Original Article

Can a New Antiseptic Agent Reduce the Bacterial Colonization Rate of Central Venous Lines in Post-Cardiac Surgery Patients?

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Abstract

Background: *Central venous (CV) catheters play an essential role in the management of critically ill patients in the Intensive Care Unit (ICU). CV lines are, however, allied to catheter-associated blood stream infections. Bacterial colonization of CV lines is deemed the main cause of catheter-associated infection. The purpose of our study was to compare bacterial colony counts in the catheter site before CV line insertion in two groups of post-cardiac surgery patients: a group receiving Sanosil (an antiseptic agent composed of H_2O_2 and silver) and a control group.*

Methods: *This interventional prospective double-blinded clinical trial recruited the patients in three post-cardiac surgery ICUs of a heart center. The participants were divided into interventional (113 patients) and control (136 patients) groups. Sanosil was added to the routine preparation procedure (Chlorhexidine bath one day before and scrub with Povidone-Iodine just before the CV line insertion). After the removal of the CV lines, the catheters tips were sent for culture and evaluation of colony counts.*

Results: *Catheter colonization occurred in 55 (22.1%) patients: 26 (23%) patients in the Sanosil group and 29 (21.3%) in the control group; there was no significant statistical difference between the two groups (p value = 0.75, RR = 1.05, 95%CI: 0.76-1.45). The most common organism having colonized in the cultures of the catheter tips was staphylococcus epidermis: 20 cases in the control group and 16 cases in the intervention group.*

Conclusion: *Catheter colonization frequently occurs in post-cardiac surgery patients. However, our results did not indicate the effectiveness of adding Sanosil to the routine preparation procedure with respect to reducing catheter bacterial colonization.*

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Introduction

Central venous (CV) catheters play an essential role in the modern management of critically ill patients, especially in the Intensive Care Unit (ICU). An estimated 5 million CV lines are used in the USA hospital wards per year.[1] Intravenous catheters are utilized for the management of fluids, drugs, nutritional products, and monitoring of central vascular pressure. Be that as it may, CV lines are associated with catheter bacterial colonization (20-49%), which may cause blood stream infection (bacteremia or sepsis) (3-7%).[2-7] Catheter-associated blood stream infection (CABSI) accounts for a mortality incidence rate of about 20% and could not only lengthen hospital stay for up to one week but also impose extra hospitalization costs.[8] As a result, it is of vital importance that a remedy be found to reduce the bacterial colonization allied to CV lines. There are some principal risk factors for CABSI such as duration of catheterization, catheter insertion sites, number of lumens, type of the intravenous fluid, type of the skin disinfectant, nursing, and underlying diseases like diabetes and malignancy.[9-11]

CABSI can be reduced with topical operational antiseptics[12] and disinfectants, which are known to decrease resident flora bacteria.[13] In recent years, many different antimicrobial products have become available for use as antiseptics (on skin and live organs) and they have revolutionized the traditional methods of infection control.[14] One of these novel concepts is the use of silver-containing products as antiseptic agents.[15,16] Silver has an inhibitory effect on bacterial replication due to its DNA binding properties; it is an effect that can last for thirteen days after the application of silver on a surface.[17]

Sanosil is an antiseptic agent, composed of H_2O_2 and silver. Sanosil can draw upon its main component, H_2O_2, for the destruction of bacteria, spores, and biofilms.[18] There has been some research on the antibacterial efficacy of Sanosil. For example, Szymanska[19] in 2003 showed a decrease in viral infectivity and bacterial load within the dental water line system after the addition of Sanosil. Yousefshahi et al.[20] in 2009 demonstrated that Sanosil could lessen contamination risk in the ventilation tubes of the ICU patients.

Given that the bacterial colonization rate of CV lines is regarded as one of the main causes of CABSI, we sought to compare bacterial colony counts in the catheter site before CV line insertion in two groups of post-cardiac surgery ICU patients: a group receiving Sanosil (an antiseptic agent composed of H_2O_2 and silver) and a control group.

Methods

Approval for this interventional prospective double-blinded clinical trial was granted by the Ethics Committee of Tehran University of Medical Sciences. Three post-cardiac surgery ICU wards of a heart center were participated in this survey on account of the fact that the patients in these units had CV line catheters for the measurement of their central venous pressure. The participants were divided into interventional (113 patients) and control (136 patients) groups. The CV lines used in this study were double lumen catheters.

