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Short Report

Peripheral venous catheter colonization after skin disinfection with 0.5% aqueous sodium hypochlorite, preceded or not by one application of 70% ethanol (DACLEAN): a single-centre, randomized, open-label, pilot study

B. Drugeon^a, M. Pichon^{b,c}, N. Marjanovic^a, S. Mousse^a, S. Seguin^a,
C. Raynaud^{a,d}, A. Rahoui^{a,d}, D. Frasca^{a,e}, O. Mimoz^{a,c,d,*}, J. Guenezan^a

^a CHU de Poitiers, Service des Urgences et SAMU 86, Poitiers, France

^b CHU de Poitiers, Département des agents infectieux, Laboratoire de Bactériologie-Hygiène, Poitiers, France

^c Université de Poitiers, INSERM U1070, Pharmacologie des Agents Anti-Infectieux et Résistance (PHAR2), Poitiers, France

^d Université de Poitiers, UFR de Médecine-Pharmacie, Poitiers, France

^e Université de Nantes, INSERM U1246, Methods in Patient-centered Outcomes and Health Research – SPHERE, Nantes, France

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SUMMARY

Few data are available on the efficacy of 0.5% aqueous sodium hypochlorite (SH) for skin disinfection before peripheral catheter insertion. A total of 239 patients were randomly assigned to either one application of SH alone or one application of SH preceded by one application of 70% ethanol (ET-SH). Catheter colonization, defined as a catheter tip culture growing >1000 cfu of a micro-organism per millilitre, occurred in 29 patients (33% of 89 colonizations per 1000 catheter-days) in the SH group and in 31 patients (33% of 126 colonizations per 1000 catheter-days) in the ET-SH group.

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Introduction

Peripheral venous catheter (PVC) is the medical device most commonly used in hospitals. About two billion are sold each year worldwide. Unfortunately, complications occur in about 50% of

* Corresponding author. Address: CHU de Poitiers, Service des Urgences et SAMU 86, Poitiers, France.

E-mail address: Olivier.MIMOZ@chu-poitiers.fr (O. Mimoz).

patients on average, requiring premature catheter removal before end of treatment. Treatment interruption may be detrimental to patients [1,2]. Catheter replacement results in patient discomfort and additional costs due to the use of new medical devices and paramedical resources. Though fortunately rare, infectious complications are associated with prolonged hospitalization, increased treatment costs, and mortality.

Optimal skin disinfection before catheter insertion is crucial to prevent infectious complications. Recently, the superiority of 2% alcoholic chlorhexidine over 5% alcoholic povidone-iodine was demonstrated for PVCs in medical wards, as well as with central venous and arterial catheters in critically ill patients [3,4]. The widespread use of chlorhexidine for hand disinfection, mouthwashes, or body baths, the risks of allergies and the risk of emergence of strains less susceptible to chlorhexidine necessitate alternatives [5].

Whereas aqueous sodium hypochlorite (SH), a cheaper antiseptic solution, is recommended in several countries to disinfect the healthy skin of children aged <30 months before performing an invasive procedure, few studies have evaluated its efficacy as a skin disinfectant in adults [6]. However, no alcoholic formulation is available, even though the use of such solutions is recommended in this setting due to the quick and deep microbicidal activity of alcohol.

The present study sought to estimate the incidence of PVC colonization after skin disinfection with 0.5% SH alone or preceded with 70% ethanol (ET-SH). The findings will be used to design a larger study comparing the efficacy of this antiseptic to 5% alcoholic povidone-iodine, the only alternative currently available to 2% alcoholic chlorhexidine for skin disinfection before catheter insertion.

Methods

DACLEAN is a single-centre, randomized, open-label, pilot study approved by the CPP Ouest IV (Nantes Institutional Review Board) and registered at [ClinicalTrials.gov](https://clinicaltrials.gov), identifier NCT04391660.

Adult patients (aged ≥ 18 years) requiring hospital admission in medical wards and the insertion of one PVC for ≥ 48 h were enrolled. Exclusion criteria were known hypersensitivity to SH, history of epilepsy, PVC insertion in life-saving situations, predictable difficult vascular access, antibiotics use during the last 15 days, participation in another study modifying the risk of catheter infection, and previous participation in the study. Written informed consent was obtained prior to study inclusion.

