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REVIEW ARTICLE

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Strategies for prevention of catheter-related bloodstream infections

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Abstract Prevention of catheter-related bloodstream infections is critically dependent on an accurate knowledge of the two main routes by which intravascular devices become contaminated: the extraluminal (skin-related) and the intraluminal (hub-related) routes. Extraluminal catheter seeding results from infection of the catheter entry site by microorganisms and leads to bacteremia most often during the week following catheter placement. The main ways of preventing it are appropriate skin disinfection and the adoption of maximal antiseptic barriers at the time of catheter insertion. Avoiding the internal jugular and the femoral veins, whenever possible, will reduce the likelihood of bacteremia. Intraluminal contamination is the consequence of improper handling of the catheter hub at the time of connection and disconnection of the administration set. It is the most common origin of catheter infections after the first week of catheter placement. Multiple-lumen catheters, side-ports and multipurpose catheters particularly increase the risk of endoluminal contamination. To prevent it, strict asepsis should be observed in hub handling and hubs should be protected against environmental soiling with an antiseptic impregnated gauze at all times. New technology is available for prevention of catheter infections: antibiotic and antiseptic-coated catheters, antiseptic hubs, disinfecting caps and flushing solutions are currently undergoing scientific assessment.

Key words Catheter · Bloodstream infections · Skin · Hub · Prevention

Introduction

Catheter-related bloodstream infection (CRBI) is the most frequent cause of hospital-acquired bacteremia (1). In the United States, 400,000 episodes of CRBI may occur every year (2), with a mean cost of 3,700 $ per episode and an average prolongation of hospital stay by 1 week (3). Around 20% of patients with CRBI die, and in one third of these cases death can be directly attributed to CRBI. The risk of CRBI is higher with either short-term or long-term central venous catheters (1–20%) than with peripheral cannulae, Swan-Ganz or arterial catheters (0–7%) (4). Well-known risk factors are the access site, emergency insertion, multiple manipulations and number of catheter lumens.

Pathogenesis of CRBI

For successful implementation of strategies for CRBI prevention, it is essential that the health care personnel dealing with intravascular access devices have precise knowledge of the mechanisms by which catheters become contaminated.

Although it has long been believed that catheters are contaminated almost exclusively by microorganisms

present at the skin entry site, it is now widely accepted that most of the CRBI associated with long-term catheters (>10 days) stem from endoluminal bacterial seeding from the catheter hub. Thus, it is now established that the main routes by which microorganisms gain access to an intravascular device are the extraluminal (skin-related) route and the endoluminal (hub-related) route. Contamination can also originate, albeit rarely, from bacteremia arising from a distant focus (hematogenous seeding) or from contaminated fluids or parenteral nutrition mixtures.

The extraluminal route

The implication of skin microorganisms in CRBI has been exhaustively documented by both conventional and molecular biology bacterial identification techniques (5, 6, 7). Contamination of the insertion wound is followed by capillary progression of microorganisms (6), which then adhere to the catheter's external surface until a critical number is reached after which they pass into the bloodstream. The highest risk for skin-related infection – as in general for all clean surgical wounds – is during the first week after insertion, although catheter site infection in implanted devices has been well documented even years after the implantation procedure. Different skin areas have different levels of risk of skin-related infections, probably as the result of local conditions, such as bacterial density, skin pH and/or facilitating conditions (hair, wrinkling, etc.). The insertion areas can be classified from low to high risk of extraluminal infection as follows: antecubital fossa < subclavian < femoral < jugular (8).

The endoluminal route

In the mid-1980s it was evident that some findings relating to CRBI could not be explained with reference to the extraluminal contamination route. Many patients with CRBI did not have clinical infection at the insertion site; others experienced CRBI associated with loosening of the catheter–infusion set junction; in some studies, bacteria present in the catheter tip and blood did not match those recovered at the catheter entry site. These facts were correctly interpreted when the relevance of endoluminal contamination was recognized (9, 10). Cultures of the inner surface of the catheter hub showed that in TPN catheters that were in place for a mean of 3 weeks the main route of contamination was via the endoluminal hub (11, 12). At that time, it was suggested that the recognition of endoluminal contamination would substantially change the strategies for prevention, diagnosis and treatment of CRBI (10). Catheter hubs are contaminated during manipulation of the junctions when microorganisms present on the external hub surface or in the vicinity (patient's skin, tracheostomy, wounds) are transferred to the hub lumen by the fingers of the nurse or physician handling them (13). Multiple-lumen catheters and multiple sideports increase the patient's risk of acquiring infection through endoluminal contamination.

