

The curative effects of acupuncture for gastrointestinal motility disorder in diabetes : A protocol for systematic review

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Abstract. Background: Diabetic gastrointestinal motility dysfunction, a leading long-term complication of diabetes, seriously affects the quality of life of the diabetes population. Apart from therapeutic drugs that control blood glucose levels and stimulants, acupuncture also play a critical role in the management of diabetic patients with gastrointestinal motility dysfunction symptoms. However, these therapeutic strategies and their effectiveness lack evidence. Therefore, this study was designed to systematically evaluate the curative effects of acupuncture for gastrointestinal motility disorder in diabetes.

Methods: RCTs on acupuncture treating Diabetic gastrointestinal motility dysfunction will be searched from the databases, from their inception to June 2022. The main outcome of the study was gastrointestinal motility disorder symptom score and clinical efficiency. Study selection, data collection, and quality assessment were independently completed by researchers. We will perform the meta-analysis by using RevMan software. Heterogeneity was assessed using Cochran's Q test. If the heterogeneity was high, sensitivity and subgroup analysis were further carried out.

Results: We will evaluate the curative effects of acupuncture for gastrointestinal motility disorder in diabetes.

Conclusion: In this study, results will provide supporting evidence for the use of acupuncture in treating diabetic gastrointestinal motility dysfunction in clinical settings.

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Keywords: Diabetic gastrointestinal motility disorders, acupuncture, meta-analysis, protocol

1. Introduction

All Diabetes neuropathy is a chronic complication of diabetes that affects 60% of diabetes patients [1]. Diabetic gastrointestinal motility dysfunction is one of the diabetic autonomic neuropathy, and the clinical manifestations include fullness, belching, nausea, vomiting, abdominal distension and pain, constipation, diarrhea, etc [2-3]. Recent reports suggest autonomic neuropathy occurs at an early stage of the disease, and the incidences are high. Further, gastrointestinal motility dysfunction may be related to diet, poor blood glucose control, and side effects of hypoglycemic drugs [4-5].

Although these classical symptoms is not fatal, the long-term abdominal uncomfortable can seriously impair the quality of life of patients with Diabetic gastrointestinal motility dysfunction .Therefore identifying strategies for treating and preventing the disease is the need of the hour. Along with the use of therapeutic drugs including blood glucose control and stimulants, acupuncture also play a critical role in the management of diabetic patients with gastrointestinal motility dysfunction symptoms. By stimulating acupoint, acupuncture can affect Yin and Yang, regulatethe gastrointestinal functions.For thousands of years, in Chinese traditional medicines, acupuncture have been considered effective in treating gastrointestinal dysfunction diseases.

It is used as adjuvant therapy for treating diabetic gastrointestinal motility dysfunction symptoms in clinical settings. The mechanism may be related to regulating gastrointestinal motility, enhancing visceral sensitivity, and regulating intestinal dysmotility. [6]. In clinical research, acupuncture can effectively enhance the Gastrointestinal Symptoms Index (GCSI) of gastric retention and gastroparesis[7]. In vivo studies have also shown that electroacupuncture can promote gastric smooth muscle contraction, improve the symptoms of gastric motility deficiency in diabetes by up-regulating the expression of RhoA/ROCK signaling pathway[8]. Despite the underlying mechanism of acupuncture having immense potential to regulatethe gastrointestinal functions , systematic review of diabetic gastrointestinal motility disorders treated by acupuncture are lacking.

Several clinical trials have shown that acupuncture effectively treats diabetic gastroparesis. However, its efficacy in treating diabetic gastrointestinal motility dysfunction has not been systematically evaluated. Hence, The aims of this study were to systematically analyze the existing randomized controlled trials (RCT) and assess the curative effects of acupuncture for gastrointestinal motility disorder in diabetes. The results of this study will aid in clinical decision-making for the treatment of this condition.

2. Methods

The systematic review will be reported following the guideline “Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)”. [9].

