

## **Curative effect of traditional Chinese medicine combined with metformin hydrochloride on diabetes and its effect on TNF- $\alpha$ , MCP-1 and NO.**

**Wei Li, Mingmin Wang, Wei Wu, Yunyun Bai, Qingxi Wang\***

Sixth People's Hospital of Qingdao, No. 9, Fushun Road, Qingdao, PR China

### **Abstract**

**Objective:** To analyse the curative effect of traditional Chinese medicine combined with metformin hydrochloride on diabetes and its effect on TNF- $\alpha$ , MCP-1 and NO.

**Methods:** 80 cases of diabetics who were treated at XX hospital from January of 2014 to January of 2015 were chosen as research subjects, according to random indicator method divided into control group and experimental group with 40 cases in each group. The patients in the control group were treated with metformin hydrochloride alone, and the patients in the experimental group received Chinese medicine combined with metformin hydrochloride. To compare the TCM syndrome points, Fasting Blood Glucose (FBG) and 2 h postprandial blood glucose (2 h PG), Fasting Insulin (FINS) and 2 h postprandial insulin (2 h INS) levels of two groups of patients before and after the implementation of treatment, at the same time observing the levels of TNF- $\alpha$ , MCP-1 and NO before and after treatment.

**Results:** After treatment, the TCM syndromes in the experimental group were significantly better than those in the control group ( $P < 0.05$ ), and FBG, 2 h PG, FINS, 2 h INS were significantly lower than those in the control group ( $P < 0.05$ ), as same as the levels of TNF- $\alpha$ , MCP-1 and NO.

**Conclusion:** Chinese Medicine combined with metformin hydrochloride tablets can effectively treat diabetes and reduce the concentration of TNF- $\alpha$ , MCP-1 and NO in the blood.

**Keywords:** Traditional Chinese medicine, Metformin hydrochloride, Diabetes.

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### **Introduction**

Diabetes is a metabolic disease characterized by high blood sugar. Hyperglycemia is caused by insulin-secretion or biological damage, or both. Diabetes and high blood sugar can lead to chronic damage and dysfunction of some tissues, especially the eyes, kidneys, heart, blood vessels, and nerves. At present the main treatment method of diabetes oral glucose-lowering drugs which can reduce blood sugar. Metformin is the most commonly used first-line drugs, mainly by reducing liver glycolysis [1], the inhibition of intestinal mucosa cells to absorb glucose give play to the role of hypoglycemic, which has definite curative effect on treatment of diabetes [2]. For the treatment of diabetes, hypoglycemic drug treatment effect is not ideal, and long-term use of the effect will be reduced [3], so there is still lack of effective treatments [4]. In this study, a combination of metformin hydrochloride and metformin hydrochloride was used to investigate the effect of metformin in the treatment of diabetes mellitus and the influence of TNF- $\alpha$ , McP-1 and NO concentration in the blood.

### **Materials and Methods**

#### **General information**

Ethical approval was given by the medical ethics committee of Sixth People's Hospital of Qingdao with the following reference number: 2015006, 80 patients with diabetes in XX hospital between January 2014 and January 2014 were selected as the research object, In accordance with the table method randomly divided all the research object into two groups, control group and experimental group, respectively, 40 cases in each group. In the control group, the treatment of metformin hydrochloride was made in the experimental group. There were 21 males and 19 females in the control group, aged 35 to 62 y, with an average of  $(43.35 \pm 5.12)$  y. In the observation group, 23 cases of males and 17 cases of female, age 38 to 69 y old, the average  $(55.16 \pm 5.36)$  y of age. By comparison, there was no statistically significant difference between the two groups in terms of gender, age, and other general data ( $P > 0.05$ ).

#### **Standard of diagnosis**

Diagnosis standard reference pacing "internal medicine" [5] (7<sup>th</sup> edition) in the relevant diagnostic criteria for type 2 diabetes: Fasting Blood Glucose (FBG)  $\geq 7.0$  mmol/L, or

patients with postprandial blood glucose 2 h (2 h PBG)  $\geq$  11.1 mmol/L.

### Inclusion and exclusion criteria

**Inclusion criteria:** 1. voluntary participation in this study and the signing of informed consent to diabetes. 2. To be able to be followed the doctor's advice.

