

Application Progress of Ziwu Liuzhu Theory in Type 2 Diabetes

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Keywords: Meridional flow theory, Type 2 diabetes mellitus, Research progress

Abstract: Ziwu liuzhu originated from ancient China, originated from the "internal meridian", reflecting the law of qi, blood and Yin and Yang flowing into the meridians at 24 hours, which can be used for acupuncture, drug selection, health and so on. Meridian flow can be linked with the rhythm of human body clock and used to guide the treatment of metabolic diseases caused by circadian rhythm disorder. Therefore, the application progress of meridian flow theory in type 2 diabetes was analyzed from the sources of meridian flow theory, the influencing factors of blood glucose, the imbalance of Yin and Yang, and the dysfunction of zang-fu organs. In order to achieve better clinical therapeutic effect, meridional flow theory was used to guide drug use.

1. Introduction

Type 2 diabetes is a metabolic disease of sugar, fat and protein caused by insulin resistance and secretion deficiency [1] A. With the aging of China and the change of modern human lifestyle, the prevalence of diabetes increased from 0.67 percent in 1980 to 12.8 percent in 2020 [2] A. People with type 2 diabetes are at increased risk of heart and peripheral vascular disease due to blood vessel damage caused by long-term high blood sugar. The treatment of diabetes in modern medicine is mainly drug therapy (sulfonylurea, glycinide, biguidine, thiazolidinedione, α glucosidase inhibitor and insulin, etc.), diet control and exercise strengthening. In order to eliminate the side effects and dependence caused by long-term use of drug therapy, to find a more safe and effective treatment method has become the focus of modern medical research.

Type 2 diabetes is called "quench thirst" in Traditional Chinese medicine. The pathogenesis of type 2 diabetes is deficiency of Yin and jin, and excess heat, which is based on Yin deficiency and excess heat. Therefore, the treatment of diabetes is to clear heat and moisten dryness, nourish Yin and produce jin. Based on this theory, this paper discusses the application of meridian flow in type 2 diabetes mellitus.

2. Sources of meridional flow theory

The theory of Meridian flow is based on the theory of "correspondence between heaven and man", which is used to explore the ebb and flow of qi, blood, Yin and Yang and the circulation of

the twelve meridians at different times [3] A. During the 24 hours of the day, the organs correspond to different times. "Ziwu" refers to zi time (23:00) and noon time (11am to 1pm). Each time and its corresponding zang-fu organs are: Zi (Dan), Chou (liver), Yin (lung), MAO (Dachang), Chen (stomach), Si (spleen), Wu (heart), Wei (small intestine), Shen (bladder), you (kidney), Xu (pericardium), hai (sanjiao). The body of qi, blood, Yin and Yang with the change of time, cyclic infusion to the viscera, the eight veins, etc. Through the combination of meridian flow theory, the pathogenesis and occurrence and development law of the disease can be discussed, and the clinical diagnosis and treatment of the disease can be guided by regulating qi, blood and Yin through different time administration.

3. Influencing factors of circadian rhythm of blood glucose

Normal blood glucose, in the physiological state, presents a "stable basal blood glucose + high postprandial blood glucose", glucose homeostasis regulation is also by multiple systems and organs involved, synergistic effect. The blood glucose of healthy people showed obvious circadian rhythm, with two peaks (10am and 10pm) and troughs (6am and 6pm) within 24 hours, while the blood glucose concentration of type 2 diabetes patients showed obvious circadian rhythm disorder. There is also a certain biological rhythm in the changes of blood glucose concentration. When abnormal blood glucose occurs in the body, it will further develop into diabetes. Hyperglycemia in the body can also increase the incidence of complications.

3.1. Circadian rhythm of glucose metabolism

Circadian rhythms raise blood sugar in terms of decreasing insulin sensitivity by regulating glucose metabolism [4] A. In the process, pancreatic function can also be reduced. Insulin sensitivity also shows a circadian rhythm. Generally, insulin sensitivity is lower at night than during the day, and glucose concentration is at a high level. It has been shown in experiments that when healthy adults are given a continuous infusion of glucose over a 24-hour period, blood sugar rises at night and falls at dawn. When rats were fed ¹⁴C-labeled deoxyglucose at night, the circadian rhythm of glucose uptake also existed in the tissues. When circadian rhythms are disrupted, changes in plasma glucose occur. So circadian rhythms are linked to glucose metabolism. Ran Meng [5] The circadian system may influence glucose tolerance through insulin sensitivity and liver glucose output in 31-40-year-old women, and insulin resistance is significantly increased in those with circadian disorder. Other studies have shown that the effect of circadian rhythm disturbance on glucose tolerance is mainly mediated by decreased insulin sensitivity rather than decreased pancreatic cell function.

