A wash twice a day keeps MRSA away?

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Every year, 180 000 patients in Australia have health care-associated infections that increase hospital length of stay and use 2 million hospital bed-days.[1] Health care-acquired bloodstream infections (BSI), especially those caused by *Staphylococcus aureus*, remain one of the most important contributors to morbidity, mortality and to the economic burden caused by health care-associated infections.[1,2] Patients admitted to the intensive care unit (ICU) are among those at greatest risk of infection,[3] and in an effort to reduce this risk, there is growing interest in "universal decolonisation strategies" in the ICU. The use of daily patient bathing with chlorhexidine gluconate to decrease skin colonisation with microbial pathogens is one such strategy.[4-6]

Topical chlorhexidine has a broad spectrum of action. Moreover, it destabilises the cell walls of gram-positive and gram-negative bacteria and fungi, and can have prolonged activity after application.[7,8] Proponents of chlorhexidine bathing argue that it is relatively simple to implement because it does not require significant change from routine patient bathing practices.[4] Furthermore, although serious allergic reactions to topical chlorhexidine have been reported,[9] these are rare.[4,5] Nonetheless, concern exists that decolonisation strategies applied universally at population-based levels may accelerate the emergence of resistance.[10] There are reports of reduced susceptibility of methicillin-resistant *S. aureus* (MRSA) to chlorhexidine, with resistance possibly associated with plasmid-mediated *qacA* and *qacB* genes encoding for multidrug efflux pumps.[11,12] Gram-negative bacteria can also exhibit reduced sensitivity.[13] In addition, coresistance can exist between antiseptics and antibiotics in vitro.[14] The use of chlorhexidine bathing could theoretically promote selection of resistant bacterial strains.

Chlorhexidine bathing in ICU has been studied as part of recent large, open-label, cluster-randomised trials in the United States.[4-6] In a cohort of 7727 ICU and bone marrow transplant patients admitted to six hospitals, Climo and colleagues[4] reported that daily chlorhexidine bathing reduced acquisition of vancomycin-resistant enterococci (–1.07 cases/1000 patient-days; $P = 0.05$) and health care-acquired BSI (relative risk, 0.69; 95% confidence interval [CI], 0.47–0.99), including central-line associated BSI (CLABSI) (–1.75/1000 catheter-days; $P = 0.004$), but not MRSA acquisition. Similarly, Huang and colleagues[5] found that a universal multicomponent decolonisation strategy including chlorhexidine bathing reduced health care-acquired BSI (hazard ratio [HR], 0.56; 95% CI, 0.49–0.65) and MRSA-positive non-surveillance cultures (HR, 0.63; 95% CI, 0.52–0.75) and was more effective than a strategy targeting only high risk patients in a cohort of 74 256 patients admitted to ICUs in 43 hospitals. However, in the latter study the attributable benefit of chlorhexidine bathing is uncertain, as the intervention was applied simultaneously with other decolonisation interventions. In contrast, a more recent single-centre cluster-randomised crossover study of 9340 patients admitted to five ICUs reported that chlorhexidine bathing did not reduce the composite primary outcome of CLABSI, ventilator-associated pneumonia, catheter-associated urinary tract infection or *Clostridium difficile* infection (rate difference, –0.04; 95% CI, –1.10 to 1.01; $P = 0.95$).[6] The choice of this complex composite outcome and the fact that overall rates of health care-associated infection were relatively low increased the likelihood of accepting the null hypothesis. Meta-analyses of studies examining chlorhexidine bathing suggest that effectiveness may depend on the underlying baseline risk of health care-associated infection in a given ICU population.[15,16] Notably, chlorhexidine was well tolerated in all three of these cluster-randomised trials, but the reported data on chlorhexidine resistance and barriers to implementation of chlorhexidine bathing were limited.

In this issue of *Critical Care and Resuscitation*, Urbancic and colleagues[17] conducted a unit-wide chlorhexidine bathing study for ICU patients in the Australian setting. Using a prospective, sequential period, open-label study design, the authors evaluated over 4000 ICU admissions in a tertiary centre during a 2-year period. The use of chlorhexidine wipes for patient bathing did not lower the primary outcome of CLABSI when compared with washes with triclosan, the antiseptic used for bathing during the 12-month standard-care period. Similarly, there was also no reduction in rates of positive blood cultures or rates of vancomycin-resistant enterococci isolates. However, the authors observed a reduction in the incidence of MRSA acquisition during the chlorhexidine-bathing period — a reduction of more than two acquisitions per 1000 patient-days (95%CI, –3.65 to –0.60; $P = 0.007$). While this secondary outcome is not patient-centred, this modest reduction may be important because *S. aureus* colonisation usually precedes infection, and the acquisition of a new strain greatly increases the risk of invasive infection.[18,19] Furthermore, *S. aureus* transmission between patients is particularly likely to occur in high acuity settings such as the ICU,[20] and Australian ICUs already invest significant resources in an attempt to prevent transmission.[21] It is important to note that baseline rates of ICU-acquired CLABSI and BSI were already low

before the use of chlorhexidine in this study, due partly to robust infection control measures, including high hand hygiene rates. Such infrequent event rates increased the risk of β error.[22] The results of this current study are applicable to the Australian and New Zealand health care setting, and provide preliminary evidence that chlorhexidine bathing may be effective in decreasing MRSA acquisition in the local ICU environment. However, given the risk of bias due to study design — single-centre, open-label, before-and-after, and comparison to triclosan — and that MRSA acquisition was a secondary outcome, which is not patient-centred, data must be interpreted with caution and are insufficient to support widespread change at this stage. In particular, data from other units in Australia would be important in confirming or refuting the reproducibility of these findings.

Future studies of chlorhexidine bathing should evaluate resistance and loss of efficacy to determine whether there are unintended microbiological consequences, establish cost-effectiveness, and compare chlorhexidine bathing to targeted infection control strategies such as the use of intranasal mupirocin to reduce MRSA carriage.[23]

Competing interests

None declared.

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