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Trends in Chlorhexidine Use in US Neonatal Intensive Care Units: Results From a Follow-Up National Survey

Chlorhexidine gluconate (CHG) is a broad-spectrum topical antiseptic frequently used to prevent healthcare-associated infections. Common uses include antisepsis for central venous catheter (CVC) insertion and maintenance, preoperative bathing, and daily bathing of patients with CVCs.[1,2] In neonates, CHG bathing has been associated with a reduction in central line–associated bloodstream infections.[3]

A 2009 survey of US neonatal intensive care units (NICUs) with fellowship training programs found that 57% of responding institutions used CHG in the NICU, many restricting use by age or weight.[4] Respondents cited concerns regarding off-label use, as well as limited availability of safety data in preterm infants. Two other surveys have investigated CHG use in the broader context of infection control practices but did not elicit the full scope of CHG use within NICUs.[5,6]

In May 2012, the US Food and Drug Administration modified the labeled indications for CHG from "do not use in premature or low birthweight infants […] or children less than 2 months of age" to "use with care in premature infants or infants under 2 months of age." To ascertain trends in CHG use in the setting of this new indication, we resurveyed US NICUs with fellowship training programs to assess several key facets of CHG use.

In 2014, a survey was sent via email to neonatology training program directors in the United States. Follow-up surveys were sent to nonresponding institutions. Study participants completed an online survey about the use of CHG within the NICU, specific infection control practices, associated adverse effects, and concerns regarding the antiseptic's use in the neonatal population. Data were analyzed using Stata, version 13.0 (StataCorp). This study was approved by the Johns Hopkins Medicine Institutional Review Board.

Of 98 training programs surveyed, 58 (59%) responded (Table 1). Among 46 respondents to the question, there was a mean (SD) of 23 (10.3) years of experience practicing neonatology, and all practiced at level III-IV NICUs. Fifty respondents (86%) reported CHG use within their NICUs, 5 (9%) reported no CHG use, and 3 (5%) did not know whether CHG was used within their NICU. Among NICUs utilizing CHG, the most common uses included skin preparation for CVC insertion, CVC dressing changes, CVC maintenance, and skin preparation for peripheral IV insertion. CHG baths were less frequently utilized, including preoperative baths, decolonization for methicillin-resistant *Staphylococcus aureus*, and routine bathing. Among 50 NICUs in 2014, 32 restricted CHG use: 21 did so by age, whereas 5 used weight-based criteria and 6 used both age- and weight-based restrictions. Among respondents who provided comments on open-ended questioning, the most common age requirement and weight requirement for CHG use were greater than 28 weeks gestation at birth and weighing more than 1 kg. A variety of CHG concentrations were utilized, ranging from 0.25% to 4.0%; the most common concentration used was 2.0%. Adverse effects of CHG were reported by 24 (53.3%) respondents, all of which were dermatologic. Those who provided specific information on dermatologic adverse events most often described skin irritation or burns. Concerns about CHG use were reported by 27, with common themes from open-ended questions regarding potential skin effects, systemic absorption, and potential neurotoxicity.

Among NICUs with fellowship training programs, CHG use has increased over the past 6 years from 57% to 86%. The benefit of using CHG in hospitalized neonates was investigated in a 2014 study conducted in a tertiary care NICU.[3] Among

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TABLE 1. Chlorhexidine Gluconate (CHG) Use by Indication Among Institutions in the Neonatal Intensive Care Unit

Indication for use	2009 CHG use, no. (%) (n = 55)	2014 CHG use, no. (%) (n = 50)
Skin preparation for PIV insertion	33 (60%)	27 (54%)
Skin preparation for umbilical line placement	28 (51%)	19 (38%)
Skin preparation for CVC insertion	40 (73%)	36 (72%)
CVC maintenance	43 (78%)	30 (60%)
CVC dressing changes	NA	32 (64%)
Scrubbing catheter hub	NA	24 (48%)
Impregnated dressing or disc	NA	10 (20%)
Preoperative bathing	NA	9 (18%)
MRSA decolonization	4 (7%)	8 (16%)
Routine bathing	1 (2%)	4 (8%)

NOTE. CVC, central venous catheter; MRSA, methicillin-resistant *Staphylococcus aureus*; NA, item not queried in 2009 survey; PIV, peripheral intravenous catheter.

infants with CVCs in place who met age and weight criteria, the rate of central line–associated bloodstream infections decreased from 6.00 cases/1,000 CVC-days to 1.92 cases/1,000 CVC-days after CHG bathing was implemented.[3] As evidence of the efficacy of CHG in reducing infection risk in hospitalized neonates continues to emerge, routine CHG use in NICUs is likely to continue to rise.

Despite 86% of sites reporting CHG use, many respondents had ongoing concerns regarding potential side effects of CHG in the neonatal population. CHG use is commonly restricted in neonates by age or weight, though specific restrictions vary considerably among institutions, reflecting a lack of specific guidelines. Practitioners were particularly concerned about potential dermatologic effects. Whether burns associated with CHG use are due to chlorhexidine or due to the alcohol in the preparation remains unclear.

