INPLASY PROTOCOL

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Review Stage at time of this submission: Preliminary searches.

Conflicts of interest:
None declared.

Efficacy and safety of C-Type Natriuretic Peptide Analogue in the treatment of achondroplasia : A Systematic Review and Meta-Analysis

Zhu, ZW[1]; You, L[2]; Qiao, J[3].

Review question / Objective: P:achondroplasia;; I:C-Type Natriuretic Peptide Analogue; C:placebo group, or any other approved medication for managing achondroplasiaor no control group; O:annualized growth velocity; S:randomized controlled trial.

Condition being studied: Achondroplasia is a rare disorder of asymmetrical short stature, which is caused by a mutation in the fibroblast growth factor receptor 3 gene. It is an autosomal dominant disorder characterized by shortening of the proximal extremities of the long bones, macrocephaly, and distinctive facial features (forehead protrusion, midface dysplasia with posterior concave and nose bridge collapse).C-type natriuretic peptide (CNP) analogues are an emerging therapeutic approach. CNP antagonizes FGFR3-induced mitogen-activated protein kinase signaling pathway activation in longplate chondrocytes by binding to natrinatritic peptide receptor B, thereby counteracting the effect of FGFR3 gene variation.CNP antagonizes may increase the annualized growth velocity in children with achondroplasia before the fusion of the epiphyses.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 May 2023 and was last updated on 12 May 2023 (registration number INPLASY202350049).

INTRODUCTION

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METHODS

Participant or population: Achondroplasia.

Intervention: C-Type Natriuretic Peptide Analogue.

Comparator: Placebo group,or any other approved medication for managing achondroplasia.

Study designs to be included: Randomized controlled trial.

Eligibility criteria: Inclusion criteria：Studies that meet all of the following conditions: P:achondroplasia; I:C-Type Natriuretic Peptide Analogue;C:placebo group, or no control group;O:Efficacy and safety;S:Randomized controlled trial. Exclusion criteria：1)Abstracts or full texts are not available; 2)Studies where data cannot be accurately extracted; 3)For repeated studies, the data with the most comprehensive report and the longest follow-up period were selected; 4)Studies with inconsistent outcome indicators.

Information sources: We will search PubMed, EMBASE,Web of Science and the Cochrane Library without placing any limitations on language or publication year.

Main outcome(s): Impact of C-Type Natriuretic Peptide Analogue on annualized growth velocity.

Additional outcome(s): Height outcomes, skeletal outcomes and any adverse effects.

Quality assessment / Risk of bias analysis: Two authors will independently assess the risk of bias using the risk of bias assessment tool in Review Manager (Revman) Version 5.4 software. Any discrepancies will be resolved through discussion.

Strategy of data synthesis: Review Manager 5.4 software was used to analyze the outcome indicators. The risk ratio (RR) of dichotomous variables was used as analysis statistic, and the meandifference (MD) of measurement data was used as effect analysis statistic.All statistics were represented by 95% confidence interval.The heterogeneity of each group will be tested. When $I^2 \le 50\%$ and $P>0.1$, the fixed-effect model was used. When $I^2 >50\%$ and $P<0.1$,the heterogeneity of the study was high. Random effects model was used for analysis, and subgroup or sensitivity analysis was performed.The results are presented as forest maps. Publication bias was tested by funnel plot.

Subgroup analysis: Subgroup analysis was not planned for this meta-analysis except if there is a heterogeneity. The heterogeneity of each group will be tested. When $I^2 \le 50\%$ and $P>0.1$, the fixed-effect model was used. When $I^2 >50\%$ and $P<0.1$,the heterogeneity of the study was high. Random effects model was used for analysis, and subgroup or sensitivity analysis was performed.

Sensitivity analysis: We will use RevMan 5.4 software for sensitivity analysis. After deleting one of the articles, the sensitivity of the article was reflected by the change of the effect size.

Country(ies) involved: Medical School of Tongji University, China.

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