

## Original Paper

# The Value of Combining Wu Ling San Plus and Minus with Repaglinide in the Treatment of Obese Type 2 Diabetes

Mingxuan Wang<sup>2\*</sup>, Huijie Yin<sup>3</sup>, Haitao Li<sup>2</sup>, Penghua Fang<sup>1</sup> & Wenxuan Wu<sup>1</sup>

<sup>1</sup> The First College of Clinical Medicine, Nanjing University of Traditional Chinese Medicine, Nanjing 210023, China

<sup>2</sup> College of Pharmacy, Nanjing University of Traditional Chinese Medicine, Nanjing 210023, China

<sup>3</sup> School of Chinese Medicine, School of Integrated Chinese and Western Medicine, Nanjing University of Traditional Chinese Medicine, Nanjing 210023, China

\* Corresponding author.

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### Abstract

**Objective:** To investigate the clinical value and practical effects of the treatment of obese type 2 diabetes mellitus patients with Wu Ling San plus and minus combined with Repaglinide. **Methods:** Twenty-two obese type 2 diabetic patients attending the outpatient clinic of Yixing Traditional Chinese Medicine Hospital from September 2020 to March 2022 were randomly selected as the subjects of this study, and all of them were divided into treatment group (n=11, Wu Ling San plus and minus + Repaglinide) and control group (n=11, single Repaglinide) according to the computerized random series grouping method. The clinical data and overall efficacy of the two groups were compared. **Results:** After treatment, the treatment group had better blood glucose, blood lipids and other basic indicators than the control group ( $P<0.05$ ); all Chinese medicine symptoms scores and complication rates of the treatment group were lower than those of the control group ( $P<0.05$ ). **Conclusion:** The treatment of obese type 2 diabetes mellitus patients with Wu Ling San plus reduction + Repaglinide has significant efficacy and high drug safety, and can stabilize many indicators of blood glucose and blood lipids, reduce the risk of complications and control their body weight, which can be promoted and used in the treatment of related clinical conditions.

### Keywords

Wu Ling San, Repaglinide, Obese type 2 diabetes mellitus

## 1. Introduction

Obesity type 2 diabetes mellitus (T2DM) is the most prevalent form of diabetes and is associated with polygenic genetics, environment and insulin resistance in the body (Kong, 2020). Clinical medicine generally advocates the use of pharmacological control of this condition, supplemented by nutrition and moderate exercise, to treat obese T2DM, while also regulating blood pressure, lipid levels and restoring platelet function (Yu, 2020). Reglanet is generally used clinically for the treatment of obese T2DM, however, although it is effective, it is not optimal. To further improve the overall treatment effect, it was decided to add Wu Ling San to the Reglanet drug therapy. In order to study the clinical efficacy of using Wu Ling San with addition + Repaglinide in the treatment of obese T2DM patients, the results of the study are reported as follows.

## 2. Materials and Methods

### 2.1 General Information

Twenty-two patients with obese T2DM who attended the outpatient clinic of Yixing Traditional Chinese Medicine Hospital between September 2020 and March 2022 were randomly selected as the subjects of this study, and all of them were divided into treatment group and control group based on computerized random series grouping, 11 cases/group. The number of patients in the control group was male/female = 5/6, age 42-79 years, mean ( $58.03 \pm 2.47$ ) years, disease period 3-5 years, mean ( $3.24 \pm 0.76$ ) months, height 1.53- 1.78m, mean ( $1.61 \pm 0.02$ ) m, weight 61.90- 121.50kg, mean ( $160.00 \pm 2.90$ ) kg. Number of male/female patients in the treatment group = 7/4, age 45-80 years, mean ( $60.09 \pm 2.41$ ) m, disease period 2-4 years, mean ( $2.68 \pm 0.32$ ) months, height  $1.50 \pm 1.92$  m, mean ( $1.63 \pm 0.02$ ) m, weight 65.00- 136.00 kg, mean ( $161.00 \pm 5.80$ ) kg. The study was reviewed and agreed by the Medical Ethics Committee of Yixing Traditional Chinese Medicine Hospital, and all obese T2DM patients and their families were informed of the purpose, methods and related procedures of the study, and all signed the consent form and the informed consent form, and voluntarily participated in the subject study. The differences between the above two groups of case information were small and negligible ( $P > 0.05$ ).

