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Network Meta-Analysis of Two Different Formulations of Recombinant Human Growth Hormone for the Treatment of Short Stature in Children

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ADMINISTRATIVE INFORMATION

Support - The funding source for this study is self-funded by the research team.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202530020

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 5 March 2025 and was last updated on 5 March 2025.

INTRODUCTION

Review question / Objective Network Meta-Analysis of Two Different Formulations of Recombinant Human Growth Hormone for the Treatment of Short Stature in Children P: Short Stature; I: recombinant human growth hormone (rhGH) injection solution; C: rhGH powder for injection; O: bone age, height, insulin-like growth factor 1 (IGF-1) levels, growth velocity, IGFBP-3 levels, and predicted adult heightin; S: Randomized Controlled Trial.

Condition being studied Short stature (SS) is a common pediatric endocrinological disorder characterized by a child's height being significantly lower than the average for their age, gender, and ethnicity. The etiology of short stature is multifactorial, encompassing genetic factors, nutritional deficiencies, endocrine disorders, as well as socio-psychological issues. Epidemiological surveys conducted both domestically and internationally indicate that short stature in children is a widespread concern. Data from the World Health Organization (WHO) reveals that in 2020, 151 million children under the age of five worldwide were affected by short stature, accounting for 21% of all children globally. Asia and Africa are the primary regions with the highest prevalence of childhood short stature, contributing 55% and 39% respectively to the global burden. In China, the prevalence rate of short stature among children is approximately 3%.In clinical practice, the selection between the two formulations of recombinant human growth hormone (rhGH) is a frequently discussed social hot topic among parents of pediatric patients and is also a clinical issue urgently needing discussion among clinicians and pharmacists. Currently, there are relatively few direct comparative studies on the use of the two short-acting rhGH formulations in pediatric patients. Evidence synthesis is needed to support

clinical decision-making regarding the choice of different formulations.

METHODS

Participant or population Children diagnosed clinically with idiopathic short stature or growth hormone deficiency were treated with recombinant human growth hormone (rhGH) either in the form of an injection solution or as a powder for injection.

Intervention Recombinant human growth hormone (rhGH) injection solution.

Comparator rhGH powder for injection.

Study designs to be included Randomized Controlled Trial.

Eligibility criteria Inclusion Criteria
Children clinically diagnosed with idiopathic short stature (ISS) or growth hormone deficiency (GHD), following the diagnostic criteria outlined in the "Clinical Practice Guidelines for Short Stature in Children" and the "Chinese Expert Consensus on the Diagnosis and Treatment of Idiopathic Short Stature in Children (2023 Edition)".
Primary Diagnostic Criteria for ISS: Children whose height is below the 3rd percentile or more than 2 standard deviations (–2SD) below the mean for age- and gender-matched healthy children; absence of systemic diseases, other endocrine disorders, nutritional issues, or chromosomal abnormalities; GH stimulation test peak ≥10 μg/L; normal or delayed bone age.
Primary Diagnostic Criteria for GHD: Children whose height is below the 3rd percentile or more than 2 standard deviations (–2SD) below the mean for age- and gender-matched healthy children; normal birth height and weight; normal intelligence; delayed bone age compared to chronological age; both GH stimulation tests show GH peak <10 μg/L.
Treatment with recombinant human growth hormone (rhGH) either as an injection solution or powder for injection.
Published randomized controlled trials (RCTs) from both domestic and international sources.
Exclusion Criteria
Literature focusing on the use of growth hormone for Turner syndrome, Prader-Willi syndrome, Noonan syndrome, and SHOX gene defects.
Duplicate publications, where only one instance will be counted.
Literature for which the full text cannot be obtained.
Review articles, research progress reports, and theoretical discussions.

Information sources PubMed、Web of Science、EMBase、the Cochrane Library、CNKI、VIP、Wanfang、SinoMed.

Main outcome(s) Height.

Quality assessment / Risk of bias analysis Cochrane Risk of Bias Tool.

Strategy of data synthesis Perform network meta-analysis using Stata 18.0 software, with the mean difference (MD) as the effect measure for continuous variables, calculating and describing the effect sizes and their 95% confidence intervals. If closed loops are present among the studies, consistency testing should be conducted. If the P-value of this test is greater than 0.05, a consistency model will be used for analysis. If no closed loops are formed among the studies, indicating that only indirect comparisons are available, the analysis will default to being conducted under a consistency model. The efficacy of the interventions will be ranked using the surface under the cumulative ranking curve (SUCRA), and comparison-adjusted funnel plots will be drawn to assess publication bias among the included studies.

Subgroup analysis The study did not perform subgroup analyses because of the homogeneity of the participants.

Sensitivity analysis Perform sensitivity analyses on all outcome measures. It was found that after sequentially excluding studies, the results of the outcome measures did not show significant changes.

Country(ies) involved China.

Keywords rhGH; short stature; idiopathic short stature; rhGH injection solution and powder for injection; Network Meta-analysis.

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