Research paper

Chlorhexidine-impregnated gel dressing compared with transparent polyurethane dressing in the prevention of catheter-related infections in critically ill adult patients: A pilot randomised controlled trial

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ARTICLE INFORMATION

ABSTRACT

Background: In patients with short-term percutaneous central venous catheter (CVC), it is recommended that a dressing be applied to the catheter insertion site to prevent catheter-related infections.
Objectives: The objective of this study was to assess the feasibility of a randomised controlled trial to compare the efficacy of chlorhexidine-impregnated dressing with that of polyurethane dressing in the prevention of catheter-related infections in critically ill adult patients with short-term percutaneous CVC.
Methods: One hundred fifteen patients with a CVC were randomised to chlorhexidine-impregnated gel dressing (chlorhexidine gel group) or transparent polyurethane dressing (polyurethane group) between April and December 2014. Feasibility outcomes included data on eligibility, recruitment, missing data, and protocol violation. The primary outcome measure of efficacy was the presence of colonisation with the same microorganism in both the skin swab around catheter insertion site and the catheter tip.
Results: Of 526 patients assessed for eligibility, 411 (78%) did not meet inclusion criteria, and 115 (22%) were randomised. Among participants of both groups, there were 14 missing primary outcomes of which 10 were due to failure to collect the catheter tip (a protocol violation). The final sample had 47 and 54 individuals in the chlorhexidine and polyurethane groups, respectively. Skin and catheter tip were colonised by the same microorganism for 13% of the participants in the chlorhexidine group and 8% in the polyurethane group, although the difference was not statistically significant (p = 0.51). There were no differences between the two groups for catheter tip colonisation, skin site colonisation, catheter insertion site infection, catheter-related bloodstream infection, skin irritation, and the number of unplanned dressing changes.
Conclusions: Our preliminary results found that a large randomised controlled trial would be feasible. This study provides valuable information that can be used to design more robust studies to prevent infection among patients with short-term percutaneous CVC when using either chlorhexidine or polyurethane dressing.

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Central venous catheters (CVCs) are necessary for the treatment of critically ill patients and are useful for infusion, blood withdrawal, haemodynamic monitoring, intravenous administration of complex drug treatments and blood components, and nutritional support.[1,2] In the United States, it is estimated that five million patients per year need central venous access.[3]

The benefits of CVC are well known, but there is a risk of catheter-related infections that might increase mortality, length of hospital stay, and costs for patients with CVC.[1,4,5] According to the Centers for Disease Control and Prevention, there are four routes for contamination of short-term percutaneous catheters: migration of skin microorganisms from the CVC insertion site to the catheter tip; direct contamination of catheter by hand contact or contaminated fluids; catheter hematogenously contaminated from another focus of infection; and infusate contamination. The most common route is migration of skin microorganisms.[5]

For short-term percutaneous CVCs, the most important strategies to prevent catheter-related infections are those that decrease contamination via the extraluminal route. Therefore, skin antisepsis and dressing applied to the CVC insertion site are expected to be effective strategies for the prevention of infections via migration of microorganisms from the skin to the catheter tip.[3,6]

Bashir et al.[7] demonstrated that the skin flora is not completely eliminated during antisepsis. Various types of dressings have been used to protect the insertion site of central venous access devices.[2,8] These dressings have the objective of reducing the migration of microorganisms to the tip of the catheter, a situation that could increase the probability of bloodstream infection (BSI). Chlorhexidine-impregnated dressing was developed to improve the prevention of growth of microorganisms in the insertion site. Chlorhexidine dressing releases the active compound directly in the skin, allowing for longer periods of time between dressing changes.[6,7]

In Brazil, at the time of this writing, chlorhexidine dressings are about three times more expensive than other dressings such as polyurethane and sterile gauze. In situations in which the healthcare system has limited resources, it would be helpful to know if and by how much the chlorhexidine dressing decreases the rate of catheter-related infection. Meta-analyses by Safdar et al.[3] and Ullman et al.[8] showed some evidence that the chlorhexidine dressing reduces those infections, but their findings were general and not specific to types of CVCs, patient populations, or routes of infection.

We were interested in assessing the effect of the chlorhexidine dressing in reducing infections via migration from skin to the catheter tip in critically ill adult patients with short-term percutaneous CVCs. Recent studies and meta-analyses have used very general definitions of catheter-related infections, including catheter-related bloodstream infection (CRBSI) and colonisation of the tip of the catheter, both of which do not necessarily imply the migration route. Therefore, for the purpose of identifying when an infection is most likely caused by migration of a microorganism from the skin to the tip, one must assess the presence of the same microorganism in a culture from the skin around the catheter insertion site and in the catheter tip. This is the same definition used by Roberts and Cheung[9] in 1998 to establish infection via migration.

