INPLASY PROTOCOL

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Conflicts of interest: None declared.

Efficacy of Regimens in the Treatment of Latent Autoimmune Diabetes in Adults: A Network Meta-Analysis

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Review question / Objective: Efficacy of Regimens in the Treatment of Latent Autoimmune Diabetes in Adults: A Network Meta-Analysis.

Condition being studied: Latent autoimmune diabetes mellitus (LADA) in adults is a highly heterogeneous autoimmune disease with clinical and genetic characteristics between Type 1 Diabetes（T1DM） and Type 2 Diabetes（T2DM）, and therefore there are no uniform criteria for the selection of therapeutic agents. We conducted a web-based meta analysis to evaluate the efficacy of various therapeutic agents for LADA by comparing their effects on various indicators reflecting LADA disease.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 October 2022 and was last updated on 18 October 2022 (registration number INPLASY2022100072).

INTRODUCTION

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efficacy of various therapeutic agents for LADA by comparing their effects on various indicators reflecting LADA disease.

METHODS

Participant or population: Patients aged 18 years or older;patients' glutamic acid decarboxylase antibody (GADAb)、protein tyrosinephosphatase antibody(IA-2A) or islet cell antibody(ICA) positive;patients having no history of ketosis within the first 6 months after diagnosis.

Intervention: Diamyd, Sitagliptin, Pioglitazone, Saxagliptin,Insulin & Sulphonylurea, Sulphonylurea, Linagliptin, Glimepiride,Insulin & MT, Insulin & VD, Tripterygium & OHA, OHA,Diet & OHA, Sitagliptin & Insulin,Tangyikang & Insulin, Rosiglitazone, Rosiglitazone & insulin, Insulin and Chinese medicine were the interventions.

Comparator: Insulin was the main comparator.

Study designs to be included: RCTs.

Eligibility criteria: (1) Randomized clinical trials in any stage were included;(2) study efficacy outcomes were glycosylated hemoglobin, type A1c (HbA1c), fasting C-peptide fasting blood glucose (FBG), postprandial blood glucose (PBG), fasting C-peptide (FCP), postprandial C-peptide (PCP), change from baseline in HbA1c (ΔHbA1c), serum C-peptide values during the oral glucose tolerance test (∑ C-piptide) and body mass index (BMI).The criteria for excluding studies were as follows:(1)non-RCTs, case reports,studies with insufficient data,conference reports, duplicated publications, summaries or systematic reviews;(2)women who were pregnant、lactating or planning on becoming pregnant;(3) patients with liver、kidney disorders or impaired hepatic/renal function;(4) patients have any severe systemic disease such as cancer, stroke, heart failure,or recent surgery.(5)patients suffering from serious cardiovascular diseases or cerebrovascular conditions or having a history of ketoacidosis or having unstable or rapidly progressive diabetic nephropathy, or neuropathy.

Information sources: Since the inception to June 2022, we PubMed and Cochrane Central Register of Controlled Trials searches were conducted by computer-based retrieval integrated with manual retrieval of related references.

Main outcome(s): Study efficacy outcomes were glycosylated hemoglobin, type A1c (HbA1c), fasting C-peptide fasting blood glucose (FBG), postprandial blood glucose (PBG), fasting C-peptide (FCP), postprandial C-peptide (PCP), change from baseline in HbA1c (ΔHbA1c), serum C-peptide values during the oral glucose tolerance test (∑ C-piptide) and body mass index (BMI).

Quality assessment / Risk of bias analysis: Two researchers evaluated the methodological quality of RCTs by using Cochrane Collaboration's tool for assessing risk of bias.The tool covers six domains, including selection bias, performance bias, detection bias, attrition bias, reporting bias and other bias.Each domain was judged as "yes," "unclear" or "no" to rate a grade as low(with no domain deemed "unclear" or "no"),moderate(with one domain deemed "unclear" or "no") or high(with more than one weak ratings). Quality assessment and investigation of publication bias were conducted by Review Manager 5 (RevMan 5.4, Cochrane Collaboration, Oxford, UK).Only one paper get a high grade in selection bias.Most of the other studies probably have moderate risks of selection bias and few of the articles are get moderate risks in other domains of the bias risk scale.Both data extraction and quality assessment were independently performed by the aforementioned reviewers.In case of disagreement, an independent third researchers will resolve inconsistencies through discussion.

Strategy of data synthesis: The heterogeneity test we selected are the

effect model on the basis of I-square(I2) test and P-value. The network funnel plot will be used to scrutinize the criterion of symmetry visually. STATA16.0 software will be used to conduct meta-analysis and draw network graphs. For meta-analysis, continuous variables are expressed as MD and 95%CI is calculated for each effect indicator. As mentioned earlier,I2 will indicate the degree of heterogeneity among multiple studies.We will conduct the node-splitting method to estimate the extent of inconsistency.If we get a result as $P > 0.05$ when the consistency check step is completed,a netleague table will give expression to the consistency among the studies.The surface under the cumulative ranking (SUCRA) will be estimated for each management,and we will use netleague command to show the statistical significance of data which were arranged in order hierarchically.The forest plots can imply the effectiveness of therapies visually.The number of control group of studies performed by three-arm trials was divided by two(the odd number was divided by two after adding one) before compared with the other groups in forest plots, subgroup analysis and sensitivity analysis.All analyses were conducted in Stata 16.0 (Stata, College Station, TX,USA).

Subgroup analysis: Subgroup analysis will be applied to explain the appearance of heterogeneity further. The subgroup analysis will be performed in the following aspects: the course of study, medicine type and the treatment with or without Insulin.

Sensitivity analysis: Sensitivity analysis will sustain the stability of our analysis results or explicate the reason why the dissertation became the cause of the heterogeneity.

Country(ies) involved: China.

Keywords: Latent autoimmune diabetes in adults; Network meta-analysis; Efficacy; Randomized controlled trials; Insulin; Immunosuppressive therapies.

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