Inclusion criteria: 1) Patients with obese T2DM with appropriate clinical symptoms and sound medical records; 2) Patients with no abnormalities in cardiac, renal or liver function; 3) Patients with no comorbidities of other organs of the body; 4) Patients who were not taking other weight loss drugs that would affect the results of this study before the study was conducted; 5) Patients with no genetic or psychiatric disorders.

Exclusion criteria: (i) patients with T1DM; (ii) patients with secondary metabolic syndrome, various infections or tumour lesions; (iii) patients with poor compliance and unable to cooperate with treatment and care; (iv) patients with incomplete follow-up data and at risk of discontinuing the study; (v) patients who are pregnant or breastfeeding.

Diagnostic criteria: (1) Western medicine: (a) Refer to the Asian adult body mass index grading standards: overweight BMI  $\geq 24$  kg/m<sup>2</sup>, obese BMI  $\geq 28$  kg/m<sup>2</sup>; for abdominal obesity: waist circumference  $\geq 90$  cm (male), waist circumference  $\geq 85$  cm (female) having either of the above conditions can confirm the diagnosis; (b) Meet the corresponding T2DM clinical diagnostic criteria. (2) Chinese medicine: those who meet the relevant diagnostic criteria for obese T2DM as described in the Internal Medicine of Chinese Medicine. (3) Chinese medicine: those who meet the diagnostic criteria for obese T2DM as described in the Internal Medicine of Traditional Chinese Medicine, and who also meet the corresponding symptomatic manifestations. Secondary symptoms: fatigue, swelling of the limbs, stuffiness of the abdomen and stomach, light in the morning and heavy at night, marked after fatigue, normal or little food, previous history of overeating, reduced urine output, poor urination, loose stools, constipation; pale tongue, thin, white and greasy coating, teeth marks on the sides, weak pulse. The diagnosis is confirmed by the presence of any two of the above main symptoms or any one of the main symptoms and two secondary symptoms, and the tongue and pulse are compatible.

## 2.2 Methodology

Patients in the control group were treated with Repaglinide tablets (Vulaid/Hausen) alone, manufactured by Jiangsu Hausen Pharmaceutical Group Co. Repaglinide tablets are usually administered orally 15-30 min before a main meal as prescribed and produce a pro-insulin response within 30 min. The exact dose depends on the actual disease progression and the level of blood glucose indicators in obese T2DM patients. Generally, the initial dose is 0.5 mg, which can be adjusted on a weekly or 2-weekly basis, but the maximum daily dose should not exceed 16 mg.

The treatment group is based on the control group with the addition and subtraction of Wu Ling San. The formula combination of Wu Ling San is: 30g of smallpox powder, 20g of poria, 15g each of yam, northern sage and coix seed, 10g each of maitong, atracylodes and zedoary, 8g each of gui zhi and pig ling, and 6g of raw licorice. For patients with blood stasis, 10g of Rhizoma Chuanxiong and 10g of Radix Salviae Miltiorrhiza; for patients with Yang deficiency, 10g of Radix Astragali and 15g of Radix Codonopsis Pilosulae; for patients with liver fire, 10g of Danpi and 10g of Gardenia; the above formula should be taken after decoction with water, 1 dose/day, 1 dose in two portions, taken in the morning and in the evening respectively, while paying attention to the patient's diet and moderate outdoor exercise training during taking the medicine, the whole treatment cycle is 2 months.

## 2.3 Observation Indicators

(1) To compare the condition of body indexes in the two groups. (a) Blood glucose: fasting blood glucose FPG, 2h postprandial blood glucose 2h FPG, glycosylated haemoglobin HbA1c; (b) Blood lipids: total cholesterol TC, triglyceride TG, HDL-C, LDL-C; (c) Basic indexes: body mass index BMI, waist-hip ratio, etc.

(2) The TCM evidence scores of the two groups were recorded and analysed, following the Guidelines for Clinical Research on New Chinese Medicines and applying the semi-quantitative point method, before and after treatment, respectively, with reference to normal, mild, moderate and severe

discomfort symptoms, scoring 0- 2-4-6 for the main symptoms and 0- 1-2-3 for the secondary symptoms.

