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Major article

Chlorhexidine-silver sulfadiazine-impregnated venous catheters save costs

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Background: Previous cost-effectiveness analyses have found that the use of chlorhexidine-silver sulfadiazine (CHSS)-impregnated catheters is associated with decreased catheter-related bloodstream infections (CRBSI) and central venous catheter (CVC)-related costs. However, in these analyses, the CVC-related cost included the increase of hospital stay.
Objective: Our aim was to determine the immediate CVC-related cost (including only the cost of CVC, diagnosis of CRBSI, and antimicrobials for the treatment of CRBSI) of using a CHSS or a standard catheter in internal jugular venous access.
Methods: We performed a prospective, observational, cohort study of patients admitted to the intensive care unit (ICU), Hospital Universitario de Canarias (Tenerife, Spain), who received 1 or more internal jugular venous catheters.
Results: The study included 245 CHSS-impregnated catheters and 391 standard catheters. Exact logistic regression analysis showed that CHSS-impregnated catheters were associated with a lower incidence of CRBSI, controlling for catheter duration, than standard catheters (0 vs 5.04 CRBSI per 1,000 catheter-days, respectively; odds ratio, 0.80; 95% confidence interval: 0.712-0.898; $P < .001$). Poisson regression showed that CHSS-impregnated catheters were associated with lower CVC-related cost per day than standard catheters (€3.78 ± €4.45 vs €7.28 ± €16.71, respectively; odds ratio, 0.52; 95% confidence interval: 0.504-0.535; $P < .001$). Survival analysis showed that CHSS-impregnated catheters were associated with increased CRBSI-free time compared with standard catheters ($\chi^2 = 14.9$; $P < .001$).
Conclusion: The use of CHSS-impregnated catheters reduced the incidence of CRBSI and immediate CVC-related costs in the internal jugular venous access.

A proposed strategy to reduce the incidence of central venous catheter-related bloodstream infection (CRBSI) is the use of chlorhexidine-silver sulfadiazine (CHSS) impregnated catheters. A meta-analysis by Veenstra et al, which included 11 randomized controlled trials (RCTs) and 2,603 catheters, showed a lower incidence of CRBSI with the use of first-generation CHSS-impregnated catheters (only the external surface was impregnated) compared with nonimpregnated catheters (odds ratio [OR], 0.56; 95% confidence interval [CI]: 0.37-0.84; $P = .005$).[1]

Second-generation CHSS-impregnated catheters (both external and internal surfaces impregnated) were subsequently introduced. The use of these second-generation CHSS-impregnated catheters was associated with a lower incidence of catheter tip colonization and CRBSI in a RCT.[2] Similarly, these second-generation CHSS-impregnated catheters showed a lower incidence of catheter tip colonization but only a nonsignificant trend to lower incidence of CRBSI in 3 RCTs[3-5] and in 1 observational study.[6] However, one other RCT did not show differences in catheter tip colonization or CRBSI.[7] Hockenhull et al,[8] in a meta-analysis including 1,176 patients from 3 RCTS,[2,3,5] found a lower incidence of catheter tip

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colonization (OR, 0.49; 95% CI: 0.33-0.74) and CRBSI (OR, 0.34; 95% CI: 0.14-0.81) with second-generation CHSS-impregnated catheters compared with standard catheters.[8]

The use of CHSS-impregnated catheters has also been found to decrease CVC-related cost in some cost-effectiveness analyses.[8-10] The mean additional cost because of CRBSI in these studies was approximately $10,000 per patient; but, in other studies, this was as high as $71,000[11] and $40,000.[12] However, in these cost-effectiveness analyses, the CVC-related cost included the increase of hospital stay, and this varied greatly in the different studies, even exceeding 20 days in some of them[11,12]; to our knowledge, there are no studies reporting CVC-related cost excluding the cost of increased hospital stay. Thus, the objective of this study was to determine the immediate CVC-related cost (including only the cost of CVC, diagnosis of CRBSI, and antimicrobials for the treatment of CRBSI) using second-generation CHSS-impregnated or standard catheters in internal jugular venous access.

