

Epidemiology of bloodstream infection associated with parenteral nutrition

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Epidemiology: Catheter-related bloodstream infections (CR-BSIs) occur in 1.3% to 26.2 % of patients with central venous catheters used to administer parenteral nutrition (PN). Because of their nutritional components, PN solutions can support microbial growth. Contamination during preparation and handling is rare in hospitals and home-infusion pharmacies but may be difficult to control in a home setting. The risk of infection is increased in hospitalized patients because of malnutrition-associated immunosuppression, hyperglycemia exacerbated by dextrose infusion, microbial colonization/contamination of catheter hubs and the skin surrounding insertion site, and poor nursing care. During long-term catheter use for PN, an intraluminal biofilm, catheter-tip fibrin sheath or tail, or central venous thrombosis creates sites for microbial seeding and infection. Chronic conditions and psychosocial issues also increase the risk of infection. In hospitalized patients with BSIs, the most common organisms are coagulase-negative *staphylococcus*, *Staphylococcus aureus*, *Enterococcus*, *Candida* spp, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*. In the long-term PN population, approximately 60% of CR-BSIs are caused by coagulase-negative *Staphylococcus*.

Treatment: The best plan of care for a suspected or known infected catheter in a hospitalized patient is to reinsert a new central line after 48 hours of antibiotic treatment and negative blood cultures. In patients who receive long-term PN, hospitalization increases the risk of a nosocomial infection because the catheter can be contaminated by staff. A patient with fungemia must always be admitted and catheter removed. With gram-positive and gram-negative organisms, the catheter may not need to be removed. In most patients receiving PN at home, removing a long-term venous-access device is challenging. Peripheral vein access or peripherally inserted central catheters are needed until a new permanent device can be inserted after negative blood cultures are obtained. Evaluation of remote site infection also is necessary. Strategies to reduce or prevent infection include catheter lock therapy, daily evaluation of continued need for PN, enteral rather than PN support, and avoiding overfeeding. More studies are needed to demonstrate conclusively the benefits of immunonutrition, such as the use of omega-3 or glutamine supplements to reduce CR-BSIs in patients receiving PN. (Am J Infect Control 2008;36:S173.e5-S173.e8.)

EPIDEMIOLOGY

Parenteral nutrition (PN) is indicated to prevent malnutrition in patients unable to receive adequate nutrients by the oral or enteral route. Examples include patients with enterocutaneous fistula, anastomatic leak, postoperative ileus, short bowel syndrome associated with ischemic bowel, Crohn's disease, abdominal trauma, radiation enteritis, or intestinal obstruction. PN has been identified as a risk factor for catheter-related bloodstream infection (CR-BSI) in critically ill, acute, and chronic care patients.¹⁻³

Several central venous access devices are used to administer PN. These include polyurethane and silicone

percutaneous single-, double-, and triple-lumen catheters; percutaneously inserted central catheters; tunneled catheters; and ports. Catheters inserted at the bedside or in the emergency department may have a higher risk of becoming infected than those inserted in a more controlled environment, such as the operating room or radiology setting. Infection occurs in 1.3% to 26.2 % of central venous catheters used to administer PN. This wide range of reported findings is related to differences in study design, definition of CR-BSIs, and varying populations and sites studied.⁴

PN formulations are susceptible to microbial growth because of their components: amino acids and dextrose that support fungal growth and fat emulsions that sustain bacteria and fungi. Current practice standards require that parenteral preparations be compounded in a clean room using a laminar-flow hood to minimize microbial contamination. Proper storage, refrigeration, and infusion time of no more than 24 hours reduce the chance of microbial contamination or growth in the PN formulation. In hospitals and home infusion pharmacies that adhere to these strict standards, contamination rarely occurs. In the home setting, storage conditions and infusion times may be difficult to control. Home PN patients may leave parenteral solutions unattended in hot weather, increasing the risk of CR-BSIs.

