INPLASY PROTOCOL

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None declared.

Efficacy comparison of 21 interventions to prevent retinopathy of prematurity: a Bayesian network meta-analysis

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Review question / Objective: **The objective of this study was to evaluate the comparative efficacy of current interventions for the prevention of retinopathy of prematurity (ROP) in premature infants.**
Condition being studied: **There have been lots of studies on the potential interventions to prevent retinopathy of prematurity (ROP) in premature infants. However, little attention has been paid to integrating various categories of preventive strategies for ranking the efficacies.**
Eligibility criteria: **In accordance with the Population, Intervention, Comparison, Outcomes, and Study (PICOS) selection criteria, randomized controlled trials (RCTs) were included if they enrolled infants of <37 weeks GA, compared any of the interventions of interest, and demonstrated the incidence of any-stage ROP.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 01 November 2022 and was last updated on 01 November 2022 (registration number INPLASY2022110002).

INTRODUCTION

Review question / Objective: **The objective of this study was to evaluate the comparative efficacy of current interventions for the prevention of retinopathy of prematurity (ROP) in premature infants.**

Condition being studied: **There have been lots of studies on the potential interventions to prevent retinopathy of prematurity (ROP) in premature infants.**

However, little attention has been paid to integrating various categories of preventive strategies for ranking the efficacies.

METHODS

Search strategy: Full search terms used for PubMed were presented as follows: ("Retinopathy of Prematurity"[Title/Abstract] OR "Retinopathy of Prematurity"[Title/Abstract] OR "prematurity retinopath*"[Title/Abstract] OR "retrolental fibroplasia*"[Title/Abstract] OR "retrolental fibrosis"[Title/Abstract] OR "retrolental fibroplasias"[Title/Abstract] AND ("infant"[Title/Abstract] OR "infants"[Title/Abstract] OR "newborn*"[Title/Abstract] OR "baby"[Title/Abstract] OR "babies"[Title/Abstract] OR "neonat*"[Title/Abstract] OR "NICU"[Title/Abstract] OR "preterm"[Title/Abstract] OR "pre-term"[Title/Abstract] OR "VLBW"[Title/Abstract] OR "very low birth weight"[Title/Abstract] OR "prematur*"[Title/Abstract] OR "pre matur*"[Title/Abstract]) AND ("randomized controlled trial"[Publication Type] OR "controlled clinical trial"[Publication Type] OR "randomized"[Title/Abstract] OR "placebo"[Title/Abstract] OR "clinical trials as topic"[MeSH Terms:noexp] OR "drug therapy"[MeSH Subheading] OR "randomly"[Title/Abstract] OR "trial"[Title/Abstract] OR "groups"[Title/Abstract]) NOT ("animals"[MeSH Terms] NOT "humans"[MeSH Terms])) AND ("diet*"[Title/Abstract] OR "parenteral"[Title/Abstract] OR "enteral"[Title/Abstract] OR "gastric feed*"[Title/Abstract] OR "force feed*"[Title/Abstract] OR "artificial feed*"[Title/Abstract] OR "amino acid*"[Title/Abstract] OR "protein*"[Title/Abstract] OR "lipid*"[Title/Abstract] OR "breast milk"[Title/Abstract] OR "human milk"[Title/Abstract] OR "maternal milk"[Title/Abstract] OR "mother milk"[Title/Abstract] OR "mothers milk"[Title/Abstract] OR "woman milk"[Title/Abstract] OR "breast feeding"[Title/Abstract] OR "breastfeeding"[Title/Abstract] OR "infect*"[Title/Abstract] OR "antiinfective*"[Title/Abstract] OR "anti infective*"[Title/Abstract] OR "sepsis"[Title/Abstract] OR "pyohemia*"[Title/Abstract] OR "septicemia*"[Title/Abstract] OR "pyemia*"[Title/Abstract] OR "blood poisoning*"[Title/Abstract] OR "bacter*"[Title/Abstract] OR "antibacter*"[Title/Abstract] OR "bactericid*"[Title/Abstract] OR "fungal"[Title/Abstract] OR "fungemia*"[Title/Abstract] OR "fungus"[Title/Abstract] OR "antifungal"[Title/Abstract] OR "fungicid*"[Title/Abstract] OR "anti-fungal"[Title/Abstract] OR "mycosis"[Title/Abstract] OR "mycoses"[Title/Abstract] OR "mycotic"[Title/Abstract] OR "clabsi"[Title/Abstract] OR "antimicrobial*"[Title/Abstract] OR "anti microbial*"[Title/Abstract] OR "microbicid*"[Title/Abstract] OR "antiseptic*"[Title/Abstract] OR "anti septic*"[Title/Abstract] OR "transfusion*"[Title/Abstract] OR "hemotherap*"[Title/Abstract] OR "Nonsteroidal anti-inflammatory drugs"[Title/Abstract] OR "NSAIDs"[Title/Abstract] OR "cyclooxygenase inhibitors"[Title/Abstract] OR "cyclooxygenase inhibitor"[Title/Abstract] OR "indomethacin"[Title/Abstract] OR "ibuprofen"[Title/Abstract] "adrenal cortex hormones"[Title/Abstract] OR "adrenal cortex hormone"[Title/Abstract] OR "dexamethasone"[Title/Abstract] OR "steroids"[Title/Abstract] OR "caffeine"[Title/Abstract] OR "corticosteroids"[Title/Abstract] OR "antioxidants"[Title/Abstract] OR "D-penicillamine"[Title/Abstract] OR "superoxide dismutase"[Title/Abstract] OR "SOD"[Title/Abstract]).