MATERIALS AND METHODS

We performed a prospective, observational cohort study of patients admitted to the intensive care unit (ICU) of the Hospital Universitario de Canarias (Tenerife, Spain) who received 1 or more internal jugular venous catheters. The study was approved by the Institutional Review Board, and informed consent was obtained from the patients or their legal guardians.

The following catheters were used: (1) ARROWg^{+}ard Blue (Arrow, Reading, PA), which are CHSS-impregnated; and (2) ARROW (Arrow), which are standard catheters. The decision to use a CHSS or standard catheter was made by the patient's physician.

Microbiologic surveillance included twice weekly cultures of urine, tracheal aspirate, throat flora, and wounds during ICU stay. Evidently, necessary clinical samples were taken when infection was suspected. Catheter tips were cultured using the method described by Maki et al.[13]

CRBSI was defined according to the following criteria: positive blood culture obtained from a peripheral vein, signs of systemic infection (fever, chills, and/or hypotension), no apparent source of bacteremia except the catheter, and catheter tip colonization (significant growth of a microorganism $\geq$ 15 colony-forming units) with the same organism as the blood culture (the same species with identical antimicrobial susceptibility).

The diagnosis of CRBSI was made by an expert panel blinded to the type of catheter used (CHSS or standard). Information about the type of catheter (CHSS impregnated or standard) was removed before the expert reviewers examined the patient charts.

Immediate CVC-related cost included only the cost of CVC, the cultures for diagnosis of CRBSI, and the antimicrobials used for the treatment of CRBSI. Data on the cost of CVC and antimicrobial agents were obtained from the hospital accounts department: each CHSS-impregnated catheter cost €26, and each standard catheter cost €15.

Statistical analysis was performed with SPSS 17.0 (SPSS Inc, Chicago, IL), LogXact 4.1, (Cytel Co, Cambridge, MA), and StatXact 5.0.3 (Cytel Co). Continuous variables are reported as means and standard deviations and categorical variables as frequencies and percentages. We compared catheters groups (CHSS impregnated or standard) by Student t test for continuous variables and Kruskal-Wallis test or Jonckeree-Terpstra test for categorical variables.

We used exact logistic regression analysis to calculate the magnitude of the effect of the type of catheter (CHSS or standard) on the occurrence of CRBSI, controlling for duration of catheter insertion. We combined CVC-related cost and duration of catheter insertion as a Poisson variable. We used exact Poisson regression analysis to test whether the type of catheter (CHSS impregnated or standard) influenced the CVC-related cost per catheter-day. The magnitude of the effect was expressed as OR and 95% CI. Survival analysis was carried out using catheter duration as the dependent variable and type of catheter (CHSS or standard) as the independent variable; curves were represented using Kaplan-Meier method, and log-rank test was used to compare distributions of CRBSI-free time between both groups. P values less than .05 were considered statistically significant.

RESULTS

We found 8 CRBSI in 636 (1.26%) internal jugular catheters during 3,271 catheter-days (2.45 CRBSI per 1,000 catheter-days). As shown in Table 1, patients with standard catheters were older and had a higher rate of diabetes mellitus and mechanical ventilation than patients with CHSS-impregnated catheters. On the other hand, patients with CHSS-impregnated catheters showed higher Acute Physiology and Chronic Health Evaluation (APACHE) II scores, higher rate of chronic obstructive pulmonary disease, steroid agents, hematologic tumor, tracheostomy, and paralytic agents and a lower rate of antimicrobials than patients with standard catheters. In addition, patients with CHSS-impregnated catheters compared with standard catheters showed a lower rate of CRBSI (0 vs 2.0%, respectively; $P = .03$), incidence density of CRBSI (0 vs 5.04 CRBSI per 1,000 catheter-days, respectively; $P < .001$), and lower CVC-related cost per catheter-day (€7.28 $\pm$ €16.71 vs €3.78 $\pm$ €4.45, respectively; $P < .001$).

CHSS-impregnated catheters were associated with a lower risk of CRBSI, controlling for catheter duration, and with lower CVC-related cost per catheter day than standard catheters (Table 2). CHSS-impregnated catheters were associated with more prolonged CRBSI-free time than standard catheters ($\chi^2 = 14.9$; $P < .001$) (Fig 1).

