Preventing Vascular Catheter-Related Infections: Current Controversies

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Prevention of vascular catheter-related infection remains an important priority. This review focuses on salient controversies regarding optimal preventive methods. Intensity of surveillance for nosocomial infections was the single most important predictor of prevention in the Study of the Efficacy of Nosocomial Infection Control (SENIC). Used suboptimally by most hospitals in the SENIC study, surveillance is probably conducted even less today. There has been one randomized trial of the optimal method of aseptic insertion for central venous catheters and none comparing the 2 most frequently used sites. Scheduled replacement did not prevent infection in multiple randomized trials but, according to a recent survey, was still being used frequently. Chlorhexidine preparation of skin before and during catheterization has significantly reduced colonization of catheters in multiple randomized trials and should be used. Impregnation of catheter and/or hub surfaces with antiseptics raises less concern about fostering the development of antibiotic resistance than does the use of antibiotics for this purpose.

Here we are not afraid to follow truth wherever it might lead, nor to tolerate any error so long as reason is left free to combat it.

Thomas Jefferson, 1820

When a thing ceases to be a subject of controversy, it ceases to be a subject of interest.

William Hazlitt, 1830

Multiple guidelines for preventing vascular catheter infection have been published. One of these was the guideline by the Hospital Infection Control Practice Advisory Committee of the Centers for Disease Control and Prevention (CDC), published in 1996, which contained 80 recommendations for preventing vascular catheter infection [1]. The present review will focus on a few important questions regarding prevention of catheter-related infection that have remained or become controversial since publication of that guideline.

First, it is important to emphasize that more studies are needed. Many of the recommendations in current guidelines are not based on data from randomized trials, and some are based on data from a single randomized trial. As advocated by Hill [2], preventive practices should be based, whenever possible, on consistent results from different studies of different populations that were undertaken by different investigators, as a guide to epidemiologic “truth.” This is necessary because of the obvious problem that some epidemiologic studies produce false results due to chance or bias [3].
For optimal prevention of nosocomial infections, in general, and vascular catheter-related infections, in particular, it should first be noted that many hospitals do not perform adequate surveillance for nosocomial infections. The importance of surveillance was perhaps most strongly demonstrated in the Study of the Efficacy of Nosocomial Infection Control (SENIC) [4]. Using a probability sample of hospitals throughout the United States, SENIC demonstrated a 32% lower rate of nosocomial infections in hospitals with the most effective infection control programs, compared with hospitals that had no infection control program. The average infection control program in the SENIC study prevented only 6% of nosocomial infections [4]. Many infection control programs have since been downsized and are now doing less surveillance. The components of infection control programs that predicted greater effectiveness in a multivariate analysis done by SENIC included the following (in decreasing order of importance): intensity of surveillance, intensity of control measures, adequacy of the ratio of infection control practitioners to patient beds, and presence of a physician trained in infection control. These components were associated with a 35% reduction in primary bloodstream infections. The ratio of infection control practitioners to hospital beds that appeared adequate during SENIC (1:250) no longer seems sufficient, according to a recent consensus panel report [5]. A recent study confirmed the SENIC finding that surveillance allowed one to address local problems in a timely manner. For example, if a majority of cases of infection are questionable because there is only 1 culture positive for coagulase-negative staphylococci, and in many cases the blood sample for culture was drawn through an indwelling catheter, there may be a problem with overdiagnosis and overtherapy. This situation should be addressed differently from another in which they have been used. For this reason, during the past few decades, more attention has been devoted to studying the continuing importance of this approach, despite the availability of other, new preventive methods.

Surveillance allows one to address local problems in a timely manner. For example, if a majority of cases of infection are questionable because there is only 1 culture positive for coagulase-negative staphylococci, and in many cases the blood sample for culture was drawn through an indwelling catheter, there may be a problem with overdiagnosis and overtherapy. This situation should be addressed differently from another in which there are too many cases of bacteremia caused by methicillin-resistant Staphylococcus aureus [8]. Because of the risks associated with the latter infection, some clinicians might be tempted to buy an expensive device to prevent catheter infections, but performance of basic epidemiologic procedures, such as active surveillance cultures and isolation of infected patients, can simultaneously prevent infections due to this pathogen at all body sites [8]. By contrast, using a device to prevent catheter sepsis does nothing to prevent bacteremia that is secondary to infections at other sites, such as the lung, which multiple studies have shown to be significantly more lethal than catheter-related bloodstream infections (CRBSI) [9–14]. Surveillance lets one know how things are going and whether policies are being followed. Eggiman et al. [15] found that some of their hospital’s policies were not being followed and reimplemented the same policies. This action was followed by a significant (3-fold) reduction in the rate of infections. It is important to recognize that infection control measures may require application in an iterative fashion such as this, because compliance can fade.