The patients enrolled were: 1) all patients candidated for open heart surgery in Tehran Heart Center who granted consent for participation in the study; 2) all patients for whom the catheter was inserted for a minimum period of two days; and 3) all patients without any evidence of infection at the time of admission. Patients fulfilling the aforementioned criteria were divided into two groups of intervention and control. Patients were excluded if there was sepsis on arrival, obvious evidence of infections such as pneumonia, CV line insertion site other than the internal jugular vein, or catheter exchange prior to post-cardiac surgery ICU admission. The other exclusion criteria were having a catheter for less than 48 hours and not being admitted to the post-cardiac surgery ICU for any reason.

As a routine, first the patients took a shower and then the bacterial colonization rate was minimized by having them bath with Chlorhexidine 2%.

About half an hour to one hour before surgery, all the patients were separated into the intervention and control groups based on simple randomization and entry sequence to the pre-operation room. Each day, a simple coin randomization technique was used to determine the group for the first patient and the spraying of pure water or Sanosil 2% on the catheter location (from the upper chest to the mandible). Subsequently, odd and even numbers were used to determine the group of the other patients. This process was performed by a trained nurse, who also recorded date and time and the type of solution sprayed for each patient. Both spray bottles were similar in shape and cover. Sanosil does not have any color or smell and is similar to water, and the patients were blinded to the study.

In the operating room, sterile gloves were used, and the catheterization area was covered with a sterile gown. The area was disinfected by scrubbing it with gauze soaked in 10% Povidone-Iodine, starting from the site of catheter insertion and then moving outward in a circular motion. This process was repeated with two more pieces of gauze. No other antibacterial solution or ointment was applied on the site of catheter insertion or the catheter itself. For all the patients, double lumen catheters were inserted by anesthesiologists, blinded to the group type of the patients. The site of the CV line was determined via an anterior approach to the right internal jugular vein, and the skin was penetrated at the apex of the anterior triangle, formed by the clavicle and the two heads of the sternocleidomastoid muscle. The catheters were sutured in place and the area was covered with sterile dressing.

In the operating room and before extubation and at least

during the first eighteen hours of ICU stay, the central venous pressure was measured continuously and digitally through the CV line. However, after the transfer of the patients to the post-cardiac surgery ICU, the measurement of the central venous pressure was carried out intermittently and manually with a ruler.

Each day, two trained ICU nurses, blinded to the group type of the patients, collected the tips of five removed catheters aseptically via a simple randomization technique and sent them to the laboratory for the bacterial culture of both the outside and inside of the tube.

When a bed was not occupied or when a patient was excluded, the last number was replaced. The post-cardiac surgery ICU patients were treated with intensive care medicine irrespective of their group types. In the post-cardiac surgery ICU, the infusion of most of the medicines was done through the CV line and based on the standard criteria. Data on the type and duration of antibiotic therapies, creatinine clearance, urinary output, total parenteral nutrition therapies, recurrent surgery, reintubation, blood pressure, laboratory results, and presence of any infection signs and symptoms (fever ≥38 °C, chills, and shivering), sepsis, pneumonia, or CV line insertion site infection were recorded on standard data collection sheets by expert nurses.

Each day, the patients were evaluated for any evidence of infection signs in the post-cardiac surgery ICU. Sepsis was diagnosed on the basis of the Centers for Disease Controland Prevention (CDC) criteria. In the presence of any sign of infection in the patients, 5 cm of the catheter and the peripheral blood were cultured.

Before the transfer of the patients to the general wards, the catheters were removed and the culture of their tip was sent to the laboratory.

The distal end of the catheter was held over a sterile container and the last 5 to 6 cm was cut with sterile scissors. The specimen was not placed in saline or a transport medium, and the container was sealed and transported to the central laboratory within one hour. The tips were laid on Blood Agar Plates (BAP) and rolled back and forth across the entire surface and then placed into thioglycollate broth.

Normal distribution of the continuous variables was assessed via the Kolmogorov-Smirnov test; and because there was no normality, the continuous variables were compared between the control and intervention groups via the Mann-Whitney test. The independent t-test was employed for the normal variables, and the qualitative variables were compared between the two groups with the chi-squared test.

