Effects of neonatal nutrition interventions on neonatal mortality and child health and development outcomes: a systematic review

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Title of the review

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Background

Global child mortality is on the decline with 52% fewer under-five deaths in 2015 compared to 1990 (GBD 2015 Child Mortality Collaborators, 2016). However, the decrease in neonatal (0-28 days) mortality was lower (42%) during this period (GBD 2015 Child Mortality Collaborators, 2016). The main causes of neonatal morality include complications of preterm birth, birth asphyxia, congenital anomalies and infections (GBD 2015 Child Mortality Collaborators, 2016; GBD 2016 Causes of Death Collaborators, 2017).

Poor nutritional management at birth increases the risk of neonatal morbidity and mortality and adversely affects neonatal growth (Bhutta, 2013; Christian, 2015; Imdad, 2013). Early initiation of breastfeeding and exclusive breastfeeding during the first 6 months have been shown to reduce the risk of neonatal morbidity and mortality due to infections (Bhutta, 2013). Kangaroo Mother Care, or newborn skin-to-mother contact, has been shown to reduce mortality in low birth weight and preterm babies (Bhutta, 2013; Imdad, 2013). Other potential nutrition interventions include vitamin A supplementation in full-term and low birth weight babies, vitamin K supplementation, delayed cord clamping, and neonatal probiotic/prebiotic supplementation (Bhutta, 2013; Christian, 2015; Deshpande, 2017; Nguyen, 2017; Pammi, 2017). Previous reviews has addressed these interventions; however, some of the review were published a long time ago and recent data has not been incorporated, some have conflicting results and some of the interventions are new and an up-to-date synthesis of evidence is needed. For example, Cochrane review on vitamin K supplementation was published 18 years ago and no updates has been published since then (Puckett 2000). Similarly, two reviews on neonatal vitamin A supplementation reached different conclusion (Haider 2017 and Gogia 2009) and the probiotics/prebiotics for prevention of necrotizing enterocolitis is a relatively new intervention and the last Cochrane review was published 4 years ago (AlFaleh 2014). Furthermore, most of the previous reviews have not assessed programmatic evaluation of neonatal nutrition intervention and long term outcome after supplementation during the neonatal period have not been assessed in these reviews. This review will evaluate up-to-date evidence related to neonatal nutrition interventions for the prevention of morbidity and mortality and improved child health and development.

Objectives

1. What is the effectiveness of delayed neonatal cord clamping on neonatal mortality and child health and development?
2. What is the effectiveness of neonatal vitamin A supplementation on neonatal mortality and child health and development?
3. What is the effectiveness of Kangaroo Mother Care on neonatal mortality and child health and development?
4. What is the effectiveness of early initiation of breastfeeding on neonatal mortality and child health and development?
5. What is the effectiveness of neonatal probiotic/prebiotic supplementation on neonatal mortality and child health and development?
6. What is the effectiveness of neonatal vitamin K supplementation on neonatal mortality and child health and development?

Existing reviews

Objective 1: Delayed neonatal cord clamping

McDonald SJ, Middleton P, Dowswell T, Morris PS. Effect of timing of umbilical cord clamping of term infants on maternal and neonatal outcomes. Evid Based Child Health. 2014 Jun;9(2):303-97.
doi: 10.1002/ebch.1971. PubMed PMID: 25404605.

Rabe H, Díaz-Rossello JL, Duley L, Dowswell T. Effect of timing of umbilical cord clamping and other strategies to influence placental transfusion at preterm birth on maternal and infant outcomes. Cochrane Database Syst Rev 2012, Issue 8. Art. No:CD003248.
doi:10.1002/14651858.CD003248.pub3.

Chapman J, Marfurt S, Reid J. Effectiveness of Delayed Cord Clamping in Reducing Postdelivery Complications in Preterm Infants: A Systematic Review. J Perinat Neonatal Nurs 2016; 30(4):372-78.
doi: 10.1097/JPN.0000000000000215.

