Chlorhexidine for Umbilical Cord Care:

A new, low-cost intervention to reduce newborn mortality

Cord care with 7.1% chlorhexidine digluconate saves newborn lives

Key points

- Each year about 3 million newborns die globally, and infection causes approximately 15% of these deaths.[1] Poor hygiene and lack of antisepsis at birth and in the first week of life increases the risk of deadly but preventable infections.
- Chlorhexidine digluconate (7.1%, in aqueous or gel form) was added to the 2013 World Health Organization (WHO) List of Essential Medicines for Children, specifically for umbilical cord care.
- In January 2014, the WHO issued a new recommendation for umbilical 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.*"[2]

- Although policy makers in any setting could consider adopting use of chlorhexidine as part of routine care on the day of birth, use should be especially prioritized in countries that still have high rates of newborn mortality (where, in most cases, sepsis will be an important cause).
- To determine if chlorhexidine is a good fit for a specific country requires the ministry of health and implementing partners to consider the neonatal mortality rates (NMR) and the percentage of neonatal deaths from sepsis (if available), as well as umbilical cord care practices and hygienic conditions in both community and facility settings.
- Chlorhexidine remains an important component of essential newborn care, where appropriate.
- It is estimated that approximately 1 million lives would be saved if chlorhexidine for umbilical cord care is used at every home birth in 49 high-burden countries between 2015 and 2030.[3]

Product description

- Chlorhexidine digluconate is an antiseptic with a broad spectrum of activity against gram-negative and gram-positive bacteria.
- When used as directed, the safety record has been well established in adults as well as in newborns. For umbilical cord care, a concentration of 7.1% was selected to be sufficiently potent as an antiseptic.[4] Chlorhexidine for umbilical cord care is a well-tolerated intervention in infants regardless of gestational age.

Photo credit: PATH/Patrick McKern

- Beyond the direct antiseptic effect, chlorhexidine cord care may replace common, harmful practices such as applying unhygienic substances to the cord.

Product availability

Chlorhexidine for umbilical cord care comes in both gel and aqueous solution (liquid) forms (pictured above). A gel sachet is also available (not pictured). To ensure the

sustainable availability of good-quality 7.1% chlorhexidine digluconate, the global Chlorhexidine Working Group has worked with manufacturers to establish local/regional production bases in several locations in sub-Saharan Africa and South Asia. For more information and a list of current manufacturers of 7.1% chlorhexidine for umbilical cord care, see:

http://www.healthynewbornnetwork.org/hnn-content/uploads/List-of-CHX-suppliers-_Final_June-6.pdf. 7.1% chlorhexidine digluconate for umbilical cord care can also be purchased from the UNICEF Supply Division Catalogue (https://supply.unicef.org).

Pathogenesis and prevention

The recently-cut umbilical cord is an entry point for bacteria that can cause newborn sepsis and death. Bacteria rapidly colonize the freshly-cut cord stump and have direct access to the bloodstream through umbilical vessels that remain somewhat patent for the first few days after birth. In addition, bacterial colonization may lead to cord infection (omphalitis) with potential spread to the surrounding tissues and blood stream. Ensuring optimal cord care at birth and in the first week of life (including use of chlorhexidine), especially in settings with poor hygiene, is a crucial strategy to prevent life-threatening sepsis and cord infections, and to avert preventable neonatal deaths.

How to apply

Immediately after cutting the cord, apply chlorhexidine to the tip of the cord, the stump, and around the base of the stump. Wash hands before and after use and keep chlorhexidine away from eyes and ears. Repeat application once daily through the first week of life. It is most important that chlorhexidine be applied within the first 24 hours of birth. Applied once daily for 7 days can reduce risk of local infection and may displace non-hygienic traditional applications. Discard product at the end of the specified application period.

Delivery strategies

Chlorhexidine can be delivered through existing health services and initiatives such as antenatal and delivery care, and postnatal care in the first days and week of life. It can be provided in public facilities and/or communities (e.g., traditional birth attendants) and by community health workers who have contact with pregnant women. In addition, retail outlets including pharmacies can be considered if countries have strong private sector channels and can provide oversight to assure product quality. It can be easily administered by health professionals, as well as by community health workers and family members.

