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Use of Disinfectants To Reduce Microbial Contamination of Hubs of Vascular Catheters

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The vascular catheter hub is a potential portal of entry for microorganisms that cause catheter-related sepsis. Thus, a reduction in catheter hub contamination might reduce the incidence of catheter-related sepsis. To develop a regimen suitable for reducing microbial contamination of the catheter hub, we experimentally contaminated catheter hubs and assessed the efficacies of disinfectant solutions. Catheter hubs were incubated overnight with suspensions of *Staphylococcus epidermidis*, *Pseudomonas aeruginosa*, or *Candida parapsilosis*. After removal of unattached microorganisms, the catheter hubs were swabbed by rotating cotton swabs dipped in 1% chlorhexidine, 1% chlorhexidine in 70% ethanol, 70% ethanol, 97% ethanol, or normal saline. Posttreatment swabs of the catheter hub were obtained and cultured quantitatively. The cleaning regimens containing ethanol were the most effective. Seventy percent ethanol was more effective than chlorhexidine and is likely to be the safest treatment. We conclude that cleaning of the catheter hub with disinfectant can dramatically reduce microbial contamination.

Vascular catheter-related sepsis is an important cause of mortality and morbidity of hospitalized patients. The reported incidence of central venous catheter-related sepsis (CRS) has varied between 3.5 and 48% in studies of hospitalized patients (2, 8, 12, 13, 16, 21, 22). The skin entry site is the usual portal of entry for the microorganisms that cause CRS. However, there is growing evidence that the catheter hub, the female part of the junction where tubing connects into the intravascular catheter, is also an important portal of entry. In a study of 190 central venous catheters in adults receiving parenteral nutrition, there were 13 episodes of CRS caused by coagulase-negative staphylococci. The same coagulase-negative staphylococci were isolated from the catheter tip, blood, and hub for 12 patients and the catheter tip, blood, and skin for 1 patient (3). The authors concluded that the majority of central venous catheter-related episodes of bacteremia secondary to coagulase-negative staphylococcal infection were hub related. At our institution, we prospectively obtained surveillance cultures three times per week from the catheter hubs of central venous catheters in infants in the neonatal intensive care unit (17). Among 88 patients with 113 catheters, there were 28 episodes of CRS. In 10 of the 28 episodes, the same species was isolated from the catheter hub prior to the onset of clinical sepsis. In an additional five episodes, the same species was isolated from the hub at the time of clinical sepsis. Thus, 54% of the episodes of CRS were preceded by or coincided with contamination of the hub, indicating that many episodes of CRS originated with contamination of the catheter hub.

We reasoned that routine treatment of the interior of the catheter hub with a disinfecting agent could reduce contamination of the hub and thereby prevent or diminish CRS originating in the catheter hub. The present study was intended to study the effectiveness of disinfecting agents for reducing the biological load of the catheter hub. Potentially useful agents include ethanol, povidone-iodine, chlorhexidine, and hydrochloric acid (23). We compared the efficacies of chlorhexidine and ethanol in eradicating microorganisms in an in vitro model of catheter hub contamination.

MATERIALS AND METHODS

Three microorganisms were chosen to contaminate the catheters: *Staphylococcus epidermidis* ATCC 35983, *Pseudomonas aeruginosa* ATCC 27853, and *Candida parapsilosis* (isolated from the catheter hub of a neonate with catheter-related candidemia). *S. epidermidis* is a common etiologic agent of CRS. This particular strain was selected for its capacity to produce slime, since the majority of *S. epidermidis* isolates involved in catheter-related bacteremia elaborate exopolysaccharides (4–6, 10). *P. aeruginosa* represents gram-negative bacteria and has been established as an agent of CRS. *C. parapsilosis* was selected because it is the most common species of *Candida* associated with CRS in our neonatal intensive care unit.