3.2. Influence of clock gene rhythm on blood glucose

Circadian rhythms are mainly regulated by clock genes. Currently, CLOCK genes are PER1, PER2, PER3), CRY1, CRY2, CLOCK, BMAL1, TIM, etc. As the core clock gene of circadian rhythm, BMAL1's genome binding site is in B cells, while type 2 diabetes is mainly characterized by islet B cell dysfunction [6] A. Moreover, the B-cell clock is an important regulator of impaired insulin secretion and glucose homeostasis. The expression of BMAL1 and B cells in vivo begins with the formation of B cells specifically inducing overexpression of BMAL1. The study showed that mice with B-BMAL1^oVM showed enhanced islet circadian rhythm amplitude, enhanced impaired insulin secretion in vivo and in vitro, and a protective effect on obesity-induced glucose tolerance. In addition, BMAL1 also increases the secretion of B cells, which is associated with an increased risk of type 2 diabetes, in which the circadian rhythm of B cells is disrupted. Some researchers have found that CLOCK and BMAL1 are related to a variety of metabolic diseases such

as type 2 diabetes and obesity. After the CLOCK/BMAL1 gene of the central system of mice is knocked out, the ratio of day and night activity in mice changes, accompanied by changes in dietary rules, and glucose and lipid metabolism disorders, which are manifested as: obesity caused by excess energy, decreased glucose sensitivity in vivo, insulin resistance, and metabolic syndrome[7]. Studies have shown that mice with the circadian gene mutation have reduced circadian rhythms in their feeding behavior and develop obesity, overeating, reduced energy expenditure and visceral obesity, as well as dysregulation of glucose and lipid metabolism [8].

3.3. Effects of physiological hormone secretion on blood glucose

The Suprachiasmatic nucleus of the hypothalamus not only regulates circadian rhythms, but also controls the release of hormones that affect blood sugar. Such as insulin, glucocorticoid hormone cortisol, melatonin, growth hormone, the secretion of these hormones also presents circadian rhythm. As the most important hormone regulating blood glucose, insulin secretion has a "biological rhythm", with secretion peaks in the morning and troughs in the night. Glucocorticoid secretion antagonizes insulin, such as growth hormone and glucocorticoid cortisol. Under the influence of SCN, the circadian secretion of glucocorticoid has a peak before the start of the active phase, with the first secretion peak at 4 or 5 o'clock, the second secretion peak at 6 or 9 o'clock, and the lowest level at midnight. Moreover, glucocorticoid cortisol affects insulin signal transmission and reduces insulin secretion and insulin sensitivity, thus affecting the blood glucose level of the human body. The secretion of growth hormone is released in pulses. Nearly 50 percent of the secretion occurs during the third or fourth period of non-REM sleep, and the largest secretion waves occur during deep sleep, which affects blood sugar by antagonizing insulin in the liver and muscles. Melatonin is secreted by the pineal gland and is mainly affected by the light-dark cycle. When light-dark signals are felt, it is transmitted to SCN and binds with receptors on SCN. The production rate of melatonin also shows a circadian rhythm, which is very low during the day and gradually increases, and peaks at 3 to 4 o'clock, and also affects insulin secretion. By studying the relationship between melatonin and 5-hydroxytryptamine secretion and circadian rhythm in mice, Li Haiyan et al. found that melatonin secretion increased during sleep and 5-hydroxytryptamine secretion decreased while 5-hydroxytryptamine secretion increased during wakefulness, and the two interact to jointly regulate circadian rhythm.

3.4. Influence of lifestyle changes on blood glucose

Lifestyle changes are closely linked to circadian rhythms and may increase the risk of developing type 2 diabetes to some extent. Fasting/eating, sleep/wake, rest/activity, postural cycles, and light/dark cycles can all contribute to circadian dysrhythmia. When the circadian system is inconsistent with the behavioral environment (sleep/wake, rest/activity, postural cycle), it controls the daily changes in blood glucose, and the behavioral cycle significantly reduces insulin sensitivity. Other studies have found that the light/dark cycle is synchronized with the circadian clock, and exposure to light can also have an earlier or later effect on the circadian clock, which affects the circadian clock and causes it to be out of sync with the circadian rhythm.

