INPLASY PROTOCOL

Probiotics to Prevent Necrotizing Enterocolitis in Very Low Birth Weight Infants: A Network Meta-Analysis

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Review question / Objective: The search strategy was constructed around the PICOS tool: (P) Population: very low birth weight infants; (I) Intervention: probiotics; (C) Comparator: control group with only placebo or another probiotic usage; (O) Outcomes: necrotizing enterocolitis. (S) Study type: RCTs.

Condition being studied: Necrotizing enterocolitis(NEC), a disease that has plagued pediatricians for a long time, is still relatively common in very low birth weight infants. The disease is associated with neurodevelopmental delays, growth retardation, intestinal strictures and adhesions, and short bowel syndrome with or without intestinal failure. Regrettably, the prevalence and mortality of NEC in very low birth weight infants had barely changed over the decades. Most studies in the past decade had claimed that probiotics could significantly reduce the risk of NEC, but which combination of probiotics, such as single or multiple, was more effective, was still inconclusive. Therefore, this study aimed to compare the effects of multiple probiotic use regimens on NEC through a network meta-analysis, direct or indirect comparisons, and to estimate the rank order of each intervention.

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 INPLASY2022110001).

INTRODUCTION

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METHODS

Participant or population: Very low birth weight infants.

Intervention: Probiotics.

Comparator: control group with only placebo or another probiotic usage.

Study designs to be included: Randomized controlled trials.

Eligibility criteria: Inclusion criteria:(1) Study design as RCT; (2) Neonates with birth weight <1500 g; (3) Interventions included probiotics; (4) Reported outcomes included NEC stage ≥ II (Bell staging criteria); (5) The incidence of outcomes given by the study.

Information sources: PubMed, EMBASE, Cochrane Library, and Web of Science.

Main outcome(s): Incidence of necrotizing enterocolitis in the study population.

Quality assessment / Risk of bias analysis: Two researchers independently assessed the risk of bias (ROB) according to the Cochrane Handbook version 5.1.0 tool for assessing ROB in RCTs. Seven items were considered:(1) random sequence design, (2) concealment of allocation, (3) blinding of participants and (4) personnel, (5) incomplete outcome data, (6) selective reporting and (7) other sources of bias. Based on the number of potentially high ROB structures, studies were classified into three levels: high risk (five or more), medium risk (three or four), and low risk (two or less).

Strategy of data synthesis: In studies using probiotics as an intervention, outcome variables were dichotomized and expressed as risk ratios (RR) and 95% confidence intervals (CI).Due to potential differences between studies, it was decided to use a random-effects model rather than a fixed-effects model to analyze the data.

Data were compiled and analyzed using Markov chain Monte Carlo simulation chains of Stata software (version 15.1) based on a Bayesian framework according to the PRISMA NMA instruction manual. To quantify and demonstrate the agreement between indirect and direct comparisons, we used the nodal method calculated according to the instructions in Stata. The consistency test was passed if the P value was >0.05.

We presented and described network diagrams for different probiotic usage using Stata software. In the presented network diagrams, each node represents a different probiotic usage, and the lines connecting the nodes represent a direct comparison between interventions. The size of each node and the width of the connecting lines are proportional to the number of trials.

Subgroup analysis: No subgroup analysis was performed in this study.

Sensitivity analysis: No sensitivity analysis was performed in this study.

Country(ies) involved: China.

Keywords: necrotizing enterocolitis; very low birth weight infants; probiotics; network meta-analysis.

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