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Chlorhexidine bathing and *Clostridium difficile* infection in a surgical intensive care unit

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ABSTRACT

Background: *Clostridium difficile* is the most common causative pathogen for hospital-acquired infections in the intensive care unit. This study evaluated the effect of chlorhexidine bathing every other day in preventing hospital-acquired *C. difficile* infection (CDI) using data from the CHlorhexidine Gluconate BATHing (CHG-BATH) randomized trial.

Methods: The primary endpoint was the proportion of patients acquiring CDIs among patients at risk for incident CDIs. Infections detected >48 h after randomization were classified as incident CDIs. Infections detected before or within 48 h of randomization were classified as prevalent CDIs.

Results: Of 38 patients (11.7%) who met criteria for potential CDI and underwent adjudication, 24 (7.4%) received oral or enema vancomycin, 18 (5.5%) had a positive *C. difficile* molecular assay, 14 (4.3%) received an International Classification of Diseases, Ninth Revision, Clinical Modification code for CDI, and 2 (0.6%) had possible pseudomembranous colitis on histopathology reports. The prevalence of CDI was 3.7% (6 of 164) in the soap and water arm and 4.3% (7 of 161) in the chlorhexidine arm. Compared with daily soap and water bathing, 2% chlorhexidine bathing every other day was not associated with the prevention of hospital-acquired CDI (1.3% [2 of 152] soap and water *versus* 2.0% [3 of 148] chlorhexidine, $P = 0.68$).

Conclusions: It is inconclusive if there was an association between chlorhexidine bathing and incidence of CDI among surgical intensive care unit patients in this study as statistical power was limited. There are limited published data evaluating the association between chlorhexidine bathing and CDI, and this study provides data for future systematic reviews and meta-analyses.

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Introduction

Routine bathing of intensive care unit (ICU) patients with chlorhexidine gluconate has been shown to reduce the incidence of hospital-acquired blood stream infection (BSI) by 28% to 44% in multiple randomized trials.[1-5] Our research team previously conducted the CHlorhexidine Gluconate BATHing (CHG-BATH) trial, a single-center, pragmatic, randomized controlled trial, which concluded that chlorhexidine bathing every other day decreased the risk of acquiring four hospital-acquired infections (HAIs) (primary BSI, catheter-associated urinary tract infection [CAUTI], ventilator-associated pneumonia [VAP], and incisional surgical site infection) compared with soap and water bathing by 44.5% in surgical ICU patients.[5] *Clostridium difficile* is the most commonly reported causative pathogen for HAIs in the ICU.[6] Patients with advanced age, long duration of hospitalization, long exposure to antimicrobials, and exposure to multiple antimicrobials have shown to be at increased risk for *C. difficile* infection (CDI).[7-10] However, the effectiveness of chlorhexidine bathing for preventing CDI remains unclear.[11,12] CDI was not included as an infectious outcome in the CHG-BATH trial. This study evaluates the effects of chlorhexidine bathing every other day in preventing hospital-acquired CDI using data from patients enrolled in the CHG-BATH trial.

Methods

CHG-BATH trial

The CHG-BATH trial was approved by the Houston Methodist Hospital Institutional Review Board, which also approved this additional analysis. The CHG-BATH trial was a single-center, open-label, randomized clinical trial conducted in a 24-bed surgical ICU at Houston Methodist Hospital, a tertiary academic medical center. All adult patients admitted to the surgical ICU from July 2012 through May 2013 with an anticipated surgical ICU stay $\geq$48 h were included. Patients with a Braden Scale for Predicting Pressure Sore Risk score <9, were pregnant, had skin irritation, had known chlorhexidine allergy, or stayed in the ICU >48 h before screening were excluded. Randomized patients were bathed with 1) daily soap and water or 2) every other day with 2% chlorhexidine gluconate alternating with every other day soap and water during the intervention period. The intervention period started at randomization and ended at surgical ICU discharge, day 28, or death, whichever occurred first. Patients and bedside clinicians were aware of treatment group assignment, but investigators who determined efficacy and safety outcomes were blinded. Additional detailed inclusion and exclusion criteria, study design, patient recruitment, and bathing procedures have been previously reported.[5]

Study design

Retrospective data from the CHG-BATH trial was evaluated for hospital-acquired CDI. CDI surveillance (molecular assay, colonoscopy, and biopsy of colon tissue) was performed by the treating medical team per standard of care. *C. difficile* in stool was detected using the *Illumi*gene *C. difficile* molecular diagnostic system (95% sensitivity, 95% specificity).[13] We hypothesized that among surgical ICU patients enrolled in the CHG-BATH trial, patients randomized to chlorhexidine bathing every other day would have a lower incidence of hospital-acquired CDI compared with patients randomized to soap and water bathing.

Study outcomes

The primary endpoint was the proportion of patients acquiring a CDI among patients at risk for an incident CDI. Infections detected >48 h after randomization and before the end of follow-up were classified as incident CDI. Infections detected before randomization or within 48 h of randomization were classified as prevalent CDI. Patients were not at risk for incident CDI if they had a prevalent infection or were enrolled in the study for <48 h. The 48-h threshold between prevalent and incident infections accounts for the latency time between exposure to a pathogen and clinical symptoms required for detection and is consistent with the 48-h latency period in Centers for Disease Control and Prevention surveillance criteria.[1,14] The secondary endpoint was the proportion of patients with at least one HAI of the composite endpoint of five HAIs (CDI, primary BSI, CAUTI, VAP, or incisional surgical site infection).

All patients included in this modified intention-to-treat analysis were screened for the CDI outcome using the criteria adapted from Clinical Practice Guidelines for CDI in adults.[7] At least two independent, blinded investigators evaluated patient medical records for CDI for all study patients with one or more criteria for potential CDI: 1) had a positive *C. difficile* molecular assay, 2) received an International Classification of Diseases, Ninth Revision, Clinical Modification code for CDI, 3) received oral antibiotics (vancomycin, fidaxomicin, or neomycin), or 4) had radiological evidence of pseudomembranous colitis during the hospital admission. The adjudication committee consisted of an infection prevention specialist (E.A.G.), infectious diseases pathologists (R.J.O. and S.W.L.), and clinical pharmacists (L.N.B. and J.T.S.). All patients were classified as no CDI, prevalent CDI, or incident CDI. Complex cases and discrepancies were finalized by majority vote at arbitration meetings.

Statistical analyses

According to previous studies,[2,15] the incidence of CDI in ICU patient was between 4% and 6%. Given a higher severity of illness and mortality in the CHG-BATH trial,[5] we estimated that there would be an 8% incidence of CDI in the control arm. Using an independent sample test of two proportions with a fixed sample size of 325 and an estimated incidence of 8% in the control arm, the study had 80% power to detect a 6.5% absolute risk reduction. Primary and secondary outcomes were evaluated using the Pearson's chi-square test or Fisher's exact test