4. Discuss type 2 diabetes from meridional flow

4.1. Imbalance of Yin and Yang

The interaction between Yin and Yang of qi and blood laid the foundation of meridional flow theory to some extent, and the change of Yin and Yang also has an important relationship with the

circadian rhythm of blood sugar. The theory of Yin and Yang puts forward that "Yin and Yang, the way of heaven and earth", so the theory of Yin and Yang can be used to explain the pathogenesis of diabetes. Ancient and modern doctors point out that the pathogenesis of diabetes is Yin deficiency and hot, the imbalance of Yin and Yang in the five viscera of the body, and the disease of the five viscera. In normal human body changes, blood glucose and insulin present a dynamic balance, insulin is an important hormone to regulate blood glucose. The secretion of basic insulin shows two peaks and troughs, the first peak is at 6-7 in the morning (egg hour), this time belongs to Yang in Yang, Yang qi gradually flourishing, and the corresponding viscera meridians are hand Yang Ming large intestine meridians and foot Yang Ming stomach meridians. From the perspective of Yin and Yang, blood glucose belongs to Yin, insulin belongs to Yang, Yang qi gradually hyperactive, promoting the secretion of insulin, gradually reaching the first secretion peak. The second peak is at 4 to 6 PM (Shen Youshi), which is the Yin of Yang. The corresponding meridians are the foot-sun bladder meridian and foot-shaoyin kidney meridian, and the two meridians are the outer and inner phase, which contains the yuan Yin and Yuan Yang of the body. Trough is at 11 o'clock in the evening to 2 o'clock in the morning (zi Chao), the Yin in the Yin, the Yin of the body, the peak at that time, Yin and Yang mutual restriction, insulin secretion and its sensitivity in the night at the lowest, in the morning (6-7 o'clock) and reached the peak, for normal healthy people, glucose concentration increases at night, to the morning gradually decreased, this situation is related to insulin secretion and insulin sensitivity, can regulate the physiological status of glucose steady state. In patients with type 2 diabetes, the function of the islet is reduced, and the insulin secreted in the morning cannot meet the regulation of glucose homeostasis, so type 2 diabetes is prone to "dawn phenomenon". Between 11pm and 2pm (late afternoon) is the second trough of insulin secretion, which can lead to type 2 diabetes if the amount of insulin cannot be satisfied when stimulated by lunch eating.

Therefore, when the human body's lifestyle changes, the related hormones regulating blood glucose homeostasis (insulin, glucocorticoid cortisol, melatonin, growth hormone) in the body also occur circadian rhythm disorder, which will increase the risk of diabetes. "Plain ask. Angry tongtian theory" said: "The popularity of Ping Dan, the sun and Yang qi long, the west and Yang qi has been empty, the valve is closed. It is because of the twilight and refuse, no bones, no fog, on the contrary, the shape is sleepy thin." Therefore, when the circadian rhythm of the human body is disturbed and the meridian flow runs in violation of the law, it will lead to the imbalance of Yin and Yang in the body.

4.2. Dysfunction of zang-fu organs

4.2.1. Treat from the spleen

"Taiping Shenghui Bureau fang" said, "The five flavors of the husband enter the mouth, hide in the stomach, and the spleen acts, its qi and liquid in the spleen, so that the population is sweet. When this fat beauty occurs, the person must eat the sweet, and overflow to quench thirst [9] ". The spleen is the body fluid of the stomach, long-term intake of fatty products, the spleen and stomach transport and loss of division, the body of qi, blood and body fluid, without normal transport of body fluid, long as this goes on, thick flavor of sorghum stagnation heat, consumption of water, grain and jin taste, overflow for thirst. Spleen deficiency is the key pathogenesis, in the treatment of diabetes, the use of spleen and qi, spleen and dampness, etc., can effectively control blood sugar. Zhang Cuiping [10] Through the study of the relationship between ziwuliuzhu and the viscera points out that the average blood glucose and high glycemic index are almost the highest point, at this time for foot Taiyin spleen by the time of the flow, at this time the temper does not rise, from the perspective of Western medicine, the reaction is high blood sugar. Liu Yuxin [9] From the Yin

and Yang treatment of thirst, the spleen Yin as insulin, Yang as insulin function, when the imbalance of Yin and Yang, spleen Yang and spleen Yin, deficiency of spleen Yang, its warm, promoting function is weakened, leading to the normal distribution of spleen Yin, that is to say, the weakened insulin function leads to insulin resistance or insufficient insulin secretion, resulting in increased blood sugar, decreased metabolic ability, the body retention of a large number of fat sweet taste products, endogenous thirst over time.

