Every other day bathing with chlorhexidine gluconate: what is the evidence?

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Healthcare-associated infections (HAIs) cause considerable morbidity, mortality and medical costs (1-3). Annually in the United States, approximately 722,000 people develop an HAI and 75,000 die (2). A cost analysis by Zimlichman *et al*., examining five major HAIs, found that HAIs cost the United States healthcare system $9.8 billion annually (1). A large proportion of HAIs are considered preventable and there is a substantial body of evidence-based interventions available for implementation (4,5). However, a gap continues to exist in the translation of evidence into practice for HAI prevention (6). Many interventions for HAI prevention are complex, behavioral interventions which are challenging to implement and sustain with high fidelity.

Daily bathing with chlorhexidine gluconate (CHG) is an efficacious intervention for HAI prevention. CHG is a broad spectrum cationic bis-biguanide antiseptic which is active against Gram-positive bacteria, Gram-negative bacteria, and fungi (7). CHG reduces the density of microorganisms on the skin by binding to the negatively charged bacterial cell walls, changing the bacteria's osmotic equilibrium thus causing bacterial cell death (8,9).

Daily CHG bathing in intensive care unit (ICU) patients has been proven to reduce healthcare-associated bloodstream infections (BSIs), in most but not all studies (8,10-13). O'Horo *et al*., in a meta-analysis of 12 studies including 137,392 patient-days found a 64% reduction in the incidence of BSIs following daily CHG bathing (12).

There is considerable variation in the way that CHG may be applied which may account for variation in effectiveness. Bathing with CHG on a daily basis is labor intensive. Is it possible that the benefit of CHG could be achieved by bathing less frequently? The hypothesis is biologically plausible because of the residual activity of CHG on the skin (7). In a recent issue of *Critical Care Medicine*, Swan and colleagues assessed the effect of 2% CHG bathing every other day on the incidence of four HAIs (14). These were catheter-associated urinary tract infection (CAUTI), ventilator-associated pneumonia (VAP), incisional surgical site infection (SSI), and primary BSIs. This study was a single-center randomized trial conducted in a surgical ICU from July 2012 to May 2013. The treatment group consisted of patients receiving 2% CHG bathing every other day (alternating with regular soap and water bathing) for up to 28 days. The control group consisted of patients bathed daily with regular soap and water. All bathing was performed by surgical ICU nurses and patient care assistants (14).

Authors reported that all patient 18 years and above who were expected to stay for at least 48 hours were eligible to enroll in the study. The primary outcome of this study was a composite outcome of CAUTI, VAP, incisional SSI and primary BSI. The study showed that 2% chlorhexidine bathing every other day compared to daily soap and water bathing decreased the incidence of infections (in the composite outcome) by 45.5% [hazard ratio (HR) =0.555; 95% confidence interval (CI), 0.309–0.997; P=0.049].

Adverse skin occurrences such as allergic reactions and skin infections occurred at similar rates in both groups (18.9% soap and water; 18.6% and 2% CHG; P=0.95).

CHG is used mostly at concentrations ranging from 0.5–4% of the water soluble gluconate form (8). For the purpose of patient bathing the CHG is applied either as a 4% solution or with 2% chlorhexidine-impregnated cloths (15). Two commonly used brands of CHG are the 4% CHG foam soap (Hibiclens® 4%) and the 2% CHG-impregnated wash cloths (Sage® 2% CHG cloths). Factors influencing decision-making regarding choice of product include cost and ease of use. The CHG-impregnated wipes cost about $5.52 per bath and are 74% more expensive than using the CHG soap ($3.18 per bath) (16). However, Ritz *et al*., reported that nurses thought that CHG-impregnated wipes were easier to use and took less time, hence they preferred to use them rather the 4% CHG solution (17). The study by Swan *et al*., attempted to find a common ground between the cost and nurse preference by using a 2% diluted CHG solution made by diluting equal amounts of warm tap water with 8 oz. of Bactoshield chlorhexidine 4% Surgical Scrub (STERIS, Mentor, OH, USA) at point of use. Although cost saving, the mixing process is likely to be a challenge in actual clinical practice and it is likely that variation in the final concentration of CHG would exist.