To study the efficacy of the chlorhexidine-impregnated dressing against other dressings, rigorous studies with stringent definitions of catheter-related infections and in specific populations are needed. However, these studies would be complex in nature and require a pilot study to assess feasibility and to provide information that can be used in a larger confirmatory study.

Our aim was to conduct a pilot study to compare chlorhexidine-impregnated dressing with polyurethane dressing in preventing the colonisation of the catheter tip via migration from skin in critically ill adult patients with short-term percutaneous CVC. In this study, feasibility and preliminary results are presented and discussed.

1. Methods

1.1. Design and sample

This study was a pilot randomised controlled trial to assess feasibility and potential efficacy of the chlorhexidine-impregnated gel dressing (denominated chlorhexidine gel group) compared with transparent polyurethane dressing (polyurethane group). Participants were randomly assigned to either of the groups. The study was conducted at the intensive care unit (ICU) and the cardiothoracic intensive care unit (CICU) at the General Hospital of the Medical School of Ribeirão Preto of the University of São Paulo, Brazil. The trial was registered at ClinicalTrials.gov, number NCT02472158.

Inclusion criteria were as follows patients who were admitted at the ICU or CICU, 18 years of age or older, and had a percutaneous CVC inserted in the subclavian, femoral, or jugular veins, which was expected to be in place for at least 48 h. Exclusion criteria were as follows: patients with a CVC with antimicrobial coating, with known allergic or hypersensitivity reaction to any compounds of chlorhexidine or polyurethane, with active lesions on the skin on the CVC or dressing site, and having a current BSI.

At the time of this study inception, the practice of estimating a sample size for a pilot study based on its feasibility outcomes (such as recruitment, for example) was still in its infancy and was not incorporated in our design. We found a single study that used the same primary outcome as ours,[9] but it was very small, and it is now 20 years old; thus, their findings were not useful to plan this study. Because pilot studies have the objective to provide estimates of various types (feasibility and efficacy), the larger the sample size, the better the estimate (in the sense of smaller confidence interval for the proportion). In the literature, studies of this type are usually not very large, and it is common to have around 30 individuals in each group that is being studied (although 30 is an arbitrary number). The two hospital units where the study was conducted have a total of 14 beds, and the mean length of stay is 13 days. Given the time allocated for the study, we estimated that we had the potential to recruit 140 patients, which would allow us to have reasonably robust estimates of the various outcomes we observed. Thus, we aimed to collect as large sample size as possible within the time and resources available, and a total of 115 individuals participated in the study, which is a sample size comparable to other recent catheter-related pilot studies found in the literature.[10–12] The trial was registered at ClinicalTrials.gov, number NCT02472158.

1.2. Ethical considerations

The study was approved by the committee on ethics research of the institution. Written informed consent was obtained from patients with Glasgow Coma Scale (GCS) ≥ 8. If the patient was mechanically ventilated or had GCS ≤ 8, the family was asked for permission to include the patient in the study.

1.3. Recruitment

Between April and December 2014, patients receiving short-term percutaneous CVC were approached by one of the investigators and were invited to participate in the study. Inclusion criteria were checked, and if eligible, the study was explained to the participant or his/her family. A randomisation list with equal

probability of assignment to the two groups was generated using statistical software R (R Foundation for Statistical Computing, Vienna, Austria, http://www.R-project.org/). The sequence was inserted in numbered opaque envelopes and sequentially retrieved as a person was randomised in the study.

1.4. Procedures

The insertion of the CVC was performed according to the recommendations of Centers for Disease Control and Prevention[5]; maximal sterile barrier precautions were used by the clinician who performed the procedure (use of cap, mask, sterile gloves, large sterile drape, gown, and surgical hand antisepsis). The femoral vein was avoided whenever possible. Daily chlorhexidine bathing was performed in all patients. During the first 24 h after CVC insertion, the patients received a sterile gauze and tape dressing, given the possibility of bleeding in the insertion site.

There are two types of chlorhexidine dressing: sponge and gel. We chose the chlorhexidine gel dressing because it is applied in a single step and it minimises the possibility of contamination during the procedure.[7,13,14] The chlorhexidine is in contact with the skin as soon as the dressing is applied to the skin. The gel is translucent and allows the visualisation of the CVC insertion site.

