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GUIDELINES

# Guidelines for the prevention of central venous catheter-related blood stream infections with prostanoid therapy for pulmonary arterial hypertension

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## SUMMARY

Intravenous prostanoids are the backbone of therapy for advanced pulmonary arterial hypertension (PAH) and have improved long-term outcome and quality of life. Currently, two prostanoids are approved by the US Food and Drug administration for parenteral administration: epoprostenol (Flolan) and treprostinil (Remodulin). Chronic intravenous therapy presents considerable challenges for patients and caregivers who must learn sterile preparation of the medication, operation of the pump, and care of the central venous catheter. Patients are routinely counseled and advised regarding the risks of CR-BSIs and catheter care before central line insertion. Central line infections as well as bacteremia are well documented risks of chronic intravenous therapy and may significantly contribute to morbidity and mortality. Recent reports have suggested a possible increase in CR-BSI; therefore, the Scientific Leadership Council of the Pulmonary Hypertension Association decided to provide guidelines for good clinical practice regarding catheter care. Although data exits regarding patients with central venous catheters and the risk of blood stream infections in patients with cancer or other disorders, there is little data regarding the special needs of patients with pulmonary arterial hypertension requiring central venous access. These guidelines are extrapolated from the diverse body of literature regarding central venous catheter care.

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The inception and completion of this document is the work of a collection of dedicated healthcare providers in the field of pulmonary hypertension medicine. It should be used as a guideline for best clinical practice. Every attempt was made to ensure the relevance and timeliness of the information included. Recent reports have suggested a possible increase in catheter-related blood stream infections (CR-BSI); therefore, the Scientific Leadership Council of the Pulmonary Hypertension Association decided to provide guidelines for good clinical practice regarding catheter care. Although data exist regarding patients with central venous catheters (CVC) and the risk of blood stream infections in patients with cancer or other disorders, there is little data regarding the special needs of patients with pulmonary arterial hypertension (PAH) requiring central venous access. These guidelines are extrapolated from the diverse body of literature regarding CVC care.

Intravenous prostanoids are the backbone of therapy for advanced PAH and have improved long-term outcome and quality of life (1–4). Currently, two prostanoids are approved by the US Food and Drug administration for parenteral administration: epoprostenol (Flolan) and treprostinil (Remodulin) (5). Chronic i.v. therapy presents considerable challenges for patients and caregivers who must learn sterile preparation of the medication, operation of the pump and care of the CVC. Patients are routinely counselled and advised regarding the risks of CR-BSIs and catheter care before central line insertion. Central line infections as well as bacteraemia are well documented risks of chronic i.v. therapy and may significantly contribute to morbidity and mortality.

The incidence of CR-BSI in 192 patients treated with epoprostenol at two PH centres (335,285 medicine days) was 0.15 per 1000 medicine days, with

 

*Staphylococcus aureus* and *Micrococcus* spp. being the most common pathogens identified (6). Recently, the Centers for Disease Control (CDC) investigated a possible increase in Gram negative CR-BSIs in patients treated with treprostinil. In a retrospective evaluation of seven centres with 51,183 i.v. prostanoid medicine days, the BSI incidence by pooled mean was higher for patients receiving treprostinil than epoprostenol (1.11 vs. 0.43). In addition, treprostinil patients had a higher incidence of gram negative bacteraemia (0.73 vs. 0.06) (7). Retrospective evaluation at two centres of 224 patients with 146,093 treatment days found the incidence of BSI for patients on epoprostenol and treprostinil was 0.55 cases per 1000 medicine days; Gram negative pathogens were reported in 0.18 cases per 1000 medicine days. Patients treated with treprostinil had higher incidence of BSI in comparison with epoprostenol (1.13 vs. 0.42 per 1000 treatment days) and a higher incidence of CR-BSI caused by Gram negative pathogens (0.81 vs. 0.04 BSI per 1000 treatment days) (8).

The mechanisms for the presumed increase in Gram negative CR-BSIs in patients receiving i.v. prostacyclins are unknown. From the literature, it is clear that Gram negative pathogens predominate in patients with malignancies or compromised mucosal barriers caused by transmigration of gut bacteria (9). In the case of pulmonary hypertension patients, it is unclear if prostacyclin therapy affects mucosal integrity, or if gut oedema from right heart failure is contributing. These will be active areas of ongoing investigation. The catheter hub is known to be an important source of CR-BSI. It is also suggested that the infusion system connections may be exposed to hydrophilic Gram negative pathogens, such as *Pseudomonas*, *Stenotrophomonas*, *Acinetobacter* and *Serratia* during bathing or showering. A closed-hub system may decrease bacterial contamination of the hub (10,11); however, the type of needleless catheter connector may also impact the incidence of CR-BSI (12,13). It is important that treating physicians keep these potential mechanisms in mind when implementing and using these guidelines.

