

Newborn skin cleansing with a dilute chlorhexidine solution reduces neonatal mortality in southern Nepal: a community-based, cluster randomized trial

James M Tielsch¹, Gary L Darmstadt¹, Luke C Mullany¹, Subarna K Khatry², Joanne Katz¹, Steven C LeClerq^{1,2}, Sharada R Shrestha², Ramesh K Adhikari³

¹Johns Hopkins Bloomberg School of Public Health, Baltimore MD; ²Nepal Nutrition Intervention Project, Sarlahi (NNIPS), Nepal;

³Institute of Medicine, Tribhuvan University, Nepal

BACKGROUND

- Progress has been made in reducing childhood mortality in developing countries; significant challenges remain for neonates
- Four million infants die annually during the neonatal period; infections account for 1.44 million (36%) neonatal deaths¹

Newborn Cleansing with Chlorhexidine

- Combined maternal and vaginal cleansing of hospital-born newborns in Malawi² and Egypt³ reduced neonatal mortality
 - Malawi – 22% reduction
 - Egypt – 33% reduction
- No community-based studies of newborn cleansing with chlorhexidine have been conducted

RESEARCH QUESTIONS

Compared to placebo cleansing, what is the impact of a single full-body wipe of the newborn skin with 0.25% chlorhexidine on all-cause neonatal mortality?

DESIGN / INTERVENTION

Setting / Study Population

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



Design

- Cluster-randomized, community-based trial
 - Communities (n=413) randomized to one of two skin cleansing regimens applied once as soon as possible after birth:
 - Cleansing with 0.25% chlorhexidine wipes
 - Cleansing with placebo wipes
 - Nested within a trial of three separate umbilical cord care regimens (2x3 factorial trial)
 - Baby wipes provided by Procter and Gamble
- ### Intervention Delivery
- Women enrolled during 6th month of pregnancy
 - All received iron, folic-acid, albendazole, weekly vitamin A supplementation, tetanus toxoid
 - Local female project workers wiped infants once in the home as soon as possible after birth



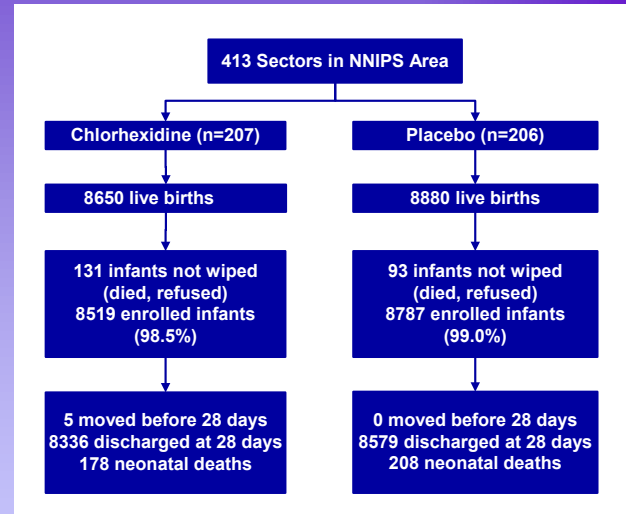
Project worker wipes infant with baby wipes

OUTCOME / ANALYSIS

- Infants were followed-up with home visits (Day 1-4,6,8,10,12,14,21,28)
- Neonatal mortality was the primary outcome**
- Axillary temperature measured at each home visit to monitor hypothermia
- Mortality estimated as deaths per 1000 live births
- Survival analysis
- Stratification by birth weight**
- Generalized estimating equations to account for cluster design
- Treatment groups were comparable at baseline on demographic and labor & delivery factors, birth weight, gestational age, socioeconomic status ethnicity, caste, etc.

- 17,306 infants participated in the trial
- The median time to intervention (skin wiping) was 5.75 hours (see table)
- There was no evidence of increased hypothermia compared to historical controls

STUDY FLOWCHART



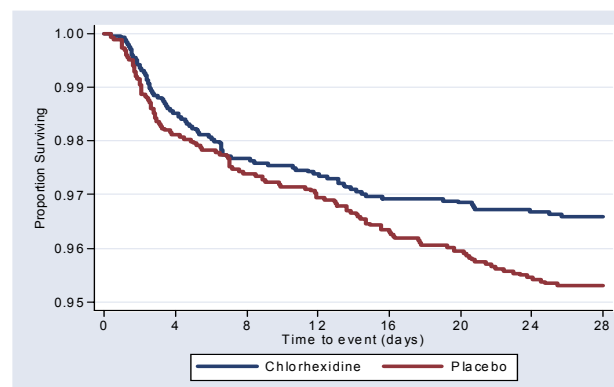
Treatment Group	N	Median	90 th %ile
CHX	8519	5.75	20.82
Placebo	8787	5.83	20.25
TOTAL	17306	5.75	20.50

IMPACT OF CLEANSING ON OVERALL NEONATAL MORTALITY

- Mortality was 11% lower among infants in the chlorhexidine clusters – not strong statistical evidence for impact

Cleansing Group	Deaths	Live Births	NMR	RR (95% CI)
Chlorhexidine 0.25%	178	8519	20.9	0.89 (0.72 – 1.10)
Placebo	208	8787	23.7	1.00

IMPACT AMONG LOW BIRTH WEIGHT INFANTS



Kaplan-Meier survival curves by treatment group

- Among low birth weight infants, mortality was significantly reduced in the 0.25% CHX group
- Neonatal mortality rate was 34/1000 in the intervention group, compared to 47/1000 in the control group
- RR for mortality: **0.72 (0.55, 0.95)**

CONCLUSIONS

- Newborn skin cleansing with 0.25% chlorhexidine reduced neonatal mortality among high risk, low birth weight infants
- These infants may be at greater risk of sepsis via percutaneous invasion of pathogens
- Chlorhexidine cleansing may prevent or reduce colonization of the skin with these pathogens
- Further research is needed to establish the efficacy of this intervention in other settings
- This inexpensive, simple intervention could significantly improve survival among high risk infants where home delivery is common and the environment is highly contaminated

ACKNOWLEDGMENT AND REFERENCES

All members of the Nepal Nutrition Intervention Project, Sarlahi (NNIPS) collaborated on the successful implementation of this research project. Gratitude goes to Procter and Gamble Company, Cincinnati, Ohio. Special appreciation goes to Data and Safety Monitoring Board members, Drs. P. S. S. Sundar Rao, Pushpa Sharma, Dharna Manandhar, and Martin Bloem. This study was supported by grants from the National Institutes of Health, National Institute of Child Health and Human Development (HD44004 and HD38753), The Bill & Melinda Gates Foundation (810-2054) and cooperative agreements between the Johns Hopkins BRN and the Office of Health and Nutrition, USAID (HRN-A-00-97-00015-00, GH-A-00-03-00019-00). (1) Lawn JC et al. 4 million neonatal deaths: when? Where? Why? Lancet 2005 March 23;365(9462):891-900. (2) Taha T et al. BMJ 1997;315:216-220. (3) Sale Af et al. J Womens Health. 2005;14(6):496-501.