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Treatment of Coronary Heart Disease from the Perspective of Liver Controlling Dispersion

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Abstract: The liver is in charge of distributing and regulating the movement of qi throughout the whole body, coordinating the transportation and transformation of the internal organs in the middle part of the body, promoting the biochemical circulation of qi, blood, and body fluids, and regulating emotions. Liver dysfunction can disrupt the transportation and transformation of qi, blood, and body fluids, causing phlegm turbidity, blood stasis, and other unwanted symptoms. Poor regulation of emotion further aggravates the accumulation of pathological substances, resulting in the obstruction of heart vessels, and ultimately coronary heart disease (CHD). Through regulating lipid metabolism, inflammatory reaction, vasoactive substances, platelet function, neuroendocrine, and other factors, liver controlling dispersing qi plays a comprehensive role in the prognosis of atherosclerosis, the primary cause of CHD. Therefore, it is recommended to treat CHD from the perspective of liver-controlling dispersion.

Keywords: Liver controlling dispersion; Coronary atherosclerotic heart disease; Atherosclerosis; Traditional chinese medicine; Treatment

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1. Introduction

Coronary atherosclerotic heart disease (CHD) is mainly caused by atherosclerosis in the coronary arteries, which partially or completely blocks the arterial lumen. Due to insufficient blood supply from the coronary arteries, the metabolic needs of the myocardium are not fulfilled, resulting in myocardial ischemia, hypoxia, and even necrosis. Atherosclerosis is the key link in coronary artery disease and is involved in many processes, including abnormal blood lipids, inflammatory reactions, platelet function, and neuroendocrine regulation. CHD falls under the scope of traditional Chinese medicine (TCM), which is categorized as "chest tightness," "heart pain," and "true heart pain." The pathogenesis of this disease is due to liver qi stagnation and heart vessel obstruction. According to the Yellow Emperor's Inner Classic, the site of onset is the meridian passage associated with the heart and liver.

The concept of the liver's function in controlling dispersion focuses on the smooth regulation of qi throughout the body by the liver, assisting in the transportation and transformation of food by the spleen and

stomach, bile secretion and excretion, improved circulation of body fluids, and emotional balance. When the liver controls the qi dispersion harmoniously, the qi flow between the internal organs and meridians operates in an orderly manner. This normalizes the metabolism of food and water, regulates the distribution of qi and blood, and stabilizes emotions. Hence, the occurrence of pathogenic factors such as phlegm and blood stasis can be avoided. If the liver fails to operate normally, the coagulation of phlegm, turbidity, and stagnant blood will likely occur. This article discussed the treatment of CHD from the perspective of liver controlling dispersion in TCM, combined with the etiology and pathogenesis of CHD and modern medical research.

2. The relationship between the liver and modern medicine in the visceral manifestation of TCM

Based on the visceral manifestation of TCM, the liver has the physiological function of controlling the dispersion and storage of blood. Modern medicine believes that the liver is an important site for the metabolism and redistribution of various substances like lipids. In TCM, the liver is a comprehensive functional complex made up of multiple systems, mainly involving the nervous, endocrine, and metabolic systems. It is closely related to the limbic system, the hypothalamus-pituitary-adrenal (HPA) axis, the smooth muscle of the blood vessels, etc. Therefore, the concept of liver in TCM overlaps with the concepts of the brain, spleen, and liver in modern anatomy [1,2].

3. The TCM concept of the liver's function in controlling dispersion

The specific process of liver controlling dispersion is as follows [3,4]. The main idea is to regulate and balance the rise, fall, entry, and exit of qi, ensuring the normal and harmonious functions of the internal organs and meridians. Liver qi promotes the transportation and transformation of food into nutrients in two aspects: coordinating the spleen's upward movement and the stomach's downward movement, and facilitating the secretion and excretion of bile. Liver qi also allows for the normal transportation and distribution of body fluids. Liver qi influences the blood vessels of the heart, facilitating blood flow to the brain and regulating emotions. Furthermore, the reproductive function of men and women benefits from the harmonious coordination between liver controlling dispersion and kidney retention.

