Impact of umbilical cord cleansing with 4% chlorhexidine on omphalitis and neonatal mortality in Nepal: a community-based, cluster randomized trial

Luke C Mullany[1], Gary L Darmstadt[1], Subarna K Khatry[2], Joanne Katz[1], Steven C LeClerq[1,2], Sharada R Shrestha[2], Ramesh K Adhikari[3], James M Tielsch[1]

[1]Johns Hopkins Bloomberg School of Public Health, Baltimore MD; [2]Nepal Nutrition Intervention Project, Sarlahi (NNIPS), Nepal; [3]Institute of Medicine, Tribhuvan University, Nepal

BACKGROUND

- Infections account for 1.44 million (36%) neonatal deaths; in areas with high NMR (> 45 / 1000), infections can account for 50% of neonatal deaths[1]
- Contamination of the umbilical cord stump may lead to omphalitis (pus, redness, swelling, foul odor)[2], systemic infection and death

Omphalitis and Topical Antiseptics

- In developed countries, topical antiseptics have been used for many years[3]
  - Antiseptics reduce bacterial colonization of the cord
  - No clear evidence for reduction in infection
- **WHO – currently promotes dry cord care for low-resource settings[2]**
- Pakistan: case control study of topical antiseptics at birth: odds of tetanus death were 60% (23%-79%) lower than among those receiving no antiseptics[4]

RESEARCH QUESTIONS

- **Compared to dry cord care, what is the impact of umbilical cord cleansing with 4.0% chlorhexidine (or soap and water) on:**
  - **Neonatal mortality risk?**
  - **Incidence of neonatal omphalitis?**

DESIGN / INTERVENTION

Setting / Study Population

- Sarlahi District, Nepal
- November, 2002 – March 2005
- Cultural, social and economic characteristics similar to northern India and Bangladesh

Design

- Cluster-randomized, community-based trial
- Communities (n=413) randomized to one of three cord care regimens
  1. 4.0% chlorhexidine cleansing of the cord
  2. Soap and water cleansing of the cord
  3. Dry cord care only
- Nested within a trial of full-body cleansing of newborn skin with 0.25% chlorhexidine (2x3 factorial trial)

Intervention Delivery

- Field workers visited infants in the home: Days 1, 2, 3, 4, 6, 8, 10, 12, 14, 21, 28; cord stump cleansed up to day 10

Cord cleansing during home visits

PRIMARY OUTCOMES

1. **Neonatal mortality (per 1000 live births)**
2. **Umbilical cord infection**
   - **Moderate or severe redness**
   - **Pus and moderate/severe redness, OR severe redness without pus**
   - **Pus and severe redness**

CLUSTERS / PARTICIPANTS

4% Chlorhexidine (N=137 sectors)	Soap and Water (N=138 sectors)	Dry Cord Care (N=138 sectors)
5168 live births	5319 live births	5317 live births
4934 enrolled infants (95.5%)	5107 enrolled infants (96.0%)	5082 enrolled infants (95.6%)

IMPACT ON NEONATAL MORTALITY

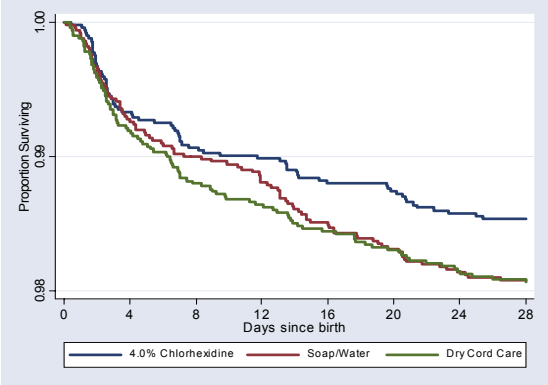
1. OVERALL

- 268 deaths among enrolled infants (17.7/1000)
- **Risk of neonatal death in chlorhexidine group was reduced by 24% [RR = 0.76 (0.55-1.04)] compared to dry cord care**
- Soap/water cleansing did not reduce mortality risk

2. AMONG INFANTS ENROLLED WITHIN FIRST 24 HOURS AFTER BIRTH

- Impact of chlorhexidine was increased; neonatal mortality was reduced by 34% (5%-55%)

Kaplan-Meier survival curves by treatment group



Cord Care Group	NMR	RR (95% CI)
Chlorhexidine 4.0%	14.4	0.66 (0.46 – 0.95)
Soap / Water	20.4	0.94 (0.67 – 1.32)
Dry cord care	21.7	1.00

IMPACT ON CORD INFECTION

Cord Care Group	Cases	Person-Time*	Rate†	IRR (95% CI)‡
Mild Infection				
Chlorhexidine 4.0%	438	4236	10.3	0.68 (0.58 – 0.80)
Soap / Water	660	4214	15.7	1.03 (0.87 – 1.22)
Dry cord care	638	4196	15.2	1.00
Moderate infection				
Chlorhexidine 4.0%	147	4676	3.1	0.46 (0.36 – 0.59)
Soap / Water	280	4702	6.0	0.88 (0.69 – 1.12)
Dry cord care	315	4652	6.8	1.00
Severe infection				
Chlorhexidine 4.0%	13	4839	0.3	0.25 (0.12 – 0.53)
Soap / Water	53	4962	1.1	1.01 (0.58 – 1.77)
Dry cord care	52	4930	1.1	1.00

**Person-time expressed as neonatal periods; †Incidence: per 100 neonatal periods; ‡ Generalized estimating equations with Poisson link were used to adjust point estimates and confidence intervals*

- **4% chlorhexidine reduced omphalitis risk (32%-75%) for all three definitions**
- **Soap/water cleansing did not reduce risk of omphalitis compared to dry cord care**

CONCLUSIONS

- **Umbilical cord cleansing with 4.0% chlorhexidine reduced the omphalitis and mortality risk**
- **Protective impact cleansing on mortality was stronger among infants enrolled within 24 hours of birth [RR=0.66 (0.46-0.95)]**
- **WHO recommendations for dry cord care may be inappropriate where baseline risk of omphalitis and mortality associated with portal of entry through the cord is high**
- **Ideal community-based intervention for mothers, traditional birth attendants, or other minimally trained persons who assist with delivery in low-resource settings**

ACKNOWLEDGMENT AND REFERENCES

All members of the Nepal Nutrition Intervention Project, Sarlahi (NNIPS) collaborated on the successful implementation of this research project. Commodity support (perfume for masking intervention groups) was provided by Procter and Gamble Company, Cincinnati, Ohio. Special appreciation goes to Data and Safety Monitoring Board members, Drs. P. S. S. Sundar Rao, Pushpa Sharma, Dharma Manandhar, and Martin Bloem. This study was supported by grants from the National Institutes of Health, National Institute of Child Health and Human Development (HD34004 and HD38753), The Bill & Melinda Gates Foundation (810-2054) and cooperative agreements between the Johns Hopkins BSPH and the Office of Heath and Nutrition, USAID (HRN-A-00-97-00015-00, GHS-A-00-03-000019-00). **(1)** Lawn JE et al. 4 million neonatal deaths: when? Where? Why? Lancet 2005 March 2;365(9462):891-900. **(2)** World Health Organization. WHO/FHE/MSM-cord care. Geneva: WHO, 1998. **(3)** Mullany LC et al. Pediatr Infect Dis J 2003;22:996-1002. **(4)** Bennett J et al. Int J Epidemiol 1997;26:897-903.