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WHAT'S NEW IN INTENSIVE CARE

What's new in catheter-related infection: skin cleansing and skin antisepsis

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Catheter-related infections (CRIs) are common, life-threatening healthcare-associated infections in intensive care unit (ICU) patients. Accumulating evidence suggests that the incidence of these infections can be decreased through discrete processes of care (Table 1) [1]. Because microorganisms from the skin at the site of catheter insertion are often the source of CRI [2], optimal skin preparation prior to short-term catheter placement is an example of such a discrete process.

The best antiseptic solution to decontaminate the skin prior to catheter insertion is still debated. One meta-analysis of eight randomized studies clearly demonstrated that 10 % aqueous povidone iodine (PVI) was associated with a twofold increase in catheter-related bloodstream infection (CR-BSI) compared to chlorhexidine gluconate (CHG), spurring recommendations to avoid aqueous PVI for skin preparation [3]. Subsequently, another study demonstrated 5 % alcoholic PVI to be more effective than 10 % aqueous PVI in preventing catheter colonization. Reductions in bacterial colonization in this study were attributed to synergy between PVI and alcohol rather than the iodine component, which was reduced by 50 % [4]. As similar synergistic effects also exist with CHG and alcohol, alcoholic formulations are now recommended as first-line antiseptic solutions for catheter care. Unfortunately, few head-to-head studies have compared alcoholic formulations of PVI to CHG such that the "active ingredient" for preventing CRI remains unclear [5]. In a single-center randomized trial of 481 central venous catheters, use of a mixture of 0.25 % CHG, 0.025 % benzalkonium chloride, and 4 % benzyl alcohol led to a 50 % reduction in catheter colonization compared to 5 % alcoholic PVI [6]. A subsequent before–after study comparing the same antiseptic formulation with 806 central venous catheters also confirmed these findings [7]. However, use of a mixture of three compounds in the CHG arm and limited statistical power attenuated insights from these studies.

Such ambiguities led to important differences in national recommendations for skin disinfection prior to catheter placement. For example, US [8] and English [9] guidelines recommended 2 % CHG in alcohol while French [10] guidelines recommend an alcoholic formulation of either PVI or CHG. Furthermore, Centers for Disease Control and Prevention recommendations [8] did not provide advise on cleansing the skin before applying the antiseptic (an approach that may improve antiseptic efficacy by reducing the amount of bacteria and proteinaceous material on the skin [11]), while French guidelines recommended cleansing the skin with a detergent before disinfection [10]. Until recently, no large randomized trials have tested skin cleansing with an antiseptic detergent before antisepsis.

To bridge these gaps, we conducted a randomized, multicenter (11 ICUs), 2 × 2 factorial design study and assigned 2349 patients (5159 catheters) to have all intravascular catheters prepared with 2 % CHG/70 % isopropyl alcohol (ChloraPrep™, CareFusion, France) or 5 % PVI/69 % ethanol (Betadine alcoolique™, Meda Pharma SAS, France), applied in one step (one antiseptic application) or four steps (cleaning the skin with antiseptic detergent, rinsing with sterile water, and drying with sterile gauzes prior to antiseptic application) [12]. We used CRI and CR-BSI as study endpoints because they are more robust and clinically meaningful than colonization outcomes. As a result of different colors and formulations of the antiseptics, masking of ICU staff was not feasible, but outcome assessors and statisticians were blinded to assignment.

Compared to PVI/alcohol use, CHG/alcohol use was associated with a fivefold to sixfold decrease in the incidence of CRI and CR-BSI. CHG/alcohol was superior

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Table 1 Basic bundle to prevent catheter-related infection

Use written protocol for catheter insertion and maintenance
Rub hands with alcohol-based solutions before each line manipulation
Respect full-barrier precaution at catheter insertion
Cleanse the skin with a 2 % chlorhexidine/70 % isopropyl alcohol sterile solution
Select subclavian vein as preferred access in the absence of contraindications[a]
Change non-adherent, soiled, or moistened dressing
Remove catheters that are clinically no longer necessary

Basic bundle to be completed with others items such as chlorhexidine dressings or use of antimicrobial coated/impregnated catheters in case of high catheter-infection rate despite adequate application and adherence to the basic bundle