Microbiology

The three most common types of organisms causing CRBI are the skin commensals coagulase-negative staphylococci (usually *S. epidermidis*), *Staphylococcus aureus* and *Candida* spp. More rarely, gram-negative bacilli such as *Pseudomonas* spp., *Acinetobacter* spp., *X. maltophilia*, enteric organisms and enterococci are implicated (14). CRBI caused by *X. maltophilia* or *Enterobacter* spp. should alert medical staff to the presence of fluid contamination.

Prevention of CRBI

Vascular catheterization brings about an unphysiological continuity of the densely contaminated external milieu with the bloodstream along two interfaces: the outer catheter surface and the catheter lumen. Preventing bacterial progression along these two breaches could ideally be achieved by permanent skin antisepsis at the catheter insertion site and by creation of an antiseptic barrier at the hub(s) level. In any circumstances, protocols aiming at CRBI prevention must focus on strategies to prevent both extraluminal and endoluminal contamination. It is unfortunate that the recently approved CDC "Guideline for prevention of intravascular-device-related infections" focuses exclusively on prevention of extraluminal contamination and offers no advice on hub protection (15). This should be amended in future recommendations if this guideline is to make a significant impact on the overall CRBI rates throughout the world.

Prevention of extraluminal contamination

Aseptic catheter insertion

Central venous catheter placement must be performed with maximal sterile barriers. Raad et al. (16) compared two groups of patients undergoing central venous catheter placement with or without maximal aseptic barriers (large drape, sterile gloves, gown, cap and mask). Maximal asepsis was associated with a sixfold improvement in the CRBI rates. As expected from a surgical point of view, in the control group, two thirds

of the CRBI occurred during the first week after catheter placement. A similar experience has been published regarding insertion of pulmonary artery catheters (17).

Skin antisepsis

Permanent exit site antisepsis is a difficult goal, but substantial progress has been made recently. Two studies have suggested the superiority of chlorhexidine-containing antiseptic solutions over iodine solutions or 70% alcohol (18, 19), particularly for the eradication of gram-positive cocci. Although transparent dressings are widely used, a meta-analysis suggests that the incidence of catheter tip colonization is higher when these are used instead of the conventional "gauze and tape" dressings (20).

Scheduled catheter replacement

Routine replacement of catheters over a guidewire every third day does not confer better protection against CRBI than replacement only when clinically indicated and, in fact, may increase the risk of infections (21). There is now growing consensus that central venous catheters should not be routinely replaced.

Endoluminal contamination

Aseptic hub handling

Aseptic handling of the catheter hub(s) is the cornerstone of prevention of endoluminal contamination. In addition, proper junctional care implies reducing the number of connections, separating the hub from the patient's skin and protecting the hub from environmental soiling at all times (22). Reducing the number of times the infusion sets are changed has helped to lessen manipulation of the hubs and consequently to reduce the chance of bacterial contamination (23).

Reduction of numbers of access ports and catheter lumens

Brismar et al. (24) have documented bacterial contamination of side-ports and stopcocks. Three-way stopcocks should be handled aseptically and must remain protected from environmental soiling, particularly when not connected to an infusion set. The use of multiple-lumen catheters increases the risk of CRBI (25, 26).

External appliances for hub protection

Hubs can be contaminated by organisms present on the patient's own skin, blankets, tracheostomies, intestinal fistulas, bladder catheters or infected surgical wounds, which are transferred to the hub by the hands of health care workers. Applying a gauze impregnated with povidone iodine around the catheter hub proved successful in controlling an epidemic of catheter sepsis caused by coagulase-negative staphylococci in our unit (23). In a controlled prospective trial (27) patients with tunneled Silastic central catheters were randomized to two groups, one (control group) managed in a standard fashion and the other managed by applying a betadine-impregnated foam around the junction between the catheter and the administration set. A 24% CRBI rate was demonstrated in the control group, while not a single case of bacteremia was found in patients whose hubs had been protected.