Objective 2: Neonatal vitamin A supplementation

Darlow BA, Graham PJ, Rojas-Reyes MX. Vitamin A supplementation to prevent mortality and short- and long-term morbidity in very low birth weight infants. Cochrane Database Syst Rev 2016, Issue 8. Art. No:CD000501. doi:10.1002/14651858.CD000501.pub4.

Haider BA, Sharma R, Bhutta ZA. Neonatal vitamin A supplementation for the prevention of mortality and morbidity in term neonates in low and middle income countries. Cochrane Database Syst Rev 2017, Issue 2. Art. No:CD006980.
doi:10.1002/14651858.CD006980.pub3.

Gogia Siddhartha, Sachdev Harshpal Singh. Neonatal vitamin A supplementation for prevention of mortality and morbidity in infancy: systematic review of randomised controlled trials BMJ 2009; 338 :b919

Objective 3: Kangaroo Mother Care

Moore ER, Bergman N, Anderson GC, Medley N. Early skin-to-skin contact for mothers and their healthy newborn infants. Cochrane Database Syst Rev 2016, Issue 11. Art. No: CD003519. doi:10.1002/14651858.CD003519.pub4.

Conde-Agudelo A, Díaz-Rossello JL. Kangaroo mother care to reduce morbidity and mortality in LBW infants. Cochrane Database Syst Rev 2016, Issue 8. Art. No:CD002771. doi:10.1002/14651858.CD002771.pub4.

Objective 4: Early initiation of breastfeeding

Balogun OO, O'Sullivan EJ, McFadden A, Ota E, Gavine A, Garner CD, Renfrew MJ, MacGillivray S. Interventions for promoting the initiation of breastfeeding. Cochrane Database Syst Rev 2016, Issue 11. Art. No:CD001688. doi:10.1002/14651858.CD001688.pub3.

Debes AK, Kohli A, Walker N, Edmond K, Mullany LC. Time to initiation of breastfeeding and neonatal mortality and morbidity: a systematic review. BMC Public Health 2013;13(3):S19. doi:10.1186/1471-2458-13-S3-S19.

Objective 5: Neonatal probiotics/prebiotics

Pammi M, Suresh G. Enteral lactoferrin supplementation for prevention of sepsis and necrotizing enterocolitis in preterm infants. Cochrane Database Syst Rev. 2017 Jun 28;6:CD007137.
doi: 10.1002/14651858.CD007137.pub5. Review. PubMed PMID: 28658720.

Deshpande G, Jape G, Rao S, Patole S. Benefits of probiotics in preterm neonates in low-income and medium-income countries: a systematic review of randomised controlled trials. BMJ Open. 2017 Dec 7;7(12):e017638. doi: 10.1136/bmjopen-2017-017638. PubMed PMID: 29222137.

AlFaleh K, Anabrees J. Probiotics for prevention of necrotizing enterocolitis in preterm infants. Cochrane Database of Systematic Reviews 2014, Issue 4. Art. No.: CD005496. DOI: 10.1002/14651858.CD005496.pub4

Objective 6: Neonatal Vitamin K supplementation

Puckett RM, Offringa M. Prophylactic vitamin K for vitamin K deficiency bleeding in neonates. Cochrane Database Syst Rev. 2000;(4):CD002776. Review. PubMed PMID: 11034761.
doi: 10.1002/14651858.CD002776.

Sankar MJ, Chandrasekaran A, Kumar P, Thukral A, Agarwal R, Paul VK. Vitamin K prophylaxis for prevention of vitamin K deficiency bleeding: a systematic review. J Perinatol. 2016 May;36 Suppl 1:S29-35. doi: 10.1038/jp.2016.30.

