INPLASY PROTOCOL

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Corresponding author:
Jing Wang

wangjingdc2022@163.com

Author Affiliation:
The TCM Hospital of Longquanyi, Chengdu.

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None declared.

Mudan Granules Adjuvant Treatment for Patients with Diabetic Peripheral Neuropathy: A Systematic Review and Meta-Analysis

Wang, J[1]; Wang, XM[2]; Yang, XL[3]; Jing, YY[4]; Zhao, WW[5]; Yue, RS[6].

Review question / Objective: **This meta-analysis selected studies on DPN with MDG as an adjuvant therapy for a pooled analysis, aiming to evaluate the therapeutic effect of this strategy on DPN patients.**
Condition being studied: **Diabetes' incidence is globally rising significantly, nearly doubling from 1980 (4.7%) to 2014 (8.5%). According to the latest data, the number of people with diabetes worldwide is 536.6 million (10.5%) in 2021 and is expected to reach 783.2 million (12.2%) by 2045. Global diabetes-related health spending is estimated at $966 billion in 2021 and is expected to reach $1.054 trillion by 2045. Diabetic peripheral neuropathy (DPN) occurs in people's approximately 30-50% with diabetes, leading to impaired quality of physical function and life. DPN is characterized by chronic paresthesias (numbness, tingling, hyperesthesia, or deep pain) and electrophysiological abnormalities, the most common type being distal symmetric polyneuropathy. It usually worsens at night, usually affects the lower legs and feet, and has a significant negative impact on the patient's quality of life and function. These individuals' 20%-30% develop painful DPN affecting mental and physical health of the patient. Worse, complications including painful DPN, foot ulcers, and lower extremity amputations were independently associated with an increased risk of death in patients.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 04 July 2022 and was last updated on 04 July 2022 (registration number INPLASY202270015).

INTRODUCTION

Review question / Objective: **This meta-analysis selected studies on DPN with MDG as an adjuvant therapy for a pooled analysis, aiming to evaluate the therapeutic effect of this strategy on DPN patients.**

Condition being studied: Diabetes' incidence is globally rising significantly, nearly doubling from 1980 (4.7%) to 2014 (8.5%). According to the latest data, the number of people with diabetes worldwide is 536.6 million (10.5%) in 2021 and is expected to reach 783.2 million (12.2%) by 2045. Global diabetes-related health spending is estimated at $966 billion in 2021 and is expected to reach $1.054 trillion by 2045. Diabetic peripheral neuropathy (DPN) occurs in people's approximately 30-50% with diabetes, leading to impaired quality of physical function and life. DPN is characterized by chronic paresthesias (numbness, tingling, hyperesthesia, or deep pain) and electrophysiological abnormalities, the most common type being distal symmetric polyneuropathy. It usually worsens at night, usually affects the lower legs and feet, and has a significant negative impact on the patient's quality of life and function. These individuals' 20%-30% develop painful DPN affecting mental and physical health of the patient. Worse, complications including painful DPN, foot ulcers, and lower extremity amputations were independently associated with an increased risk of death in patients.

METHODS

Search strategy: A systematic literature search of the PubMed, The Cochrane Library, Web of Science, Embase, China National Knowledge Infrastructure (CNKI), the Sinomed database, and the Wanfang database to June 1, 2022, for RCTs investigating the clinical efficacy of Mudan granules. The following grouped terms were used as search strategy and modified to suit each database to screen publications that might be valuable for the present review: ("Diabetic Neuropathy" OR "Diabetic Autonomic Neuropathy" OR "Diabetic Neuralgia" OR "Painful Diabetic Neuropathies" OR "Diabetic Mononeuropathies" OR "Diabetic Polyneuropathy" AND ("Mudan" OR "Mudan Granules") AND ("trial" OR "clinical trials" OR " clinical trial" OR "random" OR "random allocation" OR "randomized controlled trial" OR "RCT").

Participant or population: Patients with diabetic peripheral neuropathy (DPN); Mudan Granules(MDG) as adjuvant therapy for DPN.

Intervention: Mudan Granules(MDG) as adjuvant therapy for DPN.

Comparator: Conventional pharmaceutical therapy.

Study designs to be included: Experimental study.

