ANTISEPTIC-IMPREGNATED CENTRAL VENOUS CATHETERS: THEIR EVALUATION IN BURN PATIENTS

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SUMMARY. Central venous catheter-related infections are an important source of morbidity and mortality in burn patients. Antiseptic-impregnated catheters have been recommended to prevent infections related to central venous lines in high-risk patients who require short-term catheters. This prospective, randomized, and controlled study compared the efficacy of standard and antiseptic devices in reducing catheter-related infections in burn patients. Twenty-two patients were included in the study with an average age of 47.6 yr and an average burned total body surface area of 38.7%. Thirty-eight silver-sulphadiazine, chlorhexidine catheters were compared with 40 non-antiseptic catheters. No differences in bacteraemia or colonization rates were observed between standard and antiseptic-coated catheters. Antiseptic catheters were more effective in reducing *S. epidermidis* colonization than standard catheters (4% vs 31%, $p < 0.01$). However, Gram-negative bacilli were responsible more often than Gram-positive cocci for catheter tip colonization (53% vs 46%) and they were responsible for all the bacteraemias (5.1%) related to catheters in the present study. We conclude that antiseptic-impregnated catheters could be more effective for Gram-positive cocci and could therefore be less effective in patients with high Gram-negative bacilli bloodstream infection prevalence, as burn patients are.

Introduction

Central venous catheter (CVC)-related infections have emerged as a major source of morbidity and mortality in hospitalized patients. Catheter-related bacteraemias account for the vast majority of nosocomial bloodstream infections. The National Nosocomial Infection System hospital surveillance reported rates of CVC-related bloodstream infection as ranging from 2.1 (respiratory intensive care unit [ICU]) to 30.2 (burns ICU) bloodstream infections per 1000 central catheter-days.[1]

The micro-organisms that colonize catheter hubs and the skin surrounding the insertion site are the source of most catheter-related bloodstream infections.[2] Successful preventive strategies must therefore reduce colonization of the insertion site and hubs. In addition, these strategies can also minimize microbial spread either extraluminally from the skin or intraluminally from the hubs towards the catheter tip lying in the bloodstream. Inhibiting the adherence and growth of pathogens that reach the intravascular segment of the catheter would also be ideal.

Antimicrobial- or antiseptic-impregnated catheters have been shown to reduce bacterial adherence and biofilm formation on catheters.[3]

A large randomized controlled trial showed that catheters coated externally with chlorhexidine and silver sulphadiazine were associated with a 44% reduction in colonization and a 79% reduction in catheter-related bloodstream infections.[4] However, other studies failed to confirm the efficacy of these catheters in reducing the incidence of CVC-related bloodstream infection.[5,6] Two recent meta-analyses demonstrated that this combination of antimicrobial agents was effective in reducing catheter colonization and catheter-related bloodstream infection in high-risk patients.[7,8] "High-risk" refers to patients in an ICU and to those receiving total parenteral nutrition.

A later review of the last meta-analysis also concluded that the short-term use of these catheters reduced the risk of catheter-related bloodstream infection.[9] This last review noted that micro-organism resistance to the antimicrobial agents used in this device had not been demonstrated in clinical studies and that reports of anaphylactic reactions to the chlorhexidine component were rare.

Recent guidelines for preventing infections associated with the insertion and maintenance of CVCs recommend the use of an antimicrobial-impregnated CVC for adult patients requiring short-term (< 10 days) central venous catheterization and who are at high risk for catheter-related bloodstream infection.[10] Recently we showed a high incidence of infection related to CVCs in burn patients with an average dwelling time of six days.[11] Burn patients present differences in infection risk and bacteria associated with bloodstream infections compared with other critically ill patients. We therefore developed a prospective randomized trial aimed at evaluating the efficacy of antiseptic-impregnated catheters in reducing colonization or bacteraemia related to CVCs in burn patients.