Participants in the polyurethane group received a transparent polyurethane dressing (Tegaderm Transparent Film Dressing; 3M, St. Paul, NM, USA), whereas patients in the chlorhexidine gel group received chlorhexidine-impregnated gel dressing (Tegaderm CHG IV Securement Dressing; 3M, St. Paul, NM, USA). Dressings were changed every seven days (planned) or whenever damp, loosened, or visibly soiled (unplanned). During dressing changes, the catheter insertion site was cleaned using sterile gauze and a 0.5% chlorhexidine-alcohol preparation.

Evaluation of the skin and dressing, patients' clinical conditions, and any protocol violations were performed daily by one of the investigators and documented. The patient was followed up until the CVC was removed. When the catheter was removed, the catheter tip and a skin swab were collected for laboratory analysis. If there was suspicion of a CRBSI, two peripheral blood samples were also collected for culturing. Data collections were performed by trained nurses from each unit.

The laboratory microbiologists were blinded to the group. The two dressings were visibly different, and consequently, it was not possible to blind the patients, the ICU/CICU staff, and the investigators who collected data in the ICU/CICU. If a blood culture was positive, another investigator, blinded to the study group, reviewed the medical record to classify the finding as a CRBSI or not.

1.5. Outcomes

1.5.1. Participant and catheters characteristics

We collected the following demographic and clinical measures for each participant: age (in years), sex, hospital care unit, GCS, Acute Physiology and Chronic Health Evaluation score, length of stay in the care unit, category of admission (medical, planned surgery, and unplanned surgery), main reason for admission in critical care, presence of chronic diseases, occurrence of death during critical care (yes/no), use of parenteral nutrition (yes/no), heparin use (yes/no), and antibiotic use before catheter insertion (yes/no). For the catheter, we collected the number of lumens, type of vein used for insertion of CVC, length of time with CVC (in days), and reason for catheter removal.

1.5.2. Feasibility outcomes

For feasibility, we collected data on proportion of eligible individuals among all individuals screened, the proportion of individuals screened who accepted to participate, missing data and their reasons, and protocol violations.

1.5.3. Potential efficacy outcomes
1.5.3.1. Primary outcome

- **Skin and catheter tip positive for the same microorganism:** It is defined as the presence of the same microorganism in a culture from the skin around the catheter insertion site and the catheter tip, both with growth of more than 15 colony-forming units (CFUs) in a semiquantitative culture.[9]

1.5.3.2. Secondary outcomes

- **Skin site colonisation**: positive semiquantitative growth of more than 15 CFUs in a culture of the skin around the catheter insertion site, with or without concomitant BSI;[15]

- **Catheter tip colonisation:** growth of more than 15 CFUs from a 5-cm segment of the catheter tip by semiquantitative (roll-plate) culture;[4]

- **Clinical infection in the insertion site:** presence of erythema, induration, and/or tenderness within 2 cm of the catheter insertion site, with or without concomitant BSI;[4]

- **Catheter-related BSI**: presence of bacteraemia or fungemia in a patient who had an intravascular device and more than one positive blood culture result obtained from the peripheral vein, with clinical manifestations of infection (e.g., fever, chills, and/or hypotension) and no apparent source for BSI (with the exception of the catheter), and positive result (more than 15 CFUs) of the semiquantitative tip culture with the same microorganism as the one isolated from the peripheral blood culture.[4]

- **Planned and unplanned dressing changes**: the number of dressing changes compared with the number of planned changes according to duration of CVC.

- **Skin irritation**: The occurrence of skin irritation was defined as the presence of areas of skin loss, erythematous plaques, or vesicles in the site of CVC insertion.

The skin was sampled before the catheter removal by pressing a moist cotton swab in a 3-cm area around the catheter insertion site. A semiquantitative culture was performed by streaking the swab on blood agar plates. For the microbiological analysis, the catheter tip was cultured using blood agar plates and the semiquantitative technique.[16] The blood culture was performed using an automatised system (Bactec Dade Berhing, Dublin, Ireland), and the samples were monitored for seven days or until positive. When positive, the samples were cultured on chocolate agar, MacConkey agar, and mannitol agar. Microorganisms were identified by the VITEK® system (Biomerrieux, Marcy-l'Étoile, France) using identification and antibiotic susceptibility test.

1.5.4. Statistical analysis

Descriptive analysis was performed for all variables. Catheter characteristics were compared between the two groups using independent t-tests for time in place of catheter, whereas Fisher exact test was used for all other variables.

