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Original Article

Efficacy of Shenqi Jiangtang Granules-Assisted Western Medicine in the Treatment of Gestational Diabetes Mellitus (GDM)

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Abstract

Background: We aimed to investigate the efficacy of Shenqi Jiangtang granules-assisted Western medicine in the treatment of gestational diabetes mellitus (GDM).

Methods: A total of 147 patients with GDM treated in Qilu Hospital of Shandong University from Jan 2018 to Apr 2019 were enrolled. They were randomly divided into traditional Chinese medicine (TCM) combined with Western medicine group, Western medicine group and control group. The control group was treated with exercise combined with diet therapy, and the Western medicine group was additionally treated with metformin tablets. The TCM combined with Western medicine group was additionally treated with Shenqi Jiangtang granules.

Results: After treatment, the levels of 10 indicators in the three groups were lower than those before treatment ($P < 0.05$). These indicators were the lowest in the TCM combined with Western medicine group. However, high-density lipoprotein cholesterol (HDL-C), glutathione peroxidase (GSH-PX) and superoxide dismutase (SOD) after treatment increased in the three groups compared with those before treatment ($P < 0.05$), which was the most obvious in the TCM combined with Western medicine group. After treatment, the number of patients with natural delivery in the TCM combined with Western medicine group was the largest. The incidences of complications in pregnant women, fetuses and newborns were the lowest in the TCM combined with Western medicine group.

Conclusion: Application of Shenqi Jiangtang granules-assisted Western medicine in patients with GDM can effectively control blood glucose and lipid levels, enhance antioxidant capacity, reduce the levels of inflammatory cytokines and decrease the incidence of adverse pregnancy outcomes.

Keywords: Shenqi Jiangtang granules; Gestational diabetes mellitus; Clinical efficacy; Adverse pregnancy outcome

Introduction

Gestational diabetes mellitus (GDM) (1) refers to abnormal glucose metabolism or diabetes mellitus (DM) during pregnancy. Although the blood glucose level of most patients can return to nor-

mal after delivery, the puerperants with DM during pregnancy will present impaired glucose tolerance, which will cause great harm to themselves and fetuses, and is also an important factor eventually leading to adverse pregnancy outcomes.

The outcomes will be different due to different blood glucose control. For patients with good blood glucose control, their adverse pregnancy outcomes will also be improved (2), thus ensuring the safety of the patients. As a result, it was of great significance to control blood glucose early in patients with GDM. Metformin tablets (3,4) have a certain advantage in price, and is very convenient to take. In recent years, it has also aroused great interest in the treatment of gestational hyperglycemia, but its effect is not ideal when used alone.

Therefore, in this study, 147 patients with GDM treated in our hospital from Janu 2018 to Apr 2019, were divided into three groups for treatment, and the effect of Shenqi Jiangtang granules (5)-assisted Western medicine on the clinical efficacy of the patients was analyzed. It was reported as follows.

Materials and Methods

Clinical data

With the approval of the Ethics Committee of Qilu Hospital of Shandong University and the informed consent of patients, 147 patients with GDM (gestational age, 24-28 weeks; average (gestational age, 25.95 ± 1.91 weeks) treated in Qilu Hospital of Shandong University from Jan 2018 to Apr 2019 were enrolled. They were randomly divided into control group, Western medicine group and traditional Chinese medicine (TCM) combined with Western medicine group, with 49 patients in each group. There were no statistically significant differences in general information among the three groups (all $P > 0.05$). as seen in Table 1.

Table 1: General information of patients

Variable	*Control group(n=49)*	*Western medicine group(n=49)*	*TCM) combined with Western medicine group(n=49)*	X^2	*P*
Age (yr)				0.396	0.820
<32	31	29	28		
≥32	18	20	21		
Pregnancy BMI(kg/m^2)				1.202	0.548
<25	34	36	31		
≥25	15	13	18		
Family history of diabetes				0.843	0.656
Yes	13	17	14		
No	36	32	35		
Inoculation times				1.048	0.592
For the first time	25	30	27		
≥2	24	19	22		
The number of abortion				1.869	0.760
No	38	41	36		
1 or 2	9	7	10		
≥3	2	1	3		
Early pregnancyHb(g/L)				1.816	0.403
<130	37	35	31		
≥130	12	14	18		
Early pregnancyCRP(mg/L)				0.443	0.801
<8	34	32	35		
≥8	15	17	14		

