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Chlorhexidine cord cleansing to reduce neonatal mortality

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The rising proportional contribution of neonatal mortality to deaths in childhood has featured in international health policy discussions for more than a decade. Low-income and middle-income countries bear the burden of 99% of global neonatal deaths.¹ Many infants—perhaps 60 million every year—are born at home.² Infections account for an estimated 30% of neonatal deaths,¹ and the umbilical cord is recognised as a potential entry point for infection, especially in the first few days of life. WHO and UNICEF recommend that newborn babies are visited at home in the first week of life to ensure healthy neonatal care practices, including hygienic cord care.³

Research evidence on topical cord care is, however, scarce: most studies included in a 2004 Cochrane review⁴ were from high-income countries, and the review could not address the effect of topical care on systemic infections or mortality. The investigators called for trials in low-income settings, suggesting that “where the risk of bacterial infection appears high it might be prudent to use topical antiseptics”. The choice of antiseptic and regimen of application was unclear: “it would seem sensible, in situations where packages of care around improving umbilical cord sepsis are introduced, to conduct randomized comparisons to identify the best agents and regimens”.⁴

Two large trials^{5,6} in *The Lancet*—both of which record encouraging reductions in neonatal mortality after application of a topical antiseptic, chlorhexidine, to the umbilicus—now improve the knowledge base. The trials build on the findings of a cluster-randomised controlled trial in Nepal, which compared chlorhexidine application with education on dry cord care and showed an apparent effect on neonatal mortality of chlorhexidine application in a subgroup enrolled within 24 h of birth (relative risk 0.66; 95% CI 0.46–0.95).⁷

In Shams El Arifeen and colleagues’ randomised controlled trial⁵ in 133 clusters in Sylhet, Bangladesh, education on dry cord care was compared with two regimens: a single application of 4% chlorhexidine solution as soon after birth as possible, and the same initial application followed by daily application for 7 days. In an analysis of about 10 000 livebirths per allocation group, signs of local infection were reduced (albeit statistically significantly in only two of eight comparisons), and risk of neonatal death was lower in the single application group (relative risk 0.80; 95% CI 0.65–0.98), but not in the multiple application group (0.94; 0.78–1.14).

In Sajid Soofi and colleagues’ cluster-randomised trial⁶ in the rural Sindh province, Pakistan, families in 187 clusters were given clean home delivery kits and educational messages by traditional birth attendants. With a factorial design, two interventions were compared with advice on dry cord care. One was the provision of 4% chlorhexidine solution—the solution was applied to the umbilical cord by the traditional birth attendant at delivery, and advice was given to caregivers to repeat the application daily for 14 days. The other

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intervention was the provision of soap and handwashing advice. In an analysis of about 2350 livebirths per allocation group, risks of signs of local infection (risk ratio 0.58; 95% CI 0.41–0.82) and of neonatal mortality (0.62; 0.45–0.85) were lower in the chlorhexidine groups.

Findings for the frequency of chlorhexidine application in the Bangladesh trial—a reduction in mortality with a single application, but not when additional applications were given—are counterintuitive. We tend to agree with the investigators' suggestion that the latter might be a chance finding, especially because the trial in Pakistan showed a benefit from repeated applications. On balance, we think that sufficient evidence has accrued to claim proof-of-principle that application of 4% chlorhexidine to the cord stump can prevent omphalitis and neonatal mortality in high-mortality settings. Three cluster-randomised trials have now shown some effect of chlorhexidine application on mortality,^{5–7} and have suggested no adverse effects. The Nepal results suggest that early application is important;⁷ the results from Bangladesh suggest that a single application might be sufficient,⁵ and the results from Pakistan show a mortality effect even though families continued to apply other substances to the cord.⁶ We could argue that more research is needed—questions certainly exist about the duration and timing of application and about external validity. Evidence from high-mortality populations in Africa would be useful. Nevertheless, to demand more evidence of effectiveness might be to repeat an old public health debate: if the need is clear, the possibilities attractive, and the risk low, how much evidence is necessary before we act on plausible findings?

The next question is about evidence for the potential effectiveness of delivering cord antisepsis at scale. The trials should be seen in the context of the population health truism that the effect of an intervention is likely to diminish when it is rolled out. The Bangladesh and Pakistan trials both achieved impressive coverage, but neither worked within the confines of a government health system, which raises questions about feasibility and sustainability of delivery at scale. In Bangladesh, the intervention was delivered by specially recruited female village health workers, each covering a population of 1000 people and supervised by a community health worker. A large proportion of women were reached on the day of delivery, which could be difficult to replicate in some settings. The delivery model ran parallel to the government system, and could attract the criticism that it might not be scalable. There is, however, a precedent, in that huge areas of Bangladesh receive health services from non-governmental organisations and private-sector initiatives.

In Pakistan, the intervention was delivered by traditional birth attendants who received their delivery kits from community health workers specifically recruited for the trial. Project workers were necessary because their government counterparts (lady health workers) did not link formally with traditional birth attendants, although this might change as a result of a trial published last year, which showed that reduced neonatal mortality was associated with changes to lady health workers' activities and stronger links with traditional attendants.⁸ Working with traditional birth attendants acknowledges existing community structures, but might not be effective in settings where home deliveries are mainly done by family members, or where governments are reluctant to engage with traditional birth attendants. An alternative delivery strategy might be in families themselves. A desire to apply something (eg, ash, oil, or dung) to the umbilical cord is common.^{9–12} If we think of topical chlorhexidine as a technology, and of its adoption by families as needing diffusion of innovation, progress could be rapid, either after its inclusion in clean delivery kits or through independent access.

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