Feasibility outcomes were estimated for the two groups. Primary and secondary efficacy outcomes were categorical, and we

compared the proportion of each outcome between the two groups using the Fisher exact test. Significance level was set at 0.05, and no adjustment was performed because this was a pilot study and exploratory in nature. Data were analysed using IBM SPSS Statistics for Mac (Version 24.0, Armonk, NY: IBM Corp) and R (version 3.1.3, (R Foundation for Statistical Computing, Vienna, Austria)).

2. Results

2.1. Feasibility outcomes and participant/catheter characteristics

Fig. 1 shows the flowchart for enrolment and follow-up of participants. Of 526 patients assessed for eligibility, 411 (78%) did not meet inclusion criteria, and 115 (22%) were eligible. All patients or their families (100%) agreed to enrol and signed the consent

form and were randomised into chlorhexidine-impregnated gel dressing (n = 55) or polyurethane dressing (n = 60) groups.

In the chlorhexidine group, four patients did not have the catheters collected by staff (7.3%, protocol violation), two patients were discharged to ward with CVC, and two patients withdrew the CVC (7.3%), for a total of 14.7% of missing values. In the polyurethane group, five patients did not have catheters collected by staff (8.3%, protocol violation), and one patient was discharged to ward with CVC (1.7%), for a total of 10% of missing values. The final sample analysed was composed of 47 patients in the chlorhexidine and 54 in the polyurethane groups. There were no other protocol violations because every patient received the dressing to which he/she was randomised until the CVC was removed.

Early in the study, we made a change in the randomisation process. Initially, the randomisation was performed at the moment of the CVC insertion. However, a few severely ill individuals died
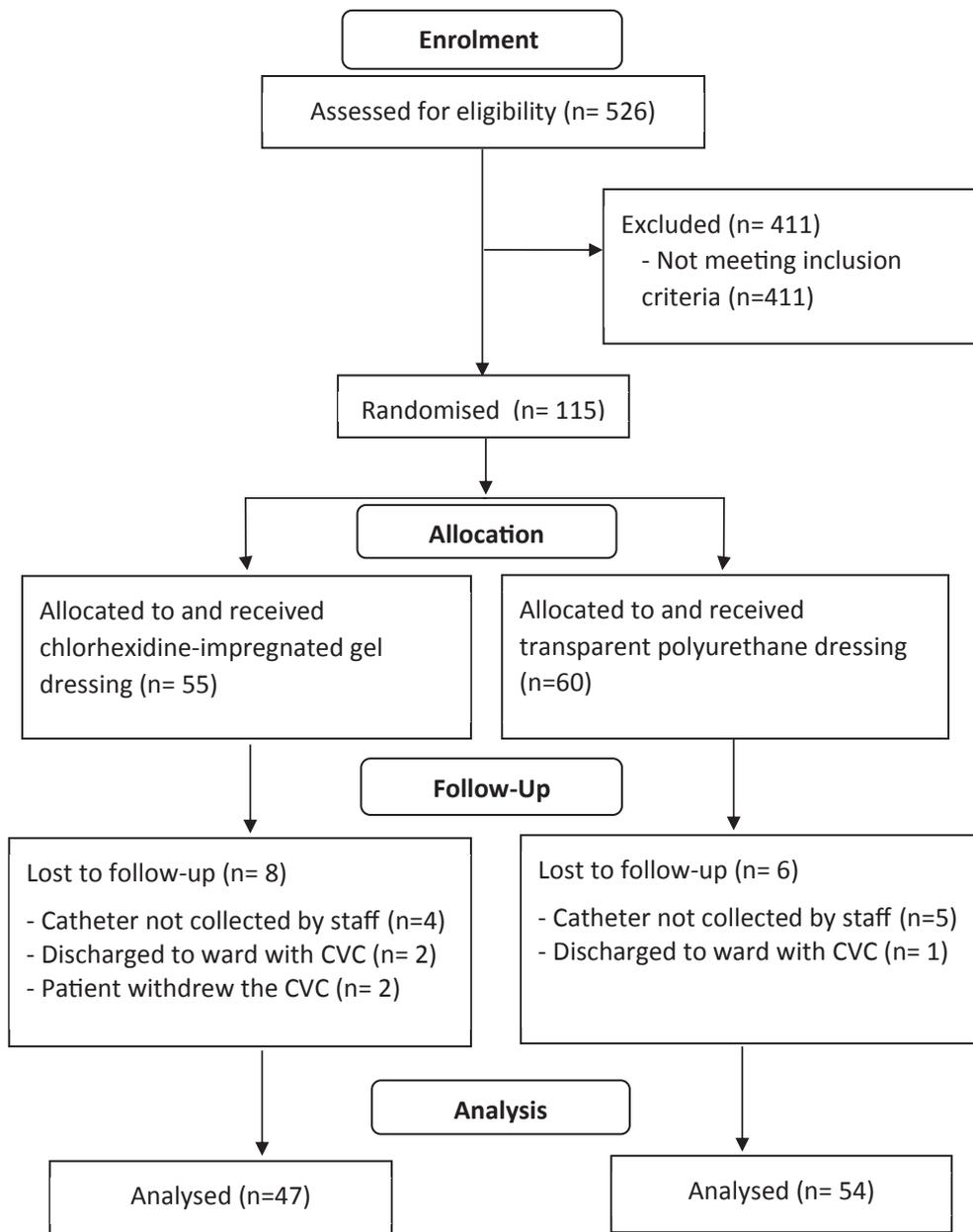

