INPLASY

The Effects of GLP-1 Receptor Agonists on Metabolic Inflam-matory Markers in Patients with Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - No.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202540020

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 7 April 2025 and was last updated on 7 April 2025.

INTRODUCTION

Review question / Objective The study utilizes the PICOS framework to construct the research question and study design, where the population comprises adult patients with T2DM, the intervention consists of GLP-1 RAs (exenatide, dulaglutide, liraglutide), the control group receives either a placebo or conventional hypoglycemic agents (such as metformin, insulin, etc.), the outcomes are the changes in inflammatory marker levels, and the study design is based on published RCTs.

Condition being studied Type 2 diabetes mellitus (T2DM), characterized by progressive β-cell dysfunction and peripheral insulin resistance, is increasingly associated with metabolic inflammation. This condition is a chronic low-grade inflammatory state that contributes to the pathogenesis of insulin resistance and the progression of T2DM. In patients with T2DM, elevated levels of metabolic inflammatory markers, including tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and C-reactive protein (CRP), are consistently observed and are positively correlated with insulin resistance and features of metabolic syndrome. These biomarkers not only contribute to insulin resistance but also accelerate β-cell degeneration and the development of vascular complications.

METHODS

Participant or population Type 2 Diabetes Mellitus.

Intervention GLP-1 Receptor Agonists.

Comparator Either a placebo or conventional hypoglycemic agents (such as metformin, insulin, etc.).

Study designs to be included Randomized Controlled Trials (RCTs): These are considered the gold standard for evaluating the efficacy of an intervention. RCTs involve randomly assigning

participants to either the intervention or control group, which helps to minimize bias.

Eligibility criteria Inclusion criteria: (1) Study subjects: Individuals diagnosed with type 2 diabetes mellitus , regardless of gender, race, or nationality; (2) Interventions: Treatment with glucagon-like peptide-1 receptor agonists , either as monotherapy or in combination with other anti-hyperglycemic drugs; (3) Control measures: The control group includes placebo, traditional anti-hyperglycemic drugs, or hormones; (4) Outcome indicators: At least one inflammatory marker C-reactive protein, tumor necrosis factor-α , or interleukin-6 is included; (5) Study type: Published randomized controlled trials . Exclusion criteria: (1) Studies for which the full text cannot be obtained, or articles with duplicate publications; (2) Conference abstracts, dissertations, and review articles; (3) Studies with incomplete data, or studies from which valid data cannot be extracted; (4) Non-English studies and studies based on animals; (5) Studies in which the study subjects have severe infections, autoimmune diseases, or other diseases that may affect the levels of inflammatory markers.

Information sources PubMed, EBSCO, Embase, Web of Science, and the Cochrane Library.

Main outcome(s) Factor-α (TNF-α), interleukin-6 (IL-6), and C-reactive protein (CRP).

Quality assessment / Risk of bias analysis In accordance with the Cochrane Handbook for Systematic Reviews of Interventions, the risk of bias of the included studies was assessed based on the following five domains: randomization process, deviations from the intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Based on the guidelines, studies were classified as having a low risk, high risk, or some concerns. The risk of bias assessment was conducted independently by two reviewers, with a third reviewer resolving any conflicts.

Strategy of data synthesis The data analysis was conducted using RevMan 5.4 software, with the effect size expressed as the weighted mean difference (WMD) and its corresponding 95% confidence interval (CI). When significant heterogeneity was not present (I^2 0.1), the fixed-effect model was used to pool the data; otherwise, the random-effects model was applied.

Subgroup analysis The subgroup analyses were conducted based on the type of glucagon-like peptide-1 receptor agonists (GLP-1 RAs), treatment duration, and dosing frequency.

Sensitivity analysis 1. Exclude studies with a high risk of bias: According to the results of the risk of bias assessment, exclude studies with a high risk of bias and conduct a meta-analysis again. Compare whether the results are consistent with those of the main analysis.
2. Analysis by the type of GLP-1 receptor agonist: Since different types of GLP-1 receptor agonists may have different effects, conduct subgroup analyses according to specific drugs (such as exenatide, liraglutide).

Language restriction English.

Country(ies) involved China.

Keywords GLP-1 receptor agonists; type 2 diabetes mellitus;inflammatory markers.

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