4.2.2. Treatment from the perspective of liver

In ziwu liuzhu hour, Zichao hour is the corresponding time of the liver and gallbladder meridian. Qi is mainly generated at this time, and the liver is the main qi machine. Professor Lu Renhe, master of Traditional Chinese medicine[11]It is believed that the patients with diabetes usually like to eat fat and sweet taste, the diet is not proper, leading to the loss of thought of the spleen and stomach transport, the dampness evil over time to generate heat stagnation of the liver and gallbladder, liver loss and drainage, affecting the function of the spleen and stomach rise and fall, the liver Yin deficiency over time, liver and kidney homology, liver Yin can affect the kidney Yin, the imbalance of Yin and Yang over time can cause thirst. From the perspective of Western medicine, the liver is an important metabolic organ of the human body. Insulin in the liver promotes glycogen synthesis and inhibits gluconeogenesis. Abnormal liver metabolism will lead to insulin resistance, and insulin resistance can reduce insulin sensitivity. Zichukuo is also a trough of insulin secretion. People with long-term shift work and circadian rhythm disorder have low liver metabolism and easy insulin resistance from the perspective of Western medicine. In terms of Chinese medicine, it can cause liver loss and drainage, imbalance of Yin and Yang and qi. From the liver treatment, liver qi chang, liver blood storage function has been improved, accelerate the regulation of blood metabolism and body metabolic waste discharge.

5. Timing of administration

Timing of drug administration is based on the changes of human physiology and pathology, giving different time for different drugs in order to achieve the best therapeutic effect. Timing therapy is widely used in clinical practice. Based on the theory of "correspondence between heaven and man" in TRADITIONAL Chinese medicine, different patients should choose the time of administration according to the ups and downs of Yin and Yang in their viscera [12] A. Based on literature research. The theory of pathogenesis of diabetes includes spleen deficiency, qi and Yin deficiency, blood stasis, phlegm-dampness and so on, with qi and Yin deficiency being the most common. Due to the change of lifestyle and constitution of modern people, the proportion of dampness-heat syndrome element is also increasing. From the perspective of traditional Chinese medicine treatment of diabetes, timing of drug administration for patients with spleen deficiency syndrome, Xu Liangyin[13] According to the timing of spleen strengthening method, the blood glucose of normal mice showed circadian rhythm, but the circadian rhythm of diabetic mice showed disorder, and the circadian rhythm recovery of 6am was more ideal than that of other times, and the spleen strengthening method could reduce the blood glucose concentration. According to the pathological rhythm of "splenic disease, noon fu wei, very early sunrise, quiet in the afternoon", it can also be concluded that the effect is best when the pathological rhythm rises most. For patients with qi and Yin deficiency syndrome, it is necessary to nourish qi and Yin, according to Yang in the day and Yin in the night, so the best effect of medication is given at night when Yin is most vigorous. For the patients with blood stasis syndrome, according to the theory of meridian circulation injection, when the meridian is the most vigorous time of qi and blood and Yang qi, drugs to promote blood circulation and remove blood stasis can get a better effect.Zhang Zhongjing

put forward that "man quench thirst, urinate more, drink a bucket, urinate a bucket, shenqi pill is the main", Shenqi pill is mainly Yang medicine, Pingdan is Yang Qi, at this time to give Yang medicine is the best effect. According to the theory of febrile diseases, "When you want to solve jue Yin disease, you should start from the Chou to the MAO". According to the syndrome differentiation of the six meridians, the liver meridian is the most vigorous from the Chou to the MAO. Some studies have pointed out that insulin is the most sensitive at 4am, and a satisfactory effect can be achieved by giving a low dose of insulin. From the perspective of timing of hypoglycemic administration in Western medicine, Xu Fangqin [14] It is suggested that hypoglycemic drugs can have the best effect when they are given at 4 o'clock in the morning. Therefore, most hypoglycemic drugs can achieve better effect when they are given in small doses in the morning. Diabetes is closely related to the secretion of various hormones. For example, for patients with spleen deficiency diabetes with insulin resistance or impaired islet function, spleen-strengthening drugs can be administered at the peak of insulin secretion (6-7 points). Therefore, according to the effect of drugs in different periods, based on the theory of meridian flow, timing of administration, to reduce drug dosage, reduce side effects, to achieve better therapeutic effect [14] A.

6. Conclusion

The theory of Meridian flow is based on the theory of Yin and Yang and Tibetan images, and the twelve meridians flow is the basic content, involving zang Fu organs, qi and blood. By studying the meridian flow theory and the factors influencing the circadian rhythm of blood glucose, we can provide a better diagnosis and treatment idea for the future treatment of diabetes from the imbalance of Yin and Yang, the dysfunction of zang-fu organs and the timing of drug administration.

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