The efficacy of our intervention, on the basis of the results of the bacterial colonization rate of the CV lines, was reported by using relative risk with a 95% confidence interval (CI). For the statistical analyses, the statistical software SPSS version 16.0 for Windows (SPSS Inc., Chicago, IL) was used.

Results

Totally, 249 CV catheters were installed for 249 patients in three post-cardiac surgery ICU wards. The study population was divided into intervention and control groups. The CV line was reinserted for 4 patients, and 2 patients had CV line insertion sites other than the internal jugular vein; the latter were excluded from the study. Five samples were excluded before culture because of disarrangement.

There was no meaningful difference between the control and intervention groups in age, sex, body mass index (BMI), last creatinine before surgery, diabetes mellitus, type of surgery, days between hospitalization and CV line insertion, days between insertion and removal of the CV line, cardiopulmonary pump time, total parenteral nutrition, inotropes use on admission day, balloon pumping on the first day of admission in the ICU, reoperation, re-intubation, and reason for CV line removal (Tables 1and 2).

None of the patients in either group had any evidence of sepsis, pneumonia, and ulcer infection during the study time. The CV lines were removed in only 5 patients because of the presence of fever (>38 °C) in at least two separate measurements: 3 patients in the control group and 2 in the intervention group (p value = 0.81). Among these 5 (2%)

Table1. Baseline characteristic of the patients

	Continuous variables Baseline characteristic according in both groups		
	No Intervention group (n=113)	Interventiongroup (n=136)	P value
Age (y)*	57.0 (51.0-64.0)	60.0 (53.0-68.0)	0.17
Days between insertion and removal of the CV line*	3.0 (2.0-3.5)	3.0 (2.0-4.0)	0.14
Days between administration in hospital and insertion of the CV line*	7.0 (6.0-7.0)	7.0 (6.0-7.0)	0.53
Creatinine (mg/dl)**	0.9 (0.8-1.1)	1.0 (0.8-1.2)	0.44
Body mass index(kg/m^2)**	25.7 (4.4)	26.7 (3.9)	0.06
Cardiopulmonary pump time (min)**	82.5 (31.7)	66.5 (24.8)	0.16

*Data are presented as median (interquartile range)
**Data are presented as mean±SD
CV Line, Central venous line

Table 2. Comparison of the qualitative variables between the two groups*

	Baseline characteristic in both groups		P value
	No Intervention (n=113)	Intervention (n=136)	
Sex			
Female	32 (23.5)	27 (23.9)	0.95
Male	104 (76.5)	86 (76.1)	
Type of surgery			
CABG	102 (75.6)	81 (72.3)	
CABG + Valve	9 (6.7)	9 (8.0)	0.89
Valve	20 (14.8)	17 (15.2)	
Congenital	4 (3.0)	5 (4.5)	
Total Parenteral Nutrition (TPN)			
No	128 (94.8)	109 (96.5)	0.53
Yes	7 (5.2)	4 (3.5)	
Diabetes			
No	91 (66.9)	84 (75.0)	0.16
Yes	45 (33.1)	28 (25.0)	
Inotropes on admission day			
No	122 (89.7)	100 (88.5)	0.76
Yes	14 (10.3)	13 (11.5)	
Balloon pumping in the first day admission in ICU			
No	134 (98.5)	108 (95.6)	0.16
Yes	2 (1.5)	5 (4.4)	
Reoperation			
No	135 (99.3)	113 (100)	0.54
Yes	1 (0.7)	0	
Re-intubation			
No	135 (99.3)	113 (100)	0.36
Yes	1 (0.7)	0	
Reason for CV line removal			
Transfer to non-critical care wards	131 (97.8)	109 (98.2)	0.81
Fever >38 °C	3 (2.2)	2 (1.8)	

*Data are presented as n (%)
CABG, Coronary artery bypass graft; ICU, Intensive care unit

Table 3. Comparison between the two procedures

	No Intervention	Intervention	RR	CI %95	P value
Result of Culture			1.05	0.76-1.45	0.75
Negative	107 (78.7%)	87 (77.0%)			
Positive	29 (21.3%)	26 (23%)			

patients, there were 2 positive CV line cultures with staphylococcus hemolyticus: one in the intervention group and the other one in the control group. In the other patients, the catheters were removed routinely after transferring the patients to the normal surgery ward for preparation before discharge.

