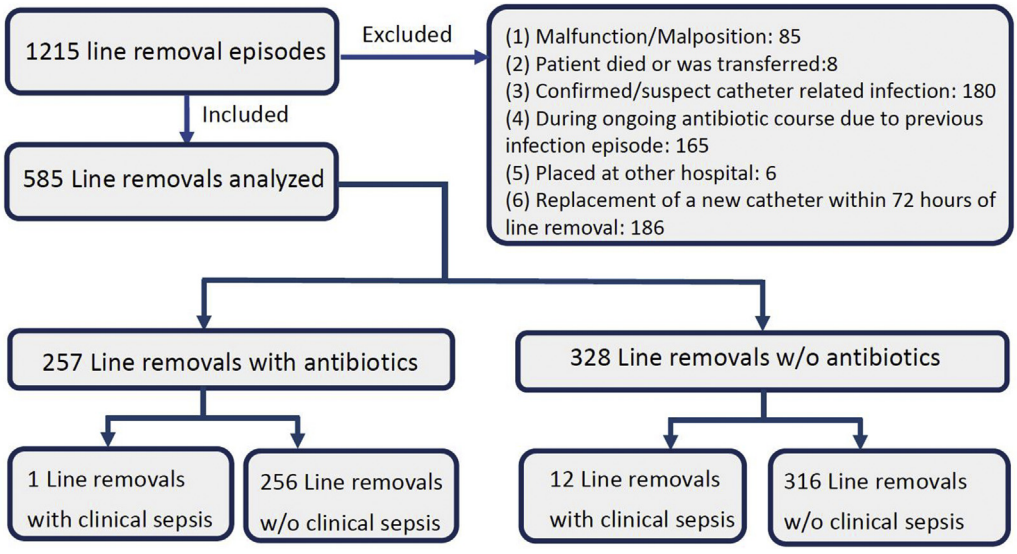

Figure 1. Flow chart of the line removal selection including recruitment, exclusion criteria, and group distribution. n = number, w/o = without.

patients had 3 line-removal events. In the 546 study patients, the mean gestational age was 29.1 ± 3.9 weeks (range 23–40 weeks), mean birth weight was 1,212.0 ± 633.0 gm (range 394–4,000 gm), with 293 (53.7%) of the subjects were male.

We evaluated each PICC removal as an individual episode. PICC lines were removed because of (1) prolonged PICC indwelling time in 18%, which required PICCs to be replaced with a new peripheral catheter or PICC set (hospital protocol dictates that catheters must be changed before the 21st day or depending on the clinical condition) and (2) resolution of indication for catheter insertion in 82%, usually upon completion of therapy or achievement of full feeding. PICCs removed due to malfunction/malposition or PICC-associated infection were excluded. Demographic and clinical data of the line removal episodes were reviewed and are summarized in Table 1. Antibiotics, including a single dose of vancomycin (223/257, 86.8%), were administered within 12 h before the removal of 257 PICCs (43.9%) in the antibiotic group, whereas antibiotics were not administered prior to the removal of 328 PICCs (56.1%). In the antibiotic exposed group, other types of antibiotics prescribed to 34 PICC cases prior to discontinuation as the end of planned therapy included penicillins: penicillin G, oxacillin, ampicillin; cephalosporins: ceftazidime, cefotaxime; carbapenems: meropenem; glycopeptides: teicoplanin, and quinolones: ciprofloxacin.

Among the 585 PICC line removal episodes, there were 13 post-catheter removal-related clinical sepsis episodes documented within 72 h (2.2%), of which two (0.3%) were blood culture-positive for methicillin-sensitive *Staphylococcus aureus* and *Klebsiella pneumoniae* in each. In the univariate analysis, we observed an association between gastrointestinal diseases with PICC in use and the onset of post-catheter removal clinical sepsis. ($p = 0.01$) There were four cases of clinical sepsis after line removal among the 82 cases of gastrointestinal diseases (6.8%) (Table 2).

There were 12 episodes of clinical sepsis in the group unexposed to antibiotics (12/328, 3.7%) and one episode received single-dose vancomycin in the group with antibiotics before line removal (1/257 0.4%). A 9.3-fold decrease in the incidence of clinical sepsis was noted in the group with antibiotics; the difference was statistically significant ($p = 0.01$). We sub-classified the antibiotic group according to the antibiotics they received, either a single dose of vancomycin or any other antibiotics as part of their planned therapy, prior to line removal. The incidence of clinical sepsis was statistically lower ($p = 0.02$) among patients who received a single prophylactic dose of vancomycin; the effect was not observed with the use of other antibiotics ($p = 0.35$). After adjusting for all confounding factors, the significant risk factors for clinical sepsis following PICC line removal were comorbidities with gastrointestinal diseases ($p = 0.01$), PICC insertion site in the scalp and neck ($p = 0.04$), and absence of a single dose of vancomycin prior to PICC removal ($p = 0.02$) (Table 3). The bacterial growth rate of the tip cultures was 2.1%. Ten cultures of coagulase-negative staphylococci (CoNS), five of aerobic gram-positive organisms, and one of *Enterococcus species* were isolated (Fig. 2).