Italics: direct quotes from *Guidelines for the Prevention of Intravascular Catheter-Related Infections* developed by the Healthcare Infection Control Practices Advisory Committee (HICPAC) of the CDC and Prevention (14).

HICPAC/CDC system for categorizing recommendations:

Category 1A: Strongly recommended for implementation and strongly supported by well-designed experimental, clinical or epidemiologic studies.

Category 1B: Strongly recommended for implementation and supported by some experimental, clinical or epidemiologic studies and a strong theoretical rationale.

Category 1C: Required by state or federal regulations, rules or standards.

Category II: Suggested for implementation and supported by clinical or epidemiologic studies or a theoretical rationale.

Unresolved issue: Represents an unresolved issue for which evidence is insufficient or no consensus regarding efficacy exists.

1. General principles (14)
   a. *Use a* cuffed and tunnelled *CVC with the minimum number of ports or lumens essential for the management of the patient. Category 1B*
   b. *No firm recommendation can be made for a preferred site of insertion to minimise infection risk for a tunnelled CVC, although the subclavian position is associated with lower overall infection risks. The risk of pneumothorax with the subclavian route should be considered. Unresolved issue*
   c. *Maintain sterile barrier precautions for insertion and aseptic technique for care of intravascular catheters. Category 1A*
   d. *Do not submerge the catheter under water. Showering should be permitted if precautions can be taken to reduce the likelihood of introducing organisms into the catheter (e.g. if the catheter and connecting device are protected with an impermeable cover during the shower.) Category II*
   e. *Swimming is not recommended. Category II*
   f. Removal of catheter is recommended if CR-BSI is clearly documented. Do not use the 'sterilise the line' approach. Category II
   g. Clearance of bacteraemia should be documented by repeat blood cultures a minimum of 4 days after institution of appropriate antibiotic therapy (ABX) and by clinical defervescence prior to reinsertion of new catheter. The time to wait postinfection to replace the central line is often based on physician judgement and may be significantly > 4 days based on pathogen and patient condition. Category II

 

h. Duration of i.v. ABX is determined both by the removal of catheter and dictated by:
   i. Type of organism.
   ii. Presence or absence of valvular heart disease (tricuspid insufficiency in PH patients). Minimum of 14 days of i.v. ABX if present and 7–10 days if absent. Category IB
   iii. Suspicion of potential endocarditis. It is recommended that a low threshold for obtaining a trans-oesophageal echocardiogram be used in the setting of *Staphylococcus* bacteraemia-related CR-BSIs. If clinical suspicion is high a minimum of 6 weeks of i.v. antibiotics is required. Category IB
   iv. Negative blood culture prior to insertion of a new catheter.