Table 3 introduces 55 cases with positive cultures of catheter tips: 29 (21.3%) in the control group and 26 (23%) in the intervention group (p value = 0.75). Considering confounding factors in a stepwise logistic regression model, there was no significant statistical difference between the two groups (RR: 1.05, 95%CI: 0.76 - 1.45).

The most common organism having colonized in the cultures of the catheter tips was staphylococcus epidermis: 36 (65.5%) of all the positive cultures (20 cases in the control group, 16 cases in the intervention group). The other isolated microorganisms of the positive cultures were mainly gram-positives, including staphylococcus hemolyticus (9 [16.4%]),

staphylococcus aureus (2 [3.6%]), and streptococcus (1 [1.8%]). Gram-negatives were found only in 4 patients (2 in each group). There was no significant difference between the two groups regarding isolated microorganisms (P value = 0.454).

Discussion

CABSI is one of the most important causes of mortality and morbidity, not least in the ICU patients, and could increase hospital stay and consequently hospitalization costs. It is, therefore, vitally important to reduce the rate of CABSI. To our knowledge, this is the first survey of its kind to use Sanosil as an antiseptic sprayed on the catheter insertion site. Our findings demonstrated no meaningful result in terms of reduction in catheter bacterial colonization after the addition of Sanosil to the routine preparation procedure (Chlorhexidine bath one day before and scrub with Povidone-Iodine) for CV line insertion in our center.

We expected a meaningful difference between our new method and the classical one because of the characteristics of Sanosil and its component, silver, such as high disinfecting and sterilizing properties and long-lasting antimicrobial effects.[18-22] We also expected to see the synergistic effects of Sanosil with the routine antibacterial agents (Chlorhexidine and Povidone-Iodine) in our intervention group. There has been some research into the synergistic effect of some antimicrobial agents. For example, the synergistic effect between Chlorhexidine and the silver sulfadiazine-coated catheter was assessed and showed a reduction in the rate of CABSI.[2,21,22] It is worthy of note, however, that there is discrepancy in the results of the investigations conducted on such synergistic effects.[23-26]

The catheter colonization rate is high (about 22.1%) even during an average of three days after insertion in post-cardiac surgery patients, who are in a more controlled situation than are other ICU patients.[2-7] In cardiac surgery patients, bacterial colonization is even more worrisome because this group of patients is at risk for endocarditic and septic vegetation, both of which are catastrophic events. Furthermore, in the case of fever and sepsis workup, catheter colonization may complicate the situation for making a definite decision and lead to inappropriate antibiotic management and its undesired consequences. It is advisable that sufficient attention be paid to the prevention of catheter bacterial colonization before and during catheter insertion and subsequently during its usage.

In the present study, there were only 5patients with fever (2% of all the patients). Such a low prevalence rate may not be of statistical significance, but the fact that there was a negative culture in the majority of these 5 patients (3 out of 5) should raise the alarm about the specificity and sensitivity of the catheter culture in follow-up for fever in the post-cardiac surgery ICU patients.

There are some probable reasons why we did not achieve meaningful differences between our two groups: 1) It seems that the patient's skin could be recontaminated readily between the pre-operation and operating rooms; consequently, using Sanosil in the operating room rather than in the pre-operation room could be more effective.2) The average time of catheter installation in our study was three days; while in other surveys, CABSI usually occurred after five days.[24] With respect to the lasting effect of Sanosil, further studies are required to evaluate the efficacy of Sanosil in long periods of catheterization. 3) There were no cases of sepsis and ulcer infection in this study; this may be in consequence of our low sample size. We would, therefore, suggest that similar surveys be undertaken with larger sample sizes in the future.

Staphylococcus epidermidis was the most frequent organism in our study, and gram-negatives accounted for the minority of the cases among our patients. These findings are consistent with those reported by some previous surveys.[27]

Conclusion

Our evaluation of bacterial colony count change after using Sanosil on the catheter site before insertion showed no significant differences between the two groups of patients in terms of either the frequency of positive cultures or the profile of isolated microorganisms. Consequently, we were unable to demonstrate that adding Sanosil to the routine preparation procedure (Chlorhexidine bath one day before and scrub with Povidone-Iodine at the time of CV line insertion) would be effective in reducing catheter bacterial colonization.

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