4. The theoretical research on the liver controlling dispersion and CHD

4.1. Liver qi affects CHD by regulating the qi mechanism of the body and promoting the circulation of fluid and blood

Obstruction of the heart arteries is the key pathogenic factor in CHD. Qi plays a crucial role in the circulation of blood. Blood flows when qi flows and stops when qi becomes stagnant. When the liver qi is functioning normally, qi flows smoothly throughout the body. This promotes the normal circulation of blood, ensuring normal function of the heart and blood vessels. Researchers have pointed out that the imbalance of qi and blood due to the loss of liver function is the basic pathogenesis in the process of coronary artery plaque development [5].

4.2. Liver qi affects CHD by promoting the transportation and transformation of food and water in the spleen and stomach, and the secretion and excretion of bile

The control of dispersion acts as a bridge between the spleen and liver in the TCM Five Element Theory [4]. The liver controlling dispersion ensures harmonious coordination between the stomach's digestion of food and the

spleen's transformation and transportation of body fluids. Abnormality in these processes causes fluid retention and blood stasis, where blood vessels become permeable and eventually lead to heart blockage. Experts have pointed out that disruptions in the liver's function in controlling dispersion and the spleen-stomach movement results in chest pain [6]. Some scholars believe that the main approach to treating chest pain is to balance the liver qi, strengthen the spleen, dissolve phlegm, and remove blood stasis [7].

In TCM, the liver and gallbladder are interdependent, with the production and function of bile regulated by the liver. Modern medicine has discovered that not only is acidic bile a risk factor for atherosclerosis but it is also closely related to other risk factors for atherosclerosis [8]. From an anatomical perspective, the vegetative nerves control the heart and bile duct and overlap at the thoracic spinal nerves. Therefore, biliary diseases may affect the great cardiac nerve fibers in the precordium, resulting in angina pectoris, a group of diseases known as the cholecystocardiac syndrome. The basic pathogenesis of the intermittent period of cholecystocardiac syndrome in TCM involves liver depression and stagnation of qi, or spleen deficiency and liver depression accompanied by dampness and heat. Relevant scholars advocated to treating it with the "Four-way Method," with Chaihu Shugan soup and Xiaoyao capsules commonly used as prescriptions [9].

4.3. Liver-qi affects CHD by regulating emotions

Chinese ancient medical practitioners believed that chest pain can be triggered by emotional changes, and proposed that liver depression is the starting factor for various mental and emotional imbalances. Chest pain caused by emotional disorders is closely related to liver depression. Chest pain caused by non-emotional disorders is also influenced by the liver's function of controlling dispersion and regulating emotions because, in TCM, the heart is made up of physical and spiritual aspects. Liver depression and emotional disorders can cause dysfunction of the physical heart through spiritual influence, resulting in the obstruction of the heart vessels.

With the advancements in biopsychosocial medical models, the concept of mood disorders has become increasingly popular, where CHD is complicated by anxiety, depression, and other psychological disorders. It was believed that mood disorders are closely related to the normal function of the heart and liver, with qi stagnation as the initial factor [10]. Relevant literature showed that the most affected organs of anxiety and depression-caused CHD are the heart and liver, and the most common syndromes were related to stagnation of qi. The core pathogenesis of the two organs can be summarized as stagnation of qi and stasis of blood [11]. Another cross-sectional study also found that qi depression was the core pathogenesis in CHD patients with mood disorders [12].

5. Research on the treatment of CHD from the perspective of the liver's function of controlling dispersion

5.1. Correlation between the liver's function of controlling dispersion and regulating lipid metabolism

The liver is the main organ in charge of lipid metabolism, which facilitates the formation of foam cells, lipid streaks, and atherosclerotic plaques in the arteries by regulating the synthesis and degradation of cholesterol, low-density lipoprotein, and very low-density lipoprotein, and clearing the remaining particles of chylomicrons [13, 14]. An experiment analyzed the molecular mechanism of lipid transformation in atherosclerosis from a metabonomic and proteomic point of view [15]. It was found that sterol carrier protein-2 (SCP2), a non-specific lipid transport protein expressed by the liver, promoted the development of atherosclerosis by regulating lipid metabolism and fatty acid metabolism [16]. Liver X receptor alpha (LXRα) plays an important role in cholesterol homeostasis and lipid metabolism. A foreign cohort study confirmed that the genetic polymorphism rs2279238

of this particular gene acts as a genetic risk factor that affects its occurrence and progression [17].