Global scale-up

Over 25 countries are now moving forward with chlorhexidine for umbilical cord care from stakeholder engagement to national scale-up. In late 2011, Nepal became the first country to introduce and scale chlorhexidine for umbilical cord care. The Government of Nepal approved the use of chlorhexidine as part of essential newborn care for both home and facility births by integrating chlorhexidine into ongoing government services and including this intervention in pre-service and in-service training curricula for professionally qualified birth attendants.

Many countries in sub-Saharan Africa and South Asia are moving forward with chlorhexidine for umbilical cord care. For example, chlorhexidine for umbilical cord care has been identified as a priority newborn health commodity by ministries of health and is being introduced for national scale-up in Bangladesh, Democratic Republic of the Congo, Ethiopia, Kenya, Liberia, Madagascar, Malawi, Mozambique, Nigeria, and Pakistan.

Cautionary note

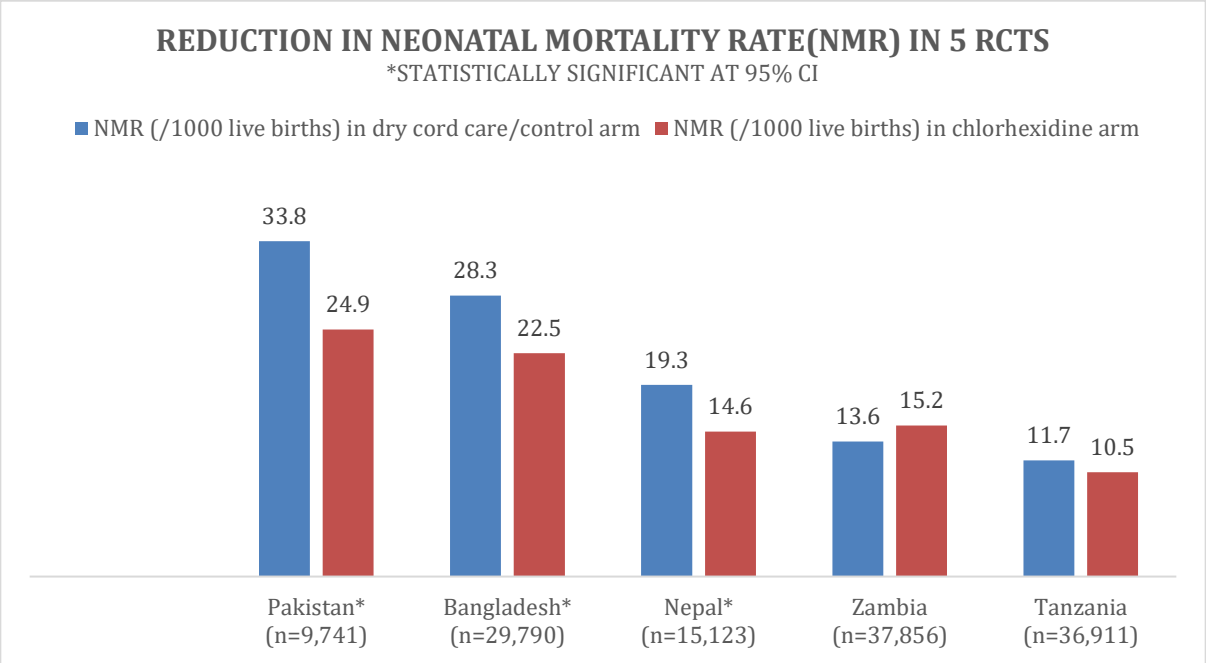
As with all medications, care must be taken to ensure that the product is used appropriately. 7.1% chlorhexidine digluconate for umbilical cord care can cause serious harm if applied to the eyes and should also not be put into the ear canal. It is important that persons and organizations responsible for chlorhexidine for umbilical cord care programs and for the distribution of the chlorhexidine for umbilical cord care product to caregivers ensure that instruction is provided on the proper use of the product, including appropriate warnings.

Chlorhexidine cord care: Evidence for health impact

Summary data on the five trials on use of 7.1% chlorhexidine digluconate for umbilical cord-stump application as a routine preventive measure are detailed in Table 1. Total sample sizes range from about 10,000 to 35,000. All of the trials used multi-day application, with the exception of one study arm in the Bangladesh trial which used a single application on the day of birth. All of the trials tried to ensure the first application as close to the time of birth as possible. The trial in Pakistan was restricted to home births assisted by traditional birth attendants; all the other trials were population-based and included both institutional and home-births.

