Chlorhexidine and newborn omphalitis and mortality

David Osrin and Tim Colbourn (November, 2016)[1] uphold a recommendation to restrict use of chlorhexidine to "infants born at home in environments with high neonatal mortality rates" and assert that "Cochrane reviews, a meta-analysis, and these two new trials have not supported an effect after hospital births". We do not think it is clear how one could come to such a conclusion from the evidence in the cited papers.

The 2013 Cochrane review cited[2] included the three large community-based trials of chlorhexidine 4% solution in which application to the cord was done at home, although in the two largest of the studies, participants included both home and facility births. The review concluded that chlorhexidine reduces risk of both omphalitis (ranging from 27% to 65% depending on severity of infection) and death (risk ratio [RR] 0·77, 95% CI 0·63–0·94). A German trial[3] of 669 healthy newborn babies was also included, with those in the intervention arm receiving chlorhexidine 1% powder applied to the cord after every diaper change, initiated in hospital and continued at home until 3 days after cord separation (and could therefore be seen as a hybrid hospital-based and community-based study). "Cord-related adverse events" (the main endpoint other than cord separation time)—including "erosion, irritation, lesion, omphalitis, erythema, umbilical granuloma, purulence, bleeding, discharge or weeping"—were seen in 29% of those receiving dry cord care and 16% receiving chlorhexidine (p=0·001). Omphalitis, as defined in the study, was seen in seven of 332 receiving dry cord care and two of 337 receiving chlorhexidine (p=0·1). This trial did not use mortality as an endpoint. The review came to no conclusions about differences in effectiveness by place of birth.

A 2015 Cochrane review[4] retained the three community-based studies mentioned above and concluded that there was high-quality evidence of reduced risk of infection or omphalitis and death. The review also included two studies in which chlorhexidine was applied in a hospital setting: the above-described German study[3] and a newer neonatal intensive care unit (NICU)-based study[5] conducted in India. On the basis of the results from these studies, the review concluded that there was moderate-quality evidence that chlorhexidine reduces risk of omphalitis or infections in hospital settings (RR 0·48, 95% CI 0·28–0·84). The Indian trial[5] enrolled only 140 participants, patients admitted to NICU of gestational age 32 weeks or older, who on admission were expected to require NICU care for at least 5 days. They received chlorhexidine 2·5% solution three times daily during their NICU stay. In addition to cord separation time, endpoints included umbilical colonisation, neonatal sepsis, culture-proven sepsis, meningitis, and death up to the time of discharge from NICU. The risk of culture-proven sepsis among these hospital births was higher in the dry cord care group than the chlorhexidine group (0·13, 0·01–0·40), although "incidence of probable sepsis and meningitis was … similar [across] groups". There were also more deaths in the dry cord care group (four of 70 patients) than in the chlorhexidine group (no deaths in 70 patients, p=0·042).

The cited meta-analytic review[6] included only trials conducted in community settings in developing countries (ie, the three large trials discussed above) and concluded that chlorhexidine reduced risk of omphalitis and newborn death. It did not include any trials in which application was done solely in a hospital setting. However, as mentioned, two of these three trials did include births at home and in facilities; the authors provided a sub-analysis focusing on about 3000 facility births and reported that mortality risk was about half among those facility births receiving chlorhexidine (RR 0·50, 95% CI 0·27–0·92).

Similar to the Nepal and Bangladesh trials, study participants in the two studies in *The Lancet Global Health*[7,8] included both home and facility births, and chlorhexidine application was done only in the home. Both studies documented that chlorhexidine reduced risk of omphalitis. In the Pemba trial,[7] relative risk for omphalitis varied from 0·61 to 0·76, depending on level of severity, with p-values for all levels <0·0001. The Zambia trial[8] found a similar effect size (RR 0·73), but with an overall rate of omphalitis of only 0·6% in the control arm there was a relatively wide confidence interval, which included 1·0 (95% CI 0·47–1·13). It is true, as Osrin and Colbourn[1] stated, that these two trials did not show an effect of chlorhexidine in reduced risk of death among those born in hospital, just as no such effect was found for home births. Indeed, no difference was seen in effect sizes when comparing home versus facility births.

For risk of infection to the cord, we see the same picture across all sources of evidence cited by Osrin and Colbourn; whether community-based[6] or hospital-based,[3–5] home births,[2–8] or facility births,[3–8] low-income settings[2,4–8] or high-income settings,[3] chlorhexidine reduces risk of such infection. As Sazawal and colleagues[7] conclude, the results of the Pemba study suggest that use of chlorhexidine is justified for its effect in reducing risk of cord infection. Further, in settings where the underlying mortality risk in the population is high, chlorhexidine cleansing reduced mortality regardless of whether babies were born in facilities or at home.

I declare no competing interests.

Stephen Hodgins
shodgins@savechildren.org

Save the Children US, Saving Newborn Lives, 899 North Capitol Street NE, Washington, DC 2002, USA

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