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Research Progress of Shenling Baizhu Powder in the Treatment of Type 2 Diabetes Mellitus Combined with Obesity

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Abstract: ***In recent years, type 2 diabetes mellitus (T2DM) is a chronic metabolic disease whose prevalence is increasing year by year [1]. T2DM is characterized by insulin resistance and impaired pancreatic β-cell function, which leads to elevated blood glucose levels. Obesity is one of the important risk factors for T2DM, and the two often coexist and influence each other, increasing the complexity of chronic disease management. Modern clinical studies [2-3] have confirmed in a large number of practices that traditional Chinese medicines (TCM) have definite efficacy in the treatment of type 2 diabetes mellitus combined with obesity, especially spleen-strengthening and dampness-dispelling TCM compound prescriptions such as Shenling Baizhu Powder, Zhi Zhu Tang, and San Ren Tang, etc., which have been proven in clinics to not only reduce the patient's body mass index (BMI), but also assist in controlling blood glucose, and delaying or reversing the disease progression of type 2 diabetes mellitus [4-5]. In this paper, by searching the relevant literature in recent years, we reviewed the recent research on the treatment of type 2 diabetes mellitus combined with obesity by Shenling Baizhu Powder to provide a basis for further in-depth study and rational use of medication.***

Keywords: Type 2 diabetes mellitus, Shenling Baizhu Powder, Obesity, Research progress**.**

1. Introduction

According to the Global Diabetes Atlas (IDFDiabetesAtlas), China has 140 million diabetic patients, ranking the first in the world [6], with type 2 diabetes as the predominant type [7]. Type 2 diabetes is a systemic chronic metabolic disease, and the prevalence rate of adults in China is as high as 10.9% [8-9]. Type 2 diabetic patients are often comorbid with obesity symptoms. According to the study, obesity rates are rising significantly worldwide while the number of people with type 2 diabetes is increasing at the same rate [10-11]. Lack of exercise and irrational diet structure are the main causes of obesity, and obese people will have visceral fat deposition, which will lead to type 2 diabetes mellitus patients' insulin resistance becoming more and more serious, resulting in a series of serious complications such as cardiovascular disease, retinopathy, stroke, renal failure, etc., which will have a serious impact on the patients' life safety and quality of life [12-13]. Detection of visceral fat can intervene in the development of obese diabetes and facilitate the subsequent development and adjustment of treatment programs. Clinical control of type 2 diabetes mellitus relies on drugs, diet and exercise, the former lowering sugar, regulating metabolic disorders, improving insulin resistance, although the effect has been recognized, but the improvement of patients' clinical symptoms is not significant, and accompanied by adverse reactions, the latter effect is slower and most of the patients are difficult to adhere to, but the appropriate exercise is conducive to the reduction of body fat, fat elimination, and regulation of glucose and lipid metabolism. Chinese medicine treatment system has been very mature, side effects are small, the efficacy of the medicine is long-lasting, and can be complementary to the advantages of Western medicine, and can achieve better therapeutic effects.

2. Explanation of Etiology, Pathogenesis and Prescription

According to the Nei Jing, the main causes of this disease are overindulgence in fat and sweet foods, insufficiency of the five viscera, and emotional disorders. Neijing believes that the main causes of this disease include excessive consumption of greasy and sweet foods, deficiency of the five zang - organs, emotional imbalance, etc. They enter the striae of the skin along the hair outside... Or it may be diabetes. Those with all the five zang - organs being weak are prone to diabetes. "According to Chinese medicine theory, the onset of diabetes is closely related to obesity, diet and emotions. Shenling Baizhu Powder is from "Taiping Huimin Heji Bing Fang", which has been used since ancient times as an important formula for treating great deficiency of the spleen and stomach, and difficulty in transforming food and drink [14]. The main components of the drug composition of white lentils, atractylodes, Poria, licorice, Platycodonopsis, lotus seeds, ginseng, sand nuts, Chinese yam, Coix lacryma. Shenling Baizhu Powder has the effect of benefiting qi, tonifying the spleen, clearing heat and resolving dampness, which can alleviate the evidence of spleen deficiency and dampness, promote qi transportation, and alleviate the internalization of dampness and heat. According to the traditional theory of Chinese medicine, ginseng in the composition of Shenling Baizhu Powder can replenish the qi of the spleen and stomach, while Atractylodes Macrocephalae and Poria cocos can strengthen the spleen and seep away dampness, and they play a key role. Yam and lotus seed meat protect the spleen and stomach and enhance the effects of ginseng and atractylodes. White lentils and Semen Coicis can enhance the transportation and digestion function of the spleen and stomach and promote the elimination of dampness. Sand nuts