**Exclusion criteria:** 1. pregnant or lactating women. 2. Patients who are allergic to all drug. 3. The liver, kidney and other functional insufficiency. 4. Patients should not strictly follow the prescribed medicine. 5. The researchers suggest that others are not suitable for this test.

### Therapeutic method

Control group adopts pure metformin hydrochloride enteric-coated metformin hydrochloride treatment (Guizhou Cheonan pharmaceutical co., LTD., approved by H52020960), 0.25 g/time, 2 times/d, continuous treatment of 12 w. Prescriptions on the basis of the experimental group in the control group used traditional Chinese medicine. Medicinal: 10 g each Fructus cnidii, lotus seed, dogeood, and cortex dictamni, 30 gram each bitter cardamon, mulberry, radix astragali preparata, Chinese yam and caulis Ionicerae, 15 g of white poria, gallnut and chicken's gizzard-membrane each 6 g, notoginseng powder 3 g. Water decoction, one dose per day, continuous treatment for 12 w.

### Score of TCM symptom

**Main symptoms:** polydipsia, polyuria, polyphagia. Accompanied by: mouth parched and tongue scorched, dry stool, skin itching, vexation, reddened tongue with yellow fur, soreness and weakness of the waist and knees, cold intolerance, emaciated body, weary-looking. The above main symptoms were graded in terms of weight (6 points), middle (4 points), light (2 points) and no (0 points). The symptoms were graded by weight (3 points), middle (2), light (1), and no (0 points).

### Observation target

1) Two groups of patients before and after the treatment of TCM syndrome integral change. 2) before and after treatment, two groups of patients with Fasting Blood Glucose detection (FBG) and 2 h postprandial blood glucose (2 h PG) level changes [5], blood glucose was detected by rapid blood glucose meter. 3) two groups of patients before and after treatment of Fasting Insulin, (FINS) and 2 h after a meal insulin (2 h insulin, 2 h INS) level change [5]. 4) two groups of patients before and after treatment was evaluated by blood TNF- $\alpha$ , MCP-1, NO change, by using enzyme-linked immunosorbent determination of human serum.

### Statistical method

The statistical software SPSS19.0 was used for statistical analysis of all the data obtained. The measurement data was

calculated  $\bar{x} \pm s$  as a representation. The test method was used for t-test, and the test standard was  $P < 0.05$ .

## Results

### The change of TCM syndrome scoring

Two groups of patients before treatment of TCM syndrome integral was not statistically significant ( $P > 0.05$ ), two groups of patients before treatment after treatment of TCM syndrome integral and there was a significant difference ( $P < 0.05$ ), and using the combined treatment of traditional Chinese medicine of TCM syndrome integral experimental group patients was significantly lower than pure metformin hydrochloride treatment of the control group ( $P < 0.05$ , Table 1).

**Table 1.** Before and after treatment of two groups of patients TCM syndrome points ( $\bar{x} \pm s$ ).

|                    | Numbers | Before treatment | After treatment     | t           | P          |
|--------------------|---------|------------------|---------------------|-------------|------------|
| Control group      | 40      | 22.15<br>12.36   | $\pm$ 16.24<br>8.13 | $\pm$ 3.233 | $P < 0.05$ |
| Experimental group | 40      | 23.21<br>11.05   | $\pm$ 10.45<br>3.61 | $\pm$ 6.370 | $P < 0.05$ |
| t                  |         | 0.155            | 5.482               |             |            |
| P                  |         | $P < 0.05$       | $P < 0.05$          |             |            |

### FBG and 2 h PG level changes

Before the treatment, two groups of patients with FBG and 2 h PG difference was not significant ( $P > 0.05$ ). After treatment, the level of FBG and 2 h PG was significantly lower than before treatment ( $P < 0.05$ ), and the experimental group the patient's level of FBG and 2 h PG significantly lower than the control group patients ( $P < 0.05$ , Table 2).