DISCUSSION

To our knowledge, this is the first study to report lower immediate CVC-related costs (cost of the catheter, diagnosis, and treatment of CRBSI) using CHSS-impregnated than standard catheters in the internal jugular site. We did not include other potential costs associated with CRBSI such as increased hospital stay, increased mechanical ventilation duration, laboratory determinations, and other costs.

The present study has certain limitations: first, this was a single-center study; thus, CVC-related costs may be different in other hospitals. Second, CHSS-impregnated or standard catheters were not randomly assigned. Third, we included only the central internal jugular venous access because, in a previous study, we found a lower incidence of CRBSI in the posterior than in central internal jugular venous access.[14]

However, our study has certain strengths: first, all patients underwent twice weekly microbiologic surveillance. Second, the diagnosis of CRBSI was made by an expert panel blinded to the type of catheter (CHSS impregnated or standard).

The findings of the current study are consistent with the results of our previous studies showing lower CRBSI and CVC-related costs associated with the use of rifampicin-miconazol-impregnated catheters compared with standard catheters.[15-17]

The following scientific societies have issued guidelines for the prevention of intravascular catheter-related infection: the Society of Critical Care Medicine (SCCM), Infectious Diseases Society of America (IDSA), Society for Healthcare Epidemiology of America (SHEA), Surgical Infection Society (SIS), American College of Chest Physicians (ACCP), American Thoracic Society (ATS), American Society of Critical Care Anesthesiologists (ASCCA), Association for

Table 1
Characteristics of patients receiving either clorhexidine-silver sulfadiazine-impregnated or standard catheter

Data	Standard (n = 391) (1,586 days)	CHSS (n = 245) (1,685 days)	*P* value
Age, y (mean ± SD)	65.72 ± 13.86	60.15 ± 15.91	<.001
Male sex, n (%)	253 (64.7)	151 (61.6)	.45
APACHE II, score (mean ± SD)	12.42 ± 7.07	16.82 ± 9.01	<.001
Admission diagnostic, n (%)			<.001
Cardiac surgery	318 (81.3)	17 (6.9)	
Cardiology	13 (3.3)	40 (16.3)	
Respiratory	10 (2.6)	78 (31.8)	
Digestive	40 (10.2)	31 (12.7)	
Neurologic	3 (0.8)	38 (15.5)	
Traumatology	1 (0.3)	26 (10.6)	
Others	6 (1.5)	15 (6.2)	
Chronic obstructive pulmonary disease, n (%)	34 (8.7)	36 (14.7)	.03
Diabetes mellitus, n (%)	158 (40.4)	78 (31.8)	.03
Chemotherapeutic agents, n (%)	9 (2.3)	11 (4.5)	.20
Steroid agents, n (%)	6 (1.5)	15 (6.1)	.002
Hematologic tumor, n (%)	6 (1.5)	11 (4.5)	.04
Solid tumor, n (%)	40 (10.2)	27 (11.0)	.79
Use of antimicrobials, n (%)	382 (97.7)	225 (91.8)	.001
Use of mechanical ventilation, n (%)	379 (96.9)	202 (82.4)	<.001
Use of tracheostomy, n (%)	14 (3.6)	36 (14.7)	<.001
Use of paralitic agents, n (%)	8 (2.0)	36 (14.7)	<.001
Duration of the catheter, days (mean ± SD)	8.64 ± 4.75	8.56 ± 4.70	.86
CRBSI, n (%)	8 (2.0)	0	.03
Number CRBSI/1,000 catheter-days	5.04	0	<.001
CVC-related cost, €/day (mean ± SD)	7.28 ± 16.71	3.78 ± 4.45	<.001

APACHE, Acute Physiology and Chronic Health Evaluation; *CHSS*, clorhexidine-silver sulfadiazine; *CRBSI*, catheter-related bloodstream infection; *CVC*, central venous catheter; *SD*, standard deviation.

