INPLASY PROTOCOL

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None declared.

Metformin, Liraglutide, Orlistat, and Phentermine for Childhood Obesity and Blood Lipids: A Systematic Review and Meta-Analysis

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Review question / Objective: **Population: Children and adolescents diagnosed with obesity (Defined as being no older than 18 years of age and having a BMI above the 95th percentile for sex and age;). No limitation of location, and gender. Intervention: one medicine of Orlistat, Phentermine, Liraglutide, and Metformin. Comparator: Placebo or Dietary control. We'll only consider random controlled trials. The other types of studies will be excluded such as animal studies, reviews, case reports, non-controlled trials, and quasi-RCTs. Outcomes: Primary outcome: BMI or body mass. Secondary outcome: Waist circumference, and blood lipid index (TC, TG, HDL-C, and LDL-C). Study design: This study is secondary, and the data were extracted from others' work.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 May 2023 and was last updated on 26 May 2023 (registration number INPLASY202350100).

INTRODUCTION

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Condition being studied: Childhood obesity is a complex chronic disease caused by an imbalance of energy gain-burn, with some genetic factors, but with a greater influence on lifestyle and dietary habits.
Obesity is a physical abnormality associated with gastrointestinal tract diseases, skeletal muscles, respiratory system, vascular circulation, neuroendocrine and other multiple systems. For example, obesity combined with obstructive apnea syndrome, type 2 diabetes induced by disorders of glucose metabolism, cardiovascular diseases induced by lipid metabolism disorders, premature death, and increased risk of tumours.
Obesity also affects children's growth and development and psychological health, such as obesity combined with precocious puberty impairs children's height reserve and brings serious psychological problems. Although the awareness of the harmful effects of obesity is increasing, the prevalence of childhood obesity continues to rise, posing high socioeconomic and social security risks. Therefore timely intervention is necessary.
Current treatment of childhood obesity is based on behavioural interventions and dietary habit therapies, and the long-term efficacy of these therapies is often difficult to guarantee. Drug and surgical therapies are more commonly used in adult obesity. However, the adverse effects of some drugs and the safety concerns and narrow indications of surgical therapies have led to a more limited use of these interventions in children. Liraglutide, oseltamivir, phentermine, and metformin are all FDA-approved drugs for treating childhood obesity, and they each have a different scope of application. Liraglutide inhibits glucagon secretion and thus lowers blood glucose while suppressing appetite. Oseltamivir inhibits digestive lipase and reduces gastrointestinal fat absorption. Phentermine is a sympathomimetic drug that suppresses appetite with the GABA agonist topiramate. Metformin inhibits hepatic gluconeogenesis and increases peripheral blood glucose uptake, lowering blood glucose and promoting lipid circulation. In the last 10 years, studies have reported the therapeutic effects of these drugs in childhood obesity, but these studies are often based on individual drugs. They are characterized by inconsistent intervention times, small sample sizes, and subject shedding, which often do not reflect the overall intervention effects of drugs on childhood obesity. This systematic review intends to summarize the combined therapeutic level of these four drugs on childhood obesity and the effect on lipid-related indicators in obese children by analyzing literature data in the past 10 years.

METHODS

Participant or population: Children and adolescent diagnosed with obesity (Defined as being no older than 18 years of age and having a BMI above the 95th percentile for sex and age;). No limitation of location, and gender.

Intervention: One medicine of orlistat, phentermine, liraglutide, and metformin.

Comparator: Placebo or dietary control.

Study designs to be included: Random controlled trials. The other types of studies will be excluded such as animal studies, reviews, case reports, non-controlled trials, and quasi-RCTs.

Eligibility criteria: Inclusion criteria of this study are as follows: 1) Obese children, aged up to 18 years, are defined as having a body mass index (BMI) greater than the 95th percentile based on their sex and age. 2) The study was a randomized controlled trial that administered one of four medications (phentermine, metformin, orlistat, or liraglutide, including phentermine/topiramate) to the trial group, while the control group was given either a placebo or dietary behavioral guidance. 3) The primary outcome measures include BMI or body mass. The secondary outcome measures include Waist circumference and

blood lipid index. The exclusion criteria for this study were: 1) Drug-related factors or other medical conditions that may cause obesity, including Prader-Willi syndrome, central precocious puberty, oral antidepressants, antiepileptic drugs, polycystic ovary syndrome, and type I diabetes mellitus, among others. 2) Concurrent administration of other medications in the test group or one of the four drugs in the control group. 3) Insufficient data are available regarding the primary outcome.

Information sources: PubMed, Embase, The Cochrane Library, Web of Science.

Main outcome(s): BMI (including BMI-Z and BMI-SDS) or body mass.

Additional outcome(s): Waist circumference and blood lipid index (TC, TG, HDL-C, and LDL-C).

Quality assessment / Risk of bias analysis: Two independent reviewers will assess the risk of bias in the chosen randomized controlled trials (RCTs) using the Cochrane Risk of Bias 2.0 tool, which comprises six domains: randomization process, deviations from intended interventions, missing data, outcome measurement, selection of the reported result, and overall bias. The studies will be categorized into three levels of bias: low, high, or some concerns. A third reviewer will resolve discrepancies between the reviewers' assessments.

Strategy of data synthesis: The study utilized Review Manager 5.3 software to perform statistical data analyses. The quality of the evidence was assessed and graded according to the GRADE methodology, and the results were presented using the GRADE profiler 3.6 software. Risk ratios (RR) with 95% confidence intervals (CI) were used to analyze dichotomous data. In comparison, mean difference (MD) or standard mean difference (SMD) with 95% confidence intervals were used to analyze continuous data. A fixed-effects model was employed to analyse homogeneous data, while a random-effects model was used for heterogeneous data. Publication bias was assessed for studies with ten or more references using funnel plots and Egger's test.

Subgroup analysis: We will investigate the source of heterogeneity by conducting a subgroup analysis that considers various interventions.

Sensitivity analysis: We will analyze the robustness and stability of the outcome results by excluding studies with low methodological quality. Our primary focus is to evaluate the effects of method quality, sample size, and missing data on the study. Additionally, we will assess the influence of individual studies on the overall outcome results to determine the strength of our findings.

Country(ies) involved: China.

Keywords: Children; Obesity; Metformin; Liraglutide; Orlistat; Phentermine; Blood lipid; Systematic review; Meta-analysis.

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