Patients were randomly assigned (1:1) to one of two groups according to the skin disinfection strategy through a secure web-based randomization system. Aside from the disinfection protocol, the insertion of PVCs followed the French Society of Hospital Hygiene recommendations, similar to US Centers for Disease Control and Prevention recommendations. According to the randomization arm, skin was disinfected with either one application of 0.5% aqueous SH (Dakin[®]; Cooper, Melun, France) or one application of 70% ethanol (Modified Alcohol[®]; Cooper) followed by one application of the 0.5% aqueous SH once alcohol had evaporated and the skin was visually dried [7]. Antiseptics were largely applied using sterile gauzes soaked with the antiseptic for ≥ 30 s. PVCs (Insyte Autoguard Blood Control Winged catheters; Becton Dickinson, Le Pont de Claix, France) were inserted once the skin was visually dry,

secured with sterile adhesive strips (Urigo Pore; Urigo, Chenôve, France) and taped with Tegaderm 1626W polyurethane dressing (3M, St Paul, MN, USA).

PVCs were continuously infused by gravity to prevent catheter occlusion. Intravenous fluids and drugs were administered through a three-way stop cock (Infu-R3; Doran International, Lyon, France). Dressings were not changed unless soiled or loose. PVCs were removed for completion of treatment, complication occurrence, and usually not later than day 4. PVC tips were cultured with a simplified quantitative broth dilution technique.

The primary outcome was the incidence of colonized catheters defined as a catheter tip culture growing >1000 cfu of a micro-organism per millilitre. Secondary outcomes were the incidence of local infections, systemic infections, catheter-related bloodstream infections, and local skin adverse events (see [Supplementary Appendix](#) for definitions).

In this pilot study, we planned to include 100 catheters per group to obtain a good estimate of catheter colonization [8]. Assuming a maximum catheter culture loss of 20%, a total of 120 patients were included per group. Demographic data and catheter characteristics were described as number and percentage or median and interquartile range. Continuous variables were compared by Mann–Whitney *U*-test. Qualitative variables were compared by χ^2 -test or Fisher's exact test. Incidence densities were calculated. Treatments effects were assessed with competing risks regression, taking into account catheters removed before having developed a complication (competing risk). The Fine and Gray model was used rather than the cause-specific Cox regression model as it better estimates the effect of covariates on the cumulative incidence function for the event of interest [9]. To make inferences about the effect of treatments, adjusted subdistribution hazard ratios (aSHR) with 95% confidence intervals (CI) were determined. Analyses were done with SAS version 9.4 and R software. All of the tests were two-tailed.

Results

Between June 15th, 2020 and January 8th, 2021, a total of 239 patients were randomized. Seventeen patients left the study prematurely (11 patients in the SH group and six patients in the ET-SH group). Of these, four patients in the SH group and three in the ET-SH group did not benefit from the study antiseptics and were secondarily excluded. All in all, 222 PVCs were analysed and 182 (82%) catheter tips were cultured ([Supplementary Figure S1](#)). Characteristics of patients ([Supplementary Table S1](#)) and catheters ([Supplementary Table S2](#)) were similar between the two study groups.

Sixty (33%) colonized catheters were identified among the catheters cultured: 29 (33% of 89 colonizations per 1000 catheter-days) in the SH group and 31 (33% of 126 colonizations per 1000 catheter-days) in the ET-SH group ([Supplementary Table S3](#), [Figure 1](#)). Local infection was noted in three patients (3%) in the SH group and four patients (4%) in the ET-SH group ([Supplementary Table S4](#)). No systemic or bloodstream infection was reported in either study group ([Supplementary Table S4](#)). Minor skin adverse events were reported in only one patient of the ET-SH group ([Supplementary Table S4](#)). The modality of skin preparation had no impact on micro-organisms growing on catheter tips ([Supplementary Table S5](#)).

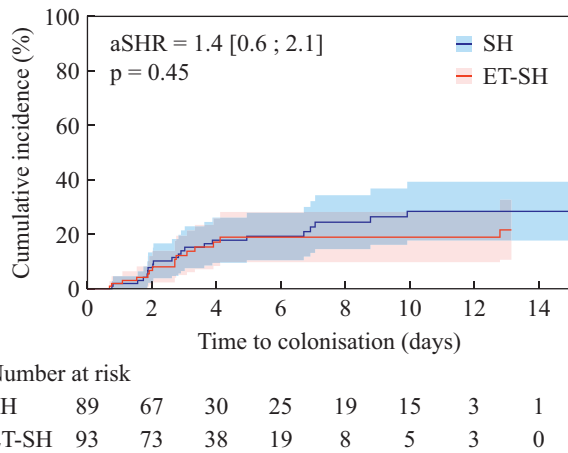


Figure 1. Cumulative incidence (with 95% CI) and adjusted sub-distribution hazard ratio (aSHR) for catheter colonization by antiseptic group allocation. SH, sodium hypochlorite.