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Malnutrition may develop in hospitalized patients with severe trauma, critical illness, and major surgery and is associated with immunosuppression, which is a risk factor for infection.⁵ During the stress response, critically ill patients may also develop hyperglycemia, which is exacerbated by infusion of dextrose. Uncontrolled hyperglycemia has a negative effect on immune response.^{6,7} Another cause of infection may be contamination or colonization at the insertion site with microbial migration from the skin along the extraluminal catheter surface into the bloodstream. The subclavian site is usually considered the “cleanest,” offering greater stability for anchoring and maintaining an intact catheter dressing. In contrast, jugular access, which has neck movement, increased beard hair, and close proximity to secretions, is less desirable.⁸ The femoral area is even less desirable because of the considerable movement in that region, pubic hair, and contamination from urine or fecal matter. Multiple-lumen catheters contribute to the incidence of infection because of frequent manipulations at the catheter hub. Minimal or no hub care, poor aseptic technique, and lack of skin site care are examples of poor nursing care that contribute to contamination of the central venous access device system (hub contamination).

In patients who receive long-term PN, the risk factors are different compared with a short-term, acute care patient. Intraluminal biofilm begins to develop shortly after a central venous access device is inserted and a denser matrix forms gradually over time.⁹ Long-term catheters may develop a fibrin sheath or tail at the distal catheter tip. Daily infusion of hypertonic parenteral solutions may cause central venous thrombosis. Clots near or on the catheter surface create prime sites for microbial seeding and eventual infection. Patients receiving long-term PN also may have chronic conditions, including Crohn’s disease, diabetes, and mitochondrial disease, that affect their immune function and place them at higher risk for developing infection. Many long-term PN have ostomies and gastrostomy tubes that can contaminate central lines. Psychosocial issues such as noncompliance, drug use, and depression also have been shown to increase risk for infection.¹⁰

In hospitalized patients, the most common organisms causing BSIs are coagulase-negative *Staphylococcus*, *Staphylococcus aureus*, *Enterococcus*, *Candida* spp, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*. In 2003, the Centers for Disease Control and Prevention reported that greater than 50% of *Staphylococcus* infections were methicillin-resistant and that 25% of *Enterococcus* infections were vancomycin-resistant infections.¹¹ These percentages may be higher today.

In the chronic, long-term PN population, the most common BSI pathogens are similar to those in the

Table 1. Characteristics of pathogens isolated in bloodstream infections from long-term parenteral nutrition patients¹²

Gram-positive	Gram-negative	Fungi
<i>Corynebacterium</i> spp	<i>Escherichia coli</i>	<i>Candida tropicalis</i>
<i>Streptococcus</i> spp	<i>Proteus</i> spp	<i>Candida lusitanae</i>
<i>Leuconostoc</i> spp	<i>Acinetobacter baumannii</i>	<i>Candida krusei</i>
<i>Lactobacillus</i> spp	<i>Serratia</i> spp	<i>Rhodotorula rubra</i>
<i>Bacillus</i> spp	<i>Pseudomonas aeruginosa</i>	<i>Malassezia furfur</i>
<i>Propionobacterium</i> spp	<i>Enterobacter cloacae</i>	<i>Aureobasidium</i> spp
	<i>Agrobacterium radiobacter</i>	
	<i>Enterobacter agglomerans</i>	
	<i>Citrobacter freundii</i>	
	<i>Acinetobacter lwoffii</i>	
	<i>Bacteriodes fragilis</i>	
	<i>Fusobacterium nucleatum</i>	
	<i>Ewingella americana</i>	
	<i>Kluyvera ascorbata</i>	

acute care population but with a higher risk for *Candida* infections. Coagulase-negative *Staphylococcus* can be attributed to approximately 60% of CR-BSIs, followed by *Klebsiella pneumoniae*, *Staphylococcus aureus*, and *Enterococcus*. *Candida parapsilosis*, *glabrata*, and *albicans* are frequently cultured from long-term central lines used for PN.^{12,13}

A descriptive, observational, epidemiologic study of home-PN patients found that in a 14-year period, 248 infections occurred in 38 patients.¹² The most common pathogens are listed in Table 1. These pathogens were cultured from both central venous access device and peripheral blood samples, but not all were verified by both methods. Patients in this study represented a wide socioeconomic, cultural, and environmental range. Some patients were in and out of prison and lived in adult homes, rooming houses, farms, and river communities. The unusual infections may have been a result of environmental contamination or drug abuse. When assessing infection in a home-PN patient admitted to the hospital, it is important to recognize that unusual organisms may be cultured and should not be disregarded as adventitious contaminants.

