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Review Paper

Neonatal mortality and topical application of chlorhexidine on umbilical cord stump: a meta-analysis of randomized control trials

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ABSTRACT

Objective: To examine the efficacy of topical chlorhexidine as an intervention on neonatal umbilical cord stumps and its association with neonatal mortality and omphalitis.
Study design: Meta-analysis of randomized controlled trials (RCTs).
Method: PubMed, EMBASE, CINAHL, IMSEAR, Google Scholar, Cochrane Central Register of Controlled Trials, Cochrane Pregnancy and Childbirth Group's Trials Register and Clinicaltrials.gov were screened until September 1, 2015 to identify RCTs that met the inclusion criteria. Pooled relative risks (RR) with 95% confidence intervals (CI) were calculated.
Results: Five RCTs, conducted in Italy, Bangladesh, Nepal, Pakistan and India with a total of 55,008 participants were identified. Analysis revealed a significant reduction in the incidence of neonatal mortality among the intervention group as compared to the control group (pooled RR = 0.8; 95% CI: 0.6–1.0; $P = 0.04$; random effects model, $I^2 = 58\%$; $\chi^2 = 9.5$; $P = 0.05$). Additionally, decreased incidence in omphalitis was seen in the intervention group as compared to the control group (pooled RR = 0.4; 95% CI: 0.3–0.7; $P < 0.001$; random effects model, $I^2 = 50\%$; $\chi^2 = 8.0$; $P = 0.09$).
Conclusions: Application of chlorhexidine to newborn umbilical cord stumps, significantly reduce the incidences of both neonatal mortality and omphalitis. However, high-quality trials from different regions and obstetric settings may help form more conclusive judgement on universal application of topical chlorhexidine.

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Introduction

With the proclamation of sustainable development goal (SDG) targets, the United Nations set out on a global crusade to end preventable deaths of newborns and children aged under 5 years, reduce neonatal mortality to at least 12 per 1000 live births, and reduce under-five mortality to at least 25 per 1000 live births by 2030.[1] In 2009, an estimated 3.3 million neonates died within the first month of life[2] with 70% of these deaths occurring in the first week. This figure only represented a 28% reduction from the 1990 estimate of 4.6 million neonatal deaths.[2] Although rates of both child (<5 years) and neonatal (<28 days) deaths declined from 1990 to 2009, the relative proportion of child deaths that were in the neonatal period increased in all regions of the world over that span.[2] Infections account for more than 30% of neonatal deaths[3] and in developing countries such as India, Nigeria, the Democratic Republic of the Congo, and Pakistan where a large proportion of all neonatal deaths occur, mortality rates from infections have been reported to be as high as 50%.

At birth, the standard practice is to clamp and cut the umbilical cord, leaving behind a remnant stump. Subsequent cord separation normally occurs 1 week postpartum[4] and is mediated through a combination of umbilical vessel spasm and thrombosis, followed by phagocyte-mediated tissue breakdown, and resolved upon epithelialization of the detachment site. During this process of repair, the stump is colonized by bacteria derived from the maternal genital tract or environment and these bacteria can precipitate umbilical or periumbilical infections (omphalitis).[5] Proper umbilical cord care is important, and many risk factors including but not limited to home delivery, unskilled birth attendants, and lack of hygiene and antiseptics at birth contribute to the incidence omphalitis, which is greater in resource-poor regions lacking aseptic care. Untreated omphalitis can rapidly progress from cellulitis to necrotizing fasciitis to life-threatening sepsis as the infection penetrates deeper beyond the epidermal barrier. Omphalitis represents a preventable sequela of improper umbilical care, and thus to reduce the under-five mortality rate as envisioned by SDG it is essential to find effective, affordable, and practical measures that best prevent neonatal omphalitis. Among the available interventions, antiseptics such as alcohol, povidone iodine, methylated spirit, or chlorhexidine (CHX) have been used with mixed results.[6]

Since 1998, the WHO has recommended aseptic dry cord care as the standard of practice for umbilical care[7] and only suggests topical antiseptics where risk of infection is high. Presently, there have been two systemic reviews evaluating the benefits of topical umbilical cord care.[7,8] A Cochrane review of 21 trials conducted by Zupan et al.[8] found inconclusive results regarding the benefits of antiseptics and/or antibiotics applied to neonatal umbilical sites. That review concluded that antiseptics prolonged the time to cord separation and reduced maternal concern, but did not demonstrate any outcome benefits compared to dry cord care or placebo.[8] Twenty of the 21 included trials were conducted in hospitals in high-income countries and not in community settings where clean dry cord care is often difficult to achieve.[7,9] Imdad et al.[7] conducted a meta-analysis of three large community-based randomized control trials to study the effectiveness of topical 4% CHX in preventing omphalitis and neonatal mortality. Unlike that of Zupan et al. their meta-analysis only included studies conducted in resource-poor community settings and evaluated only CHX as the intervention, not antiseptics as a whole. Imdad et al. concluded that CHX application in community settings significantly reduced the incidence of umbilical cord infections and all-cause mortality among home births compared to non-CHX interventions. Sinha et al.[10] evaluated both community and hospital settings separately and concluded that in the community CHX cord cleansing reduces neonatal mortality and omphalitis and that in the hospital there was no benefit to neonatal mortality and only a probable risk reduction of omphalitis. In 2013, the World Health Organization (WHO) added 7.1% chlorhexidine digluconate for umbilical cord care to its Model List of Essential Medicines for Children,[11] a decision that reflects both the perceived superiority of CHX as an umbilical care agent and the urgency to protect newborns from preventable, fatal infections. Although there have been several randomized control trials (RCTs) of topical CHX applied to neonatal umbilical cord stumps, there have not been any meta-analyses examining CHX use as the primary intervention in both hospital and community settings together. The objective of this study was to conduct a meta-analysis to evaluate the effect of topical CHX to the umbilical cord for prevention of all-cause neonatal mortality (NNM) and omphalitis in both community and hospital settings.

Objective

The objective of this study was to conduct a meta-analysis to evaluate the effect of topical CHX to the umbilical cord for prevention of all-cause NNM and omphalitis in both community and hospital settings. Additionally, this meta-analysis stratified the effects of CHX on NNM and omphalitis based on study location, either hospital setting or community setting.

Methods

Study design

Meta-analysis on randomized controlled trials (RCTs), was planned and conducted in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines (PRISMA).[12]

Eligibility criteria

To be eligible for review, studies were required to meet the following conditions:

Type of studies: Randomized control trials (RCTs) including cluster trials and factorial trials were included.

Type of participants: Late preterm and term neonates born to women aged ≥15 years.

Type of intervention: Multiple cleansing of neonate's umbilical cord stump with CHX for <10 days postpartum.

Type of comparison: Intervention (topical CHX) compared to the controls as defined by the standard of care in the region of study. Controls included no care, dry cord care, cleansing with