S. epidermidis and *P. aeruginosa* were incubated overnight at 35°C on sheep blood agar (BBL Prepared Culture Media; Becton Dickinson Microbiology Systems, Cockeysville, Md.), and *C. parapsilosis* was incubated overnight on Sabouraud agar (BBL Prepared Culture Media, Becton Dickinson Microbiology Systems). Colonies were suspended in 5% glucose–0.45% NaCl to densities of between 10^7 and 10^8 CFU/ml. This corresponded to an optical density at 490 nm (Spectronic 20; Bausch & Lomb, Rochester, N.Y.) of 0.40 for *S. epidermidis*, 0.55 for *C. parapsilosis*, and 0.26 for *P. aeruginosa*. The tips of 20-gauge intravenous catheters (Insyte; Becton Dickinson and Company, Sandy, Utah) were sealed with Seal-ease (Becton Dickinson and Company, Rutherford, N.J.), and a catheter hub was filled with a suspension of one of these organisms. The catheter hub was incubated overnight at ambient temperature, and the fluid was removed the following morning by aspiration with a 1.0-ml syringe. The hub was then carefully blotted with a

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TABLE 1. Comparison of four solutions for decreasing microbial contamination of catheter hubs

Disinfectant	Viable count (geometric mean ± SD CFU/ml [*P* value])[a]		
	S. epidermidis	*C. parapsilosis*	*P. aeruginosa*
1% Chlorhexidine in 70% ethanol	1.9 ± 4.4 (<0.0001)	220 ± 46 (0.055)	1.6 ± 2.2 (0.0008)
1% Chlorhexidine in water	210 ± 110 (0.57)	110 ± 8.8 (0.16)	11 ± 13 (0.09)
97% Ethanol	3.7 ± 3.2 (<0.0001)	21 ± 87 (0.055)	0 ± 0 (0.0002)
Normal saline	350 ± 7.3	220 ± 22	47 ± 14

[a] Viable counts in hubs after swabbing (geometric mean ± SD CFU per milliliter of solution containing the swab [n = 10 trials]). Pretreatment colony counts ranged from 10^4 to 10^6 CFU/ml. *P* values were calculated by the two-tailed Student t test in comparison with the normal saline control group.

sterile calcium alginate fiber-tipped swab (Fisher Scientific, Pittsburgh, Pa.). This swab was used instead of a cotton swab because it was thinner and was able to be maneuvered in the catheter hub, while it avoided removing the microorganisms attached to the interior wall of the hub. To obtain a pretreatment colony count, a saline-soaked sterile cotton swab was then rotated five times in the catheter hub and was placed in 1 ml of 5% glucose–0.45% NaCl, vortexed, and analyzed for the number of CFU per milliliter by spreading 0.1 ml of serial 10-fold dilutions on agar media (sheep blood agar for *S. epidermidis* and *P. aeruginosa* and Sabouraud agar for *C. parapsilosis*). *S. epidermidis* and *P. aeruginosa* were incubated overnight at 35°C; *C. parapsilosis* was incubated for 48 h. Colony counts were determined from plates that displayed between 30 and 300 colonies.

Several disinfectant solutions were prepared to assess their efficacies in decreasing microbial contamination of the catheter hub: 1% chlorhexidine digluconate (Sigma Chemical Company, St. Louis, Mo.) in 70% ethanol, 1% chlorhexidine digluconate in sterile water, 70% ethanol, and 97% ethanol. Normal saline (0.9% NaCl) served as a control. Following removal of unattached microorganisms, the catheter hubs were treated with a cotton swab moistened with a disinfectant solution or saline. The swab was rotated five times in the catheter hub. This was repeated with two additional disinfectant-moistened swabs. To remove the disinfectant, the hubs were swabbed with a second set of three cotton swabs. These swabs were moistened with normal saline in the first two sets of experiments (Tables 1 and 2), and dry cotton swabs were used in the third set of experiments (Table 3). To determine posttreatment contamination, the last swab was placed in 1 ml of 5% glucose–0.45% NaCl, vortexed, and cultured as described above. One additional saline-moistened swab was used to swab the catheter hub one additional time; this swab was used to directly inoculate a blood agar plate (for *S. epidermidis* and *P. aeruginosa*) or a Sabouraud plate (for *C. parapsilosis*) and was then placed in meat broth (9), and the agar and broth cultures were incubated for 14 days.

