A multimodality approach to prevent catheter-related bloodstream infections: the role of chlorhexidine-alcohol as a skin antiseptic before intravascular catheter insertion

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Health care-associated infection is an increasing threat to patient safety. Over 400,000 patients in the intensive care units (ICUs) and 1.2 million patients outside the ICUs were affected by hospital care-associated infections, with >30,000 deaths attributed to hospital care-associated bloodstream infections in United States in 2002 (1). Intravascular catheters play a pivotal role in the management of both ICU and non-ICU patients, but inadequate infection control precautions in using these devices may lead to catheter-related bloodstream infection (CR-BSI) resulting in prolonged hospital stay and excessive mortality (2). As such, having the best strategy to prevent CR-BSI has a potential huge benefit on both patient outcome and healthcare cost (3).

Most intravascular catheters used in the ICUs are non-cuffed and for short-term purposes, extraluminal catheter colonization derived from the cutaneous microflora is believed to be the main mechanistic cause of CR-BSI (4). With this pathogenic mechanism in mind, strategies achieving successful eradication of cutaneous bacteria, both before and after intravascular catheter insertion, would be expected to be effective in reducing CR-BSI. Consequently, the CLEAN trial assessing whether skin scrubbing, in combination with using either chlorhexidine-alcohol or povidone iodine-alcohol as skin antiseptic, is effective in reducing CR-BSI has paramount importance (5).

Methods

The CLEAN trial is an open-label, multicenter, randomized-controlled, two-by-two factorial trial. The factorial design aimed to answer three clinical questions using the same cohort of patients, including (I) is skin scrubbing before intravascular catheter insertion more effective than no skin scrubbing in preventing CR-BSI; (II) is chlorhexidine-alcohol more effective than povidone iodine-alcohol as a skin antiseptic before intravascular catheter insertion in preventing CR-BSI; and (III) does skin scrubbing work better only with a particular type of skin antiseptic (chlorhexidine-alcohol or povidone iodine-alcohol)? The study had 80% power to detect a 50% relative risk reduction in CR-BSI after using chlorhexidine-alcohol as skin antiseptic compared to povidone iodine-alcohol, assuming the baseline risk of CR-BSI in the povidone iodine-alcohol group was 5%. This was a well-designed study, including 2,349 patients (1,181 patients were randomly allocated to chlorhexidine-alcohol: 594 patients with scrubbing, 587 without; 1,168 to povidone iodine-alcohol: 580 patients with scrubbing, 588 without) from 11 French ICUs in six hospitals.

Internal validity was achieved by adequate allocation concealment through web-based randomization stratified by center, and the primary outcome, catheter-related infection and CR-BSI, was determined by microbiologists masked to group assignment. The external validity of the trial was less certain; study patients were predominantly medical patients with a substantial proportion of them with underlying immunodeficiency (6%), haematological malignancy (6%) and metastatic cancer (6%).

Findings

The average length of the intravascular catheter left in-situ was 6 days (interquartile range, 3-11 days). Chlorhexidine-alcohol was associated with a reduced risk of CR-BSI (0.7%) [0.28 *vs.* 1.32 per 1,000 catheter-days with povidone iodine-alcohol (1.1%); HR =0.21; 95% CI, 0.07-0.59]. Scrubbing was not associated with a significant reduction in catheter colonization or CR-BSI. Although systemic adverse events were not observed, severe skin reactions did occur more frequently in chlorhexidine-alcohol group (3%) than povidone iodine–alcohol group (1%). Despite a reduction in incidence of CR-BSI in the chlorhexidine-alcohol group, there was no significant reduction in length of stay or mortality.

