INPLASY

Efficacy and safety of GLP-1 receptor agonists on motor function for patients with Parkinson's disease: a meta-analysis of randomized controlled trials

INPLASY202560034

doi: 10.37766/inplasy2025.6.0034

Received: 8 June 2025

Published: 8 June 2025

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ADMINISTRATIVE INFORMATION

Support - No.

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

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202560034

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 8 June 2025 and was last updated on 8 June 2025.

INTRODUCTION

Review question / Objective P: Adult patients with a clinical diagnosis made by any physician, specialist, or otherwise of PD according to the UK Parkinson's Disease Society Brain Bank diagnostic criteria , or other equivalent clinical diagnostic criteria, or on the basis of clinical neurological assessment.
I: Intervention was defined as involved delivery of GLP-1 receptor drugs.
C: Control group was defined as received a placebo intervention or conventional PD treatment intervention or no treatment.
O: The outcomes included MDS-UPDRS Part III scores change from baseline in on-medicine state after drug period completed, MDS-UPDRS Part III scores change from baseline in off-medicine state after drug period completed, MDS-UPDRS Part III scores change from baseline in off-medicine state after drug washout period completed, MDS-UPDRS Part II scores change from baseline in on-medicine state after drug period completed, MDS-UPDRS Part IV scores change from baseline in on-medicine state after drug period completed, adverse events such as nausea and weight loss.
S: Randomized controlled trial.

Rationale Parkinson's disease (PD) is the second most common neurodegenerative disease that affects dopaminergic neurons in the mesencephalic substantia nigra, causing a progressive clinical course characterized by pre-motor, non-motor and motor symptoms. These symptoms negatively impact the quality of life of patients and cause high health care costs. PD prevalence is increasing with age and PD affects 1% of the population above 60 years. Currently, PD treatment aims at the symptomatic relief of PD patients, without being able to prevent or inhibit the process of neurodegeneration. Although dopamine replacement therapy remains a core component of PD treatment, important new approaches in the delivery of dopamine replacement are becoming available. Glucagon-like peptide-1 receptor (GLP-1R) agonists, known for their use in type 2 diabetes mellitus (T2DM)

treatment, are currently extensively studied as novel PD modifying agents.

GLP-1R are expressed in pancreatic islet cells, as well as in other organs, such as the gastrointestinal tract, lung, heart, kidney and brain, exerting indirect metabolic action. In the brain, it is expressed in the hypothalamus, the hippocampus, the subventricular zone, the striatum, the substantia nigra, the cortex and the brain stem. GLP-1 has been associated with improved endothelial function and suppression of inflammation, as well as cardio protection. Studies of animal models of PD as well as preclinical studies show that GLP1-R agonists can restore dopamine levels, inhibit dopaminergic loss, attenuate neuronal degeneration and alleviate motor and non-motor features of PD. GLP-1R agonists are divided into short-acting and long-acting, based on the time effect and the volume of injections needed. Short-acting preparations such as exenatide, and long-acting preparations such as lixisenatide, liraglutide, dulaglutide, semaglutide and albiglutide. These GLP-1R agonists are promising candidates to treat neurodegenerative diseases such as PD.

The Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS), which was designed as a comprehensive instrument for evaluating both motor and nonmotor impairments and disability in PD by the Movement Disorder Society in 2008 as a revision of the original UPDRS , was used to quantify PD progression. The MDS-UPDRS has four parts: Part I (non-motor experiences of daily living), Part II (motor experiences of daily living), Part III (motor examination) and Part IV (motor complications).

In recent years, many researchers focused on whether PD patients benefit of GLP-1R agonists. A previous meta-analysis evaluated the effectiveness and safety of GLP-1 receptor agonists for PD; nevertheless, it only included two randomized controlled trials (RCTs). Recently, there are some important researches about GLP-1R agonists for PD have been released. Therefore, we conducted this meta-analysis to investigate the efficacy and safety of GLP-1R agonists on motor function for patients with PD.

Condition being studied Parkinson's disease (PD) is the second most common neurodegenerative disease that affects dopaminergic neurons in the mesencephalic substantia nigra, causing a progressive clinical course characterized by pre-motor, non-motor and motor symptoms. These symptoms negatively impact the quality of life of patients and cause high health care costs. PD prevalence is increasing with age and PD affects 1% of the population above 60 years. Currently, PD treatment aims at the symptomatic relief of PD patients, without being able to prevent or inhibit the process of neurodegeneration. Although dopamine replacement therapy remains a core component of PD treatment, important new approaches in the delivery of dopamine replacement are becoming available. Glucagon-like peptide-1 receptor (GLP-1R) agonists, known for their use in type 2 diabetes mellitus (T2DM) treatment, are currently extensively studied as novel PD modifying agents.

