Postprint of a Randomized Controlled Trial of Gehu Tiaozhi Formula Intervention in Patients with Metabolic Syndrome

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Abstract

Background Globally, approximately one-quarter of the population suffers from metabolic syndrome (MetS). In recent years, the prevalence of MetS in China has also exhibited a year-by-year upward trend, posing a serious threat to life and health. Traditional Chinese medicine (TCM) treatment of MetS offers advantages of multiple targets and multiple pathways; however, there is currently a lack of high-quality randomized controlled trials and real-world clinical studies.

Objective To observe the effects of Gehu Tiaozhi Formula (Puerariae Radix 6 g, Dendrobii Officinalis Caulis 6 g) on waist circumference, body weight, body fat percentage, and glucose-lipid metabolism in patients with MetS.

Methods From June 2021 to November 2022, 84 patients with MetS who presented to the outpatient clinic or were hospitalized at Longhua Hospital Affiliated to Shanghai University of Traditional Chinese Medicine were prospectively selected as study subjects. Using SPSS 25.0 statistical software with a specified random seed number, the subjects were randomly allocated to the Gehu group (42 cases) and the control group (42 cases). The Gehu group received Gehu Tiaozhi Formula granules (Puerariae Radix 6 g, Dendrobii Officinalis Caulis 6 g), administered orally on an empty stomach twice daily (morning and evening), one packet per dose, for 8 consecutive weeks. The control group received placebo granules, administered orally on an empty stomach twice daily (morning and evening), one packet per dose, for 8 consecutive weeks. During the intervention period, both groups received identical health education (including guidance on dietary plans and exercise prescriptions). After 8 weeks of intervention, the two groups were compared and analyzed for waist circumference (WC), body weight, body mass index (BMI), body fat percentage (BFP), triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and fasting blood glucose (FBG).

Results Ultimately, 41 cases in the Gehu group and 41 cases in the control group completed the 8-week intervention study. Before treatment, there were no statistically significant differences between the two groups in WC, body weight, BMI, or BFP (P>0.05). Comparisons of the before-and-after treatment differences in WC, body weight, BMI, and BFP between the two groups showed statistically significant differences (P<0.05). Before treatment, there were no statistically significant differences between the two groups in TG, TC, HDL-C, LDL-C, or FBG (P>0.05). Comparisons of the before-and-after treatment differences in TG, TC, and FBG between the two groups showed statistically significant differences (P<0.05).

Conclusion Gehu Tiaozhi Formula can effectively improve WC, body weight, BMI, BFP, TG, TC, and FBG in patients with MetS, with favorable safety.

Full Text

Randomized Controlled Study on Gehu Tiaozhi Decoction Intervening Patients with Metabolic Syndrome

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Abstract

Background: Approximately one-quarter of the world's population suffers from metabolic syndrome (MetS). In recent years, the prevalence of MetS in China has also increased annually, posing a serious threat to life and health. Traditional Chinese medicine offers multi-target and multi-link advantages in treating MetS, but high-quality randomized controlled trials and real-world studies remain lacking in clinical practice.

Objective: To observe the effects of Gehu Tiaozhi Decoction (Pueraria lobatae radix 6 g, Dendrobium officinale 6 g) on waist circumference, body weight, body fat percentage, and glucose-lipid metabolism in patients with MetS.

Methods: From June 2021 to November 2022, 84 patients with MetS were prospectively enrolled from the outpatient and inpatient departments of LongHua Hospital Shanghai University of Traditional Chinese Medicine. Using SPSS 25.0 statistical software with a specified random seed, subjects were randomly allocated to the Gehu group (42 cases) and control group (42 cases). The Gehu group received Gehu Tiaozhi Decoction granules (Pueraria lobatae

radix 6 g, Dendrobium officinale 6 g) orally twice daily on an empty stomach, one bag per dose, for 8 consecutive weeks. The control group received placebo granules with identical administration. Both groups received identical health education during the intervention, including dietary guidance and exercise prescriptions. After 8 weeks, waist circumference (WC), body weight, body mass index (BMI), body fat percentage (BFP), triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and fasting blood glucose (FBG) were compared between groups.