Diagnostic criteria

According to the diagnostic criteria for GDM formulated and recommended in 2017 (6), the blood glucose of pregnant women was measured by 75 g oral glucose tolerance test (OGTT) at 24-28 weeks of gestation and the first visit after 28 weeks of gestation. GDM was diagnosed when any of the blood glucose values reached or exceeded the following criteria: fasting plasma glucose (FPG) = 5.1-6.9 mmol/L, 1-h plasma glucose (1hPG) during OGTT ≥ 10. 0 mmol/L, and 2-h plasma glucose (2hPG) during OGTT ≥ 8. 5 and <11 mmol/L.

Inclusion criteria and exclusion criteria

Inclusion criteria (7): Patients meeting the diagnostic criteria in the *Guidelines for the Diagnosis and Treatment of GDM* (Edition 2017); Patients aged 20-40 yr; Patients and their families with signed informed consent.

Exclusion criteria (8, 9): Patients with diagnosed DM before pregnancy; Patients complicated with severe abnormalities of cardiopulmonary, hepatic or renal function; Patients with mental illness; Patients who were allergic to the drugs used in this study; Patients with other diseases of the endocrine system such as Cushing's syndrome and hyperthyroidism that may affect blood glucose; Patients with a previous history of hypotension, hypoxia, major surgery or lactic acidosis.

Treatment

The control group was given routine treatment, including diet therapy and exercise therapy (10-12). 1) Diet control can not only meet the energy needed by pregnant women and fetuses and provide enough calories and reasonable nutrition for pregnant women and fetuses, but also strictly control the intake of carbohydrates, so as to maintain the blood glucose in the normal range, with healthy fetal development as the basic principle. The total daily intake of calories during pregnancy is 7,531-9,205 kJ, of which carbohydrates account for 45%-55%, fat for 25%-30% and proteins for 20%-25%. According to the standard body weight of pregnant women (standard body weight (kg) = height (cm) - 100), the daily intake of total calories per person was calculated. Small and frequent meals were recommended, with 5-6 meals a day. Based on the gestational age, blood glucose level and body mass index (BMI) of the patients, personalized catering was provided by professional dietitians. If the urinary ketone body is positive after strict diet control, the diet should be adjusted in time. After blood glucose control, FPG should be 5.3 mmol/L and 2-hour postprandial blood glucose (2hPG) should be ≤ 6.7 mmol/L. 2). Reasonable exercise was combined while diet control. Exercise mainly included slow walking, upper limb exercise and exercise with an equal amount to slow walking, 3-4 times a week, 20 min per time. On the premise of no danger to pregnant women and no influence on healthy fetal development, only upper limb exercise was recommended, which is safer.

On the basis of the control group, the Western medicine group was orally administrated with metformin hydrochloride tablets (13) (Sino-American Shanghai Squibb Pharmaceutical Co., Ltd., Guoyao Zhunzi H20023370) after meal, 0.25 g/time, twice a day. After administration for 7 d, the dose was increased to 0.5 g/time, 3 times/d in the patients whose blood glucose level was still high. The course of treatment was from 28 weeks of gestation to the end of delivery.

Based on the treatment in the Western medicine group, the TCM combined with Western medicine group was orally administrated with Shenqi Jiangtang granules (14) (Shandong Lunan Houpu Pharmaceutical Co., Ltd., Guoyao Zhunzi Z10950075), 1 g/time, 3 times/d. For the patients with high blood glucose level, the dose was increased to 3 g/time, 3 times/d. The course of treatment was from 28 weeks of gestation to the end of delivery.

Observation indicators

Clinical efficacy According to the *Guiding Principles for Clinical Research of New Drugs of Traditional Chinese Medicine*, the clinical efficacy of the three groups was evaluated after treatment (15): 1)

cured, the clinical symptoms and signs disappeared completely, and the blood glucose was controlled to the normal level; 2) markedly effective: the clinical symptoms and signs were markedly relieved, and the blood glucose level was basically normal; 3) effective: the clinical symptoms and signs were relieved, and the blood glucose level decreased slightly; 4) invalid: the clinical symptoms were not relieved or even aggravated, and the blood glucose level was not decreased. Total effective rate = (cured cases + markedly effective cases + effective cases)/total cases × 100%.