TREATMENT

Treatment for CR-BSIs depends on whether PN is being administered in the hospital or home care setting. In the hospital setting, a suspected or known infected catheter should be removed. A 24- to 48-hour central line and PN “holiday” to evaluate and treat the potential infection may decrease the incidence of recurrent or persistent bacteremia. Treatment with the appropriate antibiotic or antifungal is based on culture and sensitivity results. A new central catheter should be inserted only if needed at a different site after 48 hours of antibiotic treatment and negative blood cultures.

In patients who receive long-term PN with CR-BSIs, a critical decision is whether it is safe to treat the infection in the home setting. Hospital admission places these patients at risk for development of a nosocomial infection and contamination of their access devices by unfamiliar staff. In the case of fungemia, the patient must always be admitted and the catheter removed. In many instances, central venous access is limited because of chronic thrombosis; therefore, with gram-positive and gram-negative organisms, catheter salvage should be considered and many times is successful.

In the event that a long-term venous access device must be removed, treatment becomes challenging. Most patients on home PN have short bowel syndrome with limited absorption and large gastrointestinal fluid losses totaling 3 to 4 liters per day. Intravenous antibiotics should be used for treatment because oral absorption is questionable. Until the permanent device can be replaced, peripheral vein access or a peripherally inserted central catheter is needed for intravenous antibiotics, hydration, and electrolyte replacement, but their use is difficult because of limited venous access. Eventually, the permanent device can be replaced after negative blood cultures are obtained. Evaluation of remote site infection such as septic arthritis, infected thrombus, osteomyelitis, endophthalmitis, and endocarditis is also necessary.

Catheter lock therapy has been shown to be effective in reducing levels of intraluminal biofilm in catheters in place for more than 2 weeks.¹⁴ Antibiotics including vancomycin, gentamicin, ciprofloxacin, and amphotericin B have been used in concentrated doses as locks.¹⁵ Ethanol lock has been very successful in reducing CR-BSI in home-PN patients. In one study, 9 PN patients experienced 81 (8.3 per 1000-days) CR-BSI before ethanol lock therapy compared with 9 infections (2.7 per 1000-days) after ethanol lock therapy.¹⁶ More studies are needed to confirm the efficacy of lock therapies.

Several nutrition strategies have been suggested to prevent or reduce incidence of infection in PN patients. The continued need for administration of PN should be assessed daily. Enteral nutritional support is preferred over the parenteral route because the rate of complications is less.¹⁷ The gastrointestinal tract is the largest immune organ in the body, and keeping it active helps to prevent infection.¹⁸ Overfeeding calories, either by dextrose or fats, should be avoided in critically ill patients. Excess calories exacerbate the hyperglycemia seen in the stress response, which has a negative effect on immune function. Tight glucose control reduces mortality and morbidity in intensive care unit patients.^{19,20}

Immunonutrition is an emerging area of research in nutritional support. Most studies have evaluated

enteral formulas, but preliminary studies show that omega-3 intravenous fat emulsions decrease systemic inflammation during critical illness and reduce the liver complications commonly seen with PN therapy.²¹ These emulsions are not currently available in the United States. Another nutritional supplement is glutamine, which is a nonessential amino acid that becomes essential during stress and critical illness. Some studies show that adding glutamine to parenteral or enteral nutrition may have antioxidant effects and improve immune functions.²² More studies are needed to demonstrate the benefits of nutritional supplements in reducing CR-BSIs in patients receiving PN.

SUMMARY

Strategies to reduce or prevent infections including adherence to evidenced-based practices for inserting catheters, chlorhexidine skin preparation, and meticulous care of the intravenous site can reduce the risk of CR-BSIs. Catheter lock therapy, daily evaluation of continued need for PN, using enteral instead of PN support, glucose control, and avoiding overfeeding can reduce the risk for complications even further.