2.1 Inclusion criteria

Randomized Control Trial (RCT) which meeting following criteria:

1. patients: patients clearly diagnosed with diabetes or diabetic gastrointestinal motility disorders, and presentings indigestion symptoms.
2. The experimental group were treated by acupuncture-related methods;
3. the control group were treated with western medication, sham acupuncture, placebo, or no treatment.
4. Main outcome: dyspeptic symptoms scores; Effective rate of treatment; Secondary outcome: the quality scores of life , adverse reactions, time of gastric emptying .

2.2 Exclusion criteria

1. Multiple published studies
2. There was no control group in the trial, only comparison before and after treatment;
3. Empirical summary studies without data;
4. The patient was complicated with other diseases.

2.3 Retrieval strategy

Two researchers will independently screen and select for literature from databases: PubMed databases, Cochrane Library databases, Embase databases, Web of Science databases, China National Knowledge Infrastructure databases, Wan Fang Database databases, Chinese Biomedical Literature Database databases, VIP Database, and Clinical Trial Register (CTR) databases and extracted data. The retrieval time is from January 1990 to June 2022, and the retrieval strategy was

modified according to different databases. The literature search also included grey documents such as conference papers and dissertations. The combination of medical subject words and keywords like "acupuncture," "diabetic gastrointestinal motility dysfunction," and "Diabetic Gastroparesis" were used. Figure 1 shows the search strategy using PubMed as an example.

2.4 Studies selection

Duplicate literature will be excluded from the study using NoteExpress 3.2.0. Two researchers screen and select the literature after reading the title and abstract of the research, the retrieval process is executed separately independently. After preliminary screening, they will read the whole passage of the articles and determine whether it should be included in the study. In case of differences, the issue was resolved on further discussion, or a third researcher would intervene. The flow chart of the identifying process was shown in Figure 2.

2.5 Data extraction

Yong Wang and Ying Sun extracted the following data independently: title, first author, journal, publication time, randomization, blinding, treatment, adverse reaction events, and outcome indicators. The data were checked after extraction, and any dispute will be addressed through discussion with Zichen Guo and Shirong Zhao.

2.6 Statistical analysis

We will use Revman 5.4 software to consolidate the data during the consolidation analysis. The odds ratio (OR) was used to analyze the data for dichotomous variables, while, Mean difference (MD) will be used for continuous variables analysis. 95% confidence intervals (CI) will be used for both data.

2.7 Subgroup analysis

Subgroup analysis will be grouped according to intestinal symptoms and gastric symptoms. If there is significant heterogeneity in the study, we will conduct subgroup analysis according to treatment type or other factors.

2.8 Assessment of publication bias

We will conduct a systematic assessment using the Cochrane bias risk tool to assess the bias risk. Two reviewers will independently evaluate seven projects about bias: the bias risk of sequence generation, blindness of participants and outcome evaluation, allocation concealment, Completeness of results report, integrity of outcome data, and other bias. The risks of bias will be assessed in three cases, low, high and unclear. If there are differences opinions between the two researchers during the evaluation process, the two reviewers will discuss with the third assessor to make a decision.

2.9 Managing missing data

If any missing data or report lacked information, the corresponding authors of the articles were contacted to obtain the required relevant information.

2.10 Assessment of heterogeneity

Homogeneity test (Q test) will be used for heterogeneity test for the included studies. The homogeneity test (q test) was used for the included studies.

If $I^2 < 50\%$, indicating that the included studies have homogeneity, a fixed effect model will be used. If $I^2 > 50\%$, it indicates that there is heterogeneity between studies, and a random effect model should be used.

To identify the source of heterogeneity, sensitivity or subgroup analysis was conducted. If $I^2 > 75\%$, we will conduct system evaluation.

2.11 Sensitivity analysis

We will conduct sensitivity analysis by excluding the studies with low quality or significant weight one by one, or those with significantly different results from other studies.

If the number of studies is sufficient (greater than 10), a funnel plot will be used to detect and display publication bias.

2.12 Assessment of publication bias

We will adopt the funnel chart method to evaluate publication bias.

2.13 Assessment of the quality of evidence

We will implement quality assessment grading to assess the quality of evidence. The evidence is divided into several registers, which are high, medium, low and very low.