Results: Ultimately, 41 patients in the Gehu group and 41 in the control group completed the 8-week intervention. No statistically significant differences were found between groups in WC, body weight, BMI, or BFP at baseline ($P>0.05$). The between-group differences in changes from baseline to post-treatment for WC, body weight, BMI, and BFP were statistically significant ($P<0.05$). Similarly, no baseline differences existed for TG, TC, HDL-C, LDL-C, or FBG ($P>0.05$), but the between-group differences in changes for TG, TC, and FBG were statistically significant ($P<0.05$).

Conclusion: Gehu Tiaozhi Decoction effectively improves WC, body weight, BMI, BFP, TG, TC, and FBG in MetS patients with favorable safety profiles.

Keywords: Metabolic syndrome; Puerariae lobatae radix; Dendrobium officinale; Traditional Chinese medicine; Clinical research

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Introduction

Since the 21st century, improved socioeconomic conditions, increasingly refined and diversified food availability, and changes in lifestyle and dietary structure have contributed to the global epidemic of metabolic syndrome (MetS). According to the International Diabetes Federation, 20-25% of the worldwide population has been diagnosed with MetS [1]. Epidemiological projections estimate that global MetS prevalence will reach 53% by 2035 [2]. Data from the 2011-2016 U.S. National Health and Nutrition Examination Survey revealed that 34.7% of American adults over 20 years met MetS diagnostic criteria [3]. Analysis of Chinese national nutrition and health survey data from 2010-2012 showed an 11.0% prevalence among Chinese adults, increasing with age [4]. MetS readily induces systemic metabolic disorders and represents a major risk factor for cardiovascular and cerebrovascular diseases, making its prevention and treatment an urgent public health priority.

Current mainstream medical approaches emphasize therapeutic lifestyle intervention combined with regular medication for glucose, lipid, and blood pressure

control. However, no effective multi-target, multi-link pharmacological treatments specifically for MetS exist. These regimens demand high patient compliance, prove difficult to maintain long-term, and impose substantial economic burdens, necessitating further exploration of effective MetS interventions.

Traditional Chinese medicine classifies MetS symptoms under categories including "obesity," "thirst disease," "fullness," and "spleen heat." Numerous clinical practices have employed herbal extracts, formulas, and acupuncture for MetS treatment. Academician Tong Xiaolin proposed a four-stage MetS progression (stagnation, heat, deficiency, and damage) and suggested using Xiaoxianxiong Decoction to regulate phlegm-heat intermingling, with additions of Clematis, red yeast rice, and mulberry components to reduce lipids, glucose, and uric acid [5]. Han Xiao et al. [6] applied acupuncture combined with tuina guided by "channel-dredging and organ-regulating" principles for liver-stomach heat stagnation-type MetS, finding reductions in both laboratory indices and waist circumference.

Our research group, guided by the TCM concept of "preventive treatment," considers yin deficiency with internal heat as a critical pathological stage and important syndrome pattern in MetS development. Building upon preliminary research and clinical experience, we employed Gehu Tiaozhi Decoction for MetS patients with yin deficiency and internal heat syndrome. Through this randomized controlled trial, we compared waist circumference, body weight, body fat percentage, and lipid levels to evaluate the efficacy and safety of Gehu Tiaozhi Decoction, aiming to provide theoretical and clinical guidance for TCM treatment of MetS.

Methods

Study Design and Participants

From June 2021 to November 2022, 84 patients meeting MetS criteria were prospectively recruited from outpatient and inpatient services at LongHua Hospital Shanghai University of Traditional Chinese Medicine. Using SPSS 25.0 with a specified random seed, subjects were randomly allocated in a 1:1 ratio to the Gehu group (42 cases) and control group (42 cases). Medications were dispensed according to patient visit sequence and drug numbers, which remained constant throughout the study.

Ethics Approval

This study was registered with the Chinese Clinical Trial Registry (Registration No.: CHICTR190002685) and approved by the hospital's internal ethics committee (Approval No.: SHDC12019X16). All participants provided informed consent.

Inclusion Criteria

(1) Aged 18-75 years, both sexes; (2) Met Western diagnostic criteria for MetS and TCM syndrome differentiation of yin deficiency with internal heat; (3) Voluntary signed informed consent with commitment to follow study procedures.

