INPLASY PROTOCOL

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Review Stage at time of this submission: **Preliminary searches.**

Conflicts of interest:
None declared.

A Systematic Review and Network Meta-Analysis: Effect of of GLP-1 drugs on weight loss in obese people

Xie, YH[1]; Pang, P[2].

Review question / Objective: **1、Whether GLP-1 drugs have weight loss effect on obese people ? 2、Which GLP-1 drugs are most effective in weight loss among obese people ?**
Condition being studied: **Obesity is an important public health issue that has been on the rise over the last decades. It calls for effective prevention and treatment. Bariatric surgery is the most effective medical therapy for weight loss in morbid obesity, but we are in need for less aggressive treatments. Glucagon-like-peptide-1 receptor agonists are a group of incretin-based drugs that have proven to be productive for obesity treatment. Through activation of the GLP-1 receptor they not only have an important role stimulating insulin secretion after meals, but with their extrapancreatic actions, both peripheral and central, they also help reduce body weight by promoting satiety and delaying gastric emptying.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 June 2022 and was last updated on 17 June 2022 (registration number INPLASY202260074).

INTRODUCTION

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Condition being studied: **Obesity is an important public health issue that has been on the rise over the last decades. It calls for effective prevention and treatment. Bariatric surgery is the most effective medical therapy for weight loss in morbid obesity, but we are in need for less aggressive treatments. Glucagon-like-**

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peptide-1 receptor agonists are a group of incretin-based drugs that have proven to be productive for obesity treatment. Through activation of the GLP-1 receptor they not only have an important role stimulating insulin secretion after meals, but with their extrapancreatic actions, both peripheral and central, they also help reduce body weight by promoting satiety and delaying gastric emptying.

METHODS

Search strategy: In this systematic review study and meta-analysis, international (PubMed, CENTRAL, EMBASE and CINAHL) and national databases (Koreamed(Korea) , J-GLOBAL(Japan), CNKI CBM VIP (China)) will be searched until June 30, 2022. The following MeSH and free-text terms will be used depending on the characteristics of databases searched: Glucagon-Like Peptide 1, GLP-1, GLP 1, Glucagon Like Peptide 1, Glucagon-Like Peptide-1, Obesity, Weight loss.There is no restriction on language, publication date or publication status. Example: Pubmed_(("Glucagon-Like Peptide 1"[MeSH Terms]) OR ("Glucagon Like Peptide 1"[Title/Abstract]) OR (GLP-1[Title/Abstract]) OR ("GLP 1"[Title/Abstract]) OR ("Glucagon-Like Peptide-1"[Title/Abstract])) AND (Obesity[MeSH Terms]).

Participant or population: Obesity patients.

Intervention: GLP-1 for obesity patients with any type, time, dose, frequency and manipulate form.

Comparator: Obese patients with routine weight management methods.

Study designs to be included: RCT, Quasi-experimental studies.

Eligibility criteria: Inclusion criteria: (1) Meet the overweight/obesity standards of The Consensus of Experts on Overweight/Obesity Medical Nutrition Therapy in China (2016 edition); (2) Overweight and simple obesity, 24≤BMI≤50; (3) Aged between 18 and 65. Exclusion criteria :(1) secondary obesity, such as obesity and hypercortisolism caused by hypothyroidism; (2) pregnancy and lactation; (3) severe liver and kidney dysfunction; (4) Patients with malignant tumors.

Information sources: In this systematic review study and meta-analysis, information sources come from international (PubMed, CENTRAL, EMBASE and CINAHL) and national databases (Koreamed(Korea) , J-GLOBAL(Japan), CNKI CBM VIP (China)).

Main outcome(s): Body weight, body mass Index (BMI), body fat percentage, waist circumference, neck circumference, hip circumference, triglyceride, total cholesterol, low density lipoprotein cholesterol, uric acid, blood glucose, chronic disease self-management study measures (CDSMS).

Data management: All statistical analyses will be performed by the Rev Man Version 5.0 software. A standard X^2 test and the I^2 statistic will be used to test heterogeneity between trial results. For continuous outcome, weighted mean differences (WMD) or standardized mean differences (SMD) will be calculated. For dichotomous outcomes, relative risk(RR)and 95% confidence intervals (CI) will be estimated.

Quality assessment / Risk of bias analysis: The risk of bias assessment will be carried out by two or more authors in accordance with the recommendations set out in the Cochrane Handbook for Systematic Reviews of Interventions, including following items: sequence generation, allocation concealment, blinding of participants, personnel and outcome assessors, incomplete outcome data, selective outcome reporting, and other sources of bias. We will grade each item as “low risk”, “high risk”, or “unclear”. Disagreements will be discussed with another reviewer.

Strategy of data synthesis: The data analysis was carried out by using RevMan 5.3 software provided by Cochrane

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Collaboration. The model used to pool the data depends on the existence and extent of heterogeneity. If the I^2 statistics < 50%, the heterogeneity could be accepted, the fixed-effect model was chosen. If the I^2 statistics ≥ 50%, the significant statistical heterogeneity was identified, the random-effects model was chosen. The random-effects model was also used when subgroup analysis was adopted and heterogeneity among studies was obvious. For binary outcome, the pooled relative risk (RR) with 95% confidence interval (CI) was used as the effect measure. For the continuous outcomes, weighted mean difference (WMD) was used as the effect measure. If included studies have multiple arms, we will convert the multiple arms trial to the two arm trial according Cochrane Handbook. Publication bias will be assessed with a funnel plot and Egger's weighted regression technique.

Subgroup analysis: If the necessary data are available, subgroup analyses will be done for different type intervention (especially different type of GLP-1 drugs and dosing frequency).

Sensitivity analysis: The sensitivity of an article can be reversed by the change of effect size after deleting an article in Stata software.

Country(ies) involved: China.

Keywords: Meta-analysis; Systematic Review; GPL-1; Obesity; Weight loss.

Contributions of each author:

Author 1 - Yunhui Xie - Author 1 drafted the manuscript.
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Author 2 - Peng Pang - The author provided statistical expertise.
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