Colony counts were rounded off to two significant figures. When less than 30 colonies were present on all plates, the plate with the greatest number of colonies was used to determine the number of CFU per milliliter. When there was no growth on the plate with 0.1 ml of undiluted suspension (swab placed in 1 ml of 5% glucose–0.45% NaCl and vortexed) but the blood agar plate, the Sabouraud plate, or the meat broth that was inoculated directly with an undiluted swab had microbial growth, the number of CFU per milliliter was considered to be less than 10 and was counted as 5 for statistical analyses.

Experiments were performed to determine whether cotton fibers may be released from the swabs during the cleaning of the catheter hub. After cleaning a catheter hub with three 70% ethanol-moistened swabs and then with three dry swabs, 1 ml of normal saline was flushed through the catheter into a petri dish and the fluid was examined for fibers with a microscope under low-power magnification. This was repeated for 30 trials. A control group consisted of flushing 1 ml of normal saline through a catheter directly into a petri dish. The control group also consisted of 30 trials. A final experiment was performed to measure the amount of ethanol in the catheter after cleaning the catheter hub with three cotton swabs moistened with 70% ethanol and then with three dry cotton swabs. A clamp was placed at the base of the catheter hub to prevent ethanol from entering the catheter prematurely. After cleaning, a total of 3 ml of normal saline was flushed through the catheter and the amount of ethanol in the effluent was measured. Ethanol was measured by using the Abbott ADx REA ethanol assay (Abbott Laboratories, North Chicago, Ill.).

RESULTS

Pretreatment catheter hub cultures generally yielded between 10^5 and 10^6 CFU/ml for *S. epidermidis* and *C. parapsilosis* and between 10^4 and 10^5 CFU/ml for *P. aeruginosa*. All of the disinfectants studied initially—1% chlorhexidine digluconate in water, 1% chlorhexidine digluconate in 70% ethanol, and 97% ethanol, as well as normal saline—resulted in a significant decrease in the number of CFU recovered from the catheter hub compared with the number in pretreatment cultures (Table 1). For *S. epidermidis* and *P. aeruginosa*, 97% ethanol and 1% chlorhexidine digluconate in 70% ethanol were superior to normal saline in reducing hub contamination ($P < 0.05$), although they were not significantly different from each other ($P > 0.47$). The difference in colony counts between 1% chlorhexidine digluconate in water and normal saline was not significant. For *C. parapsilosis*, none of the three regimens was significantly more effective than normal saline ($P > 0.05$).

In a second set of experiments, the efficacies of 70 and 97% ethanol were compared with that of normal saline, as described above (Table 2). For all three microorganisms, the efficacies of 70% ethanol and 97% ethanol were not significantly different from each other ($P > 0.2$), and both were superior to normal saline ($P < 0.05$).

Seventy percent ethanol was evaluated in an additional study as described above, except the second set of three swabs was dry (Table 3). For *S. epidermidis* and *C. parapsilosis*, 70% ethanol was superior to normal saline ($P < 0.5$). Although 70% ethanol was superior to normal saline for *P. aeruginosa*, the difference was not statistically significant ($P = 0.31$), probably because saline-soaked swabs alone appeared to be more effective in decreasing contamination with *P. aeruginosa*.

Following a standard simulated cleaning regimen with 70%

TABLE 2. Comparison of 97% ethanol, 70% ethanol, and normal saline control for decreasing microbial contamination of catheter hubs

Disinfectant	Viable count (geometric mean ± SD CFU/ml [*P* value])[a]		
	S. epidermidis	*C. parapsilosis*	*P. aeruginosa*
97% Ethanol	1.9 ± 2.4 (0.0044)	10 ± 7.2 (0.012)	0 ± 0 (0.0073)
70% Ethanol	5.8 ± 6.2 (0.031)	6.9 ± 3.6 (0.0062)	2.2 ± 3.0 (0.032)
Normal saline	52 ± 11	160 ± 25	18 ± 14

[a] Viable counts in hubs after swabbing (geometric mean ± SD CFU per milliliter of solution containing the swab [$n = 5$ trials]). Pretreatment colony counts ranged from 10^4 to 10^6 CFU/ml. *P* values were calculated by the two-tailed Student *t* test in comparison with the normal saline control group; $P > 0.05$ for all comparisons between 70% and 97% ethanol.

ethanol, 1 ml of saline was flushed through the catheter and the effluent was examined for cotton strands. Among 30 trials, i.e., 180 swabs, a total of three strands resembling cotton fibers was observed under the microscope under low-power magnification. In the control group, when 1 ml of normal saline was flushed through an untreated sterile catheter, no cotton fibers were visualized.