Compared with the vancomycin antibiogram susceptibility patterns in 2010 and the results of current study, no significant differences were found over these 10 years.

Table 1 Characteristics and clinical data of the 585 PICC removal episodes.

	Episodes N = 585
Sex, male gender, No (%)	312 (53.3%)
Comorbidities, No (%)	
Respiratory tract diseases[a]	508 (86.8%)
GI diseases[b]	59 (10.1%)
CHD[c]	165 (28.2%)
CNS diseases[d]	121 (20.7%)
Renal failure[e]	66 (11.2%)
PICC insertion site, No (%)	
Four limbs (Upper limbs/Lower limbs)	527 (90.1%)
Others (Scalp and neck)	58 (9.9%)
Gestational age (weeks)	29.0 ± 3.9
Birth weight (grams)	1197.0 ± 627.7
Chronological age at PICC insertion (days)	19.3 ± 27.9
Length of PICC indwelling (days)	19.0 ± 5.1
Received TPN during PICC in use, No (%)	556 (95.0%)
TPN received during PICC in use (days)	17.2 ± 6.8
Antibiotics exposed during PICC in use (days)	5.0 ± 5.1
Mean infectious events during PICC in use (episodes)	0.2 ± 0.4
Mean operation episodes during PICC in use (episodes)	0.1 ± 0.3
Mean PICC fixation episodes adjustment (episodes)	0.3 ± 0.6

[a] Respiratory tract disease: included respiratory distress syndrome, bronchopulmonary dysplasia, chylothorax, aspiration and other condition that may induce lung function impairment or prolonged ventilation.
[b] GI diseases: gastrointestinal diseases, included necrotizing enterocolitis, intestinal perforation and other conditions that may led to mucosal destruction and impaired mesenteric perfusion.
[c] CHD: congenital heart diseases, included patent ductus arteriosus, ventricular septal defect or other congenital cardiac anomalies.
[d] CNS diseases: central nervous system diseases, included intracranial hemorrhage, intraventricular hemorrhage, epilepsy, or other CNS abnormalities.
[e] Renal failure: diagnosed when urinary output is less than 0.5–1 mL/kg/hr for a 24-hr period, and/or when the serum creatinine is above 1.5 mg/dL despite normal maternal renal function.
No = number; PICC = Peripheral inserted central catheters; TPN = Total parenteral nutrition.

Discussion

In our study, we found a statistically significant reduction in the incidence of clinical sepsis among patients who received single-dose vancomycin prior to catheter removal. Our results were similar to the results of three previous studies, which showed that the incidence of post-catheter removal-related sepsis significantly decreased in patients

Table 2 Characteristics and risk factors of the clinical sepsis within 72 h hours among the 585 PICC removal episodes.

	Clinical sepsis within 72 h (N = 13)	Non-sepsis within 72 h (N = 572)	*P* value
Sex, male gender, No (%)	10 (76.9%)	302 (52.8%)	0.09
Gestational age (weeks)	27.8 ± 3.3	29.0 ± 3.9	0.20
Birth weight (grams)	1071.5 ± 538.3	1199.4 ± 629.7	0.41
Comorbidities, No (%)			
Respiratory tract diseases[a]	11 (84.6%)	497 (86.9%)	0.81
GI diseases[b]	4 (30.8%)	55 (9.6%)	0.01
CHD[c]	5 (38.5%)	160 (28.0%)	0.41
CNS diseases[d]	2 (15.4%)	119 (20.1%)	0.63
Renal failure[e]	0 (0%)	66 (11.5%)	0.19
Chronological age at PICC insertion (days)	19.9 ± 22.4	19.3 ± 28.1	0.93
Length of PICC in use (days)	21.6 ± 5.8	19.0 ± 5.0	0.13
TPN during PICC in use, No (%)	13 (100%)	543 (94.9%)	0.41
TPN received during PICC in use (days)	20.2 ± 6.2	17.1 ± 6.8	0.11
Antibiotics exposed during PICC in use (days)	6.1 ± 3.9	4.5 ± 5.1	0.19
Infectious events during PICC in use (episodes)	0.3 ± 0.5	0.2 ± 0.4	0.42
Intubation, No (%)	8 (61.5%)	237 (41.4%)	0.15
Length of intubation during PICC in use (days)	15.1 ± 16.1	10.2 ± 16.3	0.30
Operations during PICC, No (%)	1 (7.7%)	55 (9.6%)	0.82
Mean operations frequency during PICC in use (episodes)	0.1 ± 0.3	0.1 ± 0.3	0.78
PICC insertion site, No (%)			
Four limbs (Upper limbs/Lower limbs)	3 (23.1%)/7 (53.8%)	179 (31.3%)/338 (59.1%)	
Others (Scalp and neck)	3 (23.1%)	55 (9.6%)	0.1
Attempts to insert PICC (times)	1.1 ± 0.3	1.1 ± 0.4	0.7
Mean PICC fixation adjustment (episodes)	0.4 ± 0.7	0.3 ± 0.6	0.7
Antibiotics given before PICC removal, No (%)	1 (7.7%)	256 (44.8%)	0.01
Single dosage vancomycin before PICC removal, No (%)	1 (7.7%)	222 (38.8%)	0.02