Blood glucose and lipid Fasting venous blood (5 ml) in the early morning (16,17) was collected from the three groups 1 d before and after treatment, respectively, to detect the levels of blood glucose and lipid. The levels of fasting blood glucose (FBG), 2hPG, total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) before and after treatment were observed and recorded.

Changes of oxidative stress indicators and inflammatory cytokines in the three groups before and after treatment: The above serum samples were taken to measure glutathione peroxidase (GSH-Px), superoxide dismutase (SOD), malondialdehyde (MDA), interleukin-6 (IL-6), hypersensitive C-reactive protein (hs-CRP) and tumor necrosis factor-α (TNF-α) contents by enzyme-linked immunosorbent assay (ELISA).

1) The modes of delivery in the three groups after treatment included normal delivery, cesarean section, assisted vaginal delivery and stillbirth. 2) Comparison in the incidence of complications (18) in pregnant women: The incidences of pregnancy-induced hypertension, polyhydramnios, ketoacidosis (DKA), postpartum infection and postpartum hemorrhage were observed and compared among the three groups. 3) Comparison in fetal and neonatal complications (19). The incidences of preterm birth, fetal macrosomia, neonatal distress or asphyxia, neonatal hypoglycemia and perinatal death were observed and compared among the three groups.

Statistical methods

The data were input into SPSS (Chicago, IL, USA) 23.0. The measurement data were expressed as mean ± standard deviation ($\bar{x} \pm s$) and analyzed using the *t* test. The enumeration data were expressed as percentage (%) and analyzed by the $\chi 2$ test (20). $P < 0.05$ was considered as statistically significant.

Results

Comparison in clinical efficacy among the three groups

After treatment, the total effective rate was 93.9% in the TCM combined with Western medicine group, 75.5% in the Western medicine group and 44.9% in the control group. The clinical efficacy in the treatment of GDM was higher in the TCM combined with Western medicine group and the Western medicine group compared with the control group ($P < 0.05$), and the highest in the TCM combined with Western medicine group, as seen in Fig. 1 and 2.

Comparison of blood glucose and lipid levels in the three groups before and after treatment

After treatment, the blood glucose and lipid levels in the three groups decreased compared with those before treatment ($P < 0.05$), which was more obvious in the TCM combined with Western medicine group and the Western medicine group compared with the control group ($P < 0.05$), and the most obvious in the TCM combined with Western medicine group (Fig. 3 and 4).

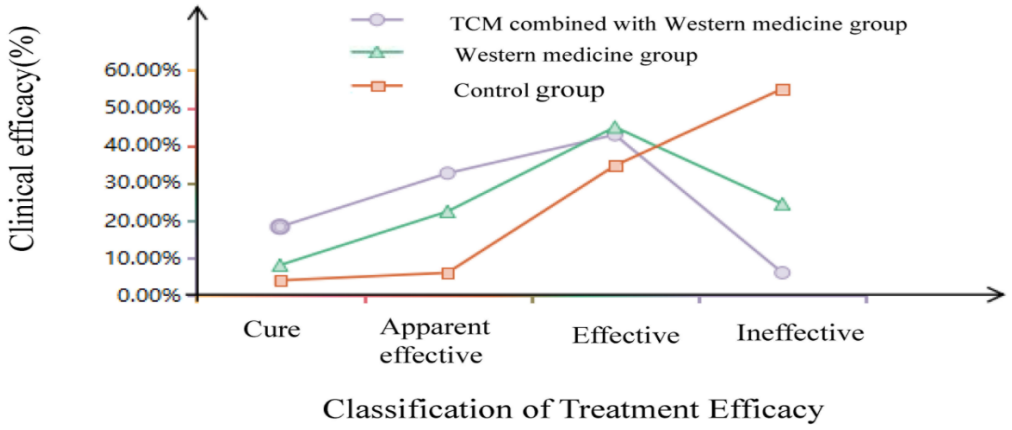

Fig. 1: Comparison in clinical efficacy among the three groups (%)

