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Catheter-Related Bloodstream Infections in the Pediatric Intensive Care Unit

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Catheter-related bloodstream infections (CRBSIs) are a significant complication for children treated in the pediatric intensive care unit (PICU). This review seeks to identify the epidemiology, risk factors, treatment, and prevention strategies for CRBSIs in the PICU. Factors such as catheter type, insertion site, number of lumens, indwelling time, and medications delivered all can influence the rate of CRBSIs. Prevention strategies include use of full-barrier techniques during insertion, use of chlorhexidine cleaning solutions during insertion and dressing change, strict adherence to catheter-care protocols, and removal of catheters as soon as possible after conclusion of therapy.
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Central venous catheters (CVCs) have become a mainstay for achieving vascular access in the critically ill child. As the use of CVCs in the pediatric population has grown, catheter-related bloodstream infections (CRBSIs) have become a significant complication of treatment in the pediatric intensive care unit (PICU). The Centers for Disease Control's (CDC's) National Nosocomial Infection Surveillance System (NNISS) reports a mean incidence of 7.6 infections per 1000 catheter days.[1] Multiple reviews of the infectious complications of CVC use have been conducted in the adult population,[2] but these reviews have not addressed CRBSI in the pediatric population. Because risk factors for the acquisition of infection, such as size, weight, underlying illness, type of device, and number of lumens, often are different for pediatric patients, a separate discussion of these issues in the pediatric population is warranted. This review will address the epidemiology of CRBSIs in the PICU, risk factors for acquiring infections, treatment of CRBSI, and prevention strategies for reducing the rate of CRBSIs.

Epidemiology

Review of the incidence of CRBSIs and the causative organisms is made difficult by the various terminologies used and the various definitions of those terms. Studies have reported such factors as the number of CVC tips that are colonized with bacteria, the number of positive blood cultures drawn from CVCs, and the number of positive peripheral blood cultures drawn from patients with CVCs. Additionally, some studies report the number of infections per CVC, whereas others report the number of infections per 100, 1000, or 10,000 catheter days. Compounding this difficulty is the presence of both clinical and surveillance definitions of CVC infections. Clinical definitions tend to underestimate CRBSI rates, whereas surveillance definitions tend to overestimate CRBSI rates. Additionally, some reports include data on catheter-associated bloodstream infections (BSIs). Definitions of clinical and surveillance CRBSI, as well as catheter-associated BSIs, are provided by the CDC[3] in Table 1.

Using the surveillance definition, the NNISS reports a mean rate of CRBSIs in PICUs of 7.3 per 1000 catheter days. This rate compares to 3.1 per 1000 catheter days in adult ICUs. Some studies also have reported higher nosocomial infection rates among children younger than 2 years of age.[1] Although the lack of standard definitions may render making exact comparisons among studies difficult, all evidence suggests that CRBSI rates are higher in the PICU population than in other hospitalized groups.

Multiple studies of the causative organisms for CRBSIs exist in the adult literature, but few such studies in the pediatric population exist. The NNISS survey of PICU patients identified coagulase-negative *Staphylococcus* spp. as the predominant organism associated with CRBSIs, accounting for 37.8 percent of reported cases. Other causative organisms included enterococcus (11.2%), *Staphylococcus aureus* (9.3%), enterobacter spp. (6.2%), *Candida albicans* (5.5%), *Pseudomonas areuginosa* (4.9%), and *Klebsiella pneumoniae* (4.1%), with a wide variety of bacteria, fungi, and viruses accounting for the remaining infections.

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Table 1 Categories and Definitions of CRBSIs

Category of CRBSI	Definition
Clinical CRBSI	Bacteremia/fungemia in a patient with an intravascular catheter with at least one positive blood culture obtained from a peripheral vein, clinical manifestations of infections (ie, fever, chills, and/or hypotension), and no apparent source for the BSI except the catheter. One of the following should be present: a positive semiquantitative (>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.
Surveillance CRBSI	Should meet at least one of the following criteria: Criterion 1: Patient has a recognized pathogen cultured from one or more blood cultures and the pathogen cultured from the blood is not related to an infection at another site. Criterion 2: Patient has at least one of the following signs or symptoms: fever (>100.4°F [>38°C]), chills, or hypotension, and at least 1 of the following: 1. Common skin contaminant (eg, diphtheroids, *Bacillus* spp., *Propionibacterium* spp., coagulase-negative staphylococci, micrococci) cultured from 2 or more blood cultures drawn on separate occasions 2. Common skin contaminant (eg, diphtheroids, *Bacillus* spp., *Propionibacterium* spp., coagulase-negative staphylococci, micrococci) cultured from at least one blood culture from a patient with an intravenous line, and the physician institutes appropriate antimicrobial therapy 3. Positive antigen test on blood (eg, *Hemophilus influenzae, Streptococcus pneumoniae, Neisseria meningitides,* group B streptococcus) and signs and symptoms with positive laboratory results that are not related to an infection at another site. Criterion 3: Patient aged <1 year has at least 1 of the following signs or symptoms: fever (>100.4°F [>38°C]), hypothermia (<98.6°F [<37°C]), apnea, or bradycardia, and at least 1 of the following: 1. Common skin contaminant (eg, diphtheroids, *Bacillus* spp., *Propionibacterium* spp., coagulase-negative staphylococci, micrococci) cultured from 2 or more blood cultures drawn on separate occasions 2. Common skin contaminant (eg, diphtheroids, *Bacillus* spp., *Propionibacterium* spp., coagulase-negative staphylococci, micrococci) cultured from at least 1 blood culture from a patient with an intravenous line, and the physician institutes appropriate antimicrobial therapy 3. Positive antigen test on blood (eg, *H. influenzae, S. pneumoniae, N. meningitides,* group B streptococcus) and signs and symptoms with positive laboratory results that are not related to an infection at another site.
Catheter-associated bloodstream infection (BSI)	Vascular access device that terminates at or close to the heart or one of the great vessels. An umbilical artery or vein catheter is considered a central line. BSI is considered to be associated with a central line if the line was in use during the 48-hour period before development of the BSI. If the time interval between onset of infection and device use is longer than 48 hours, then there should be compelling evidence that the infection is related to the central line.