2.14 Ethics and dissemination

The systematic review and meta analysis does not need ethical approval, because nothing of the information will be obtained from participant. The results of this study will be published in the near future.

3. Discussion

Diabetic gastrointestinal motility disorder significantly impacts the quality of life for patients, and the adverse reactions of drugs further add to the psychological burden on patients and their families. Acupuncture are classic traditional Chinese medicine used in therapeutics. Clinical studies have shown that acupuncture significantly relieve the symptoms of gastrointestinal motility disorders. Meta-analysis results also reveal that acupuncture can effectively treat diabetic gastroparesis[10-13]. However, the effectiveness of acupuncture in improving symptoms of gastrointestinal motor dysfunction in diabetes has not been systematically evaluated. A meta-analysis was published in 2013 on the effectiveness of acupuncture on improving symptoms of dyspepsia in diabetes gastroparesis, while some studies have been done to evaluate its effect on intestinal motor symptoms such as abdominal distension. Since 2013, new clinical trials have been carried out. Hence, in light of new evidence, it is necessary to re-evaluate the effects of acupuncture on gastrointestinal motility disorder in patients with diabetes [14].

In this study, the quality of the analysis may have depended on the quality and validity of the individual studies included. We aim to summarize and evaluate the effects of acupuncture on gastrointestinal motility disorder in patients with diabetes and provide useful evidence for clinical practice and future research.

4. Footnotes

4.1 Abbreviations

RCT = random clinical research.

4.2 Fund

This project is supported by the Chinese medicine science and technology project of Shandong Province, China (2021M068)

4.3 Conflicts

In this study, the authors did not have any conflict of interest.

4.4 Data acquisition

If there are reasonable reasons, the data in this study can be obtained from the corresponding author.

5. Figures and Tables

NO.	Search terms
#1	Diabetic gastrointestinal motility(All files)
#2	Diabetic gastroparesis(All files)
#3	(Diabetes) AND (dyspeptic symptoms)(All files)
#4	#1 OR #2 OR #3
#5	Acupuncture(All files)
#6	Complementary therapy of electroacupuncture(All files)
#7	Electroacupuncture(All files)
#8	Electro-acupuncture (All files)
#9	Acupuncture(All files)
#10	Electroacupuncture(All files)
#11	Scalp acupuncture(All files)
#12	Eye acupuncture(All files)
#13	Ear acupuncture(All files)
#14	Floating acupuncture(All files)
#15	Abdomen acupuncture(All files)
#16	#5 OR #6-15
#17	Randomized controlled trial (All files)
#18	Controlled clinical trial (All files)
#19	Randomly (All files)
#20	Randomized (All files)
#21	Placebo (All files)
#22	Double-blind method (All files)
#23	Single blind method (All files)
#24	Trials (All files)
#25	#17 OR #18-24

