

The Relationship between Intestinal Microflora and Coronary Heart Disease and the Research Status of Traditional Chinese Medicine Intervention

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Abstract: Coronary heart disease (CHD) is a disease such as angina pectoris caused by lumen stenosis caused by coronary atherosclerosis. It is one of the cardiovascular diseases with high morbidity and mortality. The pathogenesis of the disease is very complex, and there are many inducing factors. Modern studies have shown that intestinal flora is a new target for the prevention and treatment of CHD. Inflammation caused by intestinal flora imbalance and its metabolites such as short-chain fatty acids (SCFAs), bile acids (BAs) and trimethylamine oxide (TMAO) can directly or indirectly affect the development of CHD. In recent years, Chinese medicine intervention on intestinal flora in the prevention and treatment of CHD has been a hot topic. Modern doctors have made many achievements in the use of traditional Chinese medicine to intervene intestinal flora in the prevention and treatment of CHD based on the theory of "heart-to-small intestine", the theory of homology of medicine and food, and the theory of acupuncture and moxibustion. This paper summarizes the research on the intervention of traditional Chinese medicine on intestinal flora in the prevention and treatment of CHD by consulting relevant contributions in Chinese and English in recent years. It is found that monomers or extracts of traditional Chinese medicine, Chinese medicine pairs and traditional Chinese medicine preparations can regulate the occurrence and development of CHD by interfering with intestinal flora, such as regulating the risk factors of CHD, such as blood glucose and blood lipids, or increasing the production of SCFAs to prevent atherosclerosis, reducing the production of TMAO and preventing thrombosis. It is expected that this discussion can provide a new idea for traditional Chinese medicine to interfere with intestinal flora in the prevention and treatment of CHD.

Keywords: CHD; intestinal flora; TCM theory; mechanism; homology of medicine and food; traditional Chinese medicine.

Coronary heart disease (coronaryheartdisease,CHD) is due to coronary atherosclerotic lesions caused by lumen stenosis, obstruction, myocardial ischemia and hypoxia and lead to angina pectoris, acute myocardial infarction and so on, which can eventually lead to sudden death^[1]. The morbidity and mortality of this disease have been high all over the world. At present, western medicine mainly uses nitrate, lol and dipine to interfere with CHD, which can achieve the purpose of treatment in a short time, but its long-term use is easy to cause nervous system damage and side effects such as cough, allergy and abnormal renal function. The effect of some patients continues to decrease after taking medicine, and the therapeutic effect is not ideal^[2]. Studies have shown that^[3] intestinal flora is a potential source of atherosclerotic bacteria, such as intestinal flora imbalance can accelerate the progression of cardiovascular disease. According to the location and characteristics of CHD pain, it is classified into "heart failure", "chest arthralgia" and "heartache". The main pathogenesis of the disease is heart pulse obstruction, involving heart, lung, liver, spleen and kidney and so on. The heart governs the blood, the lung governs the festival, and the two coordinate with each other, so that qi and blood can run smoothly. If deficiency of qi, deficiency of yin and deficiency of yang lead to loss of nourishment of heart pulse and inability to promote blood circulation, or obstruction of heart pulse such as cold coagulation, qi stagnation, phlegm and turbid phlegm, it will be chest arthralgia and heartache, which will lead to heart failure. In recent years, under the guidance of traditional Chinese medicine theory, the research on the intervention of traditional Chinese medicine on intestinal flora in the treatment of CHD has attracted much attention, and has gradually become a new direction in the treatment of CHD. By consulting the relevant Chinese and English literature in recent years, the author summarizes the related research on

the intervention of traditional Chinese medicine in the prevention and treatment of CHD, in order to provide new ideas for the prevention and treatment of CHD.

1. An overview of intestinal flora

Intestinal microflora is a microflora colonized in intestinal anaerobic and nutritious environment^[4], which may include beneficial symbiotic microorganisms and pathogenic bacteria^[5]. Beneficial bacteria such as *Faecalibacteriumprausnitzii* and *Roseburiaintestinalis* can repair the normal function of intestinal barrier and play an anti-inflammatory role^[6]. Pathogenic bacteria such as *Escherichia coli*, *Lactobacillus*, *Streptococcus* and *Helicobacter pylori* can interact with the host to regulate immune response^[7]. After environmental changes, pathogenic bacteria can have a pathogenic effect on the host^[8]. In the case of immune dysfunction, it can be greatly increased, and can be transferred from the intestinal tract to other viscera such as the heart to cause disease^[9]. Under normal circumstances, intestinal flora can regulate human function by releasing different metabolites. Imbalance of intestinal flora can reduce beneficial substances including short-chain fatty acids (SCFA) and break the intestinal barrier. It will also produce a large number of toxic metabolites, such as lipopolysaccharide (LPS), trimethylamine-N-oxide (TMAO), phenylacetylglutamine (PAGln), etc, which enter the bloodstream and accelerate the progression of cardiovascular disease^[10].