Participant or population: Preterm infants at <37 weeks of gestational age.

Intervention: Because ROP is a typically biphasic disease, the timing of initiation of the interventions was also taken into consideration. Finally, these interventions fell into seven main categories and 21 types: (1) postnatal nutrition: human milk (HM), fish-oil-based lipid emulsion (FO), and nutritional supplementation with vitamin A (VA), vitamin E (VE), inositol (IN),

or lutein (LU); (2) blood transfusion: the use of hemoglobin transfusion guidelines (TG), early initiation of erythropoietin (early EPO, EE, initiated at 8 days of age), and all EPO (AE, early and late EPO); (3) infection reduction: fluconazole prophylaxis (FP), probiotics (PS), or lactoferrin supplementation (LS); (4) nonsteroidal anti-inflammatory drugs: indomethacin (IND), ibuprofen (IB); (5) corticosteroids: early initiation of dexamethasone (ED, initiated within the first week of life), late initiation of dexamethasone (LD, initiated at >7 days of age); (6) caffeine: early initiation of caffeine (EC, initiated at <3 days of age), late initiation of caffeine (LC, initiated at ≥3 days of age); and (7) other interventions: D-penicillamine (DP), superoxide dismutase (SOD).

Comparator: We will include studies where any of 21 interventions of interest is the only variation between the intervention group and the control group.

Study designs to be included: Randomized controlled trials (RCTs).

Eligibility criteria: In accordance with the Population, Intervention, Comparison, Outcomes, and Study (PICOS) selection criteria, randomized controlled trials (RCTs) were included if they enrolled infants of <37 weeks GA, compared any of the interventions of interest, and demonstrated the incidence of any-stage ROP.

Information sources: PubMed, Web of Science, Scopus, Embase, and the Cochrane Library were searched for pertinent literature, from their inception to May 5, 2022.

Main outcome(s): The incidence of any-stage ROP. The severity of ROP can be classified into five stages, and "any-stage ROP" refers to stages 1–5.

Quality assessment / Risk of bias analysis: We will appraise the risk of bias (ROB) in all of the included studies with the Cochrane Risk of Bias Tool (RoB 2.0). Two investigators will assess each trial independently according to the relevant quality criteria, and any disagreement will be resolved by discussion and consensus. ROB will be evaluated in Review Manager 5.4.1.

Strategy of data synthesis: We will conduct a Bayesian random-effects NMA to calculate the odds ratio (OR) and 95% credible interval (CrI), with the noninformative priors integrating direct and indirect evidence, to compare 21 preventive interventions for ROP. The extent of heterogeneity between different studies will be quantified using the I2 statistical test, and values > 50% will indicate a significant degree of heterogeneity. To adequately ensure the similarity of various strategy comparisons which could provide valid indirect inferences, we will compare the clinical and methodological characteristics such as participants and experimental designs across all the included studies to apprise the transitivity assumption. We will evaluate global inconsistency in the overall network by fitting the design-by-treatment interaction approach. Local inconsistency between direct and indirect evidence will be assessed by the node-splitting method. Evidence of publication bias will be evaluated using a funnel plot using Stata 12.0. We will use a radar plot to provide a visual representation of the relationships between each intervention and the study characteristics.

The posterior densities of the unknown parameters will be estimated using Markov-chain Monte Carlo simulations. Three parallel relevant Markov chains will be set up to run with arbitrarily chosen initial values. Each chain will use 500,000 iterations. The first 20,000 iterations will be discarded. The surface under the cumulative ranking curve (SUCRA) value for each intervention will be taken as the estimated probability used to cumulatively rank the preventive interventions. SUCRA takes a value between 0 and 1, where 0 certainly denotes the worst intervention and 1 certainly indicates the best intervention. The NMA will be performed using WinBUGS 1.4.3.

Subgroup analysis: When possible if enough data are available, we will measure males and females separately.

Sensitivity analysis: If enough studies are available, sensitivity analysis will be done.

Language restriction: English.

Country(ies) involved: China.

Keywords: Network meta-analysis; retinopathy of prematurity; prevention; neonate, preterm infant.

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