Table I - Patient features

	Aetiology	CVC number	Duration of catheterization (days)	Age (yr)	TBSA (%)	APACHE II	Inhalation injury	Length of stay (days)	Died	Catheter types	
										SSC	NA
1	Flame	4	28	85	9	20	Yes	60	No	3	1
2	Flame	3	18	24	51	8	Yes	32	No	1	2
3	Flame	7	43	28	73	9	Yes	43	No	4	3
4	Electrical burn	3	20	30	35	5	No	69	No	1	2
5	Flame	6	44	38	33	2	No	61	No	2	4
6	Scald burn	2	16	43	6	1	No	85	No	2	0
7	Flame	1	6	39	80	34	Yes	39	Yes	1	0
8	Flame	6	43	44	30	1	No	60	No	4	2
9	Electrical burn	4	41	40	22	4	No	79	No	0	4
10	Flame	6	39	42	30	5	No	50	No	4	2
11	Flame	3	20	42	55	16	Yes	49	Yes	2	1
12	Flame	2	15	77	45	23	Yes	21	No	2	0
13	Flame	2	12	23	50	5	No	51	No	1	1
14	Scald burn	2	15	82	8	6	No	39	No	0	2
15	Flame	3	20	40	75	4	No	20	No	1	2
16	Flame	6	44	89	20	9	Yes	56	No	2	4
17	Flame	5	33	60	11	3	No	78	No	3	2
18	Scald burn	1	10	21	30	0	No	40	No	0	1
19	Flame	8	60	28	30	15	Yes	31	No	3	5
20	TENS	3	12	70	100	23	No	12	Yes	1	2
21	Flame	1	7	33	24	0	No	31	No	0	1
22	Flame	6	33	71	35	9	No	70	No	4	2

SSC: silver sulphadiazine catheter

NA: no antiseptic

TENS: toxic epidermolysis necrosis syndrome

Materials and methods

A prospective randomized controlled study comparing antiseptic-impregnated CVCs with standard devices was carried out over a 21-month period (2000-2002) in burn patients. All adult patients not known to be allergic to chlorhexidine, silver, or sulphonamides and who were scheduled to receive a CVC were eligible to participate. Exclusion criteria concerned patients who did not have any site free of partial- or full-thickness burns from which to draw a blood sample for bacteriological assessment. Catheters that were withdrawn unintentionally or were in place when patients died were not included in the study. No patient was on parenteral nutrition.

The catheters were inserted by house officers wearing masks, sterile gloves, and surgical gowns and using large sterile drapes.[12]

The insertion site was prepared with 70% alcohol and then with 10% povidone-iodine, applied by scrubbing for at least 60 sec each. The catheter was then inserted percutaneously using the Seldinger technique. The insertion site was antisepticized using 10% povidone-iodine and then dressed with a piece of sterile gauze and transparent dressing on a daily basis. The dressing was removed if the sterile gauze looked stained.

Each time a catheter was scheduled to be inserted in a study patient, it was randomly assigned from a blinded pre-set randomization schedule to be a control catheter or an antiseptic catheter. The experimental unit was each CVC rather than individual patient.

All catheters were inserted in a new site; the anatomical location was chosen according to the physician's decision as to what the best insertion site was (far away from the burn wound if that was possible).

The catheters were removed as soon as they were unnecessary and moved to different sites if an infection was suspected, if the catheters had technical problems, or if catheter duration exceeded nine days.

Before removal of the catheters one blood sample was drawn for culturing. The catheter tips were also cultured.

The data obtained for each catheter included total body surface area (TBSA) burned and APACHE II[13] scores on the first day, clinical and laboratory data pertaining to infection, the anatomical location of the catheter, the reason for catheter removal, and the number of days the catheter had been in place. The Marshall Classification was used to quantify mul-

Table II - Comparison among features of patients with SSC vs NA

		SSC (n = 38)	NA (n = 40)
Age (yr)		51.2 (± 21.4)	47.3 (± 22.4)
TBSA (%)		36.6 (± 24.8)	33.9 (± 25.3)
APACHE II		9.8 (± 8.0)	7.6 (± 5.9)
MOD		2.3 (± 3.4)	2.5 (± 3.3)
Mean number hospital days of catheter insertion		17.6 (± 12.5)	15.9 (± 14.2)
Sex	Male	27 (43%)	35 (56%)
	Female	11 (57%)	8 (43%)
Aetiology	Flame burn	34 (89%)	32 (80%)
	Scald burn	2 (5%)	3 (7.5%)
	Electrical burn	1 (2.6%)	3 (7.5%)
	TENS	1 (2.6%)	2 (5%)

SSC: silver sulphadiazine catheter
NA: no antiseptic
MOD: multiple organ dysfunction

Table III - Comparison among features of catheters and procedures with SSC vs NA

		SSC (n = 38)	NA (n = 40)
Catheter type	One lumen	0	17 (42.5%)
	Two lumens	38 (100%)	23 (57.5%)
Site of Insertion	Jugular vein	8 (21%)	7 (16%)
	Subclavian vein	7 (18%)	14 (32%)
	Femoral vein	23 (60%)	19 (44%)
Reason for catheter removal	Catheter no longer needed	5 (13%)	5 (12.5%)
	Suspected infection	16 (42%)	21 (52.5%)
	Scheduled change	15 (39%)	11 (27.5%)
	Clotted catheter or displacement	2 (5%)	3 (7.5%)
Mean duration of hospital catheter insertion (days)		17.6 (± 12.5)	15.9 (± 14.2)
Median indwelling time (days)		7.0 (± 1.5)	7.0 (± 2.3)

