Research Progress of Treating Myocardial Fibrosis with Traditional Chinese Medicine

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Abstract

Myocardial fibrosis is a disease characterized by excessive accumulation of collagen fibers in myocardial extracellular matrix, unbalanced metabolism, unbalanced proportion and disordered arrangement of collagen components. Myocardial fibrosis runs through the occurrence and development of various cardiovascular diseases, and prevention and treatment of myocardial fibrosis is an important means to treat various cardiovascular diseases. The main clinical manifestations of this kind of patients are chest tightness, chest pain, dizziness, dizziness and dyspnea, etc. The main causes of this kind of diseases are myocardial hypertrophy, dilatation and fibrosis. At present, the prevention and treatment of myocardial fibrosis in western medicine is relatively simple, and the effect is not good. It is an important subject to study the prevention and treatment of myocardial fibrosis by traditional Chinese medicine, which is conducive to improving clinical efficacy and improving patients' clinical symptoms.

Keywords

Myocardial fibrosis, Chinese medicine, Mechanism, Research status

Introduction

Myocardial fibrosis refers to the excessive deposition of collagen fibers in the normal tissue structure of myocardium caused by various reasons, the concentration and volume fraction of collagen increased significantly, the ratio of various types of collagen was out of balance, and the characteristics, configuration and arrangement of collagen changed in myocardium. Myocardial fibrosis is a common pathological change when many cardiovascular diseases develop to a certain stage. The occurrence of myocardial fibrosis leads to the increase of myocardial stiffness, the loss of normal myocardial structure and pathological myocardial remodeling, which promotes the progressive deterioration of cardiac function and seriously affects the prognosis of cardiovascular diseases. Many studies have confirmed that many kinds of compound Chinese medicines and single Chinese medicine can inhibit or reverse the occurrence and development of myocardial fibrosis, which shows that Chinese medicine has certain advantages in resisting myocardial fibrosis. In this paper, the mechanism of intervention of traditional Chinese medicine on myocardial fibrosis is reviewed.

1. TCM understanding of myocardial fibrosis

Myocardial fibrosis is a pathological name put forward by modern medicine, which is not related to myocardial fibrosis in ancient Chinese medicine literature.

Corresponding disease name is recorded. However, according to the common pathological changes of various cardiovascular diseases from the development to the final stage, myocardial fibrosis can be classified into the cate-
gories of heart obstruction, palpitation, asthma syndrome and edema. In expounding the etiology and pathogenesis of myocardial fibrosis, some scholars believe that [1] the pathogenesis of myocardial fibrosis always belongs to the deficiency of the original, which is qi deficiency and yin and yang deficiency, and the excess is blood stasis, phlegm and heat toxin. In the treatment, it is often necessary to treat according to syndrome differentiation and combine symptoms with symptoms. According to the pathological changes of myocardial fibrosis induced by different primary diseases and the macroscopic syndrome differentiation of the disease in clinic, the treatment concept of "combining disease with syndrome" is embodied. Rheumatoid arthritis [2] involves the heart and causes myocardial fibrosis. The pathogenesis is always spleen deficiency and dampness excess, qi and blood deficiency, phlegm and blood stasis, and the treatment is to replenish qi, strengthen spleen and dredge collaterals. The characteristics of myocardial interstitial hyperplasia, decreased compliance and collagen deposition can be attributed to the categories of "phlegm drinking" and "accumulation" in traditional Chinese medicine; According to its clinical characteristics, it can be classified as "palpitation" and "chest arthralgia". Once MF begins, the cardiac compliance will slowly decrease, and the coordination and elasticity of myocardial movement will also decrease, which will directly affect the cardiac ejection ability and blood flow velocity, making it easier to form pathological products such as "mural thrombus" [3].

2. The effect and mechanism of traditional Chinese medicine on myocardial fibrosis

2.1 Regulating Renin-Angiotensin-Aldosterone System

Intervening myocardial fibrosis. The occurrence of myocardial fibrosis is closely related to the renin-angiotensin-aldosterone system, and the abnormal activation of renin-angiotensin-aldosterone system is closely related to myocardial fibrosis. Angiotensin II and aldosterone in circulation can cause myocardial fibrosis by promoting collagen fiber deposition, inhibiting collagen degradation and stimulating fibroblasts to synthesize collagen, respectively. Local AngII can act on cardiomyocytes to induce apoptosis through angiotensin II receptor type I and II (AT1 and AT2), and affect bradykinin (BK), NO and other cardiovascular active substances to cause myocardial fibrosis.