Antibiotic flushing

Flushing central lines with vancomycin has been shown to prevent CRBI in neonates (28, 29, 30). This practice probably delays or prevents endoluminal staphylococcal seeding. The routine infusion of antibiotics should be discouraged, however, since it may predispose patients to bacteremias caused by resistant microorganisms and to the development of resistance to the antibiotic (mainly by enterococci) and it increases the cost of catheter maintenance.

New catheter hub designs

Strict aseptic manipulation of conventional Luer connectors is cumbersome and expensive. Frequent, thorough hand-washing is essential. For this reason, protocol violations during catheter manipulations are common. For patients receiving i.v. therapy at home, training becomes painstaking and lack of compliance results in recurrent catheter infections. A solution to the problem of endoluminal contamination should be afforded by hubs incorporating antibacterial barriers. Connectors based on the piggyback concept have been shown to reduce CRBI in cases of prolonged central venous catheterization (31). The piggyback systems do not incorporate an antibacterial mechanism, however, relying on proper disinfection of the rubber membrane before puncturing. Brismar et al. (24) have shown that 10–20% of piggyback side-ports punctured six times a day become colonized. In addition, piggyback ports require a locking mechanism.

A new hub model adopting the piggyback concept and incorporating an antiseptic barrier (3% iodinated

alcohol) has been developed in our Department of Surgery. In vitro and in vivo studies (32, 33) have shown that deliberate contamination of the male component of the new hub does not result in endoluminal contamination. In a clinical trial, 151 patients with central venous catheterization for a mean of 2 weeks were randomized to receive catheters with standard Luer-lock connectors or connectors protected with Segur-Lock (34). The CRBI rate was higher in the control group (16% vs 4%), and this was due to the low rate of hub-related CRBI observed in the group fitted with the new hub (1% vs 11%, $P<0.01$). Handling of junctions equipped with this hub is simplified, since it does not require strict asepsis, which means substantial savings in dressing time and disposable materials.

Controversial issues in the prevention of CRBIs

Tunneling of catheters

Tunneling of central venous catheters per se has not been shown to reduce CRBI rates (35, 36, 37). Timsit et al., however, found that for the high-risk short-term internal jugular catheters, tunneling to the subclavian skin area significantly reduced the CRBI rates (38). What these authors did was essentially to convert an internal jugular catheter into a subclavian one. Therefore, rather than proving the efficacy of tunneling per se, their data underline once more the fact that subclavian catheters are the less prone to cause bacteremia originating from the catheter exit site than internal jugular ones.

Silver-impregnated cuffs

A silver-impregnated cuff attached to the catheter and left below the skin insertion site has been found to reduce the risk of extraluminal contamination in short-term catheters (39). Subsequent reports, however, suggest that in long-term intravenous catheterizations such catheters do not perform any better than conventional uncuffed catheters (40, 41), either because in this setting endoluminal contamination is more common (42) or because the anti-infective activity of the silver-impregnated collagen cuff is short lived or both.

In conclusion, CRBI is a preventable disease, and evidence-based protocols for intravascular catheter care should therefore be established in all institutions. These should take into account the two most common routes through which intravascular devices become contaminated: the skin at the catheter exit site and the hub. Failure to do this will inevitably lead to insufficient prevention. Accordingly, preventive strategies should aim at achieving consistent and permanent antiseptic barriers during catheter insertion, site maintenance and hub handling. Since aseptic techniques for catheter manipulation are time consuming and expensive and require trained personnel, who are not always available, new technologies should aim at making intravascular devices more resistant to bacterial and fungal colonization.