Safety concerns were explored further in a 2013 study, which measured serial serum concentrations of CHG after topical application to preterm infants' skin for peripherally inserted central catheter placement.[7] Trace levels of CHG were detectable on serum testing in 10 of 20 enrolled infants, although the clinical significance of this finding was uncertain.[8] Despite in vitro neurotoxicity,[8] it is unknown whether CHG crosses the blood-brain barrier, and no studies have been performed to assess whether trace absorbed levels reach the central nervous system and cause toxicity.

Although overall trends in CHG use can be evaluated, a limitation of this survey-based study is the inability to compare trends for specific institutions given the anonymous nature of the survey. Institutions using CHG may have been more likely to complete the survey, potentially resulting in an overestimate of use.

The heterogeneous practices among responding institutions reflect the lack of specific guidelines for CHG use in neonates. Prospective studies are needed to assess best practices for CHG use in neonates, especially with regard to dosing schedule and efficacy.

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SUPPLEMENTARY MATERIALS

For supplementary material/s referred to in this article, please visit http://dx.doi.org/10.1017/ice.2016.125

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Reduction in Acute Respiratory Infection Among Military Trainees: Secondary Effects of a Hygiene-Based Cluster-Randomized Trial for Skin and Soft-Tissue Infection Prevention

Military trainees are at increased risk for acute respiratory infection (ARI).[1,2] ARI outbreaks interrupt training and compromise troop readiness. Mitigating the risk requires prevention strategies. A skin and soft-tissue infection (SSTI) prevention trial was conducted among Army trainees.[3] Training companies were randomized to 1 of 3 groups with incrementally increasing education- and personal hygiene–based measures. The principal components were promotion of handwashing in addition to a once-weekly application of chlorhexidine-based body wash. Anticipating that these SSTI prevention measures would reduce the burden of other infections,[4] we evaluated their impact on ARI. We observed a reduction in ARI among trainees who were educated on personal hygiene practices. The use of a chlorhexidine-based cleanser had no impact on ARI.

METHODS

We conducted a cluster-randomized SSTI prevention trial among Army trainees at Fort Benning, Georgia.[3] There were 3 study groups (standard, enhanced standard, and chlorhexidine [CHG]), each with ~10,000 trainees. Each group was assigned an intervention consisting of incrementally increasing education- and personal hygiene–based measures.[3] The standard group trainees received a SSTI prevention brief upon entry. The enhanced standard group trainees received the standard group components in addition to supplemental materials (ie, a pocket card and posters in the barracks). The CHG group trainees received the enhanced standard group components in addition to a CHG-based body wash (Hibiclens, Mölnlycke Heath Care, Norcross, Georgia). Trainees were instructed to use the wash once weekly for the entire training period. All trainees sought care at a single outpatient clinic.

For a planned secondary objective of the trial, we reviewed an electronic database (Armed Forces Health Longitudinal Technology Application, AHLTA) to identify medically attended, outpatient cases of ARI in the study population. The case definition was any occurrence of the following International Classification of Disease, 9th Revision, Clinical Modification (ICD-9) symptom or disease-specific codes: 460-466, 480-488, and specifically 465.9, 482.9, 486, and 487.1. Data abstractors were blinded to group assignment.

Rate calculations included all ARI-associated visits, allowing multiple visits per individual. Rates are the number of cases per 1,000 person weeks. Binomial distributions were used to generate 95% confidence intervals (CIs). Rate ratios (RRs) were compared using Fisher's exact test.

Statistical analyses were performed using Microsoft Excel (Microsoft Corporation, Redmond, WA), Stata 12.1 (StataCorp, College Station, TX), and SAS 9.3 (SAS Institute, Cary, NC).

RESULTS

Over a 20-month period and among ~30,000 trainees, a total of 13,949 ARI episodes were identified: 4,365 (31.3%) in the standard group; 4,426 (31.7%) in the enhanced standard group; and 5,158 (36.9%) in the CHG group (Table 1). The overall ARI rate was 33.9 cases per 1,000 person weeks (95% CI, 33.3–34.5). By study group, ARI rates were 35.3 per 1,000 person weeks in the standard group (95% CI, 34.3–36.3); 29.3 in the enhanced standard group (95% CI, 28.5–30.2); and 37.7 in the CHG group (95% CI, 36.7–38.7). When compared with the standard group, ARI rates were lower in the enhanced standard group (RR, 0.82; 95% CI, 0.80–0.87) and marginally higher in the CHG group (RR, 1.07; 95% CI, 1.03–1.11). The enhanced standard:CHG group RR was 0.78 (95% CI, 0.75–0.81).

Overall rates were highest in winter. By season, enhanced standard:standard RRs were as follows: summer (RR, 0.77; 95% CI, 0.72–0.83), fall (RR, 0.97; 95% CI, 0.91–1.05), winter (RR, 0.93; 95% CI, 0.84–1.03), and spring (RR, 0.63; 95% CI, 0.57–0.70). When compared to the standard group, ARI rates in the CHG group were lower only in the spring (RR, 0.79; 95% CI, 0.72–0.86).

Case characteristics are presented in the Table 1. The most common code was acute upper respiratory infection not

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