Key messages

- ✓ The application of 7.1% chlorhexidine to the umbilical cord reduces risk of omphalitis, even in low mortality settings where there is no evidence of impact on overall newborn mortality risk.
- ✓ Although substantial reductions in mortality were seen in trials in South Asia[5], application of 7.1% chlorhexidine to the umbilical cord did not significantly reduce NMR in the study sites in Tanzania or Zambia. This means that study results have shown an impact on mortality risk in populations with high NMR (30-40 deaths/1,000 live births) and have not shown an impact on mortality risk in populations with low NMR (≤17 deaths/1,000 live births).
- ✓ In high-mortality settings, use of 7.1% chlorhexidine on the umbilical cord reduced deaths regardless of whether infants were born at home or in a facility.[6,7]
- ✓ Country programs should consider the programmatic context and level of risk in the population rather than place of birth or geographic location when deciding whether or not to prioritize chlorhexidine introduction.



* Neonatal mortality rate, from birth through 28 days, calculated from data available in study flow diagrams from the cited papers. These numbers are different than what is cited in the original articles because they are calculated variables.

Neonatal mortality rate

- A pooled analysis of the RCTs conducted in Bangladesh, Pakistan, and Nepal showed a 23% reduction in all-cause neonatal mortality in the chlorhexidine group compared with the control.
- In the three earlier studies in Asia, the overall NMR in the control arms was in the range of 30-40 deaths/1,000 live births. In contrast, in the two newly-published studies, mortality in the control arms was less than half as high (17

deaths/1,000 live births in the Tanzania study and 14 deaths/1,000 live births in the Zambia study), similar to what is generally seen in middle-income countries.

- Study results showed no evidence for mortality impact in the two study sites with comparatively low NMR (<18 deaths/1,000 live births).
- Trial results from populations with an intermediate range of NMR (18-34 deaths/1,000 live births) do not exist. Most likely, the mortality reduction benefit in these populations will be somewhat less than in the 3 original trials yet not as low as in the new studies.
- Published evidence in lower mortality settings, has generally shown a lower proportion of newborn deaths attributable to sepsis than in higher mortality settings. Chlorhexidine should still be effective in preventing sepsis due to unhygienic exposures to the cord regardless of NMR. In low mortality settings, these cases will be less frequent.

Place of birth

- Giving birth in a facility does not necessarily reduce the chance of infection. Infection prevention practices are substandard in many facilities. Furthermore, mothers and infants are frequently sent home within a few hours of birth to the same potentially harmful practices that are of concern for home birth settings.
- The proportion of facility births differed markedly between the two newly published studies and earlier trials. However, even in the earlier trials there were a significant number of facility births. Analysis of the Nepal and Bangladesh data (including ~3000 facility births) shows that the protective benefit of chlorhexidine appeared to be similar among infants born in the facility or at home.[5,6,7]

Table 1: Evidence from randomized controlled trials on chlorhexidine for umbilical cord care. All trials had neonatal mortality and omphalitis as primary outcomes. All used dry cord care as their comparison group. All trials used water-based liquid formulation of 7.1% chlorhexidine digluconate.

Publication	Mullany 2006 **Nepal**[8]	Arifeen 2012 **Bangladesh**[9]	Soofi 2012 **Pakistan**[10]	Sazawal 2016 **Tanzania**[11]	Semrau 2016 **Zambia**[12]
Total live births	15,123	29,790	9,741	36 ,911	37,856
Schedule of application	Days 1,2,3,4,6,8,10	Within 1st 24 hours, then daily for 7 days	Daily for 14 days	Daily until 3 days after cord drops	Daily until 3 days after cord drops
Intervention provider	Project staff	Project staff	Traditional birth attendant & mother/ caretaker	Mother or caretaker	Mother or caretaker
First application within 24 hours of birth	63%	87%	100%	94%	90%
Application of other substances to the cord	~ ½	few	~90%	N/A	~10%
% infants with birthweight <2500g	30%	33%	N/A	5%	7%
% health facility births	8%	7%	0%	54%	64%

Resources

For more information about chlorhexidine for umbilical cord care, please visit the chlorhexidine technical resource page on the Healthy Newborn Network site:

http://www.healthynewbornnetwork.org/issue/chlorhexidine-for-umbilical-cord-care/

The Chlorhexidine Working Group

The Chlorhexidine Working Group is an international collaboration of organizations committed to advancing the use of 7.1% chlorhexidine digluconate (delivering 4% chlorhexidine) for umbilical cord care through advocacy and technical assistance.