References

1. Vallés J, León C, Alvarez-Lerma F (1997) Nosocomial bacteremia in critically ill patients: a multicenter study evaluating epidemiology and prognosis. Clin Infect Dis 24:387–395
2. Raad I, Darouiche R (1996) Prevention of infections associated with intravascular devices. Curr Opin Crit Care 2:361–365
3. Arnow PM, Quimosing EM, Beach M (1993) Consequences of intravascular catheter sepsis. Clin Infect Dis 16:778–784
4. Rello J, Jubert P, Esandi E, Vallés J (1997) Specific problems of arterial, Swan-Ganz, and hemodialysis catheters. Nutrition 13 (Suppl):36S–41S
5. Widmer A (1993) I.V.-related infections. In: Wenzel RP (ed) Prevention and control of nosocomial infections. Williams and Wilkins, Baltimore, pp 556–579
6. Cooper GL, Schiller AL, Hopkins CC (1988) Possible role of capillary action in pathogenesis of experimental catheter-associated dermal tunnel infections. J Clin Microbiol 26:8–12
7. Maki DG (1992) Infections due to infusion therapy. In: Bennet JV, Brachman PS (eds) Hospital infections. Little, Brown, Boston, pp 849–898
8. Moro ML, Franco E, Cozzi A (1994) The central venous catheter-related infections study group. Risk factors for central venous catheter-related infections in surgical and intensive care patients. Infect Control Hosp Epidemiol 15:253–264
9. Sitges-Serra A, Liñares J (1983) Bacteria in total parenteral nutrition catheters: where do they come from? (letter). Lancet I:668
10. Sitges-Serra A, Liñares J, Garau J (1985) Catheter sepsis: the clue is the hub. Surgery 97:355–357
11. Sitges-Serra A, Puig P, Liñares J, Pérez JL, Farreró N, Jaurrieta E, Garau J (1984) Hub colonization as the initial step in an outbreak of catheter related sepsis due to coagulase negative staphylococci during parenteral nutrition. JPEN J Parenter Enteral Nutr 8:668–672
12. Liñares J, Sitges-Serra A, Garau J, Pérez JL, Martín R (1985) Pathogenesis of catheter sepsis: a prospective study using quantitative and semiquantitative cultures of catheter hub and segments. J Clin Microbiol 21:357–360
13. De Cicco M, Panarello G, Chiaradia V, Fracasso A, Veronesi A, Testa V, Santini G, Tesio F (1989) Source and route of microbial colonisation of parenteral nutrition catheters. Lancet II:1258–1260