Table 2
Exact logistic and Poisson regression analyses to estimate the risk of CRBSI and CVC-related/day cost using clorhexidine-silver sulfadiazine-impregnated catheters vs standard catheters

	OR	95% CI	*P* value
Exact logistic regression analysis			
CHSS catheter (reference category: standard catheter)	0.02	Infinite to 0.276	.001
Duration of catheter insertion (days)	1.25	1.114-1.405	<.001
Exact Poisson regression analysis			
CVC-related/day cost (euros)	0.52	0.504-0.535	<.001

CHSS, clorhexidine-silver sulfadiazine; *CRBSI*, catheter-related bloodstream infection; *CVC*, central venous catheter.

Professionals in Infection Control and Epidemiology (APIC), Infusion Nurses Society (INS), Oncology Nursing Society (ONS), American Society for Parenteral and Enteral Nutrition (ASPEN), Society of Interventional Radiology (SIR), American Academy of Pediatrics (AAP), Pediatric Infectious Diseases Society (PIDS), and the Healthcare Infection Control Practices Advisory Committee (HICPAC) of the Centers for Disease Control and Prevention (CDC), published in 2011. All recommended the use of a CHSS- or minocycline-rifampicin-impregnated catheters in patients whose catheter is expected to remain in place > 5 days and if the CRBSI rate has not decreased after implementation of a comprehensive strategy to reduce it.[18] In addition, these guidelines remarked that the use of these catheters might be cost-effective in ICU patients, burn patients, neutropenic patients, and other patient populations in which the rate of infection exceeds 3.3 per 1,000 catheter-days.

We have some comments about these recommendations. First, the guidelines did not specify which generation of CHSS-impregnated catheter is recommended. The recommendation is based on RCTs showing that second-generation CHSS-impregnated

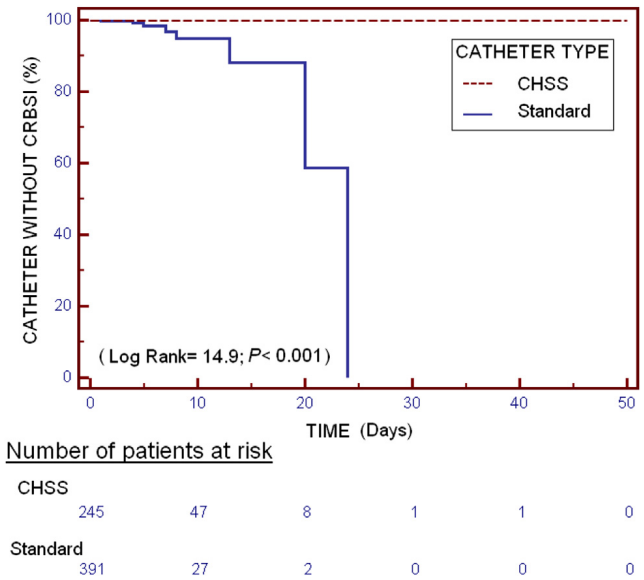

Fig 1. Comparison of the distributions of catheter-related bloodstream infection (CRBSI)-free time in jugular venous access between clorhexidine-silver sulfadiazine (CHSS)-impregnated and standard catheter.

catheters reduced the incidence of catheter tip colonization.[3-5] In these RCTs, there were no significant differences in the incidence of CRBSI with the use of second-generation CHSS-impregnated catheters; however, all showed a tendency to lower CRBSI with antimicrobial-coated catheters. On the other hand, the meta-analysis by Hockenhull et al found a lower incidence of CRBSI with second-generation CHSS-impregnated catheters compared with standard catheters.[8] We believe that our cost analysis may be a simpler analysis and could help convince health administrators to invest in the more expensive catheter.

Finally, regarding the use of CHSS-impregnated catheters, 2 other aspects are worthy of comment. One concern is the potential development of resistance to the antimicrobial agent used to coat the catheters,[19,20] an issue that has not been reported in clinical studies to date. Another concern is that, although rare, allergic reaction to the antimicrobial agent has been reported.[21-24] In the present study, no adverse effects of CHSS-impregnated catheter use was found in our ICU patients.

In conclusion, the use of CHSS-impregnated catheters reduces the incidence of CRBSI and immediate CVC-related costs in the internal jugular venous access.

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