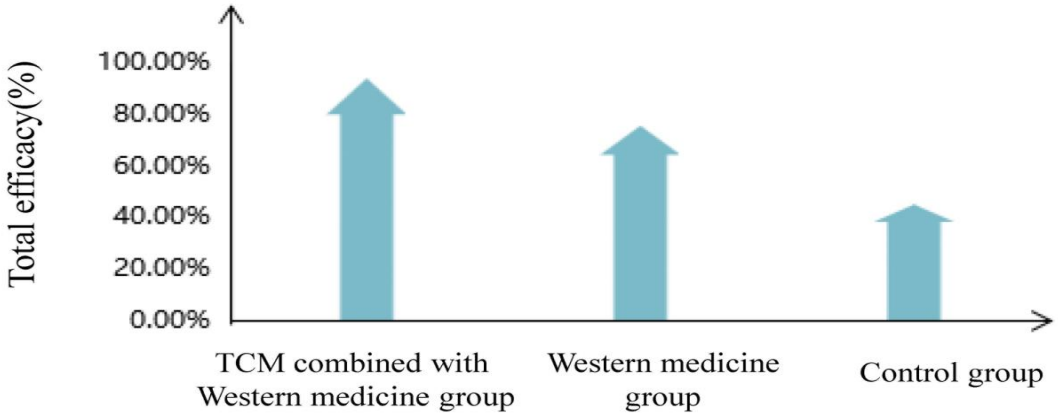

Fig. 2: Comparison in Total efficacy among the three groups (%)

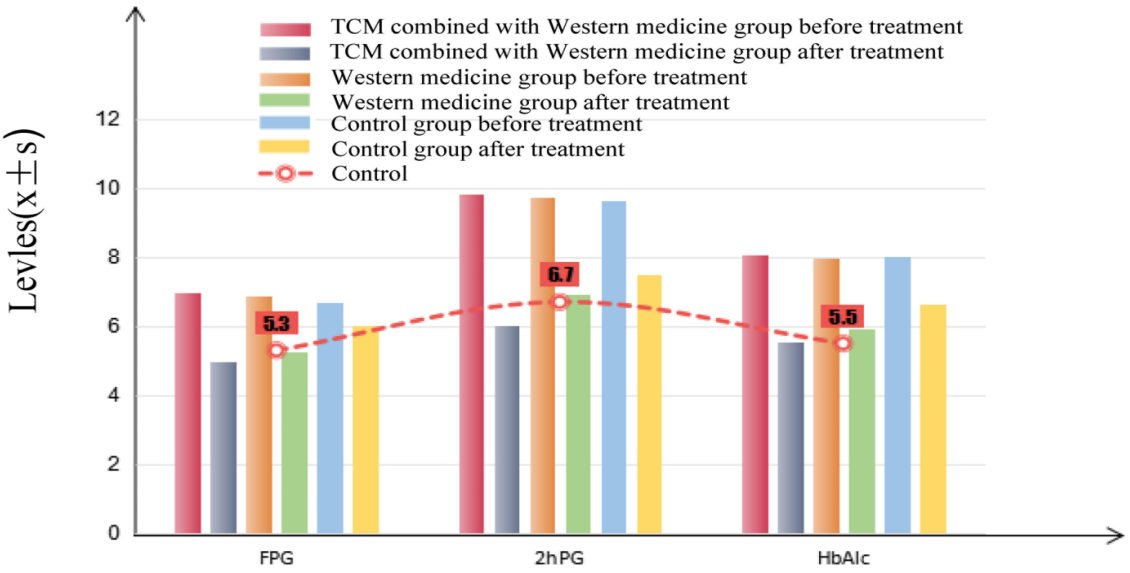

Fig. 3: Comparison of blood glucose levels in the three groups before and after treatment ($\bar{x}\pm s$)