Exclusion Criteria

(1) Pregnant or lactating women; (2) Severe hepatic or renal disease or major cardiovascular/cerebrovascular disease; (3) Allergy to intervention drugs or allergic constitution; (4) Poor compliance or psychiatric disorders; (5) Secondary obesity from hypothyroidism, hypothalamic disease, postmenopausal obesity, polycystic ovary syndrome, or drug-induced obesity.

Diagnostic Criteria

Western Medicine Criteria: Based on the *Chinese Guidelines for the Prevention and Treatment of Type 2 Diabetes (2020 Edition)* [7] and *Chinese Adult Weight Determination* [8]: (1) Central obesity: waist circumference $ $85 cm (female) or $ $90 cm (male); (2) Hyperglycemia: fasting glucose $ $6.1 mmol/L or 2-hour post-load glucose $ $7.8 mmol/L and/or diagnosed diabetes; (3) Hypertension: blood pressure $ $130/85 mmHg (1 mmHg=0.133 kPa) and/or antihypertensive treatment; (4) Fasting triglycerides $ $1.70 mmol/L; (5) Fasting HDL-C <1.04 mmol/L. MetS diagnosis required $ $3 of these 5 criteria.

TCM Criteria: Based on the *Guiding Principles for Clinical Research of New Chinese Medicines* [9], yin deficiency with internal heat syndrome was defined as: Main symptoms: obesity, dry throat and mouth, polyphagia with easy hunger; Secondary symptoms: thirst with desire for cold drinks, five-center heat, palpitations with insomnia, dry stools, scanty dark urine; Tongue and pulse: red tongue with scanty coating, thin pulse. Diagnosis required $ $1 main symptom, 1-2 secondary symptoms, and basic correspondence of tongue and pulse.

Intervention

The Gehu group received Gehu Tiaozhi Decoction granules (Dendrobium officinale 6 g, Pueraria lobatae radix 6 g) orally twice daily on an empty stomach, one bag per dose, for 8 weeks. The control group received placebo granules with identical administration. Both groups received identical health education including dietary plans and exercise prescriptions. Both granules were manufactured by Sichuan Neo-Green Pharmaceutical Technology Development Co., Ltd.

Outcome Measures

Efficacy Indicators: (1) Waist circumference (WC): measured before and after treatment with feet separated 25-30 cm, standing upright, at the midpoint between the highest point of bilateral iliac crests and the lowest point of the bony thorax; (2) Body weight, BMI, and BFP: measured using Japanese TANITA Innerscan BC-310; (3) Laboratory indices: FBG, TC, TG, LDL-C, HDL-C, with pre- and post-treatment differences recorded.

Safety Indicators: Liver and kidney function, serum electrolytes, blood routine, urine routine, and 12-lead ECG were examined before and after treatment, with adverse events monitored throughout.

Statistical Analysis

SPSS 25.0 analyzed all data. Normally distributed continuous variables were expressed as (x-±s), while skewed distributions used M(QR). Between-group comparisons of normally distributed data employed independent samples t-test or t'-test (for unequal variances); skewed data used Wilcoxon rank-sum test. Categorical data were compared using ^{2} test. Two-sided α was set at 0.05, with P<0.05 considered statistically significant.

Results

Baseline Characteristics

During the 8-week intervention, one participant from each group failed to complete follow-up due to domestic COVID-19 impacts, leaving 41 cases per group. The Gehu group comprised 20 males and 21 females with mean age (54.8$±12.3)$years; the control group had 21 males and 20 females with mean age (56.5±12.3)$years. No statistically s
P=0.825; t=-0.610, P=0.544).

WC, Body Weight, BMI, and BFP

No statistically significant baseline differences were found between groups for WC, body weight, BMI, or BFP (P>0.05). However, between-group differences in pre-post treatment changes for WC, body weight, BMI, and BFP were statistically significant (P<0.05) .

Lipid Profile and FBG

No statistically significant baseline differences existed for TG, TC, HDL-C, LDL-C, or FBG (P>0.05). Between-group differences in pre-post treatment changes for TG, TC, and FBG were statistically significant (P<0.05) .

Safety Assessment

No abnormalities were observed in ECG, routine blood/urine/stool tests, or liver and kidney function before or after treatment. No serious adverse events occurred during treatment or follow-up, indicating good safety profiles for Gehu Tiaozhi granules.