are aromatic in nature and can not only move qi and harmonize the stomach, but also remove dampness and promote the operation of qi; Platycodon grandiflorus can enhance the efficacy of the medicine. Glycyrrhiza glabra is sweet, tonic and neutral in nature, benefiting qi and neutralizing the middle, and harmonizing all medicines. The composition and ratios of Shenling Baizhu Powder reflect that it can enhance the spleen and stomach's ability of transportation and digestion, promote the elimination of water-dampness, and enhance the body's metabolic ability, thus improving many symptoms.

3. Chemical Composition

At present, the chemical composition of SLBZS has been studied more on its single herb than on its active parts [15]. Cao Shuli et al [16] established a method for the simultaneous determination of four components of SLBZS, including psoralen, isopsoralen, atractylenolide III, and isopregnanolide, using UPLC. Wang Yue et al [17] established a method for the simultaneous determination of ginsenoside Rg1, quercetin, ginsenoside Re, and rutin in SLBZS using reversed-phase high performance liquid chromatography. Li Jinglin et al [18] quantified ginsenoside Re, ginsenoside Rg1, ginsenoside Rb1, platycodonin D, atractylenolide III, and porphyrinic acid in SLBZS by using UPLC and established their fingerprints. The main components of SLBZS can be identified as ginsenoside Rg1, ginsenoside Re, ginsenoside Rb1, platycodonin D, quercetin, rutin, atractylenolide III, psoralen, isopsoralenolide, pachypoderma lucidum D, quercetin, rutin, atractylenolide III, porinic acid, psoralen, isopsoralen, isopregnanolone Porinic acid, psoralen, isopsoralen, isopregnanolone, and so on [15].

4. Pharmacological Effect

Regulating the immune system: The immune system is an important defense barrier for organisms, preventing pathogens from entering and attacking, and is closely related to health [15]. Improvement of lung function: Modern pharmacological research has found that SLBZS can improve lung function by enhancing the body's immunity. Improvement of gastrointestinal function: SLBZS, as a tonic, has an important position in the treatment of gastrointestinal diseases. Modern research shows that SLBZS has a bidirectional regulation of gastrointestinal motility, which can improve gastrointestinal function. A study showed that SLBZS could regulate gastrointestinal dysfunction and correct the malnutrition-microinflammatory state, and its mechanism of action might be related to the fact that SLBZS could regulate gastrointestinal function in both directions, reduce the level of gastrin-17 (G-17), increase nutritional indexes such as albumin (ALB), prealbumin (PA), transferrin (TRF), and body mass index (BMI), and decrease the level of hypersensitive C-reactive protein (hs-CRP), interferon-γ (IFN-γ), and up-regulate anti-inflammatory factor IL-10, and inhibit the malnutrition-microinflammatory state. It also reduces the levels of hypersensitive C-reactive protein (hs-CRP) and interferon-gamma (IFN-γ), up-regulates the anti-inflammatory factor IL-10, and suppresses malnutrition-microinflammatory state [19]. Antioxidant: Excessive oxidation of the organism will accelerate the damage and aging of the organism, and many studies have shown that SLBZS has a certain antioxidant effect. Anti-tumor: Numerous studies have shown that SLBZS can promote apoptosis of tumor cells and play an anti-tumor role, which has certain therapeutic effects on lung cancer, liver cancer and other diseases. Peng Ying et al [20] found that SLBZS synergized with chemotherapeutic agents could promote tumor cell apoptosis in H22 hepatocellular carcinoma transplanted mice after chemotherapy, and the mechanism may be related to the inhibition of apoptosis inhibitory factors and the up-regulation of pro-apoptotic factors. Anti-inflammatory: Many inflammatory diseases are caused by inflammatory factors, SLBZS can inhibit the inflammatory response by regulating the level of inflammation-related factors, thus playing a certain therapeutic effect on inflammatory bowel disease, acute sinusitis, pneumonia and other diseases. Other pharmacological effects: As to literatures, SLBZS also has pharmacological effects of improving renal function, myocardial function, fat metabolism disorders, and repairing the mechanical barrier function of the skin.