Although there have been no randomized trials comparing internal jugular with subclavian placement of catheters, 11 studies have found significantly less infection with subclavian than with internal jugular placement [16–19]. For each patient, clinicians must use reason to balance this potential benefit against the higher risk of mechanical complications at this site. Also of note, observational studies of dialysis catheters have suggested the opposite: namely, that subclavian catheter placement is associated with more infections than is internal jugular placement) [20–32]. If this finding is correct, the reason for the difference is unclear.

One randomized trial and 1 observational study suggest that wearing a cap and mask, a sterile gown and gloves, and using large drapes during placement significantly reduces the risk that a catheter will become infected [18, 33]. Additional randomized trials would be useful; they also could help demonstrate the continuing importance of this approach, despite the availability of other, new preventive methods.

Ever since the first antibiotic became available, people have tried to think of ways to harness its power to prevent catheter infections. Concern was voiced, however, that widespread use of clinically useful antibiotics for this purpose would probably result in the development of resistance, because use of these drugs has resulted in resistance in almost every other setting in which they have been used. For this reason, during the past few decades, more attention has been devoted to studying the use of antiseptics at catheter sites.

Chlorhexidine has been compared with povidone iodine and/or alcohol as an agent for the preparation of CVC sites in 4 randomized trials [43–46], as an ingredient in a patch used to dress CVCs in a fifth trial [47], and as an agent for the prep-
aration of sites for peripheral venous catheters in a sixth randomized trial [48]. Five of these 6 studies reported significantly reduced colonization of catheters [43–45, 47, 48]. Two studies also reported significant prevention of bacteremia [43, 47]. The remaining 4 were not designed to have adequate statistical power to compare rates of bacteremia. Of note, this strategy prevents only extraluminal infection and does nothing to prevent the intraluminal infections that are more common with long-term indwelling catheters. It should also be noted that 1 of these trials reported no reduction in colonization [46]. It is therefore pertinent to note that the efficacy of chlorhexidine in hand-hygiene studies has depended on what formulation was used [49, 50].

Some have argued that use of such antiseptics will result in development of resistance to antiseptics and perhaps cross-resistance to antibiotics, as suggested by an in vitro study of *Pseudomonas stutzerii* [51]. There was 1 report, in 1987, that chlorhexidine- and antibiotic-resistant *Proteus mirabilis* caused urinary tract infections when chlorhexidine began to be used in an English hospital for preparation of sites for Foley catheters [52]. Chlorhexidine has continued to be used widely and daily on the skin of patients and health care workers alike for years without reports of other such problems. Maki et al. [53, 54] have argued that the use of chlorhexidine on or at the catheter site appears to be safe, on the basis of its very widespread use on skin for so many years without more reports of problems. Chlorhexidine combined with silver sulfadiazine has been used to coat CVCs and has been shown to decrease colonization and infection by about one-half in 11 studies (which were conducted by different investigators) [55].

Low-dose infusions of vancomycin have prevented catheter infection in some studies, but this prophylactic therapy is actively opposed in existing guidelines because of the risk for promoting development of resistance [1, 56]. For 1 patient, vancomycin prophylaxis was initially administered through a peritoneal dialysis catheter, and within 3 months, peritonitis developed that was caused by *Staphylococcus epidermidis* with reduced susceptibility to vancomycin. Catheter removal was required for cure [57]. Societal reluctance to use this preventive method seems to reflect reasoning that places the projected long-term risk to the population above the expected short-term benefits to individual patients. Similar reasoning was applied by the infection control community when trials and then meta-analyses found that antibiotic decontamination of the gastrointestinal tract could prevent lethal cases of nosocomial pneumonia [58, 59]. Of note, the concern about promotion of resistance was confirmed in some later studies of that practice [60].

For preventing intraluminal infection of long-term indwelling catheters, 2 antiseptic hub products are available. One, available only in the United States, involves use of a sponge saturated with povidone iodine that fits in a casing around the hub [61]. The other, available only in Europe, involves use of a hub chamber filled with iodinated alcohol [62]. Each was studied only in a single randomized trial and appeared to prevent intraluminal infection to a significant degree. These products should not potentiate development of antibiotic resistance. Additional trials would be useful.

Almost 2 decades ago, coating catheters with antibiotics was shown to be an effective preventive measure [63], but there was no ground swell of enthusiasm because of the much-discussed risk of potentiating development of antibiotic resistance [53]. Nevertheless, several studies have been published that show such coating can be effective in vitro and in vivo [64, 65], including a randomized trial that showed that catheters coated inside and out with rifampin and minocycline prevented more infections than did catheters coated with chlorhexidine and silver sulfadiazine on the outside only [16]. This result may not be surprising, however, in light of the difference in where the coatings were applied and the delayed onset of the infections, which suggest that infection may have frequently involved the unprotected lumen. All published studies of this rifampin-minocycline product have so far involved some principal investigators with an acknowledged commercial interest in the product [16, 66, 67]. Studies of this product by other groups that do not have a vested interest are still needed. If comparison studies of the chlorhexidine–silver sulfadiazine catheter are undertaken, the product compared should probably be the second-generation version, which is now on the market, with use of higher concentrations of the agents and both luminal and extraluminal coating.