Discussion

Our results demonstrate that after 8 weeks, Gehu Tiaozhi Decoction produced superior outcomes compared to placebo, significantly improving WC, body weight, BMI, BFP, TG, TC, and FBG with favorable clinical safety.

Although MetS clinical symptoms are often subtle, underlying metabolic disturbances are already present, making early diagnosis and treatment crucial for prevention. Traditional Chinese medicine emphasizes holistic concepts, preventive treatment, and "treating different diseases with the same method," enabling comprehensive regulation of systemic metabolic disorders to delay complications. Contributing factors include improper diet, smoking, alcohol consumption, sedentary lifestyle, emotional disturbances, constitutional deficiencies, and kidney essence depletion.

Through long-term clinical observation, we identified a common syndrome pattern in early-to-mid-stage MetS patients characterized by obesity, polyphagia with easy hunger, dry throat and mouth, thirst with preference for cold drinks, five-center heat, and dry stools—representing the "yin deficiency with internal heat" pathological stage. Gehu Tiaozhi Decoction consists of two herbs with extensive historical use, high safety profiles, and proven therapeutic value. Modern pharmacological research confirms their weight-reducing, lipid-lowering, and glucose-regulating effects.

Pueraria lobatae radix is sweet and cool, entering the spleen, stomach, and lung meridians, elevating clear yang qi, generating fluids, relieving thirst, dispelling muscle heat, and unblocking collaterals. Containing puerarin, daidzein, and daidzin, puerarin exhibits vasoactive properties with clear advantages in lipid and blood pressure regulation, possibly related to enhanced endothelin and nitric oxide levels [11]. Puerarin improves insulin sensitivity in rat models, preventing MetS progression [12]. Xiang Fang [13] demonstrated that puerarin injection reduced lipids and blood pressure in 63 MetS patients while serving as an excellent insulin sensitizer.

Dendrobium officinale is sweet and cold, entering the stomach and kidney meridians, nourishing stomach yin, generating fluids, and clearing deficiency heat. Rich in polysaccharides, alkaloids, polyphenols, amino acids, trace elements, and bibenzyl compounds, it reduces serum lipids and aortic plaque deposition in high-fat/high-cholesterol-fed ApoE mice, suppressing TNF-α and IL-6 expression to attenuate atherosclerotic injury [14]. *Dendrobium officinale* polysaccha-

rides regulate cellular insulin sensitivity and improve abnormal lipid metabolism via PPAR-γ [15]. Administration of *Dendrobium officinale* dietary fiber for 11 weeks effectively alleviated obesity, inflammation, and oxidative stress in high-fat diet-fed mice [16]. Overall, *Dendrobium officinale* modulates apoptosis signaling pathways and improves inflammatory status to reduce lipids and glucose [17].

Chinese herbal formulas exert therapeutic effects through multi-level, multi-target mechanisms [18]. For this syndrome pattern, Professor Zhou Shigao, a renowned TCM physician at LongHua Hospital, selected *Pueraria lobatae radix* combined with *Dendrobium officinale* to synergistically nourish yin, clear heat, generate fluids, and relieve thirst—precisely matching the characteristics of MetS with yin deficiency and internal heat syndrome.

In summary, this study confirms the efficacy of Gehu Tiaozhi Decoction for MetS patients, particularly in improving WC, body weight, BFP, and select lipid parameters. However, this study focused primarily on these anthropometric and metabolic indices without exploring additional markers such as insulin function or inflammatory cytokines. The relatively small sample size, single syndrome pattern focus, limited statistical power, and absence of other TCM syndrome types represent study limitations. Additionally, the short observation period cannot adequately reflect long-term efficacy and prognosis. Future research should employ in vivo and in vitro studies to further elucidate mechanisms and potential targets, alongside more rigorous, in-depth, large-sample, high-quality randomized controlled trials or real-world studies to provide additional theoretical support for clinical application.

Author Contributions: Zheng Rong drafted the manuscript and performed statistical analysis; Zheng Rong, Liu Zhidong, and Chen Junlan collected and organized data; Wang Miao conducted study implementation and feasibility analysis; Zhang Xiao designed the study protocol; Zhou Shigao revised the manuscript and is responsible for overall supervision and management.

Conflict of Interest: This article has no conflict of interest.

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Note: Figure translations are in progress. See original paper for figures.