Risk Factors

Many studies have looked at various factors thought to increase or decrease the risk of acquiring a CRBSI. As mentioned previously, the NNISS data suggest that age is a risk factor, with children younger than 2 months of age being at higher risk for acquiring a CRBSI. However, at least one study found no association between age and risk of infection.[4]

The general consensus is that underlying disease and clinical course influence the risk of acquiring an infection. Neutropenia has been shown to increase risk of developing a CRBSI.[5] Because the use of total parenteral nutrition is associated with increased infection risk in multiple studies,[6] any patient with a disease necessitating such therapy can be considered at increased risk as well. Other factors that can increase risk include the need for mechanical ventilation, admission to the PICU, preexisting infections from other sources, and existing implanted devices.

One factor strongly associated with risk of acquiring an infection is catheter dwell time. Multiple studies[7,8] in pediatric patients have established that the risk of acquiring an

infection increases with device dwell time. Of clinical importance in the PICU, the risk increases significantly in percutaneously placed lines after 7 days.[4]

The type of catheter and its placement also can influence the risk of developing an infection. Catheters can be classified into percutaneously placed CVCs, peripherally inserted central catheters (PICCs), tunneled CVCs, and totally implanted vascular access devices (TIVADs). Catheters also can be divided into valved and nonvalved types. Percutanously placed CVCs and PICCs can be placed at the bedside, whereas tunneled CVCs (in pediatric patients) and TIVADs require surgical placement. Percutanously placed CVCs have been the mainstay for central venous access in the PICU setting. They can be placed quickly at the bedside during initial management of the critically ill child. These catheters carry a higher risk of causing infection than do tunneled or implanted devices,[9] possibly because they are inserted directly through skin, which is more likely to be colonized with bacteria, and because a short path exists between the skin entry site and entry into a central vein. However, this higher risk may be attributed to the fact that these lines often are inserted in less stable patients who require more frequent access. One study evaluating the use of tunneled CVCs in PICU patients did find a lower rate of catheter colonization versus percutaneously placed lines, but no decrease in CRBSI rates.[10] For long-term (>3 months) access, TIVADs generally are considered to have the lowest risk of infection, although at least one study found no difference in infection rates between TIVADs and tunneled lines.[11] PICCs generally are considered to have a lower risk of infection than percutanously placed CVCs, but they have not been studied in the PICU population. They are recommended for patients requiring access for greater than 7 days but less than 3 months. However, PICCs can be used for as long as 1 year.

Studies of valved versus nonvalved tunneled CVCs have not shown any difference in infection rates.[12] In PICCs, valved catheters have been associated with a lower complication rate, but the differences in infection rates did not rise to the level of statistical significance.[13] Many studies have looked at the risk of single-lumen versus multilumen catheters. Most of these studies have focused on adults and found an increased risk associated with multilumen catheters.[14] However, one pediatric study found no significant difference in infection rates[15] between single- and double-lumen catheters. On balance, it would seem prudent to place a catheter with the least number of lumens needed to accomplish effective therapy. However, in the PICU, this approach may create a dilemma. Frequent manipulation of lines is a well-established risk factor for the acquisition of CRBSIs[16]; therefore, the placement of a single-lumen device that requires frequent manipulations to alternate medications or deliver incompatible medications may create a greater risk than would the placement of a multilumen line that can be left untouched for longer periods of time. One final device-related issue concerns antiseptic- or antibiotic-impregnated CVCs. Studies evaluating devices impregnated with rifampin/minocycline, silver, chlorhexidine, and a platinum/silver combination have shown lower rates of catheter colonization and CRBSI than have nonimpregnated catheters.[17,18]