Ardell S, Offringa M, Soll R. Prophylactic vitamin K for the prevention of vitamin K deficiency bleeding in preterm neonates. Cochrane Database of Systematic Reviews 2010, Issue 1. Art. No.: CD008342. doi: 10.1002/14651858.CD008342. (Protocol).

Intervention

The following interventions targeting neonates will be included:

- Delayed neonatal cord clamping
- Neonatal vitamin A supplementation
- Kangaroo Mother Care
- Early initiation of breastfeeding
- Neonatal probiotics/prebiotics
- Neonatal prophylactic vitamin K supplementation

Population

The target population is neonates (aged 0-28 days), regardless of health status and gestational age, living in low- and middle-income countries as defined by the World Bank.

Outcomes

Primary outcomes:

- Neonatal all-cause mortality
- Infant all-cause mortality

Secondary outcomes:

- Cause-specific mortality
- Cause-specific morbidity
- Admission to intensive care facility
- Biochemical indicators of micronutrient status (such as retinol for vitamin A)
- Intracranial hemorrhage
- Adverse events
- Growth (Weight for age, height for age and weight for height) during infancy
- Neurodevelopmental outcomes measured by scales such as Bayley Scales of Infant Development and McCarthy Scales of Children's Ability (MSCA)

Study designs

We will include primary studies, including large-scale programme evaluations that assess the efficacy and/or effectiveness of interventions using experimental and quasi-experimental study designs that allow for causal inference:

1. Studies where participants were randomly assigned, individually or in clusters, to intervention and comparison groups.

2. Studies where non-random assignment to intervention and comparison groups is based on other known allocation rules, including a threshold on a continuous variable (regression

discontinuity designs) or exogenous geographical variation in the treatment allocation (natural experiments).

3. Controlled before-after studies in which allocation to intervention and control groups was not made by study investigators, and outcomes were measured in both intervention and control groups at baseline, and appropriate methods were used to control for selection bias and confounding, such as statistical matching (e.g., propensity score matching, or covariate matching) or regression adjustment (e.g., difference-in-differences, instrumental variables).

4. Interrupted time series studies in which outcomes were measured in the intervention group at least three time points before the intervention was implemented and at least three time points after.

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Deshpande, G., Jape, G., Rao, S., & Patole, S. (2017). Benefits of probiotics in preterm neonates in low-income and medium-income countries: a systematic review of randomised controlled trials. *BMJ Open*, 7(12):e017638. doi:10.1136/bmjopen-2017-017638.

GBD 2016 Causes of Death Collaborators. (2017). Global, regional, and national age-sex specific mortality for 264 causes of death, 1980-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet*, 390(10100):1151-1210. doi: 10.1016/S0140-6736(17)32152-9.

GBD 2015 Child Mortality Collaborators. (2016). Global, regional, national, and selected subnational levels of stillbirths, neonatal, infant, and under-5 mortality, 1980–2015: A systematic analysis for the Global Burden of Disease Study 2015. *Lancet*, 388(10053):1725–1774. http://dx.doi.org/10.1016/S0140-6736(16)31575-6.

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Pammi, M., & Suresh, G. (2017). Enteral lactoferrin supplementation for prevention of sepsis and necrotizing enterocolitis in preterm infants. *Cochrane Database of Systematic Reviews*, 6: CD007137. doi:10.1002/14651858.CD007137.pub5.

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Lead review author: The lead author is the person who develops and co-ordinates the review team, discusses and assigns roles for individual members of the review team, liaises with the editorial base and takes responsibility for the on-going updates of the review.

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Roles and responsibilities

Aamer Imdad and Rehana Salam have methodological, statistical, and information retrieval expertise. Zulfiqar Bhutta has content expertise. All additional team members (to be determined) will receive training in systematic review methods.

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Potential conflicts of interest

The authors are not aware of any conflicts of interest arising from financial or researcher interests.

Preliminary timeframe

- Date you plan to submit a draft protocol: 30 January 2018
- Date you plan to submit a draft review: 30 June 2018