INPLASY PROTOCOL

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Conflicts of interest:
All authors report no conflicts of interest in this study.

Efficacy and safety of mecobalamin combined with prokinetic agents in the treatment of diabetic gastroparesis: A protocol for a systematic review and meta-analysis

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Review question / Objective: The aim of the present study was to systematically review the efficacy and safety of mecobalamin combined with prokinetic agents in diabetic gastroparesis.

Condition being studied: Diabetic gastroparesis (DGP) is a chronic gastric dyskinesia and is characterized by delayed gastric emptying without any mechanical obstruction.Unfortunately, there are few, if any, efficient treatments for this disease. Antiemetic drugs and prokinetic agents are commonly used to alleviate the symptoms of DGP; however, long-term use is limited due to the side effects, and the recurrence rate is high following drug withdrawal. Mecobalamin is a common drug and for the past few years a number of randomized controlled trials (RCTs) have been conducted on the efficacy and safety of mecobalamin combined with prokinetic agents in DGP. However, the results of these RCTs are not completely consistent, and the sample size of a single study is limited. Furthermore, a relevant meta-analysis is still lacking to date. Thus, the aim of the present meta-analysis was to identify the efficacy and safety of mecobalamin combined with prokinetic agents in treating DGP, with a view to investigating a new therapeutic option for DGP.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 May 2020 and was last updated on 11 May 2020 (registration number INPLASY202050041).

INTRODUCTION

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dyskinesia and is characterized by delayed gastric emptying without any mechanical obstruction.Unfortunately, there are few, if any, efficient treatments for this disease. Antiemetic drugs and prokinetic agents are commonly used to alleviate the symptoms of DGP; however, long-term use is limited due to the side effects, and the recurrence rate is high following drug withdrawal. Mecobalamin is a common drug and for the past few years a number of randomized controlled trials (RCTs) have been conducted on the efficacy and safety of mecobalamin combined with prokinetic agents in DGP. However, the results of these RCTs are not completely consistent, and the sample size of a single study is limited. Furthermore, a relevant meta-analysis is still lacking to date. Thus, the aim of the present meta-analysis was to identify the efficacy and safety of mecobalamin combined with prokinetic agents in treating DGP, with a view to investigating a new therapeutic option for DGP.

METHODS

Participant or population: Participants should have a diagnosis of Diabetic gastroparesis; and age, gender and other general conditions are not limited.

Intervention: On the basis of the control of blood glucose, the experimental group was given mecobalamin combined with prokinetic drugs.

Comparator: The control group was given prokinetic drugs alone.

Study designs to be included: RCTs.

Eligibility criteria: The inclusion criteria will be as follows: i) RCTs with any follow-up duration and sample size. ii) Participants: participants should have a diagnosis of diabetes based on the WHO diagnostic criteria in 1999; participants had one or more DGP symptom, including anorexia, bloating, early satiety, abdominal pain and vomiting, persisting for >2 weeks; X-ray barium meal examination showed an objective evidence for the presence of

gastric emptying delay; endoscopic examination ruled out ulcers, tumors and other organic lesions; and ultrasound examination excluded organic lesions of the liver, gallbladder, spleen and pancreas; participants with other systemic diseases that may cause the above symptoms were excluded; and age, gender and other general conditions are not limited. iii) Intervention: on the basis of the control of blood glucose, the experimental group was given mecobalamin combined with prokinetic drugs, the control group was given prokinetic drugs alone. iv) Outcomes: total efficacy rate, the recurrence rate, gastric emptying rate, serum motilin and adverse reactions.

Information sources: EMBASE, Web of Science, China National Knowledge Infrastructure, VIP Database for Chinese Technical Periodicals, Chinese Biomedical Literature Database and WanFang Data, were searched from their inception to April 30, 2020. The ClinicalTrials.gov registry was also searched for unpublished trials and the authors were contacted for additional information if necessary. Relevant references from included studies were sought to retrieve additional eligible studies. No limits were set on language, publication year and type of publication.

Main outcome(s): Total efficacy rate, the recurrence rate, gastric emptying rate, serum motilin and adverse reactions.

Data management: Literature search and data extraction will be performed by two researchers (JY and BP) independently, and the third researcher (XG) will be involved in a discussion for any disagreements. The following information of eligible articles will be extracted to a data extraction form: author, publication year, sample size, intervention, dosage, duration, mean age, mean course of the disease, fasting blood glucose (FBG) and outcomes. When relevant details will be insufficiently reported in studies, authors will be contacted by email, and the ClinicalTrials.gov register will be searched for further information.

Quality assessment / Risk of bias analysis: According to the Cochrane collaboration's updated tool for assessing the risk of bias (version 5.1.0; updated March 2011) (3), two reviewers (JY and BP) will assess the quality of the included studies independently, and the third reviewer (XS) will be consulted for any disagreements. The risks of bias will be classified as high, unclear or low by assessing the seven components as random sequence generation, allocation concealment, blinding of outcome assessment, blinding of participants and personnel, incomplete outcome data, selective outcome reporting, and other biases. If necessary, the authors will be contacted by e-mail for further information.

Strategy of data synthesis: RevMan 5.3 and Stata 12.0 software will be used for statistical analysis. Dichotomous data will be expressed as the odds ratio (OR) with a 95% confidence interval (CI), and continuous data will be presented as the mean difference (MD) with 95% CI. Heterogeneity will be tested by χ^2-based Cochran Q statistic (P<0.10 indicated statistically significant heterogeneity) and I^2 statistic. If $I^2$0.1, a fixed-effects model will be used to pool the estimations across studies. If $I^2 \geq 50\%$ or $P \leq 0.1$, after excluding clinical heterogeneity between studies, the random-effects model will be used. Sensitivity analysis will be used to observe changes in the pooled effect size and heterogeneity between included studies, so as to assess the reliability and stability of the pooled results. Subgroup analysis will be performed according to the administration route of the included studies. The funnel plot and Egger's and Begg's test will be used to judge publication bias, and the trim and fill method will be used to correct the funnel asymmetry caused by publication bias. P<0.05 will be considered to indicate a statistically significant result.

Subgroup analysis: Subgroup analysis will be performed according to the administration route of the included studies.

Sensibility analysis: Sensitivity analysis will be used to observe changes in the pooled effect size and heterogeneity between included studies, to assess the reliability and stability of the pooled results.

Language: No language limits will be imposed on the search.

Country(ies) involved: China.

Keywords: mecobalamin; prokinetic agents; diabetic gastroparesis; meta-analysis.

Dissemination plans: After the research is completed, we will publish the research results in the journal.

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Author 1 - Jia Yao.
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