PATH is the Secretariat of the CWG, and members include individuals representing (alphabetically): ayzh, Bill & Melinda Gates Foundation, Boston University, Burnet Institute, Centre for Infectious Disease Research in Zambia, Clinton Health Access Initiative, Drugfield Pharmaceuticals Ltd. (Nigeria), Duke University, GSK (UK), Global Health Action, Jhpiego, John Snow, Inc., Johns Hopkins Bloomberg School of Public Health, Johnson & Johnson (USA), Lomus Pharmaceuticals Pvt. Ltd. (Nepal), Maternal and Child Survival Program (MCSP), Ministry of Health, DRC (Reproductive Health), Ministry of Health, Ethiopia (Maternal & Child Health), Ministry of Health, Kenya (Child & Adolescent Health), Ministry of Health, Liberia (FamilyHealth), Ministry of Health, Malawi (Reproductive Health), Ministry of Health, Mozambique (Child Health), PSI, Promoting the Quality of Medicines/United States Pharmacopeia, Save the Children/Saving Newborn Lives, SHOPS Plus/Abt Associates, Systems for Improved Access to Pharmaceuticals and Services/Management Sciences for Health, United Nations Children's Fund, United States Agency for International Development, Universal Corporation Ltd. (Kenya), University of Illinois at Chicago School of Nursing, University Research Co., LLC | Center for Human Services, World Health Organization.

References

1. Liu L, Oza S, Hogan D, et al. Global, regional, and national causes of child mortality in 2000-13, with projections to inform post-2015 priorities: an updated systematic analysis. *Lancet.* 2015 Jan 31;385(9966):430-40.
2. World Health Organization. WHO Recommendations on Postnatal Care of the Mother and Newborn. 2013. http://apps.who.int/iris/bitstream/10665/97603/1/9789241506649_eng.pdf
3. Herrick T, Harner-Jay C, Shaffer C, et al. Modeling the potential impact of emerging innovations on achievement of Sustainable Development Goals related to maternal, newborn, and child health. *BioMed Central*. 2017; 15:12.
4. Mullany LC, Darmstadt GL, Tielsch JM. Safety and impact of chlorhexidine antisepsis interventions for improving neonatal health in developing countries. *Pediatric Infectious Disease Journal.* 2006;25(8):665–675.
5. Imdad A, Mullany LC, Baqui AH, et al. The effect of umbilical cord cleansing with chlorhexidine on omphalitis and neonatal mortality in community settings in developing countries: a meta-analysis. *BMC Public Health*. 2013.
6. Hodgins S. Chlorhexidine and newborn omphalitis and mortality. *The Lancet Global Health*. 2017;5(3):270-271.
7. Mullany LC, Arifeen SE, Khatry SK, et al. Impact of Chlorhexidine Cord Cleansing on Mortality, Omphalitis, and Cord Separation Time Among Facility-Born Babies in Nepal and Bangladesh. *Pediatric Infectious Disease Journal*. 2017.
8. Mullany LC, Darmstadt GL, Khatry SK, et al. Topical applications of chlorhexidine to the umbilical cord for prevention of omphalitis and neonatal mortality in southern Nepal: A community-based, cluster-randomised trial. *Lancet.* 2006;367(9514):910–918.
9. Arifeen SE, Mullany LC, Shah R, et al. The effect of cord cleansing with chlorhexidine on neonatal mortality in rural Bangladesh: A community-based, cluster-randomised trial. *Lancet.* 2012;379(9820):1022–1028.
10. Soofi S, Cousens S, Imdad A, et al. Topical application of chlorhexidine to neonatal umbilical cords for prevention of omphalitis and neonatal mortality in a rural district of Pakistan: a community-based, cluster-randomised trial. *Lancet.* 2012;379(9820):1029–1036.
11. Sazawal, S, Dhingra U, Ali SM, et al. Efficacy of chlorhexidine application to umbilical cord on neonatal mortality in Pemba, Tanzania: a community-based randomized controlled trial. *Lancet.* 2016.
12. Semrau KEA, Herlihy J, Grogan C, et al. Effectiveness of 4% chlorhexidine umbilical cord care on neonatal mortality in Southern Province, Zambia (ZamCAT): a cluster-randomised controlled trial. *Lancet.* 2016.