[a] Assumes competency in placing subclavian catheters, including assessment of risk–benefit with respect to mechanical complications such as pneumothorax

regardless of admission category (medical or surgical patients), catheter type (arterial or central venous catheters), site of insertion (subclavian, internal jugular, or femoral veins), or bacteria isolated (gram-negative or gram-positive organisms). Cleansing the skin before CHG/alcohol or PVI/alcohol application did not reduce CRI. Severe skin reactions, although rare, were the most common adverse event, occurring more frequently with CHG/alcohol (3 % versus 1 %, $p = 0.017$). Switching from PVI/alcohol to 2 % CHG/alcohol was also cost-effective: the additional cost to prevent a single episode of CRI using CHG/alcohol was €227 on average versus the estimated cost of €19,583 per CRI in similar patients [13].

Nevertheless, several questions regarding optimal skin preparation remain. For instance, we included only short-term intravascular catheters and used a single-use applicator of 2 % CHG/70 % isopropyl alcohol sterile solution. Whether our results can be extended to catheters remaining in place for longer periods of time such as peripherally inserted devices, epidural catheters, or for skin preparation before surgery remains to be established. Similarly, because we used fixed, commercially available combinations, we could not determine the optimal concentration of CHG, type and concentration of alcohol, or the value of colored preparations in ensuring disinfection of the entire operative field. The 2 % CHG/70 % alcohol is superior to 0.5 % CHG/70 % alcohol solution for skin antisepsis before surgery [14]. Consequently the superiority of 2 % CHG/70 % alcohol preparation should not be extrapolated to CHG solution in lower concentration. Finally, although use of hands-free applicators to apply antiseptic solutions has theoretical advantages over use of sterile gauzes, further studies are required to address the optimal modality of antiseptic application on skin as well as the potential benefit of single-use vials containing sterilized antiseptic over multi-use bottles.

While bacterial resistance is important with use of any antimicrobial agent, there is no report of CHG-resistant strains or shift in a cutaneous flora less susceptible to CHG in the clinical setting despite decades of use. However, increase in minimum inhibitory concentration has been observed and needs to be cautiously monitored. It still remains far below the concentrations reached on skin in usual care [15]. Regardless, physicians must remain mindful of the risk of selection of resistant strains associated with increasing CHG use. Developing the armamentarium of effective antiseptics should therefore be a priority moving forwards. New solutions containing octenidine dihydrochloride [16], 4 % CHG [17], or new hypochlorite solutions [18] should be tested in the near future. With these advances in technology and richer understanding of factors that ensure adherence to best practices, getting to a zero rate of CRI certainly seems within reach.

In conclusion, use of sterile 2 % CHG/70 % isopropyl alcohol for skin antisepsis should be included in all bundles for intravascular short-term catheter-related infection prevention. Cleansing the skin with an antiseptic detergent before skin antiseptic application can no longer be recommended.

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Compliance with ethical standards

Conflicts of interest
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References

1. Frasca D, Dahyot-Fizelier C, Mimoz O (2010) Prevention of central venous catheter-related infection in the intensive care unit. Crit Care 14:212
2. Timsit JF, Mimoz O, Mourvillier B, Souweine B, Garrouste-Orgeas M, Alfandari S, Plantefeve G, Bronchard R, Troche G, Gauzit R, Antona M, Canet E, Bohe J, Lepape A, Vesin A, Arrault X, Schwebel C, Adrie C, Zahar JR, Ruckly S, Tournegros C, Lucet JC (2012) Randomized controlled trial of chlorhexidine dressing and highly adhesive dressing for preventing catheter-related infections in critically ill adults. Am J Respir Crit Care Med 186:1272–1278