Another controversial risk factor for the acquisition of CRBSI has been the site of insertion of the CVC. In adult literature, subclavian insertion generally is considered to have the lowest risk, followed by internal jugular and femoral insertions.[19] Researchers have speculated that these risk factors are the result of differences in bacterial colonization of the areas of insertion. However, most studies of pediatric patients have not reproduced this result, showing no difference in infection rates based on insertion site.[1] In fact, in tunneled lines, one study of neonates found the internal jugular site to be higher risk for infection than was a femoral insertion.[20]

Prevention Strategies

The CDC has issued comprehensive guidelines for the reduction of CRBSI.[21] The recommendations applicable to placement of CVCs in pediatric patients are included in Table 2. Additional prevention strategies may be more specific to the PICU. They include selecting therapies that minimize the need to manipulate the CVC and removal of the CVC as soon as possible after conclusion of therapy. Some utility may exist in replacing percutaneously placed CVCs with another type of CVC once a patient has stabilized and if the patient will need long-term central access. For example, a patient with sepsis from osteomyelitis might need a percutaneous CVC for the sepsis episode but also require 6 to 8 weeks of antibiotic therapy to treat the underlying osteomyelitis. Replacement of the percutanous CVC with a PICC might offer a lower risk of acquiring infection throughout the course of the therapy. No studies have addressed this issue to date, but the lower rates of infection associated with PICCs provide some evidence to support this strategy.

Conclusions

CRBSIs remain a significant complication for patients in the PICU. A lack of standard definitions renders establishing an exact quantification of these infections difficult. Risk factors for the acquisition of CRBSIs include age, underlying illness, catheter dwell time, type of catheter used, insertion site, and extent of catheter manipulation. These risks can be different for pediatric patients than for adults and are increased in the PICU setting. Strategies for reducing the rates of CRBSIs include use of maximum barrier techniques during insertion, implementation of standardized and diligent catheter maintenance and care, selection of the proper catheter and insertion site, and avoidance of routine catheter replacement. Central venous lines are likely to continue to be the mainstay of management of the PICU patient for years to come. Therefore, efforts to reduce the incidence of CRBSIs will be essential to providing the best possible outcomes for these patients.

Table 2 Recommendations for CVC Placement in Pediatric Patients

General principles	Use a CVC with the minimum number of ports or lumens essential for the management of the patient
	Designate personnel who have been trained and exhibit competency in the insertion of catheters to supervise trainees who perform catheter insertion.
	Use totally implantable access devices for patients who require long-term, intermittent vascular access. For patients requiring frequent or continuous access, a PICC or tunneled CVC is preferable.
Maximal sterile barrier precautions during catheter insertion	Use aseptic technique including the use of a cap, mask, sterile gown, sterile gloves, and a large sterile sheet, for the insertion of CVCs (including PICCs) or guidewire exchange.
Replacement of catheter	Do not routinely replace CVCs, PICCs, hemodialysis catheters, or pulmonary artery catheters to prevent catheter-related infections.
	Do not remove CVCs or PICCs on the basis of fever alone. Use clinical judgment regarding the appropriateness of removing the catheter if infection is evidenced elsewhere or if a noninfectious cause of fever is suspected.
	Guidewire exchange:
	Do not use guidewire exchanges routinely for nontunneled catheters to prevent infection.
	Use a guidewire exchange to replace a malfunctioning nontunneled catheter if no evidence of infection is present.
	Use a new set of sterile gloves before handling the new catheter when guidewire exchanges are performed.
Catheter and catheter-site care	General measures: Designate one port exclusively for hyperalimentation if a multilumen catheter is used to administer parenteral nutrition.
	Antibiotic lock solutions: Do not routinely use antibiotic lock solutions to prevent CRBSI. Use prophylactic antibiotic lock solution only in special circumstances (eg,in treating a patient with a long-term cuffed or tunneled catheter or port who has a history of multiple CRBSIs despite optimal maximal adherence to aseptic technique).
	Catheter-site dressing regimens:
	• Replace the catheter-site dressing when it becomes damp, loosened, or soiled or when inspection of the site is necessary.
	• Replace dressings used on short-term CVC sites every 2 days for gauze dressings and at least every 7 days for transparent dressings, except in those pediatric patients for whom the risk for dislodging the catheter outweighs the benefit of changing the dressing.
	• Replace dressings used on tunneled or implanted CVC sites no more than once per week, until the insertion site has healed.
	• No recommendation can be made regarding the necessity for any dressing on well-healed exit sites of long-term cuffed and tunneled CVCs.
	No recommendation can be made for the use of chlorhexidine sponge dressings to reduce the incidence of infection.
	Do not use chlorhexidine sponge dressings in neonates aged <7 days or of gestational age <26 weeks.
	No recommendation can be made for the use of sutureless securement devices.
	Ensure that catheter-site care is compatible with the catheter material.

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