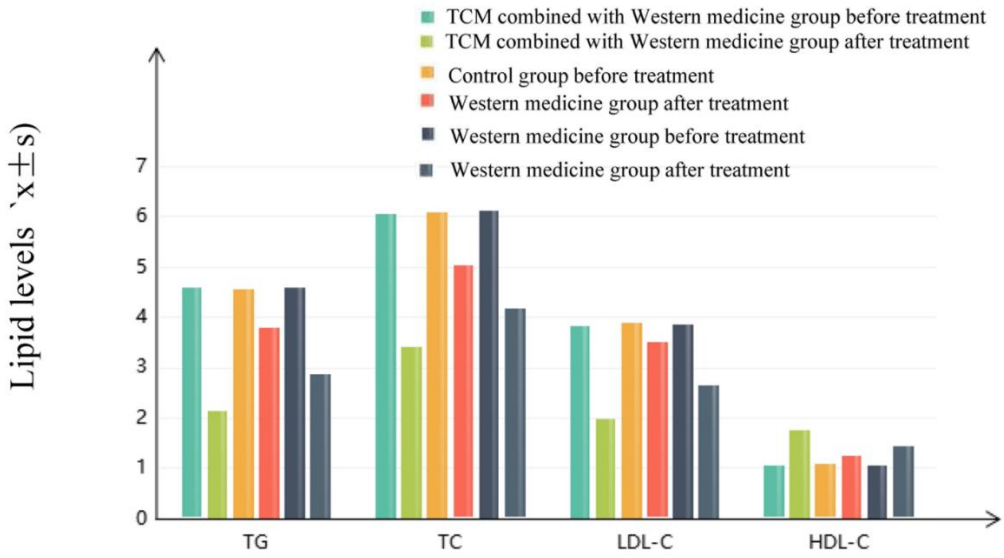

Fig. 4: Comparison of lipid levels in the three groups before and after treatment ($\bar{x}\pm s$)

Comparison in oxidative stress indicators among the three groups

In the three groups, GSH-Px and SOD levels after treatment were higher than those before treatment ($P < 0.05$). GSH-Px and SOD levels were significantly higher in the TCM combined with Western medicine group and the Western medicine group than those in the control group ($P < 0.05$), and the highest in the TCM combined with Western medicine group. After treatment, MDA level in the three groups was lower than that before treatment. MDA level was significantly higher in the TCM combined with Western medicine group and the Western medicine group compared with the control group ($P < 0.05$), and the lowest in the TCM combined with Western medicine group, as shown in Table 2.

Table 2: Comparison in oxidative stress indicators among the three groups($\bar{x}\pm s$)

Time	*Groups*	*N*	*GSH-PX(μmol/L)*	*SOD(U/mL)*	*MDA(mmol/L)*
Before Treatment	TCM combined with Western medicine group	49	17.63±2.21	107.62±13.14	74.45±8.48
	Western medicine group	49	17.72±2.18	113.25±12.07	72.36±6.59
	Control group	49	17.76±2.33	115.49±11.73	72.64±7.65
After Treatment	TCM combined with Western medicine group	49	25.04±5.36^{ab}	204.87±16.35^{ab}	48.66±4.37^{ab}
	Western medicine group	49	22.15±4.54^{ac}	182.67±17.42^{ac}	56.85±4.32^{ac}
	Control group	49	19.84±5.47^{a}	151.73±14.86^{a}	64.02±5.93^{a}
t			9.642	13.174	10.833
P			<0.05	<0.05	<0.05

Notes: Comparison in the same group before and after treatment, $^{a}P < 0.05$; compared with the control group after treatment, $^{b}P < 0.05$, $^{c}P < 0.05$; GSH-Px: glutathione peroxidase; SOD: superoxide dismutase; MDA: malondialdehyde

Comparison in inflammatory cytokines among the three groups

After treatment, the levels of inflammatory cytokines in the three groups decreased compared with those before treatment ($P < 0.05$), which was the most obvious in the TCM combined with Western medicine group, followed by the Western medicine group (Table 3).

Table 3: Changes in the levels of inflammatory cytokines ($\bar{x} \pm s$)

Time	*Groups*	*N*	*IL-6(μg/L)*	*hs-CRP(mg/L)*	*TNF-α(μg/L)*
Before Treatment	TCM combined with Western medicine group	49	195.69±21.37	6.42±0.76	7.71±0.66
	Western medicine group	49	197.24±20.57	6.50±0.73	7.58±0.73
	Control group	49	194.33±21.92	6.52±0.81	7.66±0.71
After Treatment	TCM combined with Western medicine group	49	114.78±15.05[ab]	2.71±0.43[ab]	4.95±0.54[ab]
	Western medicine group	49	139.41±16.64[a]	3.83±0.42[a]	5.67±0.52[a]
	Control group	49	167.04±15.71[a]	5.14±0.37[a]	6.15±0.46[a]
t			15.456	5.413	7.295
P			<0.05	<0.05	<0.05