[a] Respiratory tract disease: respiratory distress syndrome, bronchopulmonary dysplasia, chylothorax, aspiration and other condition that may induce lung function impairment or prolonged ventilation.
[b] GI diseases: gastrointestinal diseases, included necrotizing enterocolitis, intestinal perforation and other conditions that may led to mucosal destruction and impaired mesenteric perfusion.
[c] CHD: congenital heart diseases, included patent ductus arteriosus, ventricular septal defect or other congenital cardiac anomalies.
[d] CNS diseases: central nervous system diseases, included intracranial hemorrhage, intraventricular hemorrhage, epilepsy, or other CNS abnormalities.
[e] Renal failure: diagnosed when urinary output is less than 0.5–1 mL/kg/hr for a 24-hr period, and/or when the serum creatinine is above 1. 5 mg/dL despite normal maternal renal function.
No = number; PICC = Peripheral inserted central catheters; TPN = Total parenteral nutrition.

who received antibiotics prior to line discontinuation.[5,10,11] Our clinical sepsis rate of 2.2% and culture-positive sepsis rate of 0.3% are much lower than those in existing literature.[5,10,11] Reynolds et al. documented a clinical sepsis rate of 10.1% (22/218) within 72 h of PICC removal.[11] Van den Hoogen et al.[5] and Hemels et al. reported post-catheter removal culture-positive sepsis rates of 6.1% (21/345) within 72 h and 5.7% (5/88) within 48 h, respectively.[10] The difference among the results may be due to patient selection discrepancies. The population in the study by Reynolds et al. was more premature (mean: 26.8 ± 2.5 weeks) with lower birth weights (mean: 862 ± 212 g),[11] whereas the population in the other two studies was more comparable as they were conducted in the same hospital and shared similar patient profiles, environment, and treatment protocols.[5,10] Our lower sepsis rate may also be credited to our rigorous and standardized PICC insertion and catheter care procedures. We also minimized PICC manipulation using the lines for parenteral nutrition or intravenous drug administration only; the PICCs were not used for hemodynamic monitoring or blood sampling.

In our study, the incidence of clinical sepsis was reduced by a single prophylactic dose of vancomycin instead of other antibiotics. In a recent large multicenter cohort study, the most common pathogens associated with PICC-related bloodstream infection in neonates were CoNS and *Staphylococcus aureus*, which accounted for more than half of the catheter infections.[17] In a retrospective study focusing on the bloodstream infection in our NICU during 2008–2013, the most common organism associated with PICC infection was CoNS (32.0%).[18] There was also a predominance of CoNS (62.5%) in the tip cultures in this study. Thus, the use of prophylactic vancomycin prior to PICC removal is a reasonable choice; it complies with the antibiogram susceptibility patterns. Reynolds et al., in a study conducted in the United States, administered vancomycin to three-fourths of their patients and gentamicin and cefotaxime to the rest.[11] As such, selection of prophylactic

Table 3 Logistic regression model for risk factors of post-catheter removal-related sepsis.