The developers of the rifampin-minocycline catheter have suggested that it was reasonable to coat catheters with these particular antibiotics because they are used less frequently than β-lactams [68]. However, the rifamycins are a relatively distinctive class of antibiotics with special, well-documented abilities to penetrate and sterilize abscesses and to cure prosthetic device–related infections; they also have a number of non-mycobacterial indications [69]. For example, for almost 2 decades, rifampin has been considered a standard part of the treatment regimen for prosthetic valve endocarditis caused by coagulase-negative staphylococci, because it gives better results than other alternatives [70]. It is part of an oral regimen that has been shown to be effective for right-side *S. aureus* endocarditis [71]. It was part of a similar rifampin–quinolone regimen for severe staphylococcal infection that was quickly switched from iv to oral therapy, which, according to preliminary results from a randomized trial, resulted in equivalent outcomes but with faster hospital discharge than did standard parenteral antistaphylococcal therapy [72]. Given such data, losing the use of the rifamycins would be most unfortunate. Although the tetracyclines are not as unique as the rifamycins,
they are still clinically useful; minocycline has been the most active against and most useful for treating staphylococcal infections [73].

Although no resistance has been detected in the hundreds of rifampin-minocycline catheters that have been studied, it is clear from the history of antibiotics that clinical resistance has usually not shown up until a larger number of patients have been treated. Millions of CVCs are marketed in the United States each year; the speed at which resistance appears—if it does—could depend on the number being used.

Investigators who exposed isolates to subinhibitory concentrations of rifampin and minocycline (such as might occur on a patient’s skin under the dressing at some distance away from the catheter) found a 15-fold increase in resistance to these compounds [74]. As part of the same investigation, an experimental rat model showed that use of the rifampin-minocycline catheter or the second-generation chlorhexidine–silver sulfadiazine catheter resulted in equal protection against S. aureus infection of implanted catheter segments. This study was conducted by investigators who helped develop the chlorhexidine–silver sulfadiazine catheter, however, so confirmatory data by those without vested interest are still needed.

A recent editorial about antimicrobial-coated catheters estimated that 50,000 patients die of nosocomial bloodstream infection each year in the United States and urged that implementation of such catheters should therefore not be delayed, with the implication that much of this estimated mortality was due to CRBSIs [75]. This recommendation was controversial because of the estimates on which it was based. Deaths due to AIDS are far more common than deaths due to CRBSI in many facilities, including my institution, the University of Virginia Hospital, but the editorial estimated 50,000 deaths each year due to CRBSIs, which was 3.1-fold greater than the number of deaths due to AIDS in the US in 1999. This estimate was also 11.1-fold greater than the CDC’s most recent estimate of the number of deaths directly caused by nosocomial primary bloodstream infections in the United States [76].

The editorial did not mention that studies of nosocomial bloodstream infections have found that those that are secondary to infections in other organs, such as the lungs, have been associated with significantly higher mortality rates than have CRBSIs [9–14]. In 3 prospective studies of CRBSI at the University of Virginia Hospital that involved patients in intensive care units and bone marrow transplant recipients, none of the 24 patients with CRBSI died [36, 77, 78]. This number is significantly lower than the 6 deaths that would have been expected if the attributable mortality rate was 25%, as was suggested by the editorial ($P = .028$). This experience agrees better with the results reported by Gross et al. [79] in their study of mortality due to nosocomial infections, which found deaths due to CRBSI to be infrequent. It also agrees better with the results of a meta-analysis conducted by Byers et al. [80] regarding mortality from CRBSIs. Byers reported that the crude mortality after CRBSI was 14%, with 2.7% being due to the infection and 11.3% due to the patient’s underlying illness. A recent study of deaths due to CRBSI did not find a significant association between mortality and CRBSI after adjusting for the severity of illness during the week before onset of the bloodstream infection [81]. A more recent editorial referred to the suggestion that 50,000 US patients were dying of nosocomial bloodstream infection each year as “a myth,” citing additional studies that have reported a lower mortality rate [82].

The 1996 CDC guideline [1] advised that use of antimicrobial-coated catheters should not be the first option to consider in preventing catheter infection. In a recent review, Mermel [83] agreed with this approach. After implementing all of the other recommendations and confirming that they are indeed being followed, as discussed in the study by Eggiman et al. [15] that was mentioned above, one might need to consider use of antimicrobial catheters if rates of infection remain unacceptably high. For intraluminal protection, the antiseptic hub products mentioned above [61, 62] would appear to have virtually no risk of promoting development of antibiotic resistance. If one decides that use of antimicrobial catheters is necessary, then the contention of Maki et al. [53], that an antiseptic coating should be less likely to result in clinically important antibiotic resistance than an antibiotic coating, is probably correct.

References

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