14. Raad II, Darouiche RO (1996) Catheter-related septicemia: risk reduction. Infect Med 13:807–812, 815–823
15. Pearson ML, Hospital Infection Control Practices Advisory Committee (1996) Guideline for prevention of intravascular-device-related infections. Infect Control Hosp Epidemiol 17:438–473
16. Raad II, Hohn DC, Gilbreath J, Suleiman N, Hill LA, Bruso PA, Marts K, Mansfield P, Bodey GP (1994) Prevention of central venous catheter-related infections by using maximal sterile barrier precautions during insertion Infect Control Hosp Epidemiol 15:231–238
17. Mermel LA, McCormick RD, Springman SR, Maki DG (1991) The pathogenesis and epidemiology of catheter-related infection with pulmonary artery Swan-Ganz catheters: a prospective study utilizing molecular subtyping. Am J Med 91 (Suppl):197S-205S
18. Maki DG, Ringer M, Alvarado CJ (1991) Prospective randomised trial of povidone-iodine, alcohol and chlorhexidine for prevention of infection associated with central venous and arterial catheters. Lancet 338:339–343
19. Mimoz O, Pieroni L, Lawrence C, Edouard A, Costa Y, Samii K, Brun-Buisson C (1996) Prospective, randomized trial of two antiseptic solutions for prevention of central venous or arterial catheter colonization and infection in intensive care unit patients. Crit Care 24:1818–1823
20. Hoffmann KK, Weber DJ, Samsa GP, Rutala W (1992) Transparent polyurethane film as an intravenous catheter dressing. A meta-analysis of the infection risks. JAMA 267:2072–2076
21. Cobb DK, High KP, Sawyer RG (1992) A controlled trial of scheduled replacement of central venous and pulmonary-artery catheters. N Engl J Med 327:1062–1068
22. Stotter AT, Ward H, Waterfield AH, Hilton J, Sim AJ (1987) Junctional care: the key to prevention of catheter sepsis in intravenous feeding. JPEN J Parenter Enter Nutr 11:159–162
23. Sitges-Serra A, Liñares J, Pérez JL, Jaurrieta E, Lorente L (1985) A randomized trial on the effect of tubing changes on hub contamination and catheter sepsis during parenteral nutrition. JPEN J Parenter Enteral Nutr 9:322–325
24. Brismar B, Jordahl L, Nystrom B, Petterson N (1982) Bacterial contamination of intravenous line side ports of different designs. Clin Nutr 6:31–36
25. Clark-Christoff N, Watters VA, Sparks W, Snyder P, Grant JP (1992) Use of triple-lumen catheters for administration of total parenteral nutrition. JPEN J Parenter Enteral Nutr 16:403–407
26. Hilton E, Haslett TM, Borenstein MT, Tucci V, Isenberg HD, Singer C (1988) Central catheter infections: single versus triple-lumen catheters. Influence of guide wires on infection rates when used for replacement catheters. Am J Med 84:667–672
27. Halpin DP, O'Byrne P, MacEntee G, Hennessy TPJ, Stephens RB (1991) Effect of a betadine connection shield on central venous catheter sepsis. Nutrition 7:33–34
28. Spafford PS, Sinkin RA, Cox C, Reubens L, Powell KR (1994) Prevention of central venous catheter-related coagulase-negative staphylococci sepsis in neonates. J Pediatr 125:259–263
29. Kacica MA, Horgan MJ, Ochoa L (1994) Prevention of gram-positive sepsis in neonates weighing less than 1,500 grams. J Pediatr 125:253–258
30. Schwartz C, Henrickson KJ, Roghman K, Powell K (1990) Prevention of bacteremia attributed to luminal colonization of tunneled central venous catheters with vancomycin-susceptible organisms. J Clin Oncol 8:1591–1597
31. Inoue Y, Nezu R, Matsuda H, Fujii M, Nakai S, Wasa M, Takagi Y, Okada A (1992) Prevention of catheter-related sepsis during parenteral nutrition: effect of a new connection device. JPEN J Parenter Enteral Nutr 16:581–585
32. Segura M, Alía C, Oms LI, Sancho JJ, Torres Rodríguez JM, Sitges-Serra A (1989) In vitro bacteriological study of a new hub model for intravascular catheters and infusion equipment. J Clin Microbiol 27:2656–2659
33. Segura M, Alía C, Valverde J, Franch G, Torres-Rodríguez JM, Sitges-Serra A (1990) Assessment of a new hub design and the semiquantitative catheter culture method using an in vivo experimental model of catheter sepsis. J Clin Microbiol 28:2551–2554
34. Segura M, Alvarez F, Tellado JM, Jiménez-Farreres J, Oms L, Rello J, Baró T, Sánchez R, Morera A, Mariscal D, Marrugat J, Sitges-Serra A (1996) A clinical trial on the prevention of catheter-related sepsis using a new hub model. Ann Surg 223:363–369
35. Meyenfeldt MMF, Stapert J, De Jong PCM, Soeters PB, Wesdorp RIC, Greep JM (1980) TPN catheter sepsis: lack of effect of subcutaneous tunnelling of PVC catheters on sepsis rate. JPEN J Parenter Enteral Nutr 4:514–517
36. Sitges-Serra A, Liñares J (1984) Tunnels do not protect against venous-catheter-related sepsis (letter). Lancet I:459–460
37. Andrivet P, Bacquer A, Ngoc CV, Ferme C, Letinier JY, Gautier H, Gallet CB, Brun-Buisson C (1994) Lack of clinical benefit from subcutaneous tunnel insertion of central venous catheter in immunocompromised patients. Clin Infect Dis 18:199–206
38. Timsit JF, Sebille V, Farkas JC, Misset B, Martin JB, Chevret S, Carlet J (1996) Effect of subcutaneous tunneling on internal jugular catheter-related sepsis in critically-ill patients. A prospective randomized multicenter study. JAMA 276:1416–1420
39. Maki DG, Cobb L, Garmann JK, Shapiro JM, Ringer M, Helgerson RB (1988) An attachable silver-impregnated cuff for prevention of infection with central venous catheters: a prospective randomized multicenter trial. Am J Med 85:307–314
40. Groeger JS, Lucas AB, Coit D, Laquaglia M, Brown AE, Turnbull A, Exelby P (1993) A prospective, randomized evaluation of the effect of silver impregnated subcutaneous cuffs for preventing tunneled chronic venous access catheter infections in cancer patients. Ann Surg 218:206–210
41. Norwood S, Hajjar G, Jenkins L (1992) The influence of an attachable subcutaneous cuff for preventing triple lumen catheter infections in critically ill surgical and trauma patients. Surg Gynecol Obstet 175:33–35
42. M. Girvent, Sitges-Serra A (1995) Pathogenesis of catheter related sepsis (letter). Ann Surg 221:115–116