4% Chlorhexidine for umbilical cord care

Jamlick Karumbi
Objectives

• To understand existing guidance for dry cord care

• To understand and review the evidence available to inform decision making
Background

- Close to 50% of neonatal deaths (3 million) occur within the first 24 hours of birth and a further 25% occurring within 7 days of life.
- According to KDHS 2014, in Kenya the neonatal mortality rate currently is 22 per 1,000 live births, this is about 42% of all under five mortality
- The main causes of neonatal mortality are, asphyxia, preterm births and *infections (globally 15% Kenyan 7% sepsis*).
Background

• Cord vessels may remain potentially patent within the first 24 hours after cutting the cord offering a likely source of direct infection.

• This infection can be localized, or become systemic (sepsis – very early, early or late onset)

• Sparse data to characterize sepsis attributable to cord origin.
Background

• WHO had for a long time recommended the practice of dry cord care.

• From practice this was not happening in Kenya.

• There was need to review evidence to come up with a policy.
Its an acronym for Grading of Recommendations Assessment, Development and Evaluation.

It's a system for rating quality of evidence in systematic reviews and guidelines and grading the strength of recommendations in guidelines.

RATING QUALITY OF EVIDENCE AND STRENGTH OF RECOMMENDATIONS

GRADE: an emerging consensus on rating quality of evidence and strength of recommendations

Guidelines are inconsistent in how they rate the quality of evidence and the strength of recommendations. This article explores the advantages of the GRADE system, which is increasingly being adopted by organisations worldwide.
Overall certainty of evidence

- This refers to the combined quality of evidence across all studies for the critical outcomes.

- Consider **only** the critical outcomes, the overall grade is the **lowest** quality level assigned to the critical outcome.
### Table 2: Term babies evidence profile: antibiotic prophylaxis vs no antibiotics

**Patient or population:** preterm neonates born to mothers with no risk factors

**Settings:** Any setting

**Intervention:** Antibiotics prophylaxis

**Comparison:** no or delayed antibiotics

<table>
<thead>
<tr>
<th>Quality assessment</th>
<th>No of patients</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of studies</td>
<td>Design</td>
<td>Risk of bias</td>
</tr>
<tr>
<td>All-cause mortality (follow-up 21 days; assessed with: numbers/proportions)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. (low resource and high resource settings)
2. The study reports that there was no concealment or blinding.
3. This is a single study.
4. The choice of control is not specified.
5. The sample size was small.
6. Not estimable as there are no events in the control or no treatment arms, no details how this was done.

- **Clarification**
- **Judgements**
- **Transparency**
Three large trials

• **Nepal 2002-2005**
  – A community based cluster randomized trial
  – Three equal arms, (4%CHX, soap and water, dry care)
  – The intervention was delivered by a female community worker.
  – The population was 15,000 newborns visited in the first 10 days.
  – Follow up was up to 28 days.
  – Neonatal mortality rate was 32 per 1000
  – Omphalitis rates 105/1000 live births

*Mullany et al 2006*
Three large trials

- **Bangladesh 2007-2009**
  - Community based cluster randomized trial
  - 29,760 newborns visited within 7 days by a CHW.
  - Three similar groups (multiple cleansing with 4% CHX, single cleansing with 4% CHX and dry cord care)
  - Neonatal mortality rate was about 36/1000 live births

*Arifeen et al 2012*
Three large trials

- **Pakistan 2007-2009 (N=9,741)**
  - A community-based, cluster-randomized trial
  - Neonatal mortality rate 53/1000
  - Traditional practices are prevalent, ash, lead-based concoctions, oil, cow dung etc
  - Mainly delivered through TBAs
  - Four similar arms (two by two factorial design)
    - 4% CHX + bar soap
    - Soap
    - 4% CHX
    - No soap or CHX
  - Omphalitis rates 217/1000

*Soofi et al 2012*
Pooled results from 3 community RCTs

After adjusting for clustering, there was a 14% reduction in mortality with limits of Between 26% and 0%.