Notes: Comparison in the same group before and after treatment, [a]$P < 0.05$; compared with the control group after treatment, [b]$P < 0.05$, [c]$P < 0.05$; IL-6: interleukin-6; hs-CRP: hypersensitive C-reactive protein; TNF-α: tumor necrosis factor-α

Comparison in mode of delivery and maternal, fetal and neonatal complications among the three groups

After treatment, normal delivery was the most common in the TCM combined with Western medicine group, and there was no stillbirth. The results are shown in Table 4 ($X^2 = 6.753$, $P < 0.05$). The incidences of maternal, fetal and neonatal complications were significantly lower in the TCM combined with Western medicine group and the Western medicine group than those in the control group ($P < 0.05$), and the lowest in the TCM combined with Western medicine group (Fig. 5 and Fig. 6).

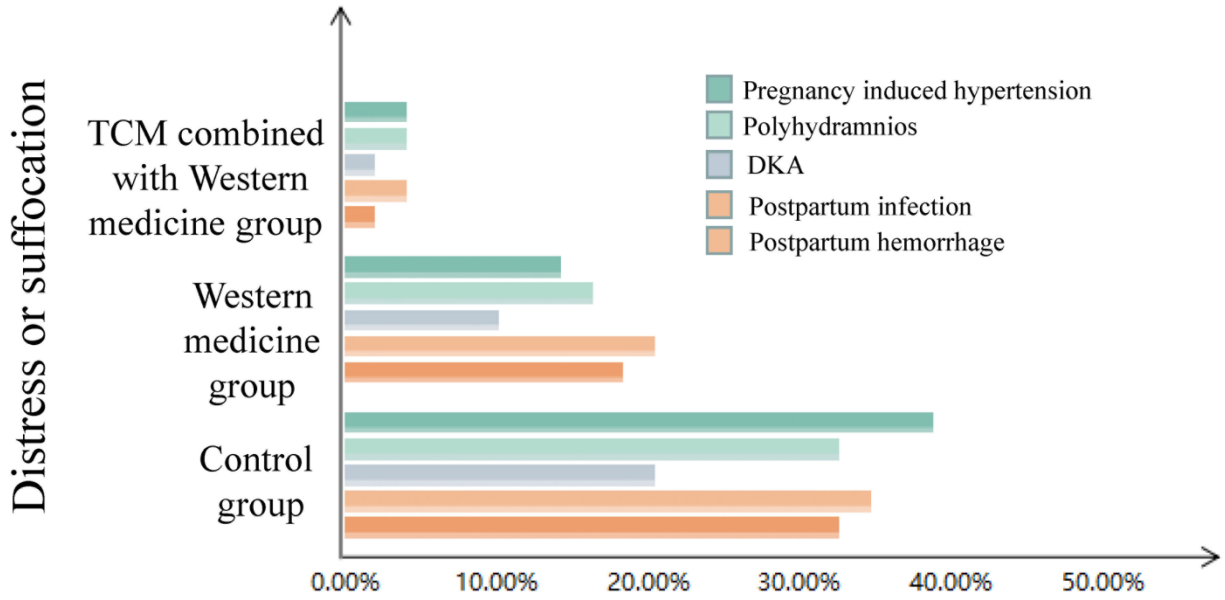

Fig. 5: Comparison of complications among three groups of pregnant women

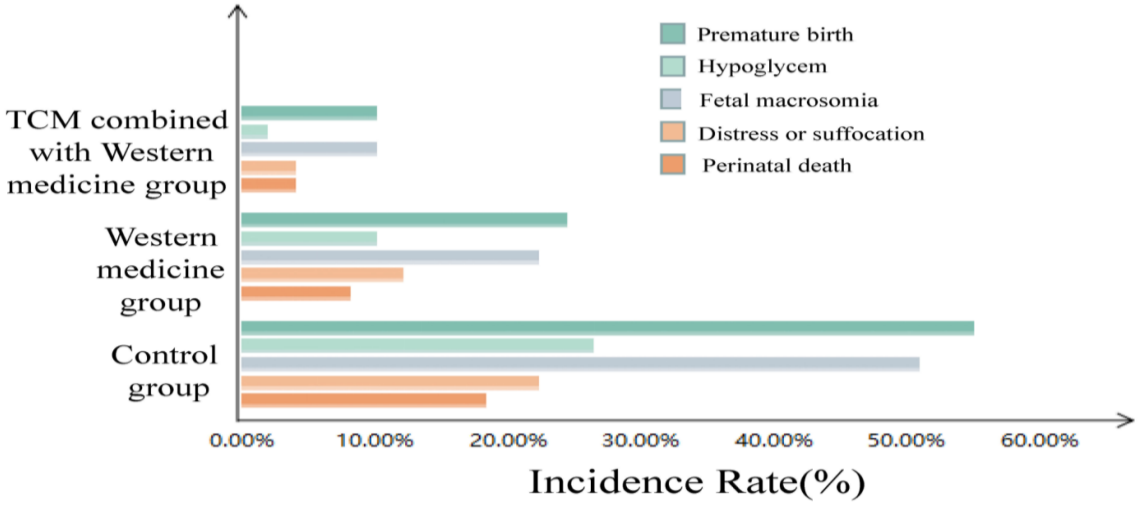

Fig. 6: Comparison of complications among three groups of fetal and neonatal

Table 4: Comparison in mode of delivery among the three groups[N(%)]

Groups	*N*	*Normal delivery*	*Cesarean delivery*	*Vaginal midwifery*	*Stillbirth induction*
TCM combined with Western medicine group	49	36 (73.50)	9 (18.37)	4 (8.16)	0 (0)
Western medicine group	49	28 (57.14)	13 (26.53)	6 (12.24)	2 (4.08)
Control group	49	17 (34.69)	16 (32.65)	11 (22.45)	5 (10.20)

Analysis of univariate logistic regression model leading to adverse pregnancy outcomes