2.2 Intervention of cell signaling pathway, multi-target regulation of myocardial fibrosis.

TGF-β is a cytokine closely related to collagen metabolism and extracellular matrix (ECM) accumulation, and its biological effects are mainly exerted through TGF-β/Smads signaling pathway. TGF-β is up-regulated and Smad expression is increased in myocardial infarction, which is related to the sustained expression of collagen and fibroblast. Under pathological conditions, Smads, as a signal integration molecule, interacts with extracellular signal-regulated kinase MAPK pathway, nuclear transcription factor-κ B (NF-κ B) and other pathways. TGF-β-mediated phosphorylation of Smads can induce CFs to differentiate into fibroblast phenotype, and promote CFs proliferation and collagen synthesis. Therefore, TGF-β/Smads pathway plays a very important role in MF caused by many factors. It is found that ShensongYangxin Capsule can inhibit MF of diabetic cardiomyopathy and improve cardiac function, and its mechanism may involve inhibiting the activity of TGF-β1/Smad signaling pathway [3]. CTGF can promote fibroblast division and collagen deposition, which is related to the occurrence and development of fibrosis in many organs.

2.3 Regulating collagen metabolism and correcting the imbalance of ECM synthesis and degradation

Myocardial fibrosis is the result of imbalance between collagen synthesis and degradation, and its formation mechanism is very complicated. Fibroblasts in the time phase of myocardial fibrosis are activated (phenotypically changed) under the stimulation of mechanical load and chemical signals, and become fibroblasts with the ability of proliferation and active secretion. Together with fibroblasts migrating to myocardial tissue, they participate in myocardial fibrosis. On the one hand, they secrete a large number of different types of collagen and other extracellular matrix (ECM) components in the form of procollagen molecules, and at the same time, they regulate the activities of collagenase, endopeptidase and other enzymes related to collagen decomposition, polymerization and maturation in ECM, thus making the collagen network structure.

Wang Zhouping [4] and others discussed the intervention effect of resveratrol on myocardial fibrosis in chronic viral myocarditis, and confirmed that resveratrol could reduce the contents of P i NP and P iii NP, significantly reduce collagen synthesis and increase degradation, and inhibit myocardial fibrosis. In vitro, it was found that matrine inhibited the proliferation and collagen synthesis of human embryonic lung fibroblasts (HFL-I) induced by AngII ii similar to cardiac fibroblasts in a concentration-dependent manner, thus playing an effective anti-fibrosis role.
2.4 Regulate gene expression and prevent myocardial fibrosis

The change of gene expression plays an important role in the occurrence and development of myocardial fibrosis. Through the study of diabetic cardiomyopathy model mice, it is confirmed that Astragalus polysaccharide treatment can significantly reduce the expression and activity of chymotrypsin gene in local myocardium of mice, and inhibit the level of AngII ii in local myocardium, thus reducing the content of type i collagen and the ratio of type i collagen to type iii collagen, and reducing collagen deposition to resist MF [5]. Puerarin can inhibit myocardial fibrosis in spontaneously hypertensive rats by reducing the content of AngII, down-regulating the mRNA expression of myocardial fibrosis chemokine MCP-1 and PAR 2, and reducing the infiltration of cardiac macrophages.

3. Treatment of myocardial fibrosis with traditional Chinese medicine extract

Traditional Chinese medicine extract is a kind of traditional Chinese medicine product with relatively clear material basis and strict quality standards, which is obtained by extracting, separating and processing traditional Chinese medicine or traditional Chinese medicine compound with modern science and technology, and can be used as the raw material of traditional Chinese medicine preparation. Traditional Chinese medicine extracts for treating MF include invigorating qi and promoting blood circulation, promoting blood circulation and removing blood stasis, and clearing away heat and toxic materials. Luteolin, a flavonoid compound, can protect myocardial cells from injury induced by hypoxia/glucose deprivation/reoxygenation through inhibiting lipoperoxide pathway and anti-inflammatory effect. Tritetanol is mainly extracted from drugs such as tonifying deficiency, hemostasis and relieving exterior syndrome (such as Radix Astragali, Radix Ginseng, Radix Glycyrrhizae, Radix Notoginseng and Radix Bupleuri). Quinones are extracted from drugs (such as salvia miltiorrhiza, cassia seed, Arnebiaeuchroma, rhubarb and aloe) that promote blood circulation and remove blood stasis, clear heat, diarrhea and diuresis. Alkaloids are mostly extracted from drugs for clearing away heat and toxic materials, promoting blood circulation and removing blood stasis (such as Coptidis Rhizoma, Sophora flavescens, Sophora Tonkinensis, Senecio scandens, Ligusticum Chuanxiong, Leonurus japonicus, etc.), while polyamines are extracted from drugs for tonifying deficiency (such as velvet antler). The multi-components of traditional Chinese medicine determine its multi-target and multi-level therapeutic effects, and the specific combination of various pharmacological active substances at the level of effective parts or active ingredients can better reflect the functional characteristics of traditional Chinese medicine.

