INPLASY

The efficacy and safety of Rybelsus in Asian patients with type 2 diabetes：A systematic review and meta-analysis

INPLASY202380046

doi: 10.37766/inplasy2023.8.0046

Received: 11 August 2023

Published: 11 August 2023

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ADMINISTRATIVE INFORMATION

Support - The National Natural Science Foundation of China(82170847).

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202380046

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 August 2023 and was last updated on 11 August 2023.

INTRODUCTION

Review question / Objective Whether different doses of Rybelsus reduce HBA1c and body weight in Asian patients with type 2 diabetes compared to placebo and active medicines? Is this better than the global average?

Rationale The current published articles ignore the racial differences in the subjects, diabetes is a chronic metabolic disease, because the basic metabolic conditions are different in different races, and the drug treatment effect is different. A systematic review and meta-analysis of Asian and non-Asian subgroup clinical trials published to date is therefore required. To evaluate the efficacy and safety of Rybelsus in Asian and global populations.

Condition being studied Diabetes is a chronic metabolic disease with a high incidence in the world, especially in patients with type 2 diabetes, the blood sugar control is very unstable, and it is easy to involve all, causing damage to multiple tissues and organs. Lifelong treatment is often required, placing a heavy burden on individuals, families and society. A 2021 epidemiological study found that more than 500 million people worldwide already have diabetes today, representing more than 10.5% of the global adult population. In Asia in particular, the countries with the highest number of people aged 20-79 with diabetes in 2021 are China, India and Pakistan. The top three positions are expected to remain the same until 2045.

METHODS

Search strategy pubmed:
((rybelsus) OR (oral semaglutide)) AND ((((((((((((Diabetes Mellitus, Type 2[MeSH Terms]) OR (Diabetes Mellitus[MeSH Terms])) OR (Diabetes Mellitus, Noninsulin-Dependent)) OR (Diabetes Mellitus, Non Insulin Dependent)) OR (Non-Insulin-Dependent Diabetes Mellitus)) OR (Diabetes Mellitus, Stable)) OR (Stable Diabetes Mellitus)) OR (Diabetes Mellitus, Type II)) OR (NIDDM)) OR (Type 2 Diabetes Mellitus)) OR (Type 2 Diabetes)) OR

(Diabetes, Type 2)) OR (Diabetes Mellitus, Adult-Onset))
cochrane:
ID Search Hits
#1 Diabetes Mellitus, Type 2
#2 Diabetes Mellitus
#3 Diabetes Mellitus, Noninsulin-Dependent
#4 Diabetes Mellitus, Ketosis-Resistant
#5 Diabetes Mellitus, Non Insulin Dependent
#6 Non-Insulin-Dependent Diabetes Mellitus
#7 Diabetes Mellitus, Stable
#8 Stable Diabetes Mellitus
#9 Diabetes Mellitus, Type II
#10 NIDDM
#11 Type 2 Diabetes Mellitus
#12 Type 2 Diabetes
#13 Diabetes, Type 2
#14 Diabetes Mellitus, Adult-Onset
#15 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14
#16 rybelsus
#17 oral semaglutide
#18 #16 OR #17
#19 #15 and #18
WanFang database:
主题:(司美格鲁肽) and 题名或关键词:(2型糖尿病)
China National Knowledge Infrastructure(CNKI):
(关键词: 司美格鲁 (模糊)) OR (关键词: GLP1受体激动剂;(模糊)AND (关键词: 2型糖尿病 (模糊)).

Participant or population Research group：Asian people with type 2 diabetes. Control group：People with type 2 diabetes worldwide.

Intervention Rybelsus 3mg, 7mg and 14mg by oral.

Comparator Placebo, empagliflozin, sitagliptin, liraglutide and dulaglutide.

