New Technologies to Prevent Intravascular Catheter-Related Bloodstream Infections

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Most intravascular catheter-related infections are associated with central venous catheters. Technologic advances shown to reduce the risk for these infections include a catheter hub containing an iodinated alcohol solution, short-term chlorhexidine-silver sulfadiazine-impregnated catheters, minocycline-rifampin-impregnated catheters, and chlorhexidine-impregnated sponge dressings. Nontechnologic strategies for reducing risk include maximal barrier precautions during catheter insertion, specialized nursing teams, continuing quality improvement programs, and tunneling of short-term internal jugular catheters.

Intravascular catheter-related bloodstream infections are an important cause of illness and excess medical cost. In prospective studies, the relative risk (RR) for a catheter-related bloodstream infection is 2 to 855 times higher with central venous catheters than peripheral venous catheters (1-3). Approximately 80,000 catheter-related bloodstream infections occur in U.S. intensive-care units each year, at a cost of $296 million to $2.3 billion (4,5). These infections are associated with 2,400 to 20,000 deaths per year. The focus of this article is on preventive strategies aimed at central venous catheters.

Chlorhexidine-Silver Sulfadiazine-Impregnated Catheters

Catheters impregnated with chlorhexidine-silver sulfadiazine are commercially available. In prospective, randomized studies of catheters left in place for an average of ≤11 days (6-14), the incidence of catheter-related bloodstream infections was reduced by using chlorhexidine-silver sulfadiazine-impregnated catheters (RR 0.4, confidence interval [CI] 0.2-0.8) (4). These catheters are cost-effective if the incidence of bloodstream infections is greater than 3.3/ 1000 catheter-days (6) or greater than 1% (15). In addition, if chlorhexidine-silver sulfadiazine-impregnated catheters in place for ≤10 days reduce infections from 5.2% to 3%, then for every 300 catheters used, approximately $60,000 would be saved and seven catheter-related bloodstream infections and one death would be prevented (15). Published studies of chlorhexidine-silver sulfadiazine-impregnated catheters were performed with catheters impregnated extraluminally. However, the U.S. Food and Drug Administration (FDA) has recently approved the use of catheters impregnated intraluminally with chlorhexidine, in addition to chlorhexidine-silver sulfadiazine extraluminal impregnation. Use of chlorhexidine-silver sulfadiazine-impregnated catheters has been associated with serious anaphylactoid reactions in Japan (16), and these catheters are not commercially available in that country. One such reaction in

the United States has been reported to the FDA (as of April 2000). Resistance to the antiseptic components of this device has not been demonstrated in clinical studies (6). However, in vitro studies of *Pseudomonas stutzeri* exposed to slowly increasing concentrations of chlorhexidine, in the absence of silver sulfadiazine, have demonstrated the development of resistance to chlorhexidine and associated resistance to several classes of therapeutic antimicrobial agents (17). Although the conditions in these experiments do not simulate clinical practice, the experiments demonstrate the potential for resistance associated with use of these devices.

Minocycline-Rifampin-Impregnated Catheters

Catheters impregnated with minocycline and rifampin are commercially available. In a prospective, randomized clinical trial of catheters in place for an average of 6 to 7 days, minocycline-rifampin-impregnated catheters were associated with lower incidence of infection than chlorhexidine-silver sulfadiazine-impregnated catheters (RR 0.1, CI 0-0.6) (18). The active ingredients of the minocycline-rifampin-impregnated catheters were on the extraluminal and intraluminal surfaces of the device, whereas the active ingredients of the chlorhexidine-silver sulfadiazine-impregnated catheters were only on the extraluminal surface. Therefore, the difference in the incidence of infection may reflect the extent of impregnation on the catheters, in addition to the difference in active ingredients. If minocycline-rifampin-impregnated catheters reduce infections from 5% to 0%, then for every 850 catheters used, approximately $500,000 would be saved (19). Resistance to active antimicrobial components of the minocycline-rifampin-impregnated catheters has not been demonstrated in clinical studies (18,19). However, when these catheters were implanted for 7 to 14 days in laboratory animals and then removed and placed on agar plates injected with *Staphylococcus aureus*, microbial growth was detected in the zones of inhibition (20); this growth may represent subpopulations of *S. aureus* with reduced susceptibility to minocycline or rifampin. In additional experiments, minocycline-rifampin-impregnated catheters were implanted in animals for 7 days, after which rifampin-resistant, minocycline-susceptible *S. epidermidis* was introduced into the insertion site and tunnel tract. In this animal model, the

minocycline-rifampin-impregnated catheters were not protective (20). These studies suggest the potential for resistance against the antimicrobial agents used to impregnate these catheters as their clinical use becomes more widespread.

Catheter Hubs Containing Iodinated Alcohol

A catheter hub containing an antiseptic chamber filled with 3% iodinated alcohol is commercially available in Europe but not in the United States. In a prospective, randomized trial of catheters in place for an average of 15 to 16 days, use of a hub with the antiseptic chamber reduced the incidence of infection (RR 0.2, CI 0.1-0.7) (21). A formal cost-benefit analysis has not been published. However, use of this device led to fourfold reduction in the incidence of infections, and the device would most likely be cost-effective when used with central venous catheters in place for approximately 2 weeks. A minute amount of iodine (0.024 mg) is estimated to enter the bloodstream each time the hub containing the antiseptic chamber is punctured (21). However, the currently marketed device has been modified, and entry of iodine into the bloodstream with daily use has not been reported.

Chlorhexidine-Impregnated Sponge Dressings

Use of a commercially available chlorhexidine-impregnated sponge dressing at the insertion site of central venous and arterial catheters led to a threefold reduction in catheter-related bloodstream infections in a recent prospective, randomized study (22).

Nontechnologic Interventions

Several strategies reduce the risk for catheter-related bloodstream infection. In a prospective, randomized study of central venous catheter insertion, use of maximal barrier precautions (large sterile sheet drape; long-sleeved sterile gown; sterile gloves, mask, and hat) resulted in lower incidence of infections, 0.08/1,000 catheter-days, compared with use of minimal precautions (small sterile drape and sterile gloves), 0.5/1,000 catheter-days (23). In another prospective, randomized trial of peripheral catheter insertions, the catheters inserted and managed by a specialized nursing team had a lower incidence of infection than catheters inserted and managed by house officers (odds ratio 0, CI 0-0.6 [24]). In prospective, cohort studies, continuing quality improvement programs aimed at appropriate insertion and maintenance of catheters substantially reduced the incidence of infection (25-29). In a prospective, randomized trial of catheters not used for blood-drawing, tunneling of short-term internal jugular central venous catheters was associated with lower incidence of infection than nontunneling of catheters (RR 0.2, CI 0.1-0.7 [30]).

Some of the nontechnologic interventions aimed at reducing the risk for catheter-related bloodstream infection, such as quality improvement programs, depend on changes in human behavior. Once implemented, whether they remain effective over the long term remains to be seen.

Future Strategies

Greater understanding of the pathogenesis of intravascular-related infections will help prevent such infections. For example, *S. aureus* binding to the catheter surface in vivo involves fibronectin-specific adhesions (31). Identification of epitopes in the *S. aureus* fibronectin-binding protein for the generation of adhesion-blocking antibodies (32) may aid in preventing future infections. The development of bacterial biofilms on the surface of foreign bodies involves cell-to-cell signaling by acyl homoserine lactone-based chemical messengers that control bacterial gene expression (33,34). Prevention of microbial growth on the surface of future intravascular catheters may be mediated by inhibitors of these chemical messengers (35).

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