Fig. 1. CONSORT 2010 flow diagram. CVC, central venous catheter.

within 24 h. We modified the protocol to randomise the patients 24 h after the CVC insertion, at which point they would have the first dressing change and the first opportunity to receive the dressing to which they were randomised. This procedure also allowed us to have more time to ask for consent from family members when the patient had GCS ≤8 because the access to the family is likely to occur during admission and visiting hours.

Table 1 shows the distribution of demographic and clinical characteristics by group. The chlorhexidine group had a larger proportion of individuals from the ICU. The two groups differed in reasons for admission and in the proportion of individuals who died during the critical care stay. It is likely that the higher proportion of death in the chlorhexidine group was associated with the higher proportion of septic shock in that group because septic shock is one of the common reasons for mortality in hospitalised patients.[17]

Table 2 shows catheter characteristics in the two groups. There was a larger proportion of individuals receiving a triple-lumen catheter in the chlorhexidine group (p = 0.04), despite the randomisation. Distributions for all other variables did not show statistical differences.

2.2. Potential efficacy outcomes

Table 3 shows the outcomes for the two groups. They did not differ statistically in percentage of individuals presenting colonisation by the same microorganism in the skin swab and catheter tip cultures (13.3% in the chlorhexidine and 8.3% in the polyurethane groups, p = 0.51). A breakdown of all observed combinations of skin swab and catheter tip results is also shown. For two individuals in the chlorhexidine and six in the polyurethane groups, the skin swab was not collected before removing the catheter. Catheter tip colonisation (any type of microorganism) was not statistically different between the groups (p = 1.0). Skin colonisation was higher in the chlorhexidine (31.1%) than in the polyurethane group (14.6%),

although not statistically significant (p = 0.08). Percentages were not statistically different for clinical infection at the insertion site (p = 0.77) and CRBSI (p = 1.0). There were 12 individuals in each group from whom blood samples were not taken, thus making the sample size much smaller for assessment of CRBSI.

Changes of dressing were categorised as planned and unplanned (1–2 more than expected and 3 or more than expected, respectively) (Table 3). The distributions of the categories were not statistically different (p = 0.51), although a higher percentage of individuals in the polyurethane group had more than three planned changes than those in the chlorhexidine group.

One patient in the chlorhexidine group and one in the polyurethane group presented skin irritation. In both cases, it was not necessary to discontinue the use of the dressing.

Table 4 shows the microorganisms identified for each outcome. The bacteria isolated from the catheter swab, tip, and blood were mainly coagulase-negative *Staphylococcus*.

3. Discussion

One of the difficulties of performing a study such as ours is missing data. In this study, the total loss in each group was less that 15%, and violations of protocol related to lack of catheter tip collection were 7–8%. We lost some data when the catheter tip was not immediately prepared to be sent to the laboratory, rendering it unusable for the research once it had been exposed to other possible contaminants. This happened in situations of stress (when the person died, for example). In addition, two patients withdrew the catheter themselves, and a few patients were discharged from the hospital with the catheter.

To minimise missing data, our research team provided verbal and written instructions for each step to be followed for data collection. Although some losses will not be under control of the researcher, in a larger study, one possible improvement would be to have some mechanism to remind the nurses who remove the CVC to keep it for the research team. Given the large percentage of ineligible individuals in the units where we recruited, it might be also necessary to add other units or institutions in a larger study to achieve the required sample size.