Karumbi et al 2013
Pooled results, community RCTs

- From 3 trials, 4% CHX reduces the risk of omphalitis when compared to dry care.
  - The risk of Omphalitis by any definition, was reduced by 39% with limits of 50% to 24% reduction.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>4% Chlorhexidine</th>
<th>Dry cord care</th>
<th>Risk Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
</tr>
<tr>
<td>Arifeen 2012</td>
<td>1044</td>
<td>23886</td>
<td>703</td>
</tr>
<tr>
<td>Mullany 2006</td>
<td>598</td>
<td>5168</td>
<td>1005</td>
</tr>
<tr>
<td>Soofi 2012</td>
<td>84</td>
<td>3131</td>
<td>182</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>32185</td>
<td>20445</td>
<td>100.0%</td>
</tr>
<tr>
<td>Total events</td>
<td>1726</td>
<td>1890</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 0.03; \text{Chi}^2 = 17.32, df = 2 (P = 0.0002); I^2 = 88\%$
Test for overall effect: $Z = 4.53 (P < 0.00001)$

Karumbi et al 2013
### Hospital data

#### Facility based interventions

<table>
<thead>
<tr>
<th>Study/setting</th>
<th>Popn</th>
<th>Interventions</th>
<th>Control</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pezzati 2003 (Italy)</td>
<td>244</td>
<td>4% CHX</td>
<td>Salicylic sugar powder</td>
<td>No beneficial effect (1 sepsis in each arm)</td>
</tr>
<tr>
<td>Ahmadvour-Kacho 2006 (Iran)</td>
<td>312</td>
<td>Breast milk, Alcohol, Silver sulfadiazene</td>
<td>No treatment (dry care)</td>
<td>No infection in any group, Breast milk shortens the time to cord separation</td>
</tr>
<tr>
<td>Erenel 2009 (Turkey)*</td>
<td>150</td>
<td>Olive oil</td>
<td>Dry care</td>
<td>No significant difference</td>
</tr>
<tr>
<td>Hsu 2010 (Taiwan)</td>
<td>150</td>
<td>Alcohol</td>
<td>Dry care</td>
<td>No infections, Alcohol prolongs time to separation</td>
</tr>
</tbody>
</table>

These facility based hospital based studies did not have data on mortality but they were not adequately powered to do that (mortality was not the primary outcome)
### Summary of findings table from the community setting

#### 4% Chlorhexidine compared to dry cord care

**Patient or population:** Newborn neonates >28 weeks and >1000g in weight  
**Settings:** Community (Nepal, Bangladesh, Pakistan)

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Impacts</th>
<th>Quality of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dry cord care</td>
<td>4% CHX</td>
</tr>
<tr>
<td></td>
<td>(per 1000)</td>
<td>(per 1000)</td>
</tr>
<tr>
<td>Mortality</td>
<td>26 per 1000</td>
<td>23 per 1000</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omphalitis/sepsis</td>
<td>109 per 1000</td>
<td>65 per 1000</td>
</tr>
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<td></td>
<td></td>
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</tbody>
</table>
RECOMMENDATION 6: Cord care

Daily chlorhexidine (7.1% chlorhexidine digluconate aqueous solution or gel, delivering 4% chlorhexidine) application to the umbilical cord stump during the first week of life is recommended for newborns who are born at home in settings with high neonatal mortality (30 or more neonatal deaths per 1000 live births).

Clean, dry cord care is recommended for newborns born in health facilities and at home in low neonatal mortality settings. Use of chlorhexidine in these situations may be considered only to replace application of a harmful traditional substance, such as cow dung, to the cord stump.

Strong recommendation based on moderate quality evidence.
DANKE!
THANK YOU
THENGIO
EROKAMANO
SHUKRAN
Xièxiè
谢谢