INPLASY PROTOCOL

To cite: Liu et al. Efficacy and safety of DPP-4 inhibitor in the treatment of patients with COVID-19 combined with diabetes mellitus a protocol for systematic review and meta-analysis. Inplasy protocol 202090015. doi: 10.37766/inplasy2020.9.0015

Received: 03 September 2020

Published: 03 September 2020

Corresponding author:
Yan Liu

liuxiaoyangas@163.com

Author Affiliation:
Affiliated Hospital/Clinical School of Chengdu University of Traditional Chinese Medicine

Support: **NSFC.**

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

Conflicts of interest: **No.**

Efficacy and safety of DPP-4 inhibitor in the treatment of patients with COVID-19 combined with diabetes mellitus a protocol for systematic review and meta-analysis

Liu, Y[1]; Xie, H[2]; Gao, H[3]; Xie, C[4].

Review question / Objective: **All patients who were diagnosed as COVID-19 will be included in our research, there will be no limitation about age, region, gender, disease severity and other factors. The experimental group is patients diagnosed with COVID-19 and diabetes, while the control group is COVID-19 patients without diabetes. Both groups of patients received conventional COVID-19 treatment.The experimental group received conventional diabetes treatment recommended by the American Diabetes Association (ADA) guidelines, including diet, exercise, hypoglycemia and lipid-lowering treatment and DPP-4 inhibitors treatment, and the control group received placebo or no treatment.The primary outcomes include mortality rate, incidence, clinical improvement, symptoms Improvement, fasting blood glucose, 2-hour postprandial blood glucose, glycosylated hemoglobin, fasting insulin, adverse reactions, etc.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 03 September 2020 and was last updated on 03 September 2020 (registration number INPLASY202090015).

INTRODUCTION

Review question / Objective: **All patients who were diagnosed as COVID-19 will be included in our research, there will be no limitation about age, region, gender, disease severity and other factors. The experimental group is patients diagnosed with COVID-19 and diabetes, while the control group is COVID-19 patients without diabetes. Both groups of patients received conventional COVID-19 treatment.The experimental group received conventional diabetes treatment recommended by the**

American Diabetes Association (ADA) guidelines, including diet, exercise, hypoglycemia and lipid-lowering treatment and DPP-4 inhibitors treatment, and the control group received placebo or no treatment.The primary outcomes include mortality rate, incidence, clinical improvement, symptoms Improvement, fasting blood glucose, 2-hour postprandial blood glucose, glycosylated hemoglobin, fasting insulin, adverse reactions, etc.

Condition being studied: In December 2019, Coronavirus disease 2019 (COVID-19) broke out in China and spread rapidly all over the world. As of the time of writing this article, a total of 90442 cases of COVID-19 have been diagnosed nationwide, 4734 cases have died, and 85169 cases have been cured. A total of 212 countries and regions overseas have reported 26215004 confirmed cases, 867865 deaths, and 18440138 cured. The prevalence of diabetes is increasing year by year and is closely related to infection. Many studies have found that DM will increase the morbidity and mortality of COVID-19. Therefore, patients with diabetes and COVID-19 may require special attention and clinical care. Dipeptidyl peptidase-4 (DPP-4) is a multi-expressed glycoprotein. Many studies have shown that membrane-associated human DPP-4, as a functional receptor of Middle East respiratory syndrome coronavirus (MERS-CoV) , interacts with MERS-CoV through the spike glycoprotein S1b domain to promote virus entry. Furthermore, blocking spike protein S1 or the receptor-binding domain (RBD) of the MERS-CoV Spike protein could directly and effectively prevent MERS-CoV binding to human DPP-4, thereby prevent MERS-CoV infection.

METHODS

Participant or population: We will include all patients diagnosed with COVID-19.

Intervention: Both groups of patients received conventional COVID-19 treatment. The experimental group received conventional diabetes treatment recommended by the American Diabetes Association (ADA) guidelines, including diet, exercise, hypoglycemia and lipid-lowering treatment and DPP-4 inhibitors treatment, and the control group received placebo or no treatment.

Comparator: The experimental group is patients diagnosed with COVID-19 and diabetes, while the control group is COVID-19 patients without diabetes.

Study designs to be included: Our research will be limited to randomized controlled trials (RCT).

Eligibility criteria: Our research will include randomized controlled trials. However, repeated publications of the same study; letters, abstracts, reviews, or animal experiments are excluded. We will include all patients diagnosed with COVID-19.This experiment involves DPP-4 inhibitor in treatment. Languages of the publications will be limited to English and Chinese.

Information sources: Electronic databases include CNKI, Wanfang, VIP, CBM database, Cochrane Library, PubMed, Web of Science, EMBASE, etc. In the meantime, for clinical trial registration and grey literature, we will manually search in Clinicaltrials.gov, the World Health Organization International Clinical Trials Registry Platform and China Conference Paper Database.

Main outcome(s): The primary outcomes include mortality rate, incidence, clinical improvement, symptoms Improvement, fasting blood glucose, 2-hour postprandial blood glucose, glycosylated hemoglobin, fasting insulin, adverse reactions, etc.

Quality assessment / Risk of bias analysis: We will evaluate all the included studies according to the guidelines of Cochrane Handbook for Systematic Reviews of Interventions. Evaluation items contain the following seven items. They are random sequence generation, allocation concealment, blinding participants and personnel, blinding evaluation of results, Incomplete outcome data, selective result

reporting, and other biases. The quality of each trial is classified as "low", "high" or "unclear" risk of bias. When there are disagreements, the two reviewers can reach a consistent conclusion through discussion or third-party consultation.

Strategy of data synthesis: We will use Review Manager software version 5.3 provided by Cochrane Collaboration to analyze the data. 95% RR is used to represent dichotomous data. And Continuous data will be represented by MD or SMD. When I2 0.01, it is shown that there is no statistical heterogeneity in this study, a fixed-effects model will be used; in contrast, when I2≥50%, P<0.01, indicating that there is considered heterogeneity, a random-effects model will be used for analysis. In addition, according to the different causes of heterogeneity, we will further conduct subgroup or sensitivity analysis. If meta-analysis is not possible, we will conduct a descriptive analysis.

Subgroup analysis: We will conduct subgroup analysis based on different reasons such as age, gender, different forms of intervention, treatment process, drug dosage, etc.

Sensibility analysis: In order to evaluate the robustness of the primary outcome measures, we will eliminate the low-quality studies and combine the data to assess the impact of the sample size, study quality, statistical methods and missing data on the meta-analysis results.

Country(ies) involved: China.

Keywords: COVID-19, diabetes mellitus, DPP-4 inhibitors, meta-analysis, protocol, systematic review.

Contributions of each author:
Author 1 - Yan Liu.
Author 2 - Hongyan Xie.
Author 3 - Hong Gao.
Author 4 - Chunguang Xie.