FIGURE 1 SEARCH STRATEGY

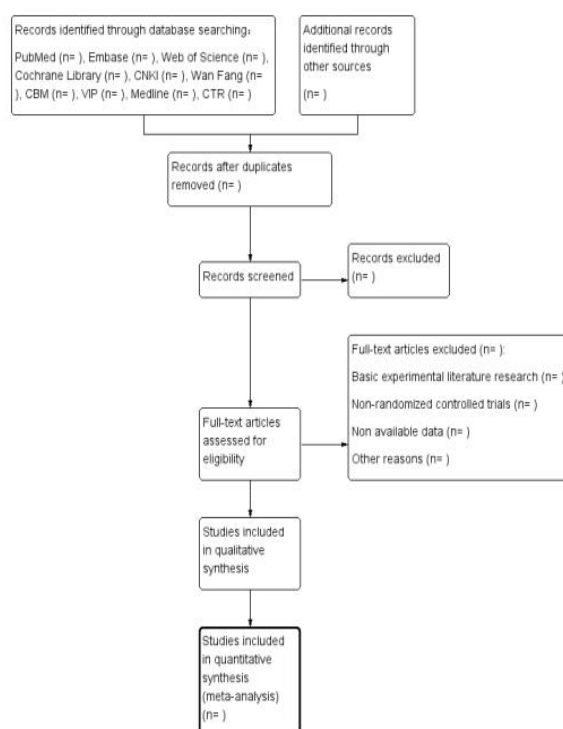


Figure 2 flow chart of the identification/identifying process

References

- [1] Wei Ni. Internal medicine – 4 th Edition [M]. People's Health Publishing House, 2016.
- [2] Du YT, Rayner CK, Jones KL, Talley NJ, Horowitz M. Gastrointestinal symptoms in diabetes: prevalence, assessment, pathogenesis, and management. *Diabetes Care*. 2018;41(3):627–37.
- [3] Sommers T, Mitsuhashi S, Singh P, Hirsch W, Katon J, Ballou S, et al. Prevalence of chronic constipation and chronic diarrhea in diabetic individuals in the United States. *Am J Gastroenterol*. 2019;114(1):135–42.
- [4] Johanson JF, Kralstein J. Chronic constipation: a survey of the patient perspective. *Aliment Pharmacol Ther*. 2007;25(5):599–608.
- [5] Meldgaard T, Keller J, Olesen AE, Olesen SS, Krogh K, Borre M, et al. Pathophysiology and management of diabetic gastroenteropathy. *Therap Adv Gastroenterol*. 2019;12:1–17.
- [6] Li H, He T, Xu Q, Li Z, Liu Y, Li F, Yang BF, Liu CZ. Acupuncture and regulation of gastrointestinal function. *World J Gastroenterol*. 2015 Jul 21;21(27):8304–13. doi: 10.3748/wjg.v21.i27.8304. PMID: 26217082; PMCID: PMC4507100.
- [7] Li G, Huang C, Zhang X, Xie H, Cheng H, Tang Y, Li Z. The short-term effects of acupuncture on patients with diabetic gastroparesis: a randomised crossover study. *Acupunct Med*. 2015 Jun;33(3):204–9. doi: 10.1136/acupmed-2014-010670. Epub 2015 Feb 17.
- [8] Wu XF, Chen XL, Zheng XN, , et al. Effects of different stimulation strength of Electroacupuncture on Gastrointestinal motility and RhoA /ROCK signaling in Gastric Antral smooth Mnscl in Diabetic Gastroparesis Rats. [J] Acupuncture research, ,2018,43(03):169-174.DOI:10.13702/j.1000-0607.170299.
- [9] Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ Clin Res* 2015;349: 7647.
- [10] Yan H, An Y, Zhang T, Zhao J, Yan J. The efficacy and safety of Tuina for diabetic gastroparesis: A protocol for systematic review and meta-analysis. *Medicine (Baltimore)*. 2021 Nov 24;100(47):e27964. doi: 10.1097/MD.00000000000027964.

- [11] Long T, Yue R, Wu T, Xu C, Yang M. The efficacy and safety of acupoint injection for diabetic gastroparesis: A protocol for systematic review and meta-analysis. *Medicine (Baltimore)*. 2020 Nov 6;99(45):e23086. doi: 10.1097/MD.00000000000023086.
- [12] Xia T, Yang Y, Li W, Tang Z, Li Z, Guo Y. Acupoint catgut embedding for diabetic gastroparesis: A protocol of systematic review. *Medicine (Baltimore)*. 2019 Oct;98(43):e17718. doi: 10.1097/MD.00000000000017718.
- [13] [13]Long T, Yue R, Wu T, Xu C, Yang M. The efficacy and safety of acupoint injection for diabetic gastroparesis: A protocol for systematic review and meta-analysis. *Medicine (Baltimore)*. 2020 Nov 6;99(45):e23086. doi: 10.1097/MD.00000000000023086.
- [14] [14] Yang M, Li X, Liu S, Li Z, Xue M, Gao D, Li X, Yang S. Meta-analysis of acupuncture for relieving non-organic dyspeptic symptoms suggestive of diabetic gastroparesis. *BMC Complement Altern Med*. 2013 Nov 9;13:311. doi: 10.1186/1472-6882-13-311.