The appearance of the two dressings precluded us from having a blind study design, although it is unlikely that knowing the type of dressing would bias our outcome. However, we would have to be attentive to the possibility that the healthcare providers would be biased by a specific type of dressing, such as neglecting changing a certain dressing because it is supposed to last longer. We did not see this happening in our study, but the potential problem could be minimised by training the research team and having a protocol that would facilitate the data collection without disrupting the workflow of the care unit.

Acceptability of the dressing was not measured in the patient in the study, given that some individuals were not able to answer questions.

In our study, there were more individuals with risk factors for CRBSI in the chlorhexidine gel group than in the polyurethane group.[5] If a larger study is undertaken in the future, the randomisation could be stratified on the reason for receiving a CVC, severity of illness, and the number of lumens in the catheter. This step would improve balance among the groups regarding risk factors for CRBSI and would allow a better assessment of the difference between the two dressings.

We did not find evidence that chlorhexidine-impregnated gel dressing was more efficacious than transparent polyurethane dressing in preventing colonisation of the catheter tip via migration. The presence of the same microorganism on skin and catheter tip occurred more often in the chlorhexidine group (13.3%) than in

Table 1
Demographic and clinical characteristics by intervention group.

Characteristics	Group	
	Chlorhexidine gel (n = 47)	Polyurethane (n = 54)
Age in years, mean (SD)	58.0 (15.8)	57.0 (18.0)
Sex, % male (n)	55.3 (26)	44.4 (24)
Care unit, % in each category (n)		
Intensive care unit	95.7 (45)	85.2 (46)
Cardiac care unit	4.3 (2)	14.8 (8)
Apache II, mean (SD)	26.8 (8.7)	24.5 (8.6)
Length of stay in days, mean (SD)	11.3 (10.6)	13.5 (14.3)
Admission category, % (n)		
Medical	87.2 (41)	81.5 (44)
Surgical (planned or unplanned)	12.8 (6)	18.5 (10)
Main reason for admission, % (n)		
Septic shock	66.0 (31)	33.3 (18)
Postsurgery care	12.8 (6)	18.5 (10)
Respiratory failure	10.6 (5)	20.4 (11)
Heart disease	4.3 (2)	11.1 (6)
Others	6.4 (3)	16.7 (9)
Presence of chronic disease, % (n)		
None	12.7 (6)	16.7 (9)
One	19.1 (9)	22.2 (12)
More than one	68.1 (32)	61.1 (33)
Occurrence of death, % (n)		
Alive at hospital discharge	36.2 (17)	61.1 (33)
Death at the critical care unit	51.1 (24)	29.6 (16)
Death in hospital after discharge from the critical care unit	12.8 (6)	9.3 (5)

APACHE II = Acute Physiology and Chronic Health Evaluation; SD = standard deviation.

Table 2
Catheter characteristics by intervention group.

Catheter characteristics	Group		P-value[a]
	Chlorhexidine gel (n = 47)	Polyurethane (n = 54)	
Number of lumens, % in category (n)			
Double (2)	83.0 (39)	96.3 (52)	0.04
Triple (3)	17.0 (8)	3.7 (2)	
Insertion vein, % in each type (n)			
Jugular	51.1 (24)	61.1 (33)	0.51
Subclavian	42.6 (20)	31.5 (17)	
Femoral	6.4 (3)	7.4 (4)	
Time in place in days, mean (SD)	7.7 (5.1)	7.7 (5.1)	0.96
Median (min, max)	6.0 (2, 23)	6.5 (1, 23)	
Parenteral nutrition, % yes (n)	12.8 (6)	9.3 (5)	0.75
Heparin use, % yes (n)	2.1 (1)	3.7 (2)	1.00
Antibiotic before catheter insertion, % yes (n)	87.2 (41)	88.9 (48)	1.00
Reason for catheter removal, % (n)			
End of treatment	40.4 (19)	53.7 (29)	0.27
Death	34.0 (16)	18.5 (10)	
Suspicion of catheter-related infection	23.4 (11)	22.3 (12)	
Other	2.1 (1)	5.6 (3)	

[a] P-value from t-test for independent samples for time in place of catheter and Fisher's exact test for all other variables.

the polyurethane group (8.3%), although the difference was not statistically significant. This might have occurred because the two groups were not completely comparable in the baseline characteristics, because the missing values (especially in the chlorhexidine group) might have biased the sample, or because there is

Table 3
Primary and secondary outcomes by randomisation group.

