Application of chlorhexidine to the umbilical cord after birth in low-income settings: two randomised controlled trials

Study design
Design: Community-based cluster-randomised trial.
Allocation: Clusters were computer randomised. There were 133 clusters, with a mean population of 4100 people.
Blinding: Interventions were not masked.

Study question
Setting: Rural area of Pakistan.
Patients: All liveborn babies were eligible for enrolment. Of 35 908 eligible infants, 29 760 were enrolled. Over 85% received the intervention within 24 h of birth. Baseline characteristics were similar between the three groups.
Intervention: Clusters were randomised to four groups: topical 4% chlorhexidine daily for 14 days plus hand washing with antiseptic soap and water, hand washing and dry cord care, chlorhexidine without hand-washing recommendations, and dry cord care without hand-washing recommendations (control group).
Outcomes: Primary outcomes were neonatal omphalitis and mortality.
Follow-up period: Outcomes were assessed at days 1, 3, 5, 7, 14 and 28.
Patient follow-up: An intention-to-treat analysis was performed. Final health status was available for 95% of patients enrolled.

Main results
Newborns in the multiple chlorhexidine group had a lower risk of severe cord redness and pus. Newborns in the single chlorhexidine group had a lower mortality rate, especially the subgroup of preterm infants. No statistically significant differences were found in mortality in the multiple chlorhexidine group. There were no adverse effects (table 1).

Conclusion
Single application of chlorhexidine reduced mortality in newborns.

Abstracted from

Source(s) of funding
PAIMAN (Pakistan Initiative for Mothers and Newborns) and John Snow Inc.

Table 1 Cord infection and mortality risks

<table>
<thead>
<tr>
<th></th>
<th>Severe redness with pus*</th>
<th>Mortality*</th>
<th>Mortality risk†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple chlorhexidine</td>
<td>0.35 (0.15 to 0.81)</td>
<td>0.94 (0.78 to 1.14)</td>
<td>26.6</td>
</tr>
<tr>
<td>Single chlorhexidine</td>
<td>0.77 (0.40 to 1.48)</td>
<td>0.80 (0.65 to 0.98)</td>
<td>22.6</td>
</tr>
<tr>
<td>Dry cord care</td>
<td>1</td>
<td>1</td>
<td>28.3</td>
</tr>
</tbody>
</table>

*Relative risk (95% CI); †Risk per 1000 livebirths.

Table 2 Cord infection and mortality risks

<table>
<thead>
<tr>
<th></th>
<th>Omphalitis*</th>
<th>Mortality*</th>
<th>Mortality risk†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorhexidine</td>
<td>0.53 (0.32 to 0.88)</td>
<td>0.64 (0.39 to 1.06)</td>
<td>20.3</td>
</tr>
<tr>
<td>+hand washing</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Hand washing</td>
<td>0.67 (0.48 to 0.93)</td>
<td>1.23 (0.82 to 1.83)</td>
<td>38.4</td>
</tr>
<tr>
<td>+dry cord care</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlorhexidine</td>
<td>0.44 (0.29 to 0.67)</td>
<td>0.74 (0.50 to 1.08)</td>
<td>24.9</td>
</tr>
<tr>
<td>Dry cord care</td>
<td>1</td>
<td>1</td>
<td>33.8</td>
</tr>
</tbody>
</table>

*Relative risk (95% CI); †Risk per 1000 livebirths.
Around 99% of neonatal deaths occur in low-income and middle-income countries, where home births remain common. Cord care may prevent infection in an undefined proportion of the 30% of sepsis-related deaths. Beyond scrupulous hygiene, however, we do not know what the optimal approach to cord care is. A cluster-randomised controlled trial (cRCT) in Nepal compared umbilical chlorhexidine application with education on dry cord care (the current WHO recommendation), and found a non-significant impact on newborn mortality.1

Two recent trials in Bangladesh and Pakistan add to the evidence. A cRCT in 133 clusters in Sylhet, Bangladesh, compared education on dry cord care with two regimens: application of 4% chlorhexidine solution soon after birth, and daily application for a week. The risk of neonatal death was lower in the single application arm, but not in the multiple application arm. A cRCT in 187 clusters in Sindh, Pakistan, provided clean home delivery kits to traditional birth attendants. In one pair of allocation arms, the kits included 4% chlorhexidine solution, to be applied by the birth attendant at delivery, and thereafter by the family for the next 2 weeks. In the other pair (the design was factorial), the kits included soap, and families were given advice on hand washing. Signs of local infection were fewer and neonatal mortality was lower in the chlorhexidine groups.

Three cRCTs have now shown some effect of chlorhexidine application on mortality. The primary implications are for low-income countries, but nosocomial infection is a significant concern for institutional births, and infection control and perinatal hygiene are critical.

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Competing interests None.

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