Eligibility criteria: The inclusion criteria were as follows: (1) patients diagnosed with diabetic peripheral neuropathy; (2) Patients in both the test and control groups received standard glycemic control (including oral hypoglycemic drugs and insulin injections), low-fat diet, physical exercise and other conventional treatments. (3) the experimental group was treated with Mudan granules + conventional pharmaceutical therapy (CPT), and the control group was treated with only the CPT, and (4) an outcome measure must include at least one of the following: effective rate, the motor nerve conduction velocity (MNCV) for common peroneal nerve, median nerve or tibial nerve, the sensory nerves conduction velocity (SNCV) for common peroneal nerve, median nerve or tibial nerve, Toronto clinical scoring system (TCSS), neuron-specific enolase (NSE), high-sensitivity C-reactive protein (hs-CRP), pain numerical rating scale(p-NRS), adverse reactions (AEs).(1) Studies combining other Traditional Chinese Medicine (TCM) non-drug treatments, (2) reviews, conference abstracts and studies with animal experiments, (3) duplicate publications, and (4) studies with incomplete or incorrect data will be excluded.

Information sources: A systematic literature search of the PubMed, The Cochrane Library, Web of Science, Embase, China National Knowledge Infrastructure (CNKI), the Sinomed database, and the Wanfang database to June 1, 2022, for RCTs investigating the clinical efficacy of Mudan granules.

Main outcome(s): Effective Rate; SNCV for common peroneal nerve, median nerve and tibial nerve (m/s); MNCV for common peroneal nerve and median nerve (m/s);Toronto clinical scoring system (TCSS);Hs-CRP in serum; Adverse Events.

Quality assessment / Risk of bias analysis: Based on the inclusion criteria, two reviewers independently reviewed the search results and extracted relevant data. Any objections will be examined by a third researcher for guidance. The subject, the first author, the basic characteristics of the subject, publication time, the sample size, the interventions of the experimental and the control groups, course of treatment, and the outcome indicators was included by the extracted data. The Cochrane Risk of Bias tool was used to evaluate the bias risk for each included study. random sequence generation, allocation concealment, blinding of personnel and participants, blinding of outcome assessments, incomplete outcome data, selective reporting, and other biases was evaluated by the two independent reviewers in each RCT. Any disagreements were settled by discussions among all reviewers.

Strategy of data synthesis: Statistical analyses were performed using RevMan 5.3 and Stata 15.0. Risk ratios (RRs) and mean difference (MD) were used to measure relative treatment effects for dichotomous and continuous data, respectively. Standard errors are calculated from 95% confidence intervals (CIs). Heterogeneity was explored using the Mantel–Haenszel χ2-test and I2 statistic. If I2≤50%, it means that the heterogeneity is small, and a fixed effect model is used. If I2>50%, it means that the heterogeneity is large, and we will conduct a sensitivity analysis to determine the reason for the heterogeneity. If heterogeneity is still large, a random effects model will be used. Further, we will conduct subgroup analysis (duration of disease, duration of medication, etc.) for outcomes with greater heterogeneity for further analysis.

Subgroup analysis: Further, we will conduct subgroup analysis (duration of disease, duration of medication, etc.) for outcomes with greater heterogeneity for further analysis.

Sensitivity analysis: Heterogeneity was explored using the Mantel–Haenszel χ2-test and I2 statistic [26]. If I2≤50%, it means that the heterogeneity is small, and a fixed effect model is used. If I2>50%, it means that the heterogeneity is large, and we will conduct a sensitivity analysis to determine the reason for the heterogeneity. If heterogeneity is still large, a random effects model will be used.

Country(ies) involved: China.

Keywords: Diabetic peripheral neuropathy; Mudan granules; Systematic Review; Meta-Analysis.

Contributions of each author:

Author 1 - Jing Wang.
Email: wangjingdc2022@163.com
Author 2 - Xiaomin Wang.
Email: waugxuaomin@163.com
Author 3 - Xinyi Yang.
Email: yxytcm@yeah.net
Author 4 - Yayi Jiang.
Email: 1261206595@qq.com
Author 5 - Wenwen Zhao.
Email: 2284327262@qq.com
Author 6 - Rensong Yue.
Email: 1580229694@qq.com