	Clinical sepsis within 72 h (N = 13)	Non-sepsis within 72 h (N = 572)	OR	95% CI	*P* value
Sex (Male), No (%)	10 (76.9%)	302 (52.8%)	3.10	0.75–12.79	0.12
Comorbid with GI diseases[a], No (%)	4 (30.8%)	55 (9.6%)	9.63	1.84–50.91	0.01
Gestational age (week)	27.8 ± 3.3	29.0 ± 3.9	0.69	0.43–1.11	0.13
Birth weight (grams)	1071.5 ± 538.3	1199.4 ± 629.7	1.00	0.99–1.00	0.56
Chronological age at PICC insertion (days)	19.9 ± 22.4	19.3 ± 28.1	0.97	0.94–1.01	0.15
PICC indwelling time (days)	21.6 ± 5.8	19.0 ± 5.0	1.06	0.82–1.35	0.67
PICC insertion site (Scalp and neck), No (%)	3 (23.1%)	55 (9.6%)	8.9	1.13–70.46	0.04
Mean PICC fixation adjustment (episodes)	0.4 ± 0.7	0.3 ± 0.6	0.88	0.34–2.32	0.80
Attempts to insert PICC (times)	1.1 ± 0.3	1.1 ± 0.4	0.43	0.07–2.59	0.35
TPN received during PICC in use (days)	20.2 ± 6.2	17.1 ± 6.8	1.03	0.83–1.28	0.78
Mean operations episodes during PICC in use (episodes)	0.1 ± 0.3	0.1 ± 0.3	0.24	0.03–1.80	0.17
Single dosage vancomycin before removal, No (%)	1 (7.7%)	222 (38.8%)	0.07	0.01–0.6	0.02
Length of intubation during PICC (days)	15.1 ± 16.1	10.2 ± 16.3	1.00	0.96–1.04	0.90

[a] GI diseases: gastrointestinal diseases, included necrotizing enterocolitis, intestinal perforation and other conditions that may led to mucosal destruction and impaired mesenteric perfusion.
No = number; PICC = Peripheral inserted central catheters; TPN = Total parenteral nutrition; n = Number.

antibiotics for reducing post-catheter removal-related sepsis should be based on the antibiotic susceptibility patterns of each region.

Several other risk factors for clinical sepsis following PICC removal were surveyed in our study. Our logistic regression model showed that diagnosis with gastrointestinal diseases during PICC in use, PICC insertion site outside of the upper or lower extremities, and catheter removal without administration of a single dose of vancomycin were associated with increased risk of post-catheter removal-related sepsis. Patients with gastrointestinal diseases were statistically associated with a higher rate of clinical sepsis after line discontinuation in both univariate and multivariate analyses. This could be because patients with gastrointestinal diseases often require prolonged parenteral nutrition; hence, the need for frequent PICC insertion or longer central line indwelling time may predispose this group to higher risk of sepsis after PICC removal. The preterm neonates, owing to their immaturities of guts or decreased intestinal integrity during diseases and operation, had potential to allow translocation of microorganisms from intestinal mucosa to bloodstream.[19–21] Among the microorganisms, CoNS were the earliest and the most abundant colonizers of the gut.[22] Recent studies have shown that CoNS leading to late-onset sepsis may be originated from the intestinal mucosal flora by genotyping and

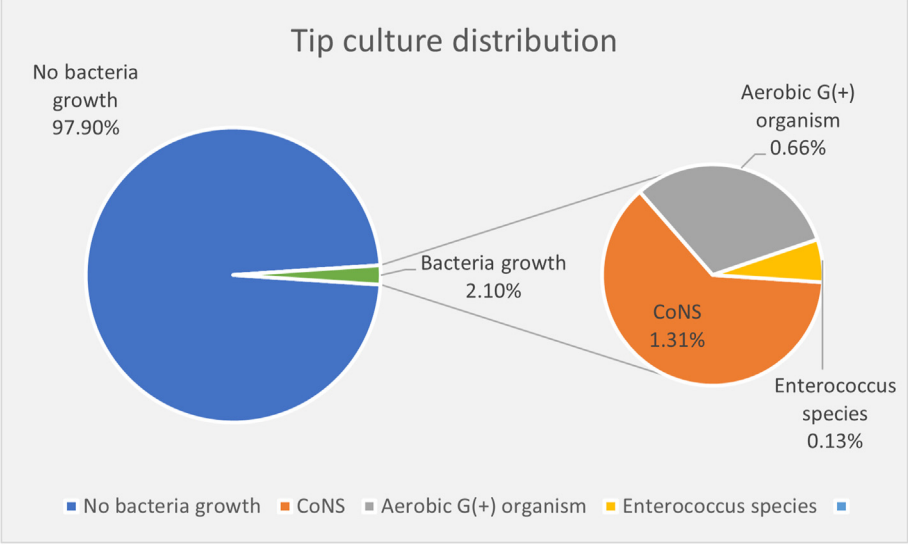

Figure 2. Organisms in the tip cultures collected after peripheral inserted central catheter removal. The figure shows the tip cultures collected after peripheral inserted central catheters (PICC) were removed. The cultured organisms include 10 coagulase-negative staphylococci (CoNS), 5 aerobic gram-positive organisms, and 1 *Enterococcus species*.

surveillance.[23–25] Extrapolating the results of these prior studies, it is reasonable that the cases with gastrointestinal diseases in our study presented with significantly higher risk of clinical sepsis after line removal. Therefore, this group requires careful attention for prevention of post-catheter removal-related sepsis.