2. Hand hygiene (14)
   a. *Observe proper hand-hygiene procedures either by washing hands with conventional antiseptic-containing soap and water or with waterless alcohol-based gels or foams. Observe hand hygiene before and after palpating catheter insertion sites, as well as before and after inserting, replacing, accessing, repairing or dressing an intravascular catheter. Category 1A*
   b. *Use of gloves does not obviate the need for hand hygiene. Category 1A*
3. Catheter hub (10–12,14,15)
   a. Closed hub system with a needleless intravascular device is recommended to decrease number of times the CVC is opened. Category II
   b. Split septum needleless intravascular device may be preferred over the mechanical valve device. Mechanical valve device with flat, smooth surface for preaccess disinfection may considered. Category II
   c. Change hub device weekly in accordance with manufacturer's recommendations and after blood draws. Category II
   d. *Minimise contamination risk by wiping access port with 70% alcohol and accessing the port only with sterile devices. Category 1B*
   e. Clean threads of CVC with alcohol wipe only when visibly soiled. Routine cleaning of the catheter threads with alcohol is not recommended. Do not allow alcohol to enter end of catheter hub. Category II
   f. Do not change needleless intravascular device attached to CVC if water is present in the connection. The connection should be dry before changing to a new device. Category II
4. Catheter site care (14,16)
   a. *Use either sterile gauze or sterile, transparent semi-permeable dressing to cover the catheter site. Category IA*
   b. *No recommendation can be made regarding the necessity for any dressing on well-healed exit sites of long-term cuffed and tunnelled CVCs. Unresolved issue*
   c. *Wear clean or sterile gloves when removing the dressing on intravascular catheters. Category 1C*
   d. Use mask and sterile gloves when cleaning catheter site. Category II
   e. *Replace the catheter-site dressing when it becomes damp, loosened or soiled, or when inspection of the site is necessary. Category 1A*
   f. *Replace dressings on CVC sites every 2 days for gauze dressing and at least every 7 days for transparent dressings. Category 1B*
   g. *Replace dressing used on new tunnelled CVC sites no more than once per week, until insertion site has healed. Category 1B*
   h. *If the patient is perspiring, or if the site is bleeding or oozing, a gauze dressing is preferable to a transparent, semipermeable dressing. Category II*
   i. *Disinfect clean skin with an appropriate antiseptic before catheter insertion and during dressing changes. Although a 2% chlorhexidine-based preparation is preferred, tincture of iodine, an iodophor or 70% alcohol can be used. Category 1A*
   j. *No recommendation can be made for the use of chlorhexidine in infants aged < 2 months. Unresolved issue*
   k. *Do not use topical antibiotic ointment or creams on insertion sites because of their potential to promote fungal infections and antimicrobial resistance. Category 1A*
   l. *No recommendation can be made for the use of chlorhexidine sponge dressings to reduce the incidence of infection. Unresolved issue*
5. Prostanoid reconstitution: Category II (14,17–20)
   a. Unopened vials may be stored at ambient room temperature according to the manufacturer's storage guidance. Do not use vials beyond expiration date on vial.
   b. Access vials with needle, bevel up at 45° angle or with split septum vial adaptor for needless reconstitution.
   c. Opened vials:
      i. Epoprostenol

 

1. Single dose vial only
2. Reconstitute using the appropriate manufacturer's sterile diluent.

ii. Treprostinil
1. Multi-use vial stable up to 30 days after opening and initial vial insertion.
2. Reconstitute with 0.9% sodium chloride or sterile water for injection.
3. Vial integrity is influenced by number of vial punctures and appropriate puncture technique.
   a. Needle access: use 20-gauge needle or smaller. Vial puncture should not exceed 30 times in 30 days.
   b. Needless access: single access with split septum vial adaptor.
4. It is preferred to store opened vial in refrigerator
5. Prefilled cassettes of normal saline are not recommended. If used, recommend storing in refrigerator.

6. Prostanoid administration (14,17,19)
   a. *Replace administration sets, including secondary sets and add-on sets, no more frequently than at 72-h intervals, unless catheter-related infection is suspected. Category 1A*
   b. Filters are recommended to remove particulate matter and air, but should not be relied on as a means of infection control. *Category* 1A
   c. Do not use catheter for administration of blood products or parenteral nutrition. Category II
   d. Prostacyclins: Category II
      i. Epoprostenol:
         1. May be administered up to 48 h after reconstitution of the solution if kept cold, 36–46 °F, (2–8°C) for a total of 48 h. Twenty-four hours in refrigerator (available for emergency use); 24 h on pump with ice packs.
         2. Reconstituted epoprostenol is stable at room temperature of < 77 °F (25 °C) for up to 8 h.
      ii. Treprostinil:
         1. May be administered up to 48 h after reconstitution at room temperature (< 37 °C).
7. Normal saline and heparin flush solutions: Category II (14)
   a. Single-dose vials are preferred to multidose vials. Refrigerate multidose vials after opened. Split septum vial adaptor or needle access is recommended for multidose vials.
   b. Prefilled syringes may be used only if 'ready for sterile field'.
8. Antibiotic lock solution (14)
   *Do not routinely use antibiotic lock solutions. Use prophylactic antibiotic lock solution only in special circumstances (e.g. in treating a patient with a long-term cuffed or tunnelled catheter or port who has a history of multiple CRBSIs despite optimal maximal adherence to aseptic technique). Category II*
9. Prophylactic antibiotics (14)
   *Do not administer intranasal or systemic antimicrobial prophylaxis routinely before insertion or during use of an intravascular catheter to prevent catheter colonization or BSI. Category 1A*
10. Surveillance (14)
    *Conduct surveillance to determine CRBSI rates, monitor trends in those rates, and assist in identifying lapses in infection control practices. Category 1A*

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