(3) Compare and analyse the complications of the two groups, such as hypertension, cardiovascular disease, cerebrovascular disease, hypoglycaemia and several others.

#### 2.4 Statistical Analysis

The data from this experiment were statistically analysed using SPSS 21.0 statistical software. The measurement data were calculated using ( $\bar{x} \pm s$ ) and the t-test was used to account for the results; the count data were expressed as a percentage (%) and the results were calculated using the  $\chi^2$  test. If  $P < 0.05$ , then there is a significant difference between the experimental studies and the results are clinically significant.

### 3. Results

#### 3.1 Comparing the Two Groups of Organismal Indicators

After treatment, the organism indexes such as TC, TG, LDL-C, FPG, 2hFPG and HbA1c decreased in both groups ( $P < 0.05$ ), while the level of HDL-C indexes increased ( $P < 0.05$ ), and the overall level of organism indexes in the treatment group was better than that in the control group ( $P < 0.05$ ), as detailed in Table 1 below.

**Table 1. Comparison of the Levels of Organismal Indicators between the Two Groups ( $\bar{x} \pm s$ )**

Relevant indicators (n=11)		Treatment group	Control group	<i>t</i>	<i>P</i>
Blood	FPG/mmol/L	5.12 $\pm$ 1.34	6.61 $\pm$ 1.28	2.667	0.014
	2hFPG/mmol/L	7.22 $\pm$ 1.46	9.35 $\pm$ 1.54	3.329	0.003
sugar	HbA1c/%	6.13 $\pm$ 0.20	7.67 $\pm$ 0.54	8.870	0.001
Blood lipids	TC/mmol/L	5.21 $\pm$ 0.37	5.85 $\pm$ 0.60	3.011	0.007
	TG/mmol/L	1.42 $\pm$ 0.36	2.65 $\pm$ 0.24	9.429	0.001
	HDL-C/mmol/L	1.74 $\pm$ 0.30	1.25 $\pm$ 0.36	3.468	0.002
	LDL-C/mmol/L	2.03 $\pm$ 0.51	2.49 $\pm$ 0.30	2.578	0.018
	BMI/kg/m <sup>2</sup>	24.16 $\pm$ 1.09	26.43 $\pm$ 1.22	4.602	0.001
Basic indicators	Waist-to-hip ratio	0.74 $\pm$ 0.06	0.95 $\pm$ 0.09	6.439	0.001

#### 3.2 Comparing the TCM Evidence Points of the Two Groups

Before treatment, there was no significant difference between the two groups ( $P > 0.05$ ); after treatment, all the TCM symptoms scores in the treatment group were lower than those in the control group ( $P < 0.05$ ), as shown in Table 2 below.

**Table 2. Comparison of TCM Evidence Points between the Two Groups [(x±s), Points]**

Group (n=11)		Treatment group		Control group	
		Before	After	Before	After
		treatment	treatment	treatment	treatment
Main symptoms	Body fat	5.41±0.23	2.08±0.32 <sup>1</sup>	5.15±2.53	2.62±0.34
	Enlarged abdomen	4.22±0.46	1.01±0.26 <sup>2</sup>	4.17±2.30	1.42±0.37
Secondary symptoms	Feeling tired and battered	2.53±0.39	0.17±0.35 <sup>3</sup>	2.58±0.52	0.62±0.44
	Heavy body weight	2.35±0.54	0.26±0.16 <sup>4</sup>	2.26±0.45	0.81±0.23
	Stiffness in the abdomen	2.52±0.64	0.37±0.23 <sup>5</sup>	2.36±0.42	0.76±0.42
	Swollen extremities	2.42±0.27	0.42±0.30 <sup>6</sup>	2.12±0.37	0.85±0.53
	Nerds	2.42±0.27	0.36±0.42 <sup>7</sup>	2.27±0.43	0.84±0.60
	Urination	2.53±0.39	0.12±0.37 <sup>8</sup>	2.20±0.79	0.61±0.53
	Poop	2.41±0.23	0.23±0.33 <sup>9</sup>	2.15±0.53	0.63±0.18