2. Intestinal flora and the mechanism of occurrence and development of CHD

Abnormal intestinal flora can form CHD by affecting lipid metabolism and inducing inflammation^[11]. The effects of imbalance of intestinal flora, metabolites produced by intestinal flora and related signal pathways on atherosclerosis may explain part of the mechanism of the occurrence and development of CHD. Intestinal microflora can maintain a normal intestinal mucosal barrier, and studies have shown that the interaction between intestinal microbiota and the host is essential for the host to maintain normal intestinal and physical function^[12]. At present, it is generally believed that intestinal flora imbalance is an important factor affecting the integrity of intestinal barrier^[13]. Overactivated inflammation caused by intestinal microflora imbalance destroys normal intestinal mucosal barrier function, such as LPS can damage intestinal mucosal barrier function and increase intestinal permeability to promote bacterial translocation, leading to endotoxemia and inflammation, thus increasing the risk of cardiovascular disease. Increase the incidence of CHD^[14]. Intestinal microflora interact with human metabolism through a series of bioactive metabolites produced^[15], such as short-chain fatty acids (SCFAs), primary and secondary bile acids (BAs), phenylacetylglutamine (PAGln), trimethylamine oxide (TMAO), etc^[16]. SCFA can regulate diet and energy intake, reduce intestinal inflammation to maintain the integrity of the barrier and prevent atherosclerosis^[17]. It can be used as a potential target for the treatment of CHD to regulate lipid metabolism and reduce inflammation^[18]. BA plays an important role in intestinal microbiota and cholesterol excretion^[19], it mainly binds to FXR and TGR5^[20], inhibition of FXR can promote BAs metabolism^[21], improve atherosclerosis and slow down the development of CHD; activation of TGR5 can reduce the area of atherosclerotic plaque and inflammation in plaque, and inhibit macrophage phagocytosis of oxLDL^[22]. TMAO can promote thrombosis and vascular endothelial injury and promote the production of atherosclerotic plaques^[23], thereby increasing the risk of CHD. ChenML et al. Nuclear factor-kappa B (NF- κ B) is one of the important signal pathways involved in thrombosis and inflammation, as well as cell survival, proliferation and activation^[24]. MaG^[25] studies have shown that TMAO can enhance monocyte adhesion by activating protein kinase C/NF- κ B/vascular cell adhesion molecule-1 pathway, and promote atherosclerosis to increase the risk of CHD.

3. The Theory of "Heart and small intestine" guided the intervention of traditional Chinese Medicine in the Prevention and treatment of CHD by intestinal microflora

The theory of "heart and small intestine" can be used to guide traditional Chinese medicine to interfere with intestinal flora in the treatment of CHD, which comes from "Lingshu Ben Shu". It is mentioned in the book: "heart and small intestine, small intestine, receive prosperous viscera". Its theory is mainly reflected in the relationship between the heart and the small intestine. in the physiological state, the heart governs the blood, which can produce and circulate blood, and the important conditions for the small intestine to be enlarged are the warmth of the heart-yang, the nourishment of the heart-blood and the promotion of the heart-qi; the small intestine is mainly affected

by the exuberant, and the main secretion of the small intestine is turbid, which can absorb the essence of water valley and water, and a strong part of it is uploaded to the spleen, and the spleen dominates the clearing, and the heart turns red into blood to nourish the heart and pulse. The filthy dregs then descend, pass through the large intestine or gasify through the bladder to become feces or urine excreted out of the body to prevent moisture from staying on the heart and lungs^[26]. The theory of "heart-intestine axis" put forward by KamoT^[27] is similar to the theory of "heart and small intestine". Heart failure is the final stage of CHD. The study explained the relationship between intestinal flora and heart failure. It is found that under the guidance of traditional Chinese medicine theory, a variety of single traditional Chinese medicine^[28] and compound^[29] can improve intestinal microbial ecology and reduce related metabolites, and they can treat or delay the occurrence and development of CHD through a variety of mechanisms.

4. Study on Prevention and treatment of CHD by intervention of intestinal microflora with traditional Chinese Medicine

4.1 Traditional Chinese medicine extract or monomer

The extract or monomer of traditional Chinese medicine can regulate the microbial composition and distribution structure of intestinal flora and play the role of anti-inflammation and anti-lipid to regulate the balance of intestinal flora^[30]. Imbalance of intestinal flora destroys the balance of glucose metabolism, lipid metabolism and protein metabolism, leading to a series of changes in corresponding metabolites^[31]. Toxic metabolites enter the blood to aggravate inflammation^[32]. Hyperglycemia and hyperlipidemia can cause atherosclerosis, which are risk factors for the occurrence and development of CHD. Inhibition of blood lipids and blood sugar can effectively prevent and treat CHD. The change of blood glucose is related to the community structure and abundance of intestinal flora^[33]. Some studies have shown that^[34] Water extract of *Atractylodes macrocephala* (RAM) can inhibit fat accumulation through Akt/PI3K pathway and play a role in the prevention and treatment of atherosclerosis in CHD. *Atractylodes macrocephala* extract fermented by *Lactobacillus* can protect intestinal mucosal barrier and resist endotoxemia^[35]. In addition, it can also improve the number of intestinal bifidobacteria, Akkerman-sia and the ratio of *Bacteroides* / thick-walled bacteria in endotoxemia rats, and increase the abundance of intestinal microorganisms such as *Bacteroides* and lactic acid bacteria^[36].

4.2 Pair of traditional Chinese medicine

BAs, an active metabolite produced by intestinal flora, can promote the absorption and transformation of intestinal lipids, and can regulate glucose and lipid metabolism through G protein coupled membrane receptors (TGR5) to prevent atherosclerosis^[37]. Mu Guohua^[38] found that *Coptis chinensis* can reduce blood glucose and reduce the release of LPS to inhibit inflammation by increasing the abundance of *Bacteroidetes*, *Actinobacteria*, *Proteobacteria* and *Verrucomicrobia*, so as to effectively interfere with the occurrence and development of CHD. Gao Ruolin^[39] and other studies found that *Coptis chinensis*-cinnamon combined exercise intervention can more effectively reduce the state of hyperglycemia in db/db mice, while significantly reduce the abundance of intestinal microflora in mice, and increase the content of butyric acid, acetic acid and propionic acid in SCFAs can effectively prevent the formation of atherosclerosis.

4.3 Compound preparation of traditional Chinese medicine

Compound preparations of traditional Chinese medicine can directly or indirectly affect the occurrence and development of CHD by interfering with intestinal flora. Qushi Huayu recipe is composed of *Artemisia officinalis*, *Polygonum cuspidatum*, *Herba Euphorbiae*, turmeric and *Gardenia jasminoides*. The study of FengQ^[40] shows that this prescription can increase the abundance of viscous spherical bacteria and verrucous microbacteria in intestinal flora, and reduce the abundance of thick-walled bacteria and non-wall bacteria, so as to inhibit the synthesis of serum lipopolysaccharide, which is helpful to reduce blood lipids and prevent CHD. Li Yubo^[41] and other studies found that Yueju Pill may reduce TC and LDL-C by inhibiting bacteria such as *Pentatomidae* and *Prevodiaceae* in intestinal flora and promoting the growth of bacteria such as *Bifidobacterium* and *Phytophagaceae*. Dong Mingxia^[42] and other studies found that Huangqin decoction could increase the number of *Lactobacillus* and *Bifidobacterium* and improve the blood glucose index and the composition of intestinal flora. Nie Kexin^[43] and other studies have shown that Wumei Pill can change the intestinal

flora structure of obese mice, reduce the ratio of thick-walled bacteria to Bacteroides, regulate SCFAs metabolism and inhibit chronic mild inflammation, promote the secretion of glucagon-like peptides, and play a positive role in the prevention and treatment of CHD.

5. Conclusion and prospect

The intervention of traditional Chinese medicine on intestinal flora under the guidance of the theory of "heart and small intestine", the theory of homology of medicine and food and the theory of acupuncture and moxibustion can effectively prevent and cure CHD. Clinical studies have shown that monomers and extracts of traditional Chinese medicine can control blood lipids and blood sugar by changing the community structure and abundance of intestinal microflora, and can also inhibit NF- κ B signal pathway to reduce the risk of atherosclerosis. Traditional Chinese medicine can interfere with the metabolites of intestinal flora to prevent the formation of atherosclerosis; traditional Chinese medicine preparations can interfere with intestinal flora at multiple levels and targets. It can increase the abundance of viscose spherical bacteria, verrucous microbacteria and other bacteria and reduce the abundance of thick-walled bacteria and non-wall bacteria effectively reduce blood lipids, increase the number of beneficial bacteria and reduce the number of pathogenic bacteria. Based on the above summary, traditional Chinese medicine can effectively prevent and treat HF by regulating the imbalance of intestinal flora, improving intestinal microenvironment and inflammation, and intervening intestinal metabolites. It can gradually replace the use of western medicine or the combination of traditional Chinese and western medicine to improve the survival and quality of life of patients. At present, the intervention of traditional Chinese medicine on intestinal flora is a new direction for the prevention and treatment of CHD, but its research still has some limitations. First of all, there are often some problems in clinical research, such as insufficient sample size, insufficient theoretical support, insufficient data processing and so on, so it is impossible to explain which components of traditional Chinese medicine act on which flora in the intestinal tract to play the role of prevention and treatment of CHD. Secondly, there are few studies on the prevention and treatment of CHD by acupuncture and moxibustion therapy, and a large number of clinical studies are needed to support it. Finally, there is a lack of a complete system to guide traditional Chinese medicine to intervene intestinal flora in the prevention and treatment of CHD. Therefore, the intervention of traditional Chinese medicine on intestinal flora in the prevention and treatment of CHD needs to be further explored.

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