5. Prevention and Treatment of Obesity Associated with Type 2 Diabetes Mellitus by Shenling Baizhu Powder

5.1 Progress of Research on the Prevention and Treatment of Type 2 Diabetes Mellitus by Shenling Baizhu Powder

Hao Lin, Yan Ling [21] selected 113 patients with type 2 diabetes mellitus of spleen deficiency and dampness-distressed type, and divided the patients into the control group (56 cases) and the treatment group (57 cases). The control group was given pioglitazone hydrochloride tablets orally; the treatment group was given Shenling Baizhu Powder (SLBZP) orally on the basis of the control group. After 8 weeks of treatment, it was found that the TCM evidence scores and DSQL scores of both groups decreased significantly ($P<0.05$), and the levels of FBG, 2hPG, HbA1c, GDF-15, FFA, and chemerin decreased significantly ($P<0.05$) in both groups, and the scores of the treatment group decreased more significantly ($P<0.05$) than those of the control group. The results demonstrated that Shenling Baizhu Powder (SLBZP) combined with pioglitazone was effective in the treatment of type 2 diabetes mellitus with spleen deficiency and dampness, and was able to promote the recovery of relevant serologic indexes while improving the patients' clinical syndromes and survival quality. LiingZhang et al [22] randomly divided 50 rats into a normal control group, a model control group, and low, medium, and high dose SLBZP groups, with 10 rats in each group. Five-week-old rats were gavaged with ultrapure water and different doses of SLBZP decoction, and feces and intestinal contents were collected from 9-week-old rats for 16SrRNA sequencing and metabolomics analysis. The results showed that SLBZP could regulate intestinal flora and metabolites and alleviate chronic inflammation, thereby controlling obesity and preventing type 2 diabetes. Wang Xiangyu [23] selected 98 cases of T2DM patients as the study subjects, which were divided into the control group and the observation group according to the random number table method, each with 49 cases. Both groups received conventional treatment, while the control group was treated with Insulin Aspart 30 Injection and the observation group was treated with SLBZP. After 3 months of treatment, the

efficacy of the two groups was compared, and the results showed that SLBZP combined with Insulin Aspart 30 Injection could improve the efficacy of treatment of T2DM and regulate the blood glucose and lipid levels.

5.2 Clinical Study on the Prevention and Treatment of Obesity by Shenling Baizhu Powder

Niu Changmiao [24] et al. detected serum triacylglycerol, total cholesterol and epididymal adipose tissue tumor necrosis factor-α, interleukin-1β, interferon-γ, and FasmRNA expression in rats by constructing a high-fat diet-induced juvenile obesity rat model, and administering SLBZS gavage. The results of animal experiments show that SLBZS has the effect of improving microinflammation and metabolic indexes in model rats, and it can regulate multiple targets and affect multiple signaling pathways through multiple active ingredients, and regulate inflammatory response, immune process, insulin resistance, glucose-lipid metabolism and other body metabolic functions through specific biological processes and related pathways, so as to play the role of improving inflammation and metabolic indexes in obese rats. The effect of this study is to improve the inflammation and metabolic indexes of obese rats. Jin Xiaoqin et al [25] divided 30 healthy male SPF-grade C57BL/6J mice into a blank group (n=5) and a high-fat chow group (n=25), with mice in the blank group fed normal chow and mice in the high-fat chow group fed high-fat chow for modeling. Ten mice with successful modeling were randomly taken and divided into model and SLBZS (2.4 g-kg-1) groups, with five mice in each group. After 4 weeks of administration of the corresponding drug intervention, it was found that compared with the model group, body mass, blood glucose and levels of TC, TG and LDL-C of mice in the SLBZS group were significantly decreased ($P<0.05$); levels of HDL-C were significantly increased ($P<0.05$); intestinal bacterial flora testing showed that the species richness and homogeneity of the intestinal community was increased by the treatment of SLBZS, and the number of species' core OTUs significantly increased; the proportion of microorganisms in the phylum Bacteroidetes and Thick-walled Bacteroidetes decreased. The experimental results showed that SLBZS could significantly improve the body mass, blood glucose and lipid-related indexes, and improve the intestinal microbial imbalance in obese mice.