The function of the liver in controlling dispersion can regulate lipid metabolism, and reduce the infiltration and obstruction of lipids in the vascular endothelium, thus preventing the formation of atherosclerotic plaques. Wang et al. [18] verified that the high, medium, and low doses of Chaihu Shugan soup had regulated the levels of these blood lipid indicators, including triglycerides, total cholesterol, and low-density lipoprotein cholesterol, in the serum of rats. It was further clarified that not only does soothing the liver directly adjust serum lipid levels but also indirectly regulates lipid metabolism by regulating LXRα [19,20].

5.2. Correlation between the liver's function of controlling dispersion and inflammatory factors as well as vascular active substances

The pathophysiological mechanism for the occurrence and development of atherosclerosis involves many inflammatory factors [21]. Some scholars believe that atherosclerosis is considered a form of inflammation on its own, and the life-threatening complications of atherosclerotic diseases are all related to acute systemic inflammation [22]. A balanced level of vascular active substances regulates the function and structure of the vascular endothelium, which is an important factor in atherosclerosis [23]. Dysregulation of lipid metabolism, inflammatory response, and vascular active substances will result in a vicious cycle that promotes the progression of atherosclerosis [23–26].

The liver's function of controlling dispersion inhibits the secretion of inflammatory factors and vascular active substances, improves vascular spasms and narrowing, and reverses atherosclerosis. TCM prescriptions with liver-soothing effects can downregulate the expression of serum endothelin-1 (ET-1), reverse endothelial dysfunction mediated by nitric oxide, reduce inflammatory factors such as C-reactive protein, interleukin-1β, interleukin-6, tumor necrosis factor-α, nuclear factor-κB, and matrix metalloproteinase-9 to alleviate inflammatory reactions [19,20]. The integrated pharmacological research on the derivative formula of Xiaoyao capsules found that the key targets of Chinese medicine components were significantly related to lipid metabolism and inflammation. *In vivo* and *in vitro* experiments confirmed that the capsule significantly reduced plasma inflammatory cytokines, reduced lipid deposition in cells, and inhibited the production of macrophages induced by oxidized low-density lipoproteins [27]. Other studies have shown that the pathological changes in the aortic tissue of rats were delayed, verifying that liver-soothing prescriptions effectively alleviated endothelial injuries [18, 20].

5.3. Correlation between the liver's function of controlling dispersion and platelet's function

Blood platelets and vascular endothelial cells accumulate around the narrow coronary artery and respond to the mechanical environment by altering the biomechanics and promoting atherosclerosis and thrombosis [28]. Excessive activation and aggregation of platelets are the main causes of coronary artery thrombosis [29].

The liver's function in controlling dispersion regulates platelet activation and aggregation, reduces blood viscosity, stabilizes hemodynamics, inhibits thrombosis, reduces the incidence of cardiovascular events, and reduces mortality [30,31]. It ultimately affects hemorheology by regulating the trimethylamine (TMA)/ flavin-containing monooxygenase 3 (FMO3)/ trimethylamine N-oxide (TMAO) pathway of gut microbiota [32].

5.4. Correlation between the liver's function of controlling dispersion and neuroendocrine regulation

When the HPA axis is overactive, the sympathetic nervous system becomes activated, causing changes in heart rate and blood pressure, which increases myocardial oxygen consumption, promotes oxidative stress and

inflammatory reactions, damages the vascular endothelium, affects platelet function, increases blood viscosity, causes coronary artery spasms, and decreases coronary blood perfusion [33].

The liver's function in controlling dispersion affects mood disorders through neuroendocrine regulation by regulating the HPA axis and the sympathetic nervous system. Chaihu Shugan soup can reduce the blood plasma levels of corticotropin-releasing hormone, correct the abnormal function of the HPA axis, and normalize the serotonin transporter of the hippocampal pathway [34].

6. Conclusion

Disruption in the liver's function in controlling dispersion leads to the disorder of qi movement throughout the body and causes blood stasis. Abnormality in the transportation and transformation of food by the spleen and stomach leads to the formation of phlegm, while emotional disturbances further aggravate the accumulation of various pathological substances, which eventually results in CHD. Modern medical research has confirmed that liver-soothing therapy can effectively regulate lipid metabolism, alleviate inflammatory reactions, balance levels of vascular active substances, change the state of coagulation, promote neurohumoral regulation, and prevent atherosclerosis. The liver's function in controlling dispersion has also been proven in TCM. Western medicine is capable of treating CHD, hence the perspective of the liver's function in controlling dispersion should be taken into consideration during the treatment of CHD.

Disclosure statement

The authors declare no conflict of interest.

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