

Treatment of Atherosclerosis Based on Inflammation-Related Pathways

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Abstract. Atherosclerosis, the primary pathological basis of cardiovascular diseases, poses a significant threat to human health. It is a chronic inflammatory disease characterized by lipid accumulation, fibrous plaque formation, and vascular wall calcification, ultimately leading to arterial stiffness and increased blood pressure. The pathogenesis of atherosclerosis is closely related to inflammatory responses triggered by vascular endothelial injury, involving key inflammatory factors such as interleukins (IL-1, IL-6), tumor necrosis factor- α (TNF- α), and thrombospondin-2 (TSP-2). These factors mediate immune cell recruitment, plaque instability, and thrombosis, significantly increasing the risk of myocardial infarction and stroke. Recent studies suggest that targeting inflammatory pathways, particularly the NF- κ B signaling pathway and ABCA1-seRNA, holds potential for innovative therapeutic approaches. Traditional Chinese medicine, including Guizhi Poria pills, and probiotics have shown anti-inflammatory effects with fewer side effects than conventional drugs. This review summarizes recent advancements in atherosclerosis treatment focusing on inflammation regulation, aiming to provide insights into more effective and personalized therapeutic strategies.

Keywords: Atherosclerosis, inflammation-related pathways, inflammation regulation, mediate immune cell recruitment, Traditional Chinese medicine.

1. Introduction

Atherosclerosis is a chronic and progressive disease, which is the main pathological basis of cardiovascular disease. It is characterized by lipid deposition in blood vessel walls, fibrous plaque formation, and persistent activation of chronic inflammatory responses. The pathological mechanism is inflammation caused by the injury of the inner cortex. White blood cells and macrophages will accumulate in the injured area to form fat blocks. In the process of coagulation, platelets will also accumulate as part of the fat blocks, which will block the arterial wall, calcify and harden the artery wall, reduce the elasticity of the artery wall and increase blood pressure. Atherosclerosis may be accompanied by angina pectoris, myocardial infarction, heart failure and other symptoms. Treatment is divided into lifestyle intervention and drug therapy. Lifestyle intervention includes diet modification, exercise and other ways. The drug treatment is to take anti-stress drugs, anti-platelet drugs and so on.

In recent years, a large number of studies have shown that inflammation not only plays a key role in the occurrence and development of atherosclerosis, but also is closely related to fatal events such as plaque rupture and thrombosis. Therefore, the regulation of inflammatory response has become a new direction to explore the treatment of atherosclerosis. In the inflammatory inhibition pathway, NF- κ B signaling pathway is a representative, and some Chinese herbal formulas can inhibit the activation of NF- κ B signaling pathway and reduce the secretion of inflammatory factors. The other is the ABCA1-seRNA pathway. In the macrophage model with ABCA1-seRNA deletion, ABCA1-seRNA can promote the ubiquitination of transcription factor P65, inhibit the activation of NF- κ B signaling pathway, and play an anti-inflammatory role. In January 2024, based on the health examination data of 10.73 million adults in China, the study showed that in the overall population, the prevalence rates of carotid intima-media thickening, carotid plaque and carotid artery stenosis were 26.2%, 21.0% and 0.56%, respectively. If arteriosclerosis is complicated by severe coronary heart disease, The 5-year survival rate after myocardial infarction is 70%-80%, and the 10-year survival rate is reduced to 50%-60%. Cerebral arteriosclerosis leads to massive cerebral infarction or

hemorrhage, with 30%-50% mortality within 1 year of onset, and the risk of recurrence within 5 years after passing the acute stage (Xu, et al., 2024).

This article reviews the progress of drug therapy for atherosclerosis based on inflammatory response. It aims to provide a comprehensive reference for patients to find a more appropriate treