INPLASY

GLP-1 receptor agonists in Parkinson's disease progression: A systematic review and meta-analysis with trial sequential analysis

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY2024110119

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 November 2024 and was last updated on 28 November 2024.

INTRODUCTION

Review question / Objective We aim to compare the protective effect of GLP1 receptor agonists with placebo in PD. Population: Parkinson's disease with or without diabetes mellitus. Intervention: patient receiving GLP1 receptor agonist. Comparison: placebo. Outcome: change of UPDRS score and levodopa equivalent daily dose.

Condition being studied Parkinson's disease (PD) is a neurodegenerative disorder with motor and non-motor symptoms. Current dopamine-related treatments are limited by side effects and diminishing efficacy over time. Other than dopamine related drugs, Glucagon-like peptide 1 (GLP-1) receptor agonists was thought to have neuroprotective effect. The effect of GLP-1 receptor agonists in PD is limited, we aim to compare the protective effect of GLP1 receptor agonists with placebo in PD.

METHODS

Search strategy We performed a comprehensive search in PubMed, Embase, and the Cochrane Library. Search term : (GLP-1 R agonist including exenatide, lixisenatide, liraglutide, dulaglutide, semaglutide) AND Parkinson's disease.

Participant or population Parkinson's disease with or without diabetes mellitus.

Intervention GLP1 receptor agonist.

Comparator Placebo.

Study designs to be included Randomized controlled trials.

Eligibility criteria Non-randomized studies, non-interventional trials, observational studies, and meeting abstracts were excluded.

Information sources We used the databases with PubMed, Embase, and the Cochrane Library.

Main outcome(s) Change of UPDRS score.

Additional outcome(s) Change of levodopa equivalent daily dose, Parkinson's Disease Questionnaire (PDQ-39), unified dyskinesia rating scale and Non-Motor Symptoms Scale for Parkinson's Disease (NMSS).

Quality assessment / Risk of bias analysis The risk of bias in the included studies was evaluated using the Cochrane Risk of Bias 2.0 (RoB2) tool for randomized clinical trials. RoB2 assessments were conducted independently by two reviewers. In instances of disagreement between the two evaluators on the risk of bias assessment, a third reviewer facilitated resolution and reached a consensus.

Strategy of data synthesis We performed random-effects meta-analysis using R software, version 4.3.1 (R Project for Statistical Computing) using the “meta” package. We calculated the risk ratios (RRs) for binary variables and the mean differences for continuous variables, each accompanied by their respective 95%CIs. Furthermore, we assessed the presence of heterogeneity in the data using Cochran's Q and I^2 tests. We considered a significance level of $P < 0.05$ (two-sided) for the Q statistic. The I^2 values were interpreted as follows: 0% to 40% might not be important; 30% to 60% may represent moderate heterogeneity; 50% to 90% may represent substantial heterogeneity; and 75% to 100% indicate considerable heterogeneity. If the number of included studies is fewer than 10, it will not be possible to conduct an Egger's regression test to assess publication bias or perform a meta-regression analysis.

Subgroup analysis Subgroup analyses will be conducted to investigate potential variations in the primary outcomes based on demographic and clinical characteristics. Pre-specified subgroups may include age, disease severity, and intervention duration. These analyses will provide insights into whether specific factors modify the effects of the intervention. We acknowledge that the exploratory nature of these analyses may limit statistical power in smaller subgroups.

Sensitivity analysis To investigate the influence of each study on the overall effect-size estimate, we conducted sensitivity analysis using the leave-one-out method.

Language restriction No language restriction.

Country(ies) involved Taiwan.

Keywords Parkinson's disease; GLP-1 receptor agonists; neuroprotection; motor symptoms; systematic review; meta-analysis.

Contributions of each author

Author 1 - Wen-Wen Tsai - Author 1 drafted the manuscript, data extraction and risk of bias assessment.
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