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Central London Intestinal Failure Partnership

ANTIBIOTIC LINE LOCK GUIDELINES FOR TREATMENT OF CRBSI IN ADULT INTESTINAL FAILURE PATIENTS

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This document aims to provide guidelines for antibiotic line lock use for treatment of CRBSI in adult intestinal failure patients

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A. Introduction

1. CRBSI is a common complication in intestinal failure patients receiving parenteral support via long-term central venous catheters and is associated with significant morbidity and mortality. The management of presumptive CRBSI includes taking paired central and peripheral blood cultures, empirical antibiotic treatment, possible catheter removal or the use of an antibiotic lock.
2. Antibiotic locks are indicated for patients with CRBSI involving long-termcatheters with no signs of exit site or tunnel infection for whom catheter salvage is the goal. Additional systemic antibiotics are needed to treat any associated bacteraemia.
3. Antibiotic lock therapy involves instilling a high concentration of an antibiotic to which the causative microbe is susceptible in the catheter lumen. The technique is based on the reasoning that bacteria in catheter lumens are usually contained within a biofilm lining the catheter. Antibiotic locks provide high luminal concentration and longer contact times allowing the antibiotic to penetrate the biofilm and reach the organisms in sufficient concentrations to be effective.
4. The likelihood of success of antibiotic lock therapy varies with the site of infection (e.g. tunnel orpocket infection are unresponsive to salvage) and with the microbe causing the infection (e.g. coagulase-negative staphylococci are likely to respond; *S. aureus* is not).
5. Antibiotic locks should only be used on the advice of Microbiology or Infectious Diseases doctors.

B. Objectives

6. The recommendations in this guideline have been based on the Infectious Diseases Society of America (IDSA) guidelines for management of intravascular catheter-related infections. There is a paucity of data for the most appropriate dosage regimens for antibiotic locks and the recommendations in this guideline are based on published case reports and expert opinion.
   a. To maximise the clinically effectiveness of antimicrobial agents used.
   b. To reduce drug related toxicity and development of antimicrobial resistance.
   c. To ensure cost effective use of antimicrobial agents.

C. Scope

7. This guideline covers (1) the empiric management of CRBSI in adults with intestinal failure on home parenteral support and (2) the use of antibiotic locks as an adjunctive to systemic treatment for associated bacteraemia. It does not cover use of antibiotic locks for prevention of CRBSI.
8. This guideline applies to all healthcare professionals involved in the prescription, administration and management of antimicrobial agents.

D. Definitions

9. CVC Central Venous Catheter
10. IV Intravenous
11. MIC Minimal Inhibitory Concentration PICC Peripherally Inserted Central Catheter

E. Intravenous Catheter Infection

12. This section discusses the empiric antibiotic management of IV catheter-associated infection. IV catheter-associated infection may be:
    a. obvious – catheter site infection with erythema and pus
    b. strongly suggested – history of pyrexia / a rigor when the catheter is flushed
13. But at other times it may only be:
    a. suspected – fever in a patient with an IV catheter but NO other alternative source of infection / sepsis. These cases can only be confirmed retrospectively with positive blood cultures or a positive catheter tip culture following IV catheter removal
14. IV catheter-associated infection may be considered to be:
    a. local (exit site infection)
    b. local but with systemic signs
    c. systemic with NO local signs

F. Systemic infection (with or without local infection)

Diagnosis

15. Systemic infection may present as pyrexia, sometimes with a rigor after flushing the IV catheter, generally feeling unwell, tachycardia, hypotension or shock.
16. Signs of infection at the catheter site include erythema, tenderness at the exit site / insertion site / skin over the tunnel / port pocket, with or without pus.

Management

17. Take blood cultures as per guidelines. This includes blood cultures from all lumens of the IV catheter, including peripherally if possible. Take a wound swab if appropriate.
18. Start empirical antibiotics as listed below.

Empiric antibiotictreatment	**Teicoplanin** 400mg or 6mg/kg if >70kg (max 1g per dose) IV bd for 3 dosesthen 400mg or 6mg/kg if >70kg (max 1g per dose) IV od

Catheter removal

19. Catheter salvage may be possible if the catheter site is not tender and the patient is not hypotensive.
20. In septic shock, if the catheter is felt to be the likely source, it is almost always appropriate to remove the catheter urgently.
21. In a non-tunnelled CVC exit site infection with pus the catheter should be removed immediately unless there are significant reasons not to.
22. In a tunnelled CVC, implantable port or PICC a superficial exit site infection will often resolve with antibiotic treatment but an infection involving the skin tunnel above the cuff or a port pocket is impossible to treat with antibiotics and requires catheter removal.
23. The date and time of catheter removal must be documented.
24. If the IV catheter is not removed use an antibiotic lock.

Ongoing management

25. If a positive blood culture a microbiologist will call the clinical team and
    a. report the gram stain microscopy result
    b. review the empiric antimicrobial prescribing and the IV catheter if not previously removed
    c. later phone with the identity and susceptibility of the blood culture isolate(s)
    d. adjust the antimicrobial prescribing, including the route and duration of treatment according to the specific pathogen.
26. Otherwise discuss with Microbiology and:
    a. check the wound swab culture and, if sent, the catheter tip culture result
    b. adjust the empiric antimicrobial prescribing at 48 hours

Microorganisms and the need for catheter removal

27. Catheter removal is mandatory for infections caused by Candida spp.
28. Catheter removal is recommended for infections caused by specific more virulent organisms:
29. Staphylococcus aureus and Pseudomonas aeruginosa.
30. CRBSI caused by some other bacteria may also require catheter removal because of persistent colonisation: Klebsiella spp., Stenotrophomonas maltophilia, and Acinetobacter spp., Corynebacterium jeikeium. Single isolates require confirmation with repeat blood cultures taken ideally from all lumens of the catheter and peripherally.
31. Although usually less pathogenic, persistent infection with coagulase-negative staphylococci may also necessitate catheter removal.