**Table 2.** Before and after treatment of two groups of patients FBG and 2 h PG levels ( $\bar{x} \pm s$ ).

|                    | Numbers | Difference       | FBG                           | 2 h PG                        |
|--------------------|---------|------------------|-------------------------------|-------------------------------|
| Control group      | 40      | Before treatment | 9.71 $\pm$ 3.11               | 13.95 $\pm$ 3.74              |
|                    |         | After treatment  | 8.22 $\pm$ 1.53 <sup>#</sup>  | 11.04 $\pm$ 2.96 <sup>#</sup> |
| Experimental group | 40      | Before treatment | 9.63 $\pm$ 3.46               | 14.25 $\pm$ 2.85              |
|                    |         | After treatment  | 7.47 $\pm$ 1.48 <sup>#*</sup> | 8.39 $\pm$ 3.18 <sup>#*</sup> |

Note: compared with the patients before treatment, <sup>#</sup> $P < 0.05$ . Compared with the control group, <sup>\*</sup> $P < 0.05$

### FINS and 2 h INS horizontal changes

Two groups of patients before treatment FINS and 2 h INS level were no obvious difference ( $P > 0.05$ ), two groups of patients after treatment of FINS and 2 h ins levels were

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significantly lower than before treatment ( $P < 0.05$ ), and the experimental group the patient's level of FINS and 2 h INS significantly lower than the control group patients ( $< 0.05$ , Table 3).

**Table 3.** Before and after treatment of two groups of patients FINS and 2 h INS levels ( $\bar{x} \pm s$ ).

|                    | Numbers | Difference       | FINS                          | 2 h INS                       |
|--------------------|---------|------------------|-------------------------------|-------------------------------|
| Control group      | 40      | Before treatment | 12.16 $\pm$ 1.21              | 14.32 $\pm$ 1.48              |
|                    |         | After treatment  | 10.23 $\pm$ 1.49 <sup>#</sup> | 12.12 $\pm$ 1.34 <sup>#</sup> |
| Experimental group | 40      | Before treatment | 12.22 $\pm$ 1.13              | 14.25 $\pm$ 1.85              |
|                    |         | After treatment  |                               |                               |

**Table 4.** Before and after treatment of two groups of patients TNF- $\alpha$ , MCP-1, NO levels ( $\bar{x} \pm s$ ).

|                    | Numbers | Difference       | TNF- $\alpha$                    | MCP-1                            | NO                               |
|--------------------|---------|------------------|----------------------------------|----------------------------------|----------------------------------|
| Control group      | 40      | Before treatment | 403.15 $\pm$ 21.61               | 444.72 $\pm$ 13.67               | 0.743 $\pm$ 0.023                |
|                    |         | After treatment  | 276.51 $\pm$ 19.36 <sup>#</sup>  | 309.56 $\pm$ 13.21 <sup>#</sup>  | 0.606 $\pm$ 0.027 <sup>#</sup>   |
| Experimental group | 40      | Before treatment | 412.48 $\pm$ 20.72               | 424.92 $\pm$ 12.34               | 0.718 $\pm$ 0.015                |
|                    |         | After treatment  | 135.82 $\pm$ 16.32 <sup>#*</sup> | 239.42 $\pm$ 11.97 <sup>#*</sup> | 0.0509 $\pm$ 0.018 <sup>#*</sup> |

Note: compared with the patients before treatment, <sup>#</sup> $P < 0.05$ ; Compared with the control group, <sup>\*</sup> $P < 0.05$

**Conclusion**

Diabetes has a higher incidence in our country especially among obese people. Traditional treatments rely on glucose-lowering drugs such as metformin hydrochloride to control blood sugar levels and weight loss. But simply by increasing the dosage of metformin hydrochloride to control the rise in blood sugar, it is easy to cause the drug resistance of the body and affect the therapeutic effect. And it is not ideal to rely solely on western medicine. Diabetes in patients with type 2 diabetes in the normal insulin secretion and self-adjustment disorder, and the ability to influence of lipid and protein metabolism, prone to metabolic disorders, and increased risk of diabetes complicated with lipid and protein metabolism lesions [6].