3. Chaiyakunapruk N, Veenstra DL, Lipsky BA, Saint S (2002) Chlorhexidine compared with povidone-iodine solution for vascular catheter-site care: a meta-analysis. Ann Intern Med 136:792–801
4. Parienti JJ, du Cheyron D, Ramakers M, Malbruny B, Leclercq R, Le Coutour X, Charbonneau P, Members of the NACRE Study Group (2004) Alcoholic povidone-iodine to prevent central venous catheter colonization: a randomized unit-crossover study. Crit Care Med 32:708–713
5. Chopra V, Shojania KG (2013) Recipes for checklists and bundles: one part active ingredient, two parts measurement. BMJ Qual Saf 22:93–96
6. Mimoz O, Villeminey S, Ragot S, Dahyot-Fizelier C, Laksiri L, Petitpas F, Debaene B (2007) Chlorhexidine-based antiseptic solution versus alcohol-based povidone-iodine for central venous catheter care. Arch Intern Med 167:2066–2072
7. Girard R, Comby C, Jacques D (2012) Alcoholic povidone-iodine or chlorhexidine-based antiseptic for the prevention of central venous catheter-related infections: in-use comparison. J Infect Public Health 5:35–42
8. O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, Lipsett PA, Masur H, Mermel LA, Pearson ML, Raad II, Randolph AG, Rupp ME, Saint S, Healthcare Infection Control Practices Advisory Committee (HICPAC) (2011) Summary of recommendations: guidelines for the prevention of intravascular catheter-related infections. Clin Infect Dis 52:1087–1099
9. Loveday HP, Wilson JA, Pratt RJ, Golsorkhi M, Tingle A, Bak A, Browne J, Prieto J, Wilcox M, UK Department of Health (2014) Epic3: national evidence-based guidelines for preventing healthcare-associated infections in NHS hospitals in England. J Hosp Infect 86(Suppl 1):S1–S70
10. Société française d'anesthésie et de réanimation, Société de réanimation de langue française (2009) Prevention of hospital-acquired sepsis in intensive care unit (except cross transmission and neonate). Ann Fr Anesth Reanim 28:912–920
11. Zamora JL, Price MF, Chuang P, Gentry LO (1985) Inhibition of povidone-iodine's bactericidal activity by common organic substances: an experimental study. Surgery 98:25–29
12. Mimoz O, Lucet JC, Kerforne T, Pascal J, Souweine B, Goudet V, Mercat A, Bouadma L, Lasocki S, Alfandari S, Friggeri A, Wallet F, Allou N, Ruckly S, Balayn D, Lepape A, Timsit JF, CLEAN trial investigators (2015) Skin antisepsis with chlorhexidine-alcohol versus povidone iodine-alcohol, with and without skin scrubbing, for prevention of intravascular-catheter-related infection (CLEAN): an open-label, multicentre, randomised, controlled, two-by-two factorial trial. Lancet 386:2069–2077
13. Schwebel C, Lucet JC, Vesin A, Arrault X, Calvino-Gunther S, Bouadma L, Timsit JF (2012) Economic evaluation of chlorhexidine-impregnated sponges for preventing catheter-related infections in critically ill adults in the dressing study. Crit Care Med 40:11–17
14. Casey A, Itrakjy A, Birkett C, Clethro A, Bonser R, Graham T, Mascaro J, Pagano D, Rooney S, Wilson I, Nightingale P, Crosby C, Elliott T (2015) A comparison of the efficacy of 70 % v/v isopropyl alcohol with either 0.5 % w/v or 2 % w/v chlorhexidine gluconate for skin preparation before harvest of the long saphenous vein used in coronary artery bypass grafting. Am J Infect Control 43:816–820
15. Milstone AM, Passaretti CL, Perl TM (2008) Chlorhexidine: expanding the armamentarium for infection control and prevention. Clin Infect Dis 46:274–281
16. Dettenkofer M, Wilson C, Gratwohl A, Schmoor C, Bertz H, Frei R, Heim D, Luft D, Schulz S, Widmer AF (2010) Skin disinfection with octenidine dihydrochloride for central venous catheter site care: a double-blind, randomized, controlled trial. Clin Microbiol Infect 16:600–606
17. Bilir A, Yelken B, Erkan A (2013) Chlorhexidine, octenidine or povidone iodine for catheter-related infections: a randomized controlled trial. J Res Med Sci 18:510–512
18. Forni C, Sabattini T, D'Alessandro F, Fiorani A, Gamberini S, Maso A, Curci R, Zanotti E, Chiari P (2015) Use of sodium hypochlorite for skin antisepsis before inserting a peripheral venous catheter: a pilot study. Biol Res Nurs 17:330–333