Discussion

In this study, use of 0.5% aqueous SH for skin antiseptics before PVC insertion was associated with ~30% of catheters colonized. Application of 70% ethanol before SH use did not reduce the risk of catheter colonization further. Both antiseptics demonstrated excellent safety profiles.

Few studies have evaluated the efficacy of aqueous SH for skin disinfection prior to vascular catheter insertion in adults. In one non-comparative study, 42 patients undergoing scheduled orthopaedic surgery and requiring PVC placement in the immediate postoperative period had their skin insertion site disinfected with 0.055% aqueous SH [10]. The average catheter dwell time was three days. Catheter colonization was 17%. Catheter colonization was higher in our study despite the use of a 10-fold more concentrated aqueous SH solution and a median catheter dwell time of only two days. This difference may be explained by the inclusion in our study of an older population (75 vs 60 years, on average) receiving fewer antibiotics at the time of catheter insertion (0 vs 55%). Additionally, in contrast to most patients visiting an emergency department, patients undergoing clean surgery usually take a shower or a bath with an antiseptic soap before going to the operating room, which reduces the bacterial burden on skin and consequently the risk of catheter colonization.

CLEAN 3 is another study conducted by our team comparing the efficacy and safety of skin disinfection with 2% alcoholic chlorhexidine or 5% alcoholic povidone iodine prior to PVC insertion in the emergency department using the same methodology as in the present study [3]. The catheter colonization rate was slightly lower (71 vs 89 colonizations per 1000 catheter-days) in patients of the 5% alcoholic-povidone iodine group in CLEAN 3 than in patients of the SH group in the present study. However, use of antibiotics was less frequent (0 vs 7%) and catheters remained in place longer (49 vs 41 h on average) in patients of the present study, two factors known to increase the risk of PVC colonization.

Alcohols exhibit rapid and intense broad-spectrum microbicidal activity against most bacteria and fungi, but their effect

disappears once the substance has evaporated. The combination of alcohol with another antiseptic with sustained activity, such as chlorhexidine and, to a lesser extent, povidone-iodine, is therefore recommended [3]. Such a synergistic effect has never been explored between alcohols and SH. Use of an alcoholic formulation of SH was not feasible because there is incompatibility between SH and ethanol, the first substance being a powerful oxidant and the second comprising a hydroxyl group which can be oxidized. We therefore applied ethanol and SH sequentially, once alcohol had dried out. Application of ethanol before SH was not associated with a decrease in the number of catheters colonized compared with application of SH alone (126 vs 89 colonizations per 1000 catheter-days, respectively).

No systemic or cutaneous adverse event following SH use was reported in our study, which is in line with its good safety profile reported in previous studies [10]. Antiseptics are usually very well tolerated. Whereas systemic manifestations are rare, local reactions are much more frequent. In the CLEAN 3 study, minor skin reactions were reported in 1% of patients exposed to 5% alcoholic povidone-iodine and 2% of patients exposed to 2% alcoholic chlorhexidine [3].

Our study has several limitations. First, we chose catheter colonization as the main endpoint rather than catheter-related infection, which would have been more clinically relevant, but would have required many more patients. However, as a preliminary step before catheter-related infection, catheter colonization has been frequently used as the main endpoint in several previous studies such as the CLEAN 3 study. Second, the number of uncultured catheters was slightly higher than estimated. However, the number of analysable catheters was enough to estimate the incidence of catheter colonization with SH use and to rule out any benefit of the combination with ethanol. Third, the study could not be performed blindly because of the typical odour and colour of the antiseptics used. However, the statistician and the microbiologist were blinded to group assignment and the primary endpoint was based on objective criteria. Finally, patients requiring surgery were not included in the study because of the high risk of catheter removal and contamination in the operating room or during transfers.

The DACLEAN study showed that aqueous SH has efficacy close to that of 5% alcoholic PVI for skin disinfection before PVC insertion with good skin tolerance. A large clinical and medico-economic study directly comparing aqueous SH to 5% alcoholic PVI should be conducted to confirm these results and thus position aqueous SH as an alternative to 2% alcoholic chlorhexidine in patients with contraindication to chlorhexidine while reducing the overall cost of care.

Conflict of interest statement

OM received personal fees and funding from Cooper and Becton Dickinson. All other investigators declare no competing interests.

Funding sources

Cooper[®], the manufacturer of the 0.5% sodium hypochlorite solutions and 70% modified alcohol used in the study, provided an unrestricted grant and solution samples for the study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jhin.2021.11.012>.

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