Outcomes	Group		P-value[a]
	Chlorhexidine gel (n = 47)	Polyurethane (n = 54)	
Primary outcome			
Sample size for primary outcome[b]	45	48	
Skin and catheter tip positive for same microorganism, % (n)	13.3 (6)	8.3 (4)	0.51
Breakdown of all categories of primary outcome, n[c]			
Skin and catheter tip positive for same organism	6	4	NA[d]
Both, skin, and tip negative	29	37	
Positive skin and negative tip	8	3	
Negative skin and positive tip	2	4	
Negative tip and skin not collected	2	5	
Positive tip and skin not collected	0	1	
Secondary outcomes, % yes (n/N)			
Catheter tip colonisation	17.0 (8/47)	16.7 (9/54)	1.00
Skin site colonisation[b]	31.1 (14/45)	14.6 (7/48)	0.08
Clinical infection at insertion site	14.9 (7/47)	11.1 (6/54)	0.77
Catheter-related bloodstream infection[e]	2.9 (1/35)	4.8 (2/42)	1.00
Changes in dressing during CVC period, % (n)			
Only planned changes	55.3 (26)	51.8 (28)	0.41
1–2 more changes than planned	38.3 (18)	31.5 (17)	
3 or more changes than planned	6.4 (3)	14.8 (8)	
One change fewer than planned	0.0 (0)	1.8 (1)	
Skin irritation	2.2 (1/47)	2.1 (1/54)	

N = total number in sample, n = total number with observed outcome.

[a] P-value from Fisher's exact test.

[b] Skin swab not collected for 2 individuals in the chlorhexidine group and 6 in the polyurethane group.

[c] Includes all individuals in the study.

[d] NA: not applicable. These data are for information only. Individuals without skin swab collected did not enter in the calculation of test for the primary outcome.

[e] Blood not collected in 12 individuals in each group, due to lack of suspicion of infection.

no real difference between the dressings. We found no statistically significant differences in the colonisation of skin swab and tip, in clinical infection at the insertion site, or in CRBSI. In this study, the majority of the infections related to the catheter were caused by coagulase-negative *Staphylococcus*, similar to other studies.[3,5,14] We observed skin irritation in only one patient of each group. Other studies have reported skin irritation or damage for both dressings.[18–22] A few case reports showed erosive contact dermatitis and skin necrosis from chlorhexidine-impregnated dressings.[23,24]

Repeated application and removal of dressings damage the skin integrity, lead to inflammatory skin reactions, and increase rates of CRBSI.[25] A randomised controlled trial showed that dressing disruptions was a common event and a risk factor for catheter-related infections.[26] We found no statistically significant difference in planned dressing changes between the groups, although the polyurethane group had more unplanned changes than the chlorhexidine group. Owing to the possible skin irritation and cost of unplanned changes, it might be important to evaluate the frequency of dressing change when evaluating the efficacy and cost-benefit of the dressing being studied.

The aforementioned results can be used to design confirmatory studies, and we will turn the focus of the discussion to the issues that we observed during the conduction of the study, which can provide subsidies for designing a confirmatory study for prevention of CRBSI in critically ill patients using a short-term percutaneous CVC.

The first issue is the definition of the primary outcome. In the literature, we found only one controlled trial with the same primary outcome and comparison groups as ours. The study was conducted in 1998, with only 17 individuals in the chlorhexidine and 16 in the polyurethane groups.[9] In the chlorhexidine group, one person had the catheter tip skin swab colonised by the same microorganism. In that study, in the polyurethane group, no patients had colonisation by the same organism on both catheter tip and skin swab.

From a conceptual point of view, if one wants to assess if a BSI was related to the catheter and that the infection was via migration, it makes sense to assess if the same microorganism is present in both the skin and catheter tip; otherwise, one cannot assume migration as the mechanism of infection. Other studies have evaluated different outcome variables, such as the presence of microorganisms in the insertion site of short-term percutaneous CVC only,[27] or used several types of catheters in the same study.[14,18] These outcomes do not address the migration mechanism that the chlorhexidine-impregnated dressing is supposed to prevent.