The study by Swan *et al*. was a randomized trial desirable when evaluating the efficacy of an intervention because it balances treatment groups on both known and unknown potential confounding factors (14). Unlike most other trials of CHG that have been cluster randomized, this trial randomized patients at the individual level. The randomization process was well described, post randomization imbalances of certain variables did not have an effect on the estimate according to results of a sensitivity analysis in which they were adjusted for in the analysis. The study followed the Consolidated Standards of Reporting Trials (CONSORT) guideline in reporting its findings and it was registered on clinical trials.gov before enrollment began (20,21).

The authors reported that this was a pragmatic design which would ensure maximum generalizability of the findings because of real world application with few inclusion and exclusion criteria, but generalizability of this study's findings is difficult. This is not only because it was conducted at a single surgical ICU of one hospital, but also because the determination of how the inclusion criteria of "patients with anticipated SICU stay of 48 hours" was met was not reported. Seventy-four percent (1,261/1,343) of all screened patients were excluded because they did not meet this inclusion criterion. This was an ICU that provided quaternary care to a high proportion of patients with liver failure and liver transplant with high rates of infections. Authors reported that the average length of stay was 7 days and 15 days for the surgical ICU and hospital stay respectively.

The findings of the study should be assessed in the context of the limitations. First, although daily auditing of bathing was performed and 83% of patients received bathing, compliance to CHG bathing with observations or measurement of CHG concentrations was not reported and the quality of CHG baths was not monitored. For complex behavioral interventions, replication and reproducibility is possible only with a careful assessment and reporting of intervention fidelity. In this study, given that front line staff were asked to undertake the preparation of the product rather than a pre-prepared product, it is essential that some measurement of intervention fidelity and variation from the protocol be conducted. The authors reported that two of the outcome assessors provided direct clinical care to the study participants. This is could have resulted in inadequate blinding and could have introduced information bias in the study (22).

The authors did not report how the nurses determined when to give a bath with which product. Every other day bathing schedule will likely have challenges in record keeping establishing CHG bathing days and non CHG bathing days. There was no measurement of skin CHG concentration after bathing. Thus, it is not possible to determine if every other day bathing delivered detectable CHG concentrations on the patients' skin, although rinsing was not done which ameliorates this concern. Importantly, although the treatment effect of the study was large (HR =0.555), the estimate had poor precision because of the wide CI of 0.309–0.997. The study was not powered to detect the impact of CHG bathing on HAIs separately rather than as solely as a composite outcome.

Few other studies have evaluated every other day CHG bathing. Except in a single quasi-experimental study by Rupp *et al*., (23) in which CHG bathing was done every other day excluding weekends, studies that have showed the efficacy of CHG against multi-drug resistant organisms incidence and colonization have used the daily bathing schedule (10,11,24). Moreover, the study by Rupp *et al*., showed that every other day bathing schedule was associated with a reduction only in the incidence of *C. difficile* which is difficult to attribute to CHG bathing because CHG is not sporicidal (23). There was no randomization in that study and fidelity to the intervention was not fully assessed. For example, direct observation of bathing or of the bathing technique was not conducted.

In conclusion, although every other day CHG bathing using 2% CHG solution is potentially cost saving and beneficial, several issues need to be addressed before embedding in routine use. We recommend that monitoring and reporting of factors influencing implementation using an established framework be undertaken. The Reach Effectiveness Adoption Implementation Maintenance (RE-AIM) is one such framework which allows assessment of the process of the intervention in addition to the clinical outcomes (25).

In the context of CHG bathing, it would be important to routinely report for example: what percentage of patients eligible for CHG bathing actually underwent CHG bathing, what percentage of nurses responsible for bathing adopted the intervention, a description of the fidelity to the intervention, and the maintenance or lack thereof over time. Ideally, a mixed methods evaluation with provider and patient interviews or focus groups, as applicable coupled with direct observations of the bathing process, and determination of CHG concentration and HAI rates should be conducted. Answering these key process questions is essential in order to effectively bridge the gap between evidence generation and practice in real world settings.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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