INPLASY PROTOCOL

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Bevacizumab for retinopathy of prematurity in Neurodevelopmental Outcomes: A Bayesian Meta-analysis

Shen, L[1]; Yang, Lu, Y[2].

Review question / Objective: **What are the effect of Bevacizumab on nuerodevelopemental outcomes of patients with retinopathy of prematurity?**
Condition being studied: **Retinopathy of prematurity is the leading cause of blindness in children.Recently, intravitreal injection of anti-VEGF has played a more important role in the treatment of ROP. Although the Bevacizumab Eliminates the Angiogenic Threat of Retinopathy of Prematurity study (BEAT-ROP) showed that VEGF inhibitors had a significant benefit than laser photocoagulation in zone I ROP, the systemic safety of VEGF inhibitors was still uncertain,especially in the neurodevelopmental outcomes.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 April 2020 and was last updated on 10 April 2020 (registration number INPLASY202040053).

INTRODUCTION

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METHODS

Participant or population: Patients with retinopathy of prematurity.

Intervention: Intravitreal injection of bevacizumab (IVB).

Comparator: Laser therapy or cryotherapy monotherapy or without treatment.

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

Eligibility criteria: Two independent author identified potential studies if they met the following criteria:(1) randomized controlled trials (RCTs) or observational studies. (2) preterm infants with ROP. (3) outcomes including the score of the composite scores of Bayley III, both in congnitive, language and motor. (4) patients treated by IVB as monotherapy or adjunctive treatment with laser therapy in the study group; patients treated by laser therapy or cryotherapy monotherapy or patients without treatment were selected in the control group. Exclusion criteria were following: (1) double reported; (2) no specific data of outcomes; (3) significant defects in study design.

Information sources: A comprehensive literature search was conducted in PubMed, EMBASE and Cochrane Library up to December 2019 in all languages. We used "retinopathy of prematurity" and "Bevacizumab" as subject terms with their free terms to search. Relevant references were retrieved if they met the objective of this meta-analysis.

Main outcome(s): Composite scores of Bayley III outcomes.

Additional outcome(s): neurodevelopmental impairment which is defined as the composite scores of Bayley III < 85 between two groups.

Quality assessment / Risk of bias analysis: We evaluated the methodological quality of eligible studies using the Newcastle-Ottowa Scale for observational studies and Jaded Scale for RCTs.

Strategy of data synthesis: The statistical analysis was performed using Stata 14.0 (Stata Corp LP, College station, TX). Heterogeneity between the results of studies was determined by $\chi 2$ test and I-squared statistics. According to the I-squared value, the random effects model (≥50%) or fixed effects model (<50%) was used for meta-analysis. The Markov chain Monte Carlo (MCMC) method was used to simulate the posterior distribution of parameters for the bayesian meta-analysis of neurodevelopmental outcomes. Subgroup analysis was based on the treatment in the experimental group and control group, GA and BW of the patients and quality control. To explore the stability and reliability of our results, we evaluated the influence of each individual study on the pooled effect size by a sensitivity analysis. Potential publication bias would be assessed with the Egger's regression asymmetry test if the number of including studies are more than 10.

Subgroup analysis: We will conduct a subgroup analysis for different reasons, such as type of studies(RCTs and observational studies) , treatment of two groups, quality control, GA (gestational age)and BW(birth weight) and so on.

Sensibility analysis: We consecutively removed each study from the statistic to perform sensitivity analysis.

Country(ies) involved: China.

Keywords: Bevacizumab; ROP; BSID III; Neurodevelopment; meta-analysis.