Among the 74 patients with adverse pregnancy outcomes, 31 (41.9%) had BMI ≥ 25 kg/m^2. Among the 73 patients without adverse pregnancy outcomes, 12 (24.5%) showed BMI ≥ 25 kg/m^2. BMI ≥ 25 kg/m^2 presented a statistically significant difference between patients with and without adverse pregnancy outcomes ($\chi 2$ = 19.828, P < 0.01). After adjusting for age and family history of DM, the logistic regression model (21,22) demonstrated that the patients with BMI ≥ 25 kg/m^2 had an increased risk of adverse pregnancy outcomes compared with those with BMI < 25 kg/m^2 (OR = 3.51, 95% CI: 1.59-7.72), as seen in Table 5.

Table 5: Logistic Regression analysis on risk factors of complications in pregnant women, fetus and neonates (P<0.01)

Variable	*Variable OR (95% CI)*
History of DM	
Yes	2.37 (1.31-3.97)
No	1.0
Age>32 years	
Yes	1.09 (1.02-1.16)
No	1.0
BMI≥25kg/m2	
Yes	3.51 (1.59-7.72)
No	1.0

Discussion

The incidence of GDM was different in different regions of China. In recent years, because of the changes in people's lifestyle and eating habits, the incidence of GDM (23) is increasing. Now it has become a common pregnancy-related complication, which has adverse effects on the physical and mental health of mothers and infants. Timely and effective clinical diagnosis and treatment can improve the incidence of adverse pregnancy outcomes, reduce perinatal mortality of mothers and infants, and help to control the probability of pregnant women developing into type 2 DM (24). At present, the etiology of GDM is unclear, and the understanding and research of its pathogenesis is still at the initial stage in international Western medicine. However, the research on GDM in TCM has been carried out for a long time in China, and TCM treatment has achieved good efficacy. The combination of TCM and Western medicine is still the main method for the treatment of GDM. According to TCM (25), GDM belongs to the category of "dispersion-thirst in pregnancy".