A second issue in the literature on the chlorhexidine dressing is that a few studies performed are specific for a certain type of catheter or population,[16–19] such as oncology patients[28,29] and ICU.[14,18] The dressing might be more efficacious in one setting or another or in populations with different levels of severity. This is an important consideration, especially in less developed countries where the costs of routine use of chlorhexidine dressings might be prohibitive. If one could find in which patient populations and types of catheter the chlorhexidine dressing is more efficacious than polyurethane dressing, then those patients should receive the chlorhexidine dressing. If in certain situations, the two dressings are equivalent, then a choice based on cost could be made. A study of equivalence of the two dressings would require a very large sample size, especially because the outcome of interest (presence of the same microorganism in both skin and catheter tip) might be a relatively infrequent event. However, a large study, possibly performed in a multicenter setting, would answer the question for a specific populations and type of catheters, whereas the same is not achievable with a meta-analysis of heterogeneous studies.[2,3] The

Table 4
Laboratory results by type of colonisation and randomisation group.

Types of microorganisms found in the culture	Group	
	Chlorhexidine gel	Polyurethane
Primary outcome		
Catheter tip and skin swab colonisation, n		
Coagulase-negative *Staphylococcus*	3	1
Staphylococcus aureus	1	
Acinetobacter baumannii and *Enterobacter cloacae*	1	
Pseudomonas aeruginosa	1	
Serratia marcescens		1
Klebsiella pneumoniae		1
Secondary outcomes		
Catheter tip colonisation, n		
Coagulase-negative *Staphylococcus*	4	3
Acinetobacter baumannii		2
Acinetobacter baumannii and *Enterobacter cloacae*	1	
Pseudomonas aeruginosa	1	
Staphylococcus aureus	1	
Fungi	1	
Serratia marcescens		1
Acinetobacter baumannii and *Proteus mirabilis*		1
Klebsiella pneumoniae		1
Skin insertion site colonisation, n		
Coagulase-negative *Staphylococcus*	8	3
Acinetobacter baumannii	2	1
Klebsiella pneumoniae		2
Acinetobacter baumannii and *Enterobacter cloacae*	1	
Morganella morganii	1	
Pseudomonas aeruginosa	1	
Staphylococcus aureus	1	
Serratia marcescens		1
Catheter-related bloodstream infection, n		
Staphylococcus aureus	1	
Acinetobacter baumannii		1
Coagulase-negative *Staphylococcus*		1

published meta-analysis can only answer a general question, but not specific ones.[2,3,30]

For future studies, one could calculate the necessary sample size using our outcome definition in the same population of patients, in a randomised trial comparing chlorhexidine with polyurethane dressing. For example, with the significance level of 0.05, power of 0.80, and a test of proportions to detect a change from 8.3% of colonisation in the polyurethane group (as we found) to 5% colonisation in the chlorhexidine group, one would need a sample size of 1059 individuals in each group, whereas for 2% colonisation, one would need 412 individuals in each group. Trials testing for equivalence instead of superiority would require larger sample sizes.

4. Conclusions

This feasibility pilot study did not show a difference in proportion of catheter-related infections between the chlorhexidine and polyurethane groups in critically ill adult patients with short-term percutaneous CVC. Both dressings were well tolerated by the patients. Our study provides results that might be used for designing and calculating the sample size for future studies that would address the question of whether chlorhexidine-impregnated dressing might be more efficacious (superior) or as efficacious (noninferior) than polyurethane dressing to prevent catheter-related infections in patients with short-term percutaneous CVC.

Despite the limitations, this study demonstrated the feasibility in performing a study, testing the colonisation of the skin and tip of catheter as an outcome and providing information for designing larger randomised controlled trials.

Author contributions

Amanda S. Margatho contributed to the conception and design of the work, acquisition of data, analysis and interpretation of data for the work; drafted and critically revised the article for important intellectual content; provided the final approval of the version to be submitted; and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Marcia A. Ciol contributed to the conception and design of the work and analysis and interpretation of data for the work; drafted and critically revised the article for important intellectual content; provided the final approval of the version to be submitted; and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Jeanne M. Hoffman contributed to the conception and design of the study and analysis and interpretation of data for the work; revised the article critically for important intellectual content; provided the final approval of the version to be submitted; and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Paula E. D. dos Reis contributed to the analysis and interpretation of data for the work; drafted and critically revised the article for important intellectual content; provided the final approval of the version to be submitted; and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Rejane K. Furuya contributed to the analysis and interpretation of data for the work; drafted the article and revised it critically for important intellectual content; provided the final approval of the version to be submitted; and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Denissani A. F. S. Lima contributed to the acquisition of data for the work; revised it critically for important intellectual content; provided the final approval of the version to be submitted; and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Anibal Basile-filho contributed to the conception and design of the work and interpretation of data for the work; revised the article critically for important intellectual content; provided the final approval of the version to be submitted; and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Renata C. C. P. Silveira contributed to the conception and design of the work and interpretation of data for the work;

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