SSC: silver sulphadiazine catheter
NA: no antiseptic

Table IV - Colonization and bacteraemic rates

	SSC	NA	*p*
Colonization (%)	42	55	0.2
Bacteraemia (%)	7.8	2	0.2
Colonization (1000 catheter/days)	60.1	79.7	0.3
Bacteraemia (1000 catheter/days)	11.2	3.3	0.2

SSC: silver sulphadiazine catheter
NA: no antiseptic

tiple organ dysfunction[14] on catheter insertion day.

Two noncuffed CVCs were studied: the standard (one- or two-lumen) catheter made of polyurethane without antiseptic (NA) and the test catheter (two-lumen) with the external surface impregnated with chorhexidine gluconate (0.75 mg) and silver sulphadiazine (0.70 mg).

Catheter-tip colonization was defined as a positive semiquantitative[15] culture of an intravascular catheter segment (> 15 CFU). If the same micro-organism was isolated from blood and CVC, this was defined as catheter-related bacteraemia. The experimental unit was each CVC rather than individual patient.

Differences between means were calculated by Student's t-test. Percentages were compared by chi-square test or Fisher's exact test, if appropriate. A p value < 0.05 was considered statistically significant. The 95% CI of the risk ratio was determined by a test-based procedure (EpiInfo program, USD, Stone Mountain, GA).

Results

During the study period 84 CVCs were inserted in 22 admitted patients. Six catheters were excluded, three because of unintentional displacement and three because the patients died with the catheters in place. The average number of catheters per patient was 5.0 (range, 1-8) and the mean duration of catheterization 26.3 days (range, 6-60). Fifteen patients (68%) had both antiseptic and non-antiseptic catheters. Sixteen patients (72%) had flame injury, eight (36%) had inhalation injury, and three (13%) died. Their average age was 47.6 yr (range, 21-89), TBSA 38.7% (range, 6-100), Apache II 9.1 (range, 0-34), and duration of stay 48.9 days (range, 12-85) (*Table I*).

Thirty-eight CVCs coated with silver sulphadiazine were compared with 40 CVCs without antiseptic. There were no differences among these cases as regards patient features (*Table II*) or catheter characteristics, except for the number of lumens. All SSC CVCs had two lumens, while only 57% of NA CVCs had two lumens (*Table III*).

SSC CVCs had 13% lower colonization rates (42% vs 55%) and 5.8% higher bacteraemic rates (7.8% vs 2%), but both these features were without any statistically significant difference (*Table IV*).

Colonized catheters in the control group had a relative risk of 1.93 (CI 95% 0.97-3.84) of being colonized by Gram-positive cocci (p < 0.05) and of 7.14 (CI 95% 0.97-52.33) of being colonized by coagulase-negative *Staphylococcus* (p < 0.02) (*Table V*) compared with SSC CVCs.

Gram-negative bacilli (*Table VI*) caused all the bacteraemias related to CVCs.

Discussion and conclusion

Burn patients fulfil the criteria for using antiseptic

Table V - Frequency and microbiological cause of catheter colonization and catheter-related bacteraemia

	SSC (n = 23)	NA (n =29)
Gram-positive cocci	7 (30%)	17 (58%)
Staphylococcus aureus	5 (21%)	6 (20%)
Streptococcus faecalis	1 (4%)	2 (6%)
Staphylococcus epidermidis	1 (4%)	9 (31%)
Gram-negative bacillus	16 (69%)	12 (41%)
Stenotrophomonas maltophilia	0	1 (3%)
Pseudomonas aeruginosa	4 (17%)	4 (13%)
Acinetobacter baumannii	5 (21%)	3 (10%)
Serratia marcescens	3 (13%)	1 (3%)
Proteus mirabilis	4 (17%)	3 (10%)

SSC: silver sulphadiazine catheter
NA: no antiseptic

Table VI - Frequency and microbiological causes of central venous catheter-related bacteraemia

	SSC (n = 3)	NA (n = 1)
Acinetobacter baumannii	0	1
Serratia marcescens	2	0
Pseudomonas aeruginosa	1	0

SSC: silver sulphadiazine catheter
NA: no antiseptic

CVCs, according to recent guidelines.[15] However, no reports have specifically assessed their efficacy in this special group of patients. In this study, we found a mild reduction in catheter colonization and an increase in bacteraemic rates with antiseptic catheters, but without any statistically significant difference. There was a bias related to catheter design. All the antiseptic catheters were double-lumen, while 42% were single-lumen in the standard group. The impact of these differences is not clear: some researchers believe that multi-lumen catheters have a higher infection risk while others disagree.