During pregnancy, women will change their previous eating habits, and have significantly increased meals compared with that during non-pregnancy. However, if the diet is not well controlled, the spleen and stomach will be damaged, resulting in excessive pressure on the spleen and stomach and gradual loss of function. Not well controlled diet is one of the main causes of GDM, while dysfunction of the spleen and stomach caused by damage is the basic cause. Based on Western medicine treatment (diet control, reasonable exercise, Western drug therapy, etc.), Shenqi Jiangtang granules was used for combined treatment in this study. Shenqi Jiangtang granules (26-28) was a common TCM preparation in clinic, mainly containing *Panax ginseng, Astragalus propinquus*, fruit of Chinese wolfberry, *Rehmannia glutinosa, Ophiopogon japonicus, Alisma orientalis, Schisandra chinensis*, etc. *Astragalus propinquus* has an important effect of invigorating Qi and promoting Yang, and can raise and clear Yang, tonify the spleen and invigorate lung Qi. Panax ginseng has the function of supplementing Qi and promoting the production of body fluid. It tastes sweet and can keep the vitality, and slightly bitter and can nourish Yin. Additionally, it can help transport function, replenish the spleen-Qi, consume Yin fluid and transport refined nutritious substances. The combined use of *Astragalus propinquus* and *Panax ginseng* can invigorate the spleen for benefiting the lung, slake thirst and help produce saliva, and tonify blood and Qi. *Schisandra chinensis* can nourish the kidney, astringe the lung, constrain sweat and promote the secretion of saliva or body fluid. The fruit of Chinese wolfberry has the effect of nourishing the liver and kidney. *Alisma orientalis* can achieve the effect of purging heat, diuresis and excrete dampness. *Ophiopogon japonicus* can play the role of moistening the lung, clearing away the heart-fire, purging heat and promoting the secretion of saliva or body fluid. The combined use of these Chinese herbal medicines can play an important role in nourishing the spleen, tonifying the kidney, replenishing Qi and nourishing Yin.

The total effective rate of the TCM combined with Western medicine group was significantly higher than that of the Western medicine group and the control group. The results showed that conventional Western medicine combined with Shenqi Jiangtang granules could effectively enhance the clinical efficacy of patients with GDM and achieve better therapeutic effect. In this study, FBG, 2hPG and HbAlc levels in the three groups after treatment were significantly lower than those before treatment, and the decrease in the TCM combined with Western medicine group was more obvious than that in the other two groups. This is resulted from that the fruit of Chinese wolfberry contains a large amount of vitamin B1, vitamin B2, carotene, niacin and various amino acids, which can protect important organs such as the liver and kidney, improve the body's immunity and significantly reduce blood glucose level. In addition, ginsenoside contained in Panax ginseng (29) can also protect the liver, stomach, heart and blood vessels, and reduce blood glucose level. Therefore, Shenqi Jiangtang

granules can not only reduce the blood glucose level of GDM patients, but also protect the function of important organs such as the liver and kidney and improve the body's immunity.

After treatment, TC, TG, LDL-C and HDL-C levels in the TCM combined with Western medicine group decreased significantly than those before treatment, and were lower compared with the other two groups. These results indicated that the combination of conventional Western medicine and Shenqi Jiangtang granules can effectively reduce the blood glucose and lipid levels in GDM patients, with definite efficacy. After treatment, the levels of IL-6, hs-CRP and TNF-α in the TCM combined with Western medicine group were lower than those in the Western medicine group and the control group, suggesting that Shenqi Jiangtang granules-assisted Western medicine can reduce IL-6, hs-CRP and TNF-α levels in patients with GDM, so as to alleviate inflammatory reaction in the patients. After treatment, GSH-Px content and SOD activity increased, while MDA content decreased in the TCM combined with Western medicine group, which resulted in reduced incidences of maternal infection and fetal macrosomia and increased maternal rate of natural delivery, indicating that Shenqi Jiangtang granules can promote oxidation in the body and antioxidant system return to normal by improving the antioxidant capacity of GDM patients and eliminating the accumulation of harmful substances, so as to reduce the incidence of pregnancy-related complications and enhance the maternal rate of natural delivery.

Conclusion

Shenqi Jiangtang granules-assisted Western medicine in the treatment of GDM can effectively reduce blood glucose and lipid levels, enhance clinical efficacy, improve body's self-healing function, alleviate oxidative stress response, decrease the incidence of pregnancy-related complications, and improve pregnancy outcomes in GDM patients. Therefore, it is worthy of clinical promotion and application.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The authors declare that there is no conflict of interest.

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