References

1. Cagatay AA, Ozcan PE, Gulec L, Ince N, Tugrul S, Ozsut H, et al. Risk factors for mortality of nosocomial bacteraemia in intensive care units. *Med Princ Pract* 2007;16:187-92.
2. Chen HS, Wang FD, Lin M, Lin YC, Huang LJ, Liu CY. Risk factors for central venous catheter-related infections in general surgery. *J Microbiol Immunol Infect* 2006;39:231-6.
3. Tokars JL, Cookson ST, McArthur MA, Boyer CL, McGeer AJ, Jarvis WR. Prospective evaluation of risk factors for bloodstream infection in patients receiving home infusion therapy. *Ann Intern Med* 1999;131:340-7.
4. Beghetto MG, Victorino J, Teixeira L, de Azevedo MJ. Parenteral nutrition as a risk factor for central venous catheter-related infection. *J Parent Ent Nutr* 2005;29:367-73.
5. Pesce-Hammond K, Wessel J. Nutrition assessment and decision making. In: Merritt R, DeLegge MH, Holcombe B, Mueller C, editors. *The A.S.P.E.N nutrition support practice manual MD: American Society for Parenteral and Enteral Nutrition*. 2nd edition; 2005 p. 3-26 Silver Spring.
6. Digman C, Borto D, Nasraway SA. Hyperglycemia in the critically ill. *Nutr Clin Care* 2005;8:93-101.
7. Forbes A. Parenteral nutrition. *Curr Opin Gastroenterol* 2007;23:183-6.
8. Centers for Disease Control and Prevention. Guidelines for the prevention of intravascular catheter-related infections. *Morb Mort Weekly Rpt* 2002;51(RR-10):6.
9. Ryder M. Evidence-based practice in the management of vascular access devices for home parenteral nutrition therapy. *J Parent Ent Nutr* 2006;30:S82-93.
10. Smith CE, Curtas S, Werkowitch M, Kleinbeck SV, Howard L. Home parenteral nutrition: does affiliation with a national support and education organization improve patient outcome? *J Parent Ent Nutr* 2002;26:159-63.
11. CDC NNIS System. National nosocomial infections surveillance (NNIS) system report data summary from January 1992 through June 2003, issued August 2003. *Am J Infect Control* 2003;31:481-98.

12. Marra AR, Opilla M, Edmond MB, Kirby DF. Epidemiology of bloodstream infections in patients receiving long-term total parenteral nutrition. *J Clin Gastroenterol* 2007;41:19-28.
13. Saqui O, Raman M, Chang A, Allard JP. Catheter-related infections in a Canadian home total parenteral nutrition program: a prospective study using US Centers for Disease Control and Prevention criteria. *J Assoc Vascular Access* 2007;12:85-8.
14. Sherertz RJ, Boger MS, Collins CA, Mason L, Raad II. Comparative in vitro efficacies of various catheter lock solutions. *Antimicrob Agents Chemother* 2006;50:1865-8.
15. Bestul MB, VandenBussche HL. Antibiotic lock technique: review of the literature. *Pharmacotherapy* 2005;25:211-27.
16. Opilla MT, Kirby DF, Edmond MB. Use of ethanol lock therapy to reduce the incidence of catheter-related bloodstream infections in home parenteral nutrition patients. *J Parent Ent Nutr* 2007;31:302-5.
17. Dhaliwal R, Heyland DK. Nutrition and infection in the intensive care unit: what does the evidence show? *Curr Opin Crit Care* 2005;11:461-7.
18. Martindale RG, Cresci G. Preventing infectious complications with nutrition intervention. *J Parent Ent Nutr* 2005;29:S53-6.
19. Van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in critically ill patients. *N Engl J Med* 2001;345:1359-67.
20. McCowen KC, Friel C, Sternbery J, et al. Hypocaloric total parenteral nutrition: effectiveness in prevention of hyperglycemia and infectious complications-a randomized clinical trial. *Crit Care Med* 2000;28:3606-11.
21. Lee S, Gura KM, Kim S, et al. Current clinical applications of omega-6 and omega-3 fatty acids. *Nutr Clin Pract* 2006;21:323-41.
22. Marik PE. Maximizing efficacy from parenteral nutrition in critical care: appropriate patient populations, supplemental parenteral nutrition, glucose control, parenteral glutamine, and alternative fat sources. *Curr Gastroenterol Rep* 2007;9:345-53.