Chlorhexidine and newborn omphalitis and mortality

Authors' reply

Stephen Hodgins says that cord application of chlorhexidine protects infants against omphalitis equally after birth at home or in hospital, and that we were incorrect to say that it was not effective for infants born in hospital.

The first point is well taken. The 2015 Cochrane review[1] suggests that risk ratios (RR) for omphalitis were similar in hospital (RR 0·48, 95% CI 0·28–0·84) and community trials (0·48, 0·40–0·57). The 2013 Cochrane review[2] included nine relevant hospital studies of chlorhexidine application. For omphalitis, one study[3] suggested a benefit versus dry cord care (0·28, 0·06–1·35); another study[4] found no benefit versus alcohol (2·77, 0·12–66·49), and another[5] found no benefit over hydrophobic gauze (1·36, 0·55–3·36). Imdad and colleagues[2] suggested that, "...compared with dry cord care, no antiseptic was convincingly advantageous to reduce the incidence of omphalitis."

The 2015 Cochrane review addressed cord cleansing, more extensive skin cleansing, and maternal vaginal washing.[1] One trial[6] in India suggested that, compared with dry cord care, chlorhexidine cord cleansing was associated with a non-significant reduction in mortality (RR 0·11, 95% CI 0·01–2·04). This and a trial in Germany[3] suggested that chlorhexidine cord cleansing was associated with lower risk of omphalitis. The review[1] made no recommendation for hospital births, saying that the "...quality of evidence for the effects on infection are moderate for cord application".

The trial in Germany[3] compared healthy term infants (>2500 g) in two neonatal nurseries treated with chlorhexidine 1% powder (337 infants) or dry cord care (332 infants). Sample size was based on the primary outcome of cord separation time but recruitment shortfalls necessitated respecification of the detectable difference. Hodgins summarises adverse events. Omphalitis was identified in two infants in the chlorhexidine group and seven in the dry cord care group. All cases but one were described as mild. The 2015 Cochrane review[1] downgraded its classification because of "...serious risk of selection bias, performance bias and detection bias".

The trial in India[6] compared application of chlorhexidine 2·5% solution to the cords of 70 infants with dry cord care for 70 infants, all of them older than 32 weeks and weighing more than 1499 g and judged on enrolment as likely to spend at least 5 days in a neonatal intensive care unit. The sample size was again based on the primary outcome of cord separation time. Culture-confirmed sepsis was lower in the chlorhexidine group (RR 0·13, 95% CI 0·02–0·40). The 2015 Cochrane review[1] downgraded its classification of bias risk because of imprecision. Together, these trials included 809 infants.

Hodgins' second point interprets a statement we made, quoting the WHO recommendation,[7] and saying that the Cochrane reviews,[1,2] a meta-analysis,[8] and the two trials in *The Lancet Global Health*[9,10] had not supported an effect after hospital births. Our Comment[11] begins with, and is permeated by, an emphasis on newborn mortality. As Hodgins says, community-based trials[8–10] suggest that the effect on neonatal mortality was similar—even when non-significant—when infants were born in hospital. We do not take issue with this. Indeed, we acknowledge the complete statement by Sazawal and colleagues:[10] "The findings in our study suggest that use of chlorhexidine for the reduction of omphalitis is justified, but in an African setting there is insufficient evidence to promote this intervention to reduce neonatal mortality."

The emphasis of our Comment was on whether cord application of chlorhexidine might achieve appreciable reductions in newborn mortality in low-income and middle-income countries. We said that two recent trials[9,10] did not provide evidence to alter current WHO guidelines,[7] which recommend it for infants born at home in environments with neonatal mortality rates of more than 30 per 1000 livebirths. We stand by this.

DO does not work with but has been a co-author of six publications in the past 5 years with Robert Black, a named author of the paper from Tanzania. The publications were produced by large working groups and DO and TC both either contributed data from their research programmes or were members of a distributed expert group.

*David Osrin, Tim Colbourn
d.osrin@ucl.ac.uk

Institute for Global Health, University College London, London WC1N 1EH, UK

1 Sinha A, Sazawal S, Pradhan A, Ramji S, Opiyo N. Chlorhexidine skin or cord care for prevention of mortality and infections in neonates. *Cochrane Database Syst Rev* 2015: CD007835.

2 Imdad A, Bautista RMM, Senen KAA, Uy MEV, Mantaring III JB, Bhutta ZA. Umbilical cord antiseptics for preventing sepsis and death among newborns. *Cochrane Database Syst Rev* 2013: CD008635.

3 Kapellen TM, Gebauer CM, Brosteanu O, Labitzke B, Vogtmann C, Kiess W. Higher rate of cord-related adverse events in neonates with dry umbilical cord care compared to chlorhexidine powder: results of a randomized controlled study to compare efficacy and safety of chlorhexidine powder versus dry care in umbilical cord care of the newborn. *Neonatology* 2009; **96:** 13–18.

4 Oishi T, Iwata S, Nonoyama M, Tsuji A, Sunakawa K. Double-blind comparative study on the care of the neonatal umbilical cord using 80% ethanol with or without chlorhexidine. *J Hosp Infect* 2004; **58:** 34–37.

5 Meberg A, Schoyen R. Hydrophobic material in routine umbilical cord care and prevention of infections in newborn infants. *Scand J Infect Dis* 1990; **22:** 729–33.

6 Gathwala G, Sharma D, Bhakhri B. Effect of topical application of chlorhexidine for umbilical cord care in comparison with conventional dry cord care on the risk of neonatal sepsis: a randomized controlled trial. *J Trop Pediatr* 2013; **59:** 209–13.

7 WHO. WHO recommendations on postnatal care of the mother and newborn: 2013. Geneva: World Health Organization, 2014.

8 Imdad A, Mullany LC, Baqui AH, et al. The effect of umbilical cord cleansing with chlorhexidine on omphalitis and neonatal mortality in community settings in developing countries: a meta-analysis. *BMC Public Health* 2013; **13** (suppl 3): 15.

9 Semrau KE, Herlihy J, Grogan C, et al. Effectiveness of 4% chlorhexidine umbilical cord care on neonatal mortality in Southern Province, Zambia (ZamCAT): a cluster-randomised controlled trial. *Lancet Glob Health* 2016; **4:** e827–36.

10 Sazawal S, Dhingra U, Ali SM, et al. Efficacy of chlorhexidine application to umbilical cord on neonatal mortality in Pemba, Tanzania: a community-based randomised controlled trial. *Lancet Glob Health* 2016; **4:** e837–44.

11 Osrin D, Colbourn T. No reason to change WHO guidelines on cleansing the umbilical cord. *Lancet Glob Health* 2016; **4:** e766.