In most clinical practice, the preferred sites for PICC insertion are the upper or lower extremities. A PICC line is usually inserted in the neck or scalp if the line cannot be inserted in the extremities. A previous study demonstrated that scalp-vein access for PICC was a safe and effective alternative route for central venous infusion in infants.[26] However, our study demonstrated there was a slightly increased risk for post-catheter removal clinical sepsis if PICC lines were inserted in these locations. PICC lines inserted in the scalp or neck were also associated with higher prophylactic antibiotic usage rates prior to catheter removal. It is equally likely that these patients had more severe medical conditions to begin with, which made inserting the PICC in the upper or lower extremities more difficult. More severe conditions also require more prolonged central venous access. As such, PICC insertions in the scalp or neck were more likely in these patients. Studies examined infectious complications based on location of the PICC insertion sites show conflicting results. One study that examined PICCs in scalp veins reported no significant difference in complication rates.[27] A recent cohort study that examined 2,574 PICCs suggested that noncentral catheters were an independent risk factor for noninfectious complications but not for infectious events.[28] Nevertheless, none of the studies examined the influence of PICC insertion sites on post-catheter removal-related sepsis rates; further studies are required.

Previous studies have shown that prolonged catheter duration increased the incidence of line infection in neonates with PICCs.[17,29] Casner et al. reported a 6.3-fold increase in the odds of culture-negative sepsis in VLBW infants with PICC indwelling time of over 21 days and no antibiotic exposure within 72 h of PICC removal in a large retrospective study.[14] While in our analysis, we found no significant difference in the PICC indwelling time between the groups with or without post-catheter removal clinical sepsis. This finding may be explained by our hospital protocol that avoids most patients with PICC indwelling duration longer than 21 days. The mean duration of PICC in place was 19.0 $\pm$ 5.1 days in our study episodes. Therefore, the extent of association with clinical sepsis following catheter removal was minimized by the short range of catheter duration.

Although our culture-positive sepsis rate was lower than the clinical sepsis rate, the effect of prophylactic antibiotic administration on post-catheter removal infection rates cannot be overlooked. The clinical symptoms observed in infants with culture-negative sepsis may be due to transient bacteremia, which is an inflammatory reaction due to extremely low colony counts of bacteria released from biofilm disruption and is not detectable in standard blood cultures. Clinical sepsis is associated with increased morbidity, prolonged antibiotic exposure, increased length of hospital stays, and increased costs. Therefore, reducing the incidence of both culture-positive and culture-negative sepsis is of clinical importance.

Our study has some limitations. First, this study was a retrospective review of cases seen in a single tertiary-level medical center. A randomized controlled trial is more ideal; however, there may be ethical issues with not administering antibiotics to a group of infants when it has been shown to reduce the risk for sepsis. Second, the number of culture-positive sepsis examined in this study is low, which made analysis in this group difficult. However, we still identified a significant reduction in post-catheter removal clinical sepsis with a single dose vancomycin, which is important for clinical practice. Lastly, there was no detailed record of the frequency of attempted venipunctures in our study, which is also a risk factor for microorganism colonization of the PICC lumen and post-catheter removal-related sepsis. The strength of our study is in our large cohort of patients. We utilized strict selection criteria and only included patients with uneventful catheter removal episodes. As such, we were able to confidently identify the value of a single dose of vancomycin in reducing the incidence of post-catheter removal clinical sepsis.

There are several measures, such as proper hand hygiene, adequate skin preparation with antibiotics, strict catheter monitoring with care bundles, implementation of designated nurse PICC teams,[30] and utilization of antimicrobial-impregnated catheters,[31] which aimed to lower overall catheter-associated infection in infants with central venous catheters. We examined the efficacy of a single dose of vancomycin hoping to minimize the burden of antimicrobial resistance. Our results suggest that a single prophylactic dose of vancomycin prior to PICC line removal might reduce the risk for post-catheter removal clinical sepsis among at-risk infants.

Declaration of competing interest

The authors have no conflicts of interest to declare.

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