INPLASY

INPLASY2023110020

doi: 10.37766/inplasy2023.11.0020

Received: 05 November 2023

Published: 05 November 2023

Influence of glucagon-like peptide-1 receptor agonists on fat distribution in patients with diabetes mellitus or obesity: A systematic review and meta-analysis of randomized control trials

Xie, WR[1]; Zhang Y[2].

Corresponding author:
Wanrun Xie

1484208294@qq.com

Author Affiliation:
Quanzhou First Hospital Affifiliated to Fujian Medical University.

ADMINISTRATIVE INFORMATION

Support - None.

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

Conflicts of interest - None declared.

INPLASY registration number: INPLASY2023110020

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 05 November 2023 and was last updated on 05 November 2023.

INTRODUCTION

Review question / Objective a)P: patients with obesity and diabetes mellitus. b)I: glucagon-like peptide-1 receptor agonists. c)C: without glucagon-like peptide-1 receptor agonists treatment. d)O: VAT, SAT, BMI, weight, BP, BG, HbA1c, HOMAIR, FIB, Blood lipid etc. e)S: randomised controlled trials.

Condition being studied Type 2 diabetes mellitus (T2DM) is a heterogeneous, chronic, progressive metabolic disease accounting for 90–95% of all diabetes. T2DM presents a severe public health problem with a global prevalence of 6059 cases per 100,000 T2DM. Male patients show a slightly higher prevalence than females. Patients with T2DM have insulin resistance, and genetically predisposed insulin deficiency clinically manifests as hyperglycemia. Patients with T2DM are usually overweight and obese . Obesity is defined as a body mass index (BMI) of 30 kg/m2 or higher. It is associated with insulin resistance, hyperinsulinemia, endothelial dysfunction, inflammation, and prothrombotic state. Obesity is a significant risk factor for the occurrence and mortality of T2DM, hypertension, cardiovascular diseases, non-alcoholic steatohepatitis, obstructive sleep apnea, orthopedic problems, mental health complications such as anxiety and depression, and cancer.

GLP-1 is a 37 amino acid long polypeptide secreted from specialized L cells primarily located in the brush border of the small and the large intestine.GLP-1 acts through a receptor (GLP-1R) that belongs to the B subfamily of the G protein-coupled receptor family. It consists of seven transmembrane domains in the form of alpha-helices, which are interconnected by six loops, of which three are intra- and three extracellular.

GLP-1 increases the synthesis and release of insulin from pancreatic β-cells. GLP-1 regulates the gene expression of pancreatic β-cells, inhibits apoptosis of β-cells, protects them from glucolipotoxicity, and improves their function. In addition, GLP-1 also reduces glucagon secretion by pancreatic α-cells. This reduces glucose production in the liver, reflected in lower blood glucose levels. GLP-1 may additionally act through the activation of visceral afferent neurons. On the other hand, it centrally regulates food intake, energy consumption, and the functioning of the digestive system, thus slowing down gastric emptying and reducing acid secretion, resulting in decreased appetite and body weight.
Novel therapeutic approaches for T2DM and obesity treatment rely on the incretin effect of GLP-1R agonists on both pancreatic β-cells and other peripheral and central mechanisms of action.

METHODS

Participant or population Patients diagnosed with diabetes or obesity.

Intervention Glucagon-like peptide-1 receptor agonists.

Comparator Without glucagon-like peptide-1 receptor agonists treatment.

Study designs to be included Randomised controlled trials.

Eligibility criteria Exclusion criteria comprised the following: (1) Irrelevance to the topic; (2) duplication of articles; (3) inclusion of case reports, abstracts, letters, reviews, or meta-analyses; (4) incomplete data.

Information sources We conducted a thorough search of the PubMed, Embase, and Web of Science databases to retrieve all available literature up to October 2023.

Main outcome(s) Out of 207 identified studies, 13 RCTs met inclusion criteria. GLP-1RA treatment led to significant reductions in VAT (SMD -0.55, 95% CI [-0.90, -0.19]) and SAT (SMD -0.59, 95% CI [-0.99, -0.19]), as well as body weight (SMD -1.07, 95% CI [-1.67, -0.47]) and BMI (SMD -1.10, 95% CI [-1.74, -0.47]) compared to control groups. Significant heterogeneity was observed for VAT, SAT, body weight, and BMI($I^2 > 50\%$, $P < 0.01$). No publication bias was detected for VAT or SAT($P > 0.05$). Additionally, GLP-1RA treatment showed favorable effects on fasting blood glucose, postprandial glucose, HbA1c, HOMA-IR, and FIB-4.

Quality assessment / Risk of bias analysis The assessment of bias risk was conducted utilizing the Cochrane risk-of-bias instrument, which considered the following criteria: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, completeness of outcome data, selectivity of reporting, and any other potential sources of bias. The evaluations were categorized as either "low risk," "high risk," or "unclear risk."

Strategy of data synthesis Data extraction for all included papers was conducted separately by two researchers. The data that were extracted included: (1) the author and year of publication; (2) population and duration; (3) age; (4) intervention, sample size, BMI, HbA1c, instrument, and key findings. Data were manually retrieved from the literature, tables, and figures when not clearly stated. When the paper lacked sufficient information, we contacted the corresponding authors via email to request further data or clarification. Two researchers addressed their disagreements through consensus.

Subgroup analysis If significant heterogeneity was observed between studies ($P < 0.10$ or $I2 > 50\%$), meta-regression analysis and sensitivity analysis were carried out by reassessing sensitivities or specificities with the omission of articles one by one. This aimed to assess the robustness of overall sensitivities or specificities and identify studies contributing to heterogeneity. Publication bias was assessed through a funnel plot and Egger's test.

Sensitivity analysis Sensitivity analysis was conducted by systematically excluding individual studies, and subgroup analysis was performed based on the number of GLP-1RA patients, intervention duration, type of GLP-1RA, baseline BMI, and diagnostic methods to identify the source of heterogeneity.

Country(ies) involved Quanzhou first Hospital, Fujian Medical University, China.

Keywords glucagon-like peptide 1 receptor agonists; fat distribution; diabetes mellitus; obesity; meta-analysis.

Contributions of each author
Author 1 - Wanrun Xie.
Email: 1484208294@qq.com
Author 2 - Yi Zhang.