Study designs to be included (1) Randomized controlled trials; (2) Comparing semaglutide taken orally to placebo or any other antidiabetic medication in adults with T2DM; (3) Need to include predetermined main outcome measures of interest, change from baseline in glycated hemoglobin (HbA1c%) or body weight; (4)results were presented in different ethnic groups (including results presented alone or obtained in conjunction with other literature analysis);(5) Duration of intervention at least 12 weeks; (6) Published in English or Chinese. RCT.

Eligibility criteria The followings are the specific inclusion criteria: (1) Randomized controlled trials; (2) Comparing semaglutide taken orally to placebo or any other antidiabetic medication in adults with T2DM; (3) Need to include predetermined main outcome measures of interest, change from baseline in glycated hemoglobin (HbA1c%) or weight body; (4)results were presented in different ethnic groups (including results presented alone or obtained in conjunction with other literature analysis);(5) Duration of intervention at least 12 weeks; (6) Published in English or Chinese. Meanwhile, the pre-set exclusion criteria were used: (1) The protocol of the trial did not focus on the efficacy and safety of semaglutide in the treatment of T2DM; (2) Abstracts from conferences, meta-analysis, hoc-analysis, systematic reviews, editorials, expert comments and case reports; (3) The study only provided semaglutide self-information on pharmacokinetics, pharmacology, dose ranging and mechanism; (4) The patient population was not T2DM, including type 1 diabetes, gestational diabetes and obesity; (5) Research based on cell or animal level; (6) Pharmacoeconomics studies of semaglutide.

Information sources The databases searched for RCTs were PubMed, EMBASE , Cochrane Library, CNKI and Wang Fang Database.

Main outcome(s) The number of Participants who achieved HbA1c <7.0% (53 millimoles per mole [mmol/mol]). They were measured at 26, 52 and 78 weeks.

Additional outcome(s) The number of Participants losing 5% or more of baseline body weight, Incidence of adverse events (AE) and Incidence of serious adverse events (SAE).

Data management The data included in the study will be extracted by two auditors using pre-designed excel tables respectively, and the two tables will be compared after completion. Any differences should be reached through negotiation. Characteristics collected in the included trials included: first author name, year of publication, journal source, NCT number, sample size, ethnicity, intervention, follow-up time point, and background disease.

Quality assessment / Risk of bias analysis Cochrane Handbook for Systematic Reviews of Interventions v5.2 was used to assess the risk of bias in the studies.The evaluation process will be carried out by two researchers.

Strategy of data synthesis Statistical analysis will be performed using Review Manager (RevMan) 5.4.1, a Cochrane's bespoke software for writing Cochrane Reviews. The continuous and

dichotomous variables adopted weighted mean difference (WMD) and risk ratio (RR), respectively, with 95% confidence intervals (95% CIs). A fixed-effects model was used to compare groups initially. The I2 statistic (I2> 50% indicates considerable heterogeneity) and Cochrane's Q test ($p<0.1$ shows significant heterogeneity) will be used to assess heterogeneity. Statistical significance was set at a p-value of 0.05.

Subgroup analysis Subgroup analyses will be conducted based on Rybelsus dosages for placebo compared (3mg 7 mg or 14 mg vs placebo) and active compared (14 mg vs active arm). The other antidiabetic agents used in active arms were empagliflozin, sitagliptin, liraglutide and dulaglutide.

Sensitivity analysis Sensitivity analyses for each study and subgroup analyses will be used to reduce the heterogeneity to acceptable level, whereas a random-effects model was applied if sensitivity analysis cannot resolve heterogeneity.

Language restriction Only English or Chinese.

Country(ies) involved Department of Endocrinology and Metabology, The First Affiliated Hospital of Shandong First Medical University andShandong Provincial Qianfoshan Hospital, Jinan, China; Shandong University of Traditional Chinese Medicine, Jinan, China.

Keywords T2DM, oral semaglutide, Rybelsus, therapy, meta-analysis.

Contributions of each author

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Author 3 - Zhao Junyu - Data Extraction.
Author 4 - Zhao Junyu - Article innovation and Paper submission.