Multi-lumen catheter insertion sites may be prone to infection because they increase trauma to the insertion site or because multiple ports increase the frequency of CVC manipulation.[16-18] Other studies have however failed to demonstrate any difference in the infection rate.[19,20]

The lowered efficacy of antiseptic catheters in burn patients could also be explained taking into consideration bacteriological differences from other critically ill patients. The skin insertion site is the commonest source of colonization and infection of vascular catheters in place for less than 10 days. Furthermore, microbiology frequently shows a predominance of Gram-positive bacteria, mainly *Staphylococcus epidermidis* and *S. aureus*. In a recent study in a medical-surgical ICU, 77% of blood stream infections were caused by coagulase-negative *Staphylococcus*.[21]

Burn patients are colonized by Gram-negative bacteria more frequently and more rapidly than other critically ill patients. In the present study, 53% of colonized catheters had Gram-negative bacilli while 19% had coagulase-negative *Staphylococcus*. Four bacteraemias (5.1%) were registered in the present study, all caused by Gram-negative bacilli. One study[22] showed that antibiotic-coated or impregnated catheters were effective in the prevention of bacterial colonization with Gram-positive bacteria. However, their activity against Gram-negative bacteria has not been well defined. Although one study demonstrated that SSCs were effective in reducing bacterial adherence, persistence, and further colonization of *Klebsiella pneumoniae*, these data cannot be extended to other Gram-negative microorganisms.[23] Gram-positive cocci were more likely to colonize the standard polyurethane catheters in the present study, as recently reported.[24,25] However, in the present study, no media containing inhibitors to chlorhexidine and silver sulphadiazine were used. Therefore, falsely low or negative catheter cultures were observed owing to antiseptic activity during culturing processes.[26]

Finally, no benefits were observed using antiseptic impregnated catheters to reduce central catheter-related infections in burn patients, even if this study is underpowered to make such a statement. Gram-positive cocci colonization was reduced with antiseptic catheters but no evident benefits were observed as regards Gram-negative bacilli, which were the main cause of colonization and bacteraemia related to CVCs in the present study. We conclude that antiseptic-impregnated catheters could be more effective for Gram-positive cocci and therefore that they could be less effective in patients with high Gram-negative bacilli bloodstream infection prevalence, as burn patients are. Future prospective, randomized controlled trials with a larger number of catheters are encouraged in order to confirm or refute these results.

RÉSUMÉ. Les infections liées à l'emploi du cathéter central veineux constituent une source importante de la morbidité et de la mortalité des patients brûlés. L'emploi du cathéter imprégné d'antiseptique a été recommandé pour prévenir les infections liées aux lignes centrales veineuses dans les patients à risque élevé qui nécessitent un cathéter de courte durée. Les Auteurs de cette étude prospective, randomisée et contrôlée ont comparé l'efficacité des appareils standard antiseptiques pour réduire les infections liées au cathéter dans les patients brûlés. Vingt-deux patients ont été inclus dans l'étude (âge moyen, 47,6 ans; surface corporelle cutanée brûlée moyenne, 38,7%). Trente-huit cathéters imprégnés de sulfadiazine argent et de chlorhexidine ont été comparés avec 40 cathéters non-antiseptiques. Aucune différence du taux de bactérémie ou de colonisation n'a été observée entre les cathéters standard et les cathéters revêtus d'antiseptique. Les cathéters antiseptiques étaient plus efficaces pour réduire la colonisation de *S. epidermi-*

dis par rapport aux cathéters standard (4% vs 31%, $p < 0,01$). Pourtant, les bacilles à gram négatif étaient responsables plus souvent, par rapport aux cocci à gram positif, de la colonisation de la pointe du cathéter (53% vs 46%) et ils étaient responsables de toutes les bacterémies (5,1%) liées aux cathéters dans cette étude. Les Auteurs concluent que les cathéters imprégnés d'antiseptiques pourraient être plus efficaces par rapport aux cocci à gram positif et pourtant moins efficaces dans les patients atteints d'une prévalence élevée d'infection de la circulation sanguine par bacilles à gram négatif, de même qu'il arrive dans les patients brûlés.

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