G. Local infection (excluding those related to small cannulas)

Diagnosis

32. Local infection may present as erythema and tenderness at the exit site / insertion site / skin over the tunnel / port pocket, with or without pus.

Management

33. In a non-tunnelled CVC exit site infection with pus the catheter should be removed immediately unless there are significant reasons not to.

34. In a tunnelled CVC, implantable port or PICC a superficial exit site infection will often resolve with antibiotic treatment. Infections involving the skin tunnel above the cuff or the port pocket are very difficult to treat and require catheter removal.
35. Send a wound swab or IV catheter tip, if removed, for culture

Empiric management	**Teicoplanin** 400mg or 6mg/kg if >70kg (max 1g per dose) IV bd for 3doses then 400mg or 6mg/kg if >70kg (max 1g per dose) IV od
Specific pathogen	Discuss with Microbiology

Ongoing management

36. Discuss with Microbiology
    a. Check the wound swab culture and, if sent, the catheter tip culture result.
    b. Adjust the antimicrobial prescribing at 48 hours, including the route and duration of treatment according to any specific pathogen.

H. Antibiotic locks

37. Antibiotic locks may be used as an adjunctive to systemic treatment for associated bacteraemias.
38. The antibiotic solution is instilled or “locked” into each catheter lumen during periods when the catheter is not being used.
39. Rapidly decreasing antibiotic concentrations may occur over time in the distal lumen of catheters instilled with an antibiotic lock, especially among ambulatory patients with femoral catheters. Thus, the antibiotic concentration used for locking should be at least 1000 times higher than the minimal inhibitory concentration of antibiotic for the bacterium (the MIC is the lowest concentration that will inhibit the growth of the bacterium). So a catheter infection caused by a coagulase negative staphylococcus (typically with a teicoplanin MIC of 1mg/L) can be locked using teicoplanin (concentration of 10mg/mL = 10 000mg/L).

Antibiotic lock concentrations to be used (adapted from refs 1,2; also used refs 3-6)

40. The most commonly used antibiotic concentrations are shown below. Any remaining antibiotic in the vial should be discarded.

Drug	How to make up the antibiotic lock	Final Concentration
Vancomycin	Reconstitute a 500mg vial with 9.8mL water for injections. Draw up 2mL of this solution and further dilute it to 10mL with sodium chloride 0.9%	10mg/mL
Teicoplanin	Reconstitute the 200mg vial with the ampoule of water for injections provided. Draw up 1mL of this solution and dilute to 6.7mL with sodium chloride 0.9%	10mg/mL
Gentamicin	Draw up the contents of one 80mg/2mL vial and furtherdilute to 16mL with sodium chloride 0.9%	5mg/mL
Amikacin	Draw up the contents of a 100mg/2mL vial and dilute to20mL with sodium chloride 0.9%	5mg/mL
Ciprofloxacin	Ready diluted. Do not further dilute.	2mg/mL

Antibiotic lock volumes

41. If the fill (luminal) volume is clearly marked on the lumen, use that volume for the antibiotic lock even if the catheter is known to have been trimmed.
42. Where the fill (luminal) volume is not printed on the lumen, use the guide below for antibiotic lock volume.
43. When using lumens for antibiotic locks, it is important to ensure the "locked" lumen is easy to identify e.g. attach a label to the locked catheter.

Type of CVC catheter	Lumen volume (if not marked on lumen)[7]
PICC	1mL per lumen
Hickman catheter	2mL per lumen
Portacath	2mL per lumen
Vascath	2mL per lumen
Temporary CVC (e.g. jugular / femoral)	0.5mL per lumen

Addition of heparin to catheter lock

44. Addition of heparin is not generally recommended. There is poor evidence of the role of heparin in reducing central venous catheter thrombosis.
45. In addition, precipitation occurs when some antibiotics are mixed with heparin, especially with increasing antibiotic concentrations.

Antibiotic lock dwell time

46. Ideally the antibiotic lock should be left in place for 24 hours and generally should not exceed 48 hours before re-installation. If necessary the catheter may be used between antibiotic locks unless this gives rise to rigors or fever.
47. For in-patients, the antibiotic lock should be aspirated and replaced every 24 hours. For patients on thrice-weekly dialysis, the antibiotic lock solution can be changed after every dialysis session.

Re-installation of the antibiotic locks

48. The antibiotic lock should be aspirated before infusion of the next dose of the antibiotic lock, other intravenous medication or solution.
49. Where it is difficult to aspirate the lock due to bleed back, the lock may be flushed through systemically.

Duration of antibiotic lock therapy1

50. Although the duration of antibiotic lock therapy has varied substantially among different studies (3-30 days), most studies have used 2-week duration.
51. If antibiotic lock therapy is used in conjunction with systemic antimicrobial therapy for catheter-associated infection, treat for 7–14 days.
52. For patients with multiple positive catheter-drawn blood cultures that grow coagulase-negative staphylococci or gram negative bacilli and concurrent negative peripheral blood cultures, a trial of antibiotic lock therapy may be used without systemic therapy for 10–14 days.

I. References

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