5.3 Clinical Study on the Prevention and Treatment of Obesity in Combination with Type 2 Diabetes Mellitus by Shenling Baizhu Powder

Wang Xiangge [26] et al selected 170 obese T2DM patients as study subjects and randomly divided them into conventional group (85 cases) and combined group (85 cases). Metformin was used in the conventional group, and the combined group was based on the conventional group with adjunctive SLBZS. The results showed that the total effective rate of the combined group (88.24%) was higher than that of the conventional group (71.12%) ($P<0.05$); after the treatment, the changes of WHR, BMI, FPG, and HbA1c in the combined group were greater than those in the conventional group ($P<0.05$); compared with the conventional group, the HOMA-β of the combined group increased, and the FINS, and the HOMA-IR decreased in the combined group after the treatment ($P<0.05$); the combined group MCP-1 decreased and GLP-1, miR-146a, miR-221 increased ($P<0.05$). The experimental results showed that SLBZS assisted western medicine to treat obese T2DM with precise efficacy, which could alleviate patients' insulin tolerance and hyperglycemia, inhibit inflammatory response, reduce body weight, and regulate miR-146a and miR-221 expression. Luo Jintong et al [27] randomly divided 10 LZ rats as control group and 20 ZDF rats into model group as well as SLBZS treatment group. The intervention started at 5 weeks of age corresponding to gavage of ultrapure water and 24g/kg of SLBZS decoction and continued until 9 weeks of age. The experimental results showed that after SLBZS intervention, the serum FFA level of ZDF rats decreased ($P<0.01$), the morphology of pancreatic islets improved with clear boundaries, and the volume returned to normal. The expression of insulin in pancreatic islets increased ($P<0.05$), and the expression of glucagon decreased ($P<0.01$). The expression of FoxO1, Pdx1, and Nkx6. 1 proteins and mRNA was upregulated in the pancreas ($P<0.05$), and the expression of Oct4, Nanog proteins and mRNA, and Ngn3 protein was downregulated ($P<0.05$). SLBZS reduces the risk of lipotoxicity in ZDF rats, improves pancreatic β-cell dedifferentiation, and plays a role in the treatment of obese T2DM. Zhang Shuqin et al [28] randomly divided male C57BL/6J mice into five groups: normal control group, model group, metformin (200 mg/kg) positive control group and SLBZS high (24 mg/kg) and low (12 mg/kg) dose group, high-fat feeding plus small-dose injections of streptozotocin (STZ) to construct an obese T2DM mouse model, and mice in each group were given the corresponding drug for 6w. The results showed that SLBZS could improve obese T2DM and promote lipid and glucose metabolism by activating the AMPK signaling pathway, thus alleviating the symptoms of glucose-lipid metabolism disorders in high-fat feeding plus STZ-induced diabetic mice when compared with the model group.

6. Summary

In conclusion, SLBZS has unique advantages and significant efficacy in the treatment of type 2 diabetes mellitus combined with obesity. By regulating the functions of the spleen and stomach, promoting metabolism and improving insulin resistance and other aspects of the mechanism of action, the formula can effectively reduce blood glucose levels, reduce body weight and improve the clinical symptoms of patients. With the continuous deepening of research and the promotion of clinical application, SLBZS is expected to become one of the important choices for the treatment of T2DM combined with obesity. Meanwhile, further exploration and optimization of the dosing regimen are needed to improve the therapeutic effect and patients' quality of life.

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