Commentary

Extraluminal colonization is the predominant mechanism of CR-BSI related to short-term non-cuffed intravascular catheters (4). Chlorhexidine is a synthetic bisbiguanide that binds to cutaneous protein resulting in a persisting antimicrobial effect with limited systemic absorption. It has bacteriostatic, bactericidal and fungicidal activity towards a wide range of micro-organisms (6). In line with the perceived benefits of chlorhexidine, the CLEAN study has confirmed that (I) chlorhexidine-alcohol was a more effective skin antiseptic than povidone iodine-alcohol, and (II) a two-step skin cleaning process by adding skin scrubbing did not provide further improvement in skin decolonization and any subsequent catheter colonization and infection compared to an one-step skin cleaning process before intravascular catheter insertion.

Previous studies showed that CR-BSI was associated with a significant attributable morbidity and mortality in critically ill patients (2,3). So, why this study could not demonstrate any substantial reduction in length of stay or mortality despite a significant reduction in CR-BSI after using chlorhexidine-alcohol as a skin antiseptic before intravascular catheter insertion? First, this study was not powered to detect a mortality or length of stay difference between the two groups. Second, the incidence of CR-BSI in the povidone iodine-alcohol group (1.1%) was much lower than the assumption (5%) in the sample size calculation. This result suggests that the study protocol itself, regardless of the intervention allocated, was effective in reducing risk of CR-BSI. The elements of the protocol that may be effective in reducing CR-BSI include (I) the physician who inserted the catheter disinfected the skin used maximal barrier precautions; (II) the antiseptic was applied to the skin for at least 30 s before catheter insertion to maximize the contact time between the antiseptic and skin flora; (III) catheter insertion sites were inspected daily for signs of infection; (IV) manipulation of lines and three-way stopcocks was done with gauze moistened with the same antiseptic used for catheter insertion; (V) blood sampling through the central venous catheter was not allowed; and finally (VI) intravascular catheters were removed if no longer needed, usually before discharge from the ICUs or when a catheter-related infection was suspected.

As such, we should consider the use of chlorhexidine-alcohol as skin antiseptic only as one small part of the full infection control precautions needed before, during, and after intravascular catheter insertion. In addition, there are also other elements that are likely effective in reducing CR-BSI, but were not included in the protocol of this trial, including use of antiseptic or antibiotic impregnated intravascular catheters and use of chlorhexidine-impregnated dressing at the insertion site after catheter insertion (7-9). It is, thus, possible to reduce the incidence of CR-BSI further from 0.7%. Although this study did not demonstrate a significant reduction in length of stay and mortality after using chlorhexidine-alcohol instead of povidone iodine-alcohol as a skin antiseptic before vascular catheter insertion, the results would still suggest that chlorhexidine-alcohol should be used as the routine skin antiseptic for intravascular catheter insertion (with two possible exceptions). The number needed to treat (NNT) to prevent one CR-BSI demonstrated by this study was 250, and the incremental cost to prevent one episode of CR-BSI was only €350 (US$372)—much lower than the widely reported cost associated an episode of CR-BSI (>US$25,000) (3). That said, contact dermatitis as well as anaphylaxis to chlorhexidine have been well described, particularly in neonates and Japanese population, respectively, even when chlorhexidine is applied topically onto skin or mucosa in susceptible individuals (6,8). Thus, clinicians should remain vigilant to monitor patients' response to chlorhexidine either as a topical antiseptic or when chlorhexidine-impregnated catheter is used in hospitalized patients.

Implications for practice and research

(I)   Chlorhexidine-alcohol should be used as a routine skin antiseptic instead of povidone iodine-alcohol before intravascular catheter insertion, with the

exceptions in patients who have known or suspected topical or systemic reaction to chlorhexidine.

(II) Chlorhexidine-alcohol skin antiseptic should only be considered as a part of a multimodal approach to prevent CR-BSI. Other elements of infection control precautions are likely more important than the choice of skin antiseptic alone.

(III) Whether using chlorhexidine-alcohol as a skin antiseptic can further reduce CR-BSI when combined with chlorhexidine-impregnated intravascular catheter or chlorhexidine-impregnated dressing at the insertion site remains uncertain, but this merits further investigation.

Acknowledgements

Footnote

References

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