METHODS

Search strategy Databases including PubMed, The Cochrane Library, EMBASE, Web of Science were searched for relevant articles from inception to May 2025. The search terms as follows: Parkinson disease, idiopathic Parkinson's disease, glucagon like peptide 1 receptor agonists, GLP-1 receptor agonists, exenatide, liraglutide, dulaglutide, semaglutide, albiglutide, lixisenatide, randomized controlled trial. Only English records and data were included.

Participant or population Adult patients with a clinical diagnosis made by any physician, specialist, or otherwise of PD according to the UK Parkinson’s Disease Society Brain Bank diagnostic criteria , or other equivalent clinical diagnostic criteria, or on the basis of clinical neurological assessment.

Intervention Intervention was defined as involved delivery of GLP-1 receptor drugs.

Comparator Control group was defined as received a placebo intervention or conventional PD treatment intervention or no treatment.

Study designs to be included Randomized controlled trial.

Eligibility criteria Included studies had to meet the following criteria: (1)The study was a RCT; (2) Adult patients with a clinical diagnosis made by any physician, specialist, or otherwise of PD according to the UK Parkinson’s Disease Society Brain Bank diagnostic criteria , or other equivalent clinical diagnostic criteria, or on the basis of clinical neurological assessment. (3) Intervention was defined as involved delivery of GLP-1 receptor drugs, the control group was defined as received a placebo intervention or conventional PD treatment intervention or no treatment. (4) the outcomes included MDS-UPDRS Part III scores change from baseline in on-medicine state after drug period completed, MDS-UPDRS Part III scores change

from baseline in off-medicine state after drug period completed, MDS-UPDRS Part III scores change from baseline in off-medicine state after drug washout period completed, MDS-UPDRS Part II scores change from baseline in on-medicine state after drug period completed, MDS-UPDRS Part IV scores change from baseline in on-medicine state after drug period completed, adverse events such as nausea and weight loss.

Information sources Databases including PubMed, The Cochrane Library, EMBASE, Web of Science were searched for relevant articles.The relevant grey literature, like reports and conference abstracts on the Internet, was also searched.

Main outcome(s) The outcomes included MDS-UPDRS Part III scores change from baseline in on-medicine state after drug period completed, MDS-UPDRS Part III scores change from baseline in off-medicine state after drug period completed, MDS-UPDRS Part III scores change from baseline in off-medicine state after drug washout period completed, MDS-UPDRS Part II scores change from baseline in on-medicine state after drug period completed, MDS-UPDRS Part IV scores change from baseline in on-medicine state after drug period completed, adverse events such as nausea and weight loss.

Quality assessment / Risk of bias analysis One reviewer assessed the risk of bias of all included trials and completed a Risk of Bias Table as described in the Cochrane Handbook. All assessments were conducted independently.

Strategy of data synthesis Meta-analysis was conducted using Stata 18.0 software. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) evaluation was conducted with the online tool GradeproGDT (https://gradepro.org/) to grade the evidence. Continuous outcomes were presented as mean differences (MDs) with 95% confidence intervals (CIs), while dichotomous outcomes were shown as risk ratio (RR) with their 95% CIs. Heterogeneity was tested using the Q test and the I2 statistic where percentages greater than 50% were taken to indicate significant heterogeneity. If I2 $<$50%, the fixed-effect model was applied to describe the center of the distribution of intervention effects. If heterogeneity was detected for outcomes, meta regression, subgroup analysis and sensitivity analysis were performed to analyze the causes of heterogeneity. Funnel plot was used to evaluate the publication bias. The test level of meta-analysis was set as $\alpha = 0.05$.

Subgroup analysis If heterogeneity was detected for outcomes, subgroup analysis were performed to analyze the causes of heterogeneity.

Sensitivity analysis If heterogeneity was detected for outcomes, sensitivity analysis were performed to analyze the causes of heterogeneity.

Language restriction In the present analysis, only English records and data were included.

Country(ies) involved All the authors of this study are from China.

Keywords Glucagon-like peptide-1 receptor agonists; Parkinson's disease; motor function; Meta-analysis; Randomized controlled trial; Systematic review.

Contributions of each author

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