4. Problems and prospects of Chinese medicine intervention in MF

Although the research on anti-myocardial fibrosis of traditional Chinese medicine started relatively late, it has made gratifying achievements in clinical and experimental research through the unremitting efforts of many scholars. It is found that some traditional Chinese medicines and their effective components have anti-myocardial fibrosis effects, and the mechanism of action is preliminarily clarified through experiments.

Myocardial fibrosis is a complex pathological process, involving RAAS, immune system and various cytokines. Inflammation, apoptosis and cell signal regulation are all related to it, and the formation mechanism of different types of myocardial fibrosis is different in different heart diseases and even the same disease. At present, there are some problems in experimental research: the animal model of myocardial fibrosis is relatively simple; The research ideas and methods are relatively backward; The specific mechanism of action is not clear, and there is a lack of systematic and in-depth research at the cellular and molecular levels; Lack of research on anti-myocardial fibrosis of integrated traditional Chinese and western medicine [6]. In view of the above problems, in the future research, we should strengthen the research on animal modeling design, establish a model that objectively reflects the pathogenesis of human myocardial fibrosis, try our best to be scientific and rigorous in experimental design, broaden our thinking, and further clarify the specific mechanism of Chinese medicine's intervention in myocardial fibrosis by applying modern molecular biology technology from the whole, organ, cell, molecule and gene levels. Seek new breakthroughs in the following aspects: (1) find specific effective monomers in traditional Chinese medicine and couple them with corresponding monoclonal antibodies for biotherapy; Anti-myocardial fibrosis of traditional Chinese medicine compound is a field with great research value and application prospect. Traditional Chinese medicine compound has multi-directional regulation function, gives full play to the advantages of TCM syndrome differentiation, combines disease and syndrome, broadens the scope of prescription selection and seeks effective prescriptions; Carry out the research of anti-myocardial fibrosis combined with Chinese and western medicine [7]. It is believed that with the gradual deepening of research, Chinese medicine will play a greater role in the treatment of...
myocardial fibrosis.

MF is common in cardiovascular diseases, but there is no effective drug to reverse MF at present. At present, many Chinese herbal medicines, active ingredients or compounds can relieve MF in many ways to improve heart function, which fully demonstrates the great potential of traditional Chinese medicine in preventing and treating MF and provides rich ideas for developing new drugs.

Although Chinese medicine has a significant effect on improving MF, there are still many problems in the current research: first, due to the limitations of technology, the exact components of a single Chinese medicine or compound can not be fully understood, and the multi-component research can not effectively reflect the exact therapeutic effect of the research drugs on MF; Secondly, for the study of in vivo experiments, most animal experiments do not involve syndrome differentiation and treatment, but adopt the methods of warming yang and promoting diuresis, promoting blood circulation and removing blood stasis, widening chest and resolving phlegm, invigorating qi and nourishing yin, calming liver and suppressing yang, clearing away heat and detoxifying, etc., which are realistic and effective, but lack of parallel comparison, which can not reflect the characteristics of "three causes are suitable" in traditional Chinese medicine; Finally, in the investigation and clinical research, there is no large sample of randomized controlled trials to support the effectiveness of traditional Chinese medicine in treating MF. Therefore, from the point of view of clinical medication, more rigorous random and double-blind large-scale clinical trials can better confirm the exact curative effect of traditional Chinese medicine against MF; From the perspective of chemical composition, the use of high performance liquid chromatography, mass spectrometry and other technologies to clarify the composition of drugs can lay a clearer material foundation for pharmacological research; From the pharmacological point of view, the future research should be more important than the phenotype of the drug itself, which can better clarify the pharmacological effects of the chemical components of traditional Chinese medicine. There is still a long way to go to prove the safety and effectiveness of traditional Chinese medicine against MF by scientific and objective methods.

5. Summary and prospect

To sum up, myocardial fibrosis refers to the excessive accumulation of collagen fibers in the normal tissue structure of myocardium, the significant increase of collagen concentration in heart tissue or the change of collagen composition under the action of various pathogenic factors (inflammation, ischemia, hypoxia, etc.). Myocardial fibrosis is the key to the transformation of cardiac function from compensatory period to decompensated period. The regression of myocardial fibrosis can restore the balance between myocardial tissue and interstitial tissue, normalize stiffness and improve cardiac function. Therefore, it is of great significance to prevent and reverse myocardial fibrosis.

References