The amount of ethanol in the effluent of a catheter hub wash was measured after the 70% ethanol cleaning regimen. Three 1-ml washes of normal saline were used to flush a catheter after cleaning with 70% ethanol. Among 12 trials, a mean of 0.29 mg (range, 0.03 to 0.92 mg) was recovered from each 3-ml catheter wash. Most of the ethanol was recovered in the first 1-ml flush, with little ethanol recovered in the subsequent two 1-ml washes.

DISCUSSION

There are at least four possible sources of microorganisms that cause CRS. They include contaminated intravenous hyperalimentation fluid, the skin-catheter interface at the catheter insertion site, the interface of the tubing with the catheter hub, and the catheter tip, which can become infected following an otherwise transient bacteremia or fungemia. Because contaminated hyperalimentation fluid and seeding of the catheter tip by microorganisms in the blood are uncommon, the skin-catheter interface at the catheter insertion site and the interface of the tubing with the catheter hub are regarded as the major portals of entry for microorganisms that cause CRS. When the skin at the catheter insertion site is the portal of entry, sepsis is caused by extraluminal migration of organisms along the catheter. When the catheter hub is the portal of entry, sepsis occurs after intraluminal migration of microorganisms along the catheter.

There is evidence that intravenous catheters become contaminated prior to the onset of sepsis. In one study involving 38 neonates with central venous catheters, blood samples for culture were obtained every 2 weeks both from a peripheral site and through the central venous catheter. In two of three cases of bacteremia, contamination of the catheter was documented 48 h prior to bacteremia (15). Therefore, if such contamination can be prevented or if the microorganisms that contaminate a catheter can be eradicated before they migrate toward the bloodstream, the incidence of CRS might be reduced.

The catheter hub has been implicated as an important portal of entry for microorganisms that cause CRS. In 12 of 13 episodes of coagulase-negative staphylococcal bacteremia occurring in adults with central venous catheters, the same coagulase-negative *Staphylococcus* species was isolated from the catheter hub culture and the blood culture (3). Additional evidence for the hub as the portal of entry was put forth in a study involving junctional care (20). When a shield was placed around the catheter hub and the hub did not contact the skin, the incidence of catheter-related infections decreased from 39 to 8%. In another study which involved daily heating of metallic hubs, patients had a CRS rate of only 0.95% (18). Delayed tubing changes have also been shown to reduce the incidence of catheter sepsis (19), presumably by decreasing the access of microorganisms to the catheter hub.

All disinfectant solutions used to clean the catheter hub in the present study were effective in reducing the colony counts. Saline-soaked cotton swabs reduced the microbial load from about 10^5 to 10^2 organisms, suggesting mechanical removal with the cotton swab at a level greater than 99% of the total number of microorganisms. Seventy percent ethanol was even more effective, often decreasing the colony counts by 4 to 5 orders of magnitude. Ethanol was no more effective than normal saline in disinfection of *C. parapsilosis* (Table 1), but in subsequent experiments (Tables 2 and 3), the ethanol was more efficacious than normal saline. It is unclear what accounted for the observed difference in the efficacy of ethanol; differences may have occurred by chance or by differences in the amount of mechanical pressure applied to the wall of the hub.