Note. <sup>1</sup>, <sup>2</sup>, <sup>3</sup>, <sup>4</sup>, <sup>5</sup>, <sup>6</sup>, <sup>7</sup>, <sup>8</sup> indicates that the two groups were compared between groups after treatment,  $t1 = 3.836$ ,  $P1 < 0.001$ ,  $t2 = 3.007$ ,  $P2 = 0.007$ ,  $t3 = 2.655$ ,  $P3 = 0.015$ ,  $t4 = 6.511$ ,  $P4 < 0.001$ ,  $t5 = 2.701$ ,  $P5 = 0.013$ ,  $t6 = 2.342$ ,  $P6 = 0.029$ ,  $t7 = 2.438$ ,  $P7 = 0.024$ ,  $t8 = 2.514$ ,  $P8 = 0.020$ ,  $t9 = 3.529$  and  $P9 = 0.002$ .

### 3.3 Comparison of Complications between the Two Groups

The treatment group had a lower complication rate than the control group ( $p < 0.05$ ), as detailed in Table 3 below.

**Table 3. Comparison of Complication Rates between the Two Groups [n (%)]**

Group	Number of examples	Hypertensive disorders	Cardiovascular disease	Cerebrovascular disease	Hypoglycemia	Incidence (%)
Treatment group	11	0 (0.00)	1 (9.09)	1 (9.09)	0 (0.00)	2 (18.18)
Control group	11	1 (9.09)	2 (18.18)	2 (18.18)	2 (18.18)	7 (63.64)
$\chi^2$						5.310
$P$						<0.05

## 4. Discussion

With the improvement of public quality of life, more and more people prefer to consume high-calorie, high-fat and high-protein food, therefore the number of obese people is gradually increasing, and the number of patients with obese T2DM is also increasing (Guo, 2020). In China, the prevalence of T2DM is very high. According to clinical statistics, at least 20 million of the 80 million people with DM have T2DM, and 70-80% of T2DM patients are overweight or obese (Zheng, 2020).

At present, the main clinical use of Reglanet tablets is in the treatment of obese T2DM. Repaglinide is a non-sulphonylurea insulinotropic agent that has a rapid response and is easily absorbed. It acts rapidly on the patient's beta cells in a short period of time to stimulate insulin secretion, resulting in a significant reduction in postprandial blood glucose (Yao, Huang, Li, et al., 2020). Repaglinide can be used alone or in combination with other clinical hypoglycaemic agents.

Wu Ling San is a Chinese medicinal preparation commonly used in clinical practice. It has the effect of helping Yang to transform Qi, promoting dampness and moving water, and can significantly relieve swelling caused by Yang's failure to transform Qi and internal stagnation of water and dampness, as well as reduced urine output, poor urination, loose stools and constipation (Gao, Lv, Ma, et al., 2021). The Chinese medicinal preparation is safe and has no significant side effects. After treatment, the patient's clinical symptoms are rapidly relieved, resulting in stable blood lipids and blood glucose and improved insulin resistance. The patient's clinical discomfort was quickly relieved after treatment, resulting in stable blood lipids and blood glucose and improved insulin resistance.

The results of this study showed that after treatment, the treatment group had better blood glucose, blood lipids and other basic indexes than the control group ( $P < 0.05$ ); the scores of Chinese medicine symptoms in the treatment group were lower than those in the control group for both primary and secondary symptoms ( $P < 0.05$ ); and the incidence of complications such as hypertension, cardiovascular disease, cerebrovascular disease and hypoglycemia were lower in the treatment group than in the control group ( $P < 0.05$ ). This study was in high agreement with the results of Zhu (2022) and Liu (2021) studies. It can be seen that the combination of Chinese medicine agents and Western medicine agents can effectively control the development of obese T2DM patients, while speeding up the recovery of the body's pancreatic function, improving insulin resistance and returning blood glucose and lipid levels to the normal range.

In conclusion, the use of Wu Ling San + Repaglinide in the treatment of obese T2DM patients has shown remarkable results in stabilizing blood glucose and blood lipids, reducing body mass index and waist-to-hip ratio, preventing exacerbation of the disease and preventing the development of chronic complications and comorbidities of DM.

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