Diabetes is a kind of “quenching thirst” in TCM syndrome differentiation, which is considered to be the pathological basis of diabetes. The function of spleen and renal is transport water and essence of water and grain, so the spleen kidney deficiency, the unfavorable transportation is the disease machine key of diabetes [7-10]. The transformation of the spleen is dependent on the driving effect of qi, and the spleen deficiency cannot be transported, resulting in the blood glucose rising in the blood. The physiological function of the spleen in traditional medicine actually covers the physiological function of the pancreas, while the changes of pancreas belong to the pathological changes of the spleen, essentially is the pathogenesis of collateral of pixu (spleen deficient). Antibacterial anti-inflammatory in this prescription, bacteria resistance and bacteriostasis of Fructus cnidii, restrain the

After treatment 9.46  $\pm$  0.87<sup>#\*</sup> 10.23  $\pm$  1.52<sup>#\*</sup>

Note: compared with the patients before treatment, <sup>#</sup> $P < 0.05$ . Compared with the control group, <sup>\*</sup> $P < 0.05$

**Changes in the concentration of TNF- $\alpha$ , MCP-1, and NO in the blood**

The two groups of patients before treatment with TNF- $\alpha$ , MCP-1, NO concentration was no obvious difference ( $P > 0.05$ ), two groups of patients after treatment of TNF- $\alpha$ , MCP-1, the level of NO was significantly lower than before treatment ( $P < 0.05$ ). In the experimental group, TNF- $\alpha$ , McP-1, and NO level were significantly lower than those in the control group ( $P < 0.05$ , Table 4).

blood of lotus seeds, antibacterial anti-inflammatory and fall blood sugar of dogwood, bacteria resistance and bacteriostasis of cortex dictamni, fructus alpiniae oxyphyllae into the spleen meridian and warming spleen and dispel cold, mulberry into renal meridian and reinforcing kidney to replenish kidney essence, Chinese yam can tonifying spleen nourishing the stomach and generating saliva to benefit lung. Radix Astragali preparata can tonify qi and strengthen the exterior. Clearing damp and promoting diuresis of Poria locos. Gallnut of reinforcing the kidney and controlling nocturnal emission, antiseptic and anti-inflammation. Invigorating spleen and stomach of chicken's gizzard-membrane. Sanqi regulates blood sugar. Therefore, this study makes a significant therapeutic effect on the spleen, invigorating the spleen, invigorating the spleen, the biochemical fluid, and regulating the endocrine.

This experiment adopted TCM plus metformin hydrochloride in 40 patients with diabetes treatment, the results showed that after 12 w of treatment, patients with traditional Chinese medicine combined therapy with metformin enteric-coated metformin hydrochloride in FBG, 2 h PG, FINS and 2 h INS improvement is superior to pure metformin hydrochloride treatment group, shows that Chinese and western medicine can effectively reduce the patients of FBG, 2 h PG and FINS and 2 h INS, indicates that Chinese and Western medicine combination can effectively control diabetes plays a positive role to prevent or improve diabetes complications [11].

Diabetes caused by vascular disease is a major cause of damage, while inflammatory factors throughout the whole process of the onset of vascular inflammation [12-15]. The

studies have shown that people with diabetes in their blood, the concentration of the inflammatory factors significantly increased [16-18], and TNF- $\alpha$  of the Zang-Fu organs has strong toxicity, skin cell activation, it can induce organ leucocyte migration, granulocyte degranulation and blood capillary leakage, etc., thus inducing and further aggravate the inflammatory response. MCP-1 is a bisectonal molecule that is specific to mononuclear macrophages, which participates in the occurrence of inflammation. NO is a dual cell messenger molecule and cytotoxic molecule. Therefore, inflammatory factor TNF- $\alpha$ , chemokine MCP-1 and inflammatory media NO can accurately reflect the infection of the microinflammation of the body, which is an indicator of the inflammation of the body and the development of the disease. This study found that patients with traditional Chinese medicine combined therapy with metformin enteric-coated metformin hydrochloride the TNF- $\alpha$ , MCP-1, NO level significantly lower than the control group patients, showed that Chinese and western medicine combination can effectively control inflammation, diabetes and can improve the inflammatory state of diabetic patients.

So, the use of traditional Chinese medicine prescription with metformin hydrochloride therapy of diabetes can be offset by increasing dosage to improve the effect of western medicine, and improve the body immunity, strengthen the spleen and kidney, tonic Yin losses, providing a possibility for diabetes fundamentally.

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## \*Correspondence to

Qingxi Wang

Sixth People's Hospital of Qingdao

Qingdao

PR China