The quantity of microorganisms that may contaminate the catheter hub prior to sepsis is unknown, but it is probably less than 10^5 organisms. It is noteworthy that 70% ethanol was effective against both a gram-positive and a gram-negative bacterial strain and a strain of yeast, because this suggests that it may be effective against all of the hub-contaminating microorganisms likely to cause CRS. Vancomycin has successfully been used to eradicate *S. epidermidis*

TABLE 3. Comparison of 70% ethanol and normal saline control for decreasing microbial contamination of catheter hubs

Disinfectant	Viable count (geometric mean ± SD CFU/ml [*P* value])[a]		
	S. epidermidis	*C. parapsilosis*	*P. aeruginosa*
70% Ethanol	6.2 ± 20 (0.003)	1.9 ± 4.3 (<0.0001)	5.0 ± 230 (0.3090)
Normal saline	1,200 ± 47	160 ± 6.2	25 ± 40

[a] Viable counts in hubs after swabbing (geometric mean ± SD CFU per milliliter of solution containing the swab [$n = 10$ trials]). Pretreatment colony counts ranged from 10^4 to 10^6 CFU/ml. *P* values were calculated by the two-tailed Student *t* test in comparison with the normal saline control group.

from the internal surfaces of noninfused catheters (7). However, coverage for gram-negative bacteria and fungi would also need to be added. Bonding of silver sulfadiazine and chlorhexidine has been shown to reduce the incidence of CRS in an ongoing study (14). In addition, cefazolin bonded to intravascular catheters has been effective in reducing bacterial colonization of catheters (11).

Both 70 and 97% ethanol reduced microbial numbers more effectively than normal saline did. Although it is generally believed that 70% ethanol is a more effective disinfectant than higher concentrations of ethanol, this was not shown under the conditions of our present study. It was also surprising that 1% chlorhexidine digluconate in water was not significantly better than normal saline; perhaps it is necessary to leave chlorhexidine in place for a longer period of time to be a more effective disinfectant. To test this hypothesis, we left 1% chlorhexidine in the catheter hub for 30 min and compared it with a normal cleaning regimen with chlorhexidine. Although we did this test with only two catheters, there was a greater reduction of microorganisms (*S. epidermidis*) when chlorhexidine was left in place for 30 min. We did not continue this trial since it would be impractical to leave chlorhexidine in a catheter hub for an extended period of time in a clinical setting.

Ethanol treatment of the catheter hub was the most effective regimen in our studies. In order to apply this result in a clinical trial, we assessed the amount of ethanol which might enter a patient's bloodstream after cleaning the interior of the catheter hub with 70% ethanol in the manner described above. On the basis of the amount of ethanol in the effluent, the ethanol concentration in patient serum would be minimal. For example, even using this regimen in a premature 500-g neonate, assuming a volume of distribution for ethanol of 0.53 liters/kg of body weight (1), an infusion of 1.0 mg of ethanol would result in a concentration of ethanol in serum of only 0.38 mg/dl. The limit of detection in our hospital toxicology laboratory is 10 mg/dl. Since ethanol would enter the bloodstream in a relatively concentrated form, it would have the potential to cause erythrocyte lysis, coagulation, or tissue destruction at the site of entry. However, a 10% solution of ethanol is infused to treat methanol poisoning, and such problems have not been observed.

Results of our study indicate that a brief treatment of catheter hubs with 70% ethanol is extremely effective in eradicating microorganisms from the catheter hub. Because the catheter hub appears to be a portal of microbial entry for a significant subset of patients with CRS, the use of 70% ethanol at times of tubing changes might decrease the incidence of CRS. This strategy is dependent on elimination of microorganisms prior to contaminating the catheter proximally. It is likely that treatment of the catheter hub at appropriate intervals could accomplish this goal. The current study provides data which suggest that this procedure should be safe for the patient. Specifically, very little ethanol enters the patient's bloodstream; thus, the risk involved with its use is negligible. Furthermore, the number of cotton fibers which might enter a patient's bloodstream after cleaning the hub with cotton swabs appears to be extremely low, although it is possible that an occasional cotton fiber may enter the bloodstream and might serve as a nidus for clot formation or be carried to the lung. We are planning a clinical trial with 70% ethanol to clean the catheter hubs of central venous catheters of neonates at the time of tubing change to determine whether this intervention will reduce the incidence of CRS.

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