

# Safety and efficacy of whole-body chlorhexidine gluconate cleansing with or without emollient in hospitalised neonates (NeoCHG): A multicentre, randomised, open-label, factorial pilot trial

Neal Russell, Michelle N. Clements, Kazi Shammin Azmery, Adrie Bekker, Julia Bielicki, Angela Dramowski, Sally Ellis, Aaqilah Fataar, Mahbubul Hoque, Kristen LeBeau, Seamus O'Brien, Francesca Schiavone, Peter Skoutari, Mohammad Shahidul Islam, Samir K. Saha, Ann Sarah Walker, Andrew Whitelaw, and Michael Sharland

eClinical Medicine, 2024;69:  
102463

DOI:  
<https://doi.org/10.3329/dshj.v4i1.93362>

## Summary:

**Background:** Healthcare-associated infections account for substantial neonatal in-hospital mortality. Chlorhexidine gluconate (CHG) whole body skin application could reduce sepsis by lowering bacterial colonisation density, although safety and optimal application regimen is unclear. Emollients, including sunflower oil, may independently improve skin condition, thereby reducing sepsis. We aimed to inform which concentration and frequency of CHG, with or without emollient, would best balance safety and the surrogate marker of efficacy of reduction in bacterial colonisation, to be taken forward in a future pragmatic trial evaluating clinical outcomes of sepsis and mortality.

**Methods:** In this multicentre, randomised, open-label, factorial pilot trial, neonates in two hospital sites (South Africa, Bangladesh) aged 1–6 days with gestational age  $\geq 28$  weeks and birthweight 1000–1999 g were randomly assigned in a factorial design stratified by site to three different concentrations of CHG (0.5%, 1%, and 2%), with or without emollient (sunflower oil) applied on working days vs alternate working days. A control arm received neither product. Caregivers were unblinded although laboratory staff were blinded to randomisation. Co-primary outcomes were safety (change in neonatal skin condition score incorporating dryness, erythema, and skin breakdown) and efficacy in reducing bacterial colonisation density (change in total skin bacterial log<sub>10</sub> CFU from randomisation to day-3 and day-8). The trial is registered at the ISRCTN registry, ISRCTN 69836999.

**Findings:** Between Apr 12 2021 and Jan 18 2022, 208 infants were randomised and 198 were included in the final analysis. Skin condition scores were low with mean 0.1 (sd = 0.3; N = 208) at baseline, 0.1 (sd = 0.3; N = 199) at day 3 and 0.1 (sd = 0.3; N = 189) at day 8, with no evidence of differences between concentration (1% CHG vs 0.5% estimate = -0.3, 95% CI = (-1.2, 0.6), p = 0.55. 2% CHG vs 0.5% CHG estimate = 0.5 (-0.4, 1.4), p = 0.30), increasing frequency (estimate = -0.4; 95% CI = (-1.1, 0.4), p = 0.33), emollient (estimate = -0.5, (-1.2, 0.3), p = 0.23) or with control (estimate = -0.9, (-2.3, 0.4), p = 0.18). Mean log<sub>10</sub> CFU was 4.9 (sd = 3.0; N = 208) at baseline, 6.3 (sd = 3.1; N = 198) at day 3 and 8.4 (sd = 2.6; N = 183) with no evidence of differences between concentration (1% CHG vs 0.5% estimate = -0.4; 95% CI = (-1.1, 0.23); p = 0.23. 2% CHG vs 0.5% CHG estimate = 0.0 (-0.6, 0.6), p = 0.96), with increasing frequency (estimate = -0.4; 95% CI = (-0.9, 0.2); p = 0.17), with emollient (estimate = 0.4, 95% CI = (-0.2, 0.9); p = 0.18) or with control (estimate = -0.2, 95% CI = (-1.3, 0.9); p = 0.73). By day-8, overall 158/183 (86%) of neonates were colonised with Enterobacterales, and 72/183 (39%) and 69/183 (9%) with Klebsiella spp resistant to third-generation cephalosporin and carbapenems, respectively. There were no CHG-related SAEs, emollient-related SAEs, grade 3 or 4 skin scores or grade 3 or 4 hypothermias.

**Interpretation:** In this pilot trial of CHG with or without sunflower oil, no safety issues were identified, and further trials examining clinical outcomes are warranted. The relatively late start application of emollient, at a mean of 3.8 days of life, may have reduced the impact of the intervention although no subgroup effects were detected. There was no clear evidence in favour of a specific concentration of chlorhexidine, and there was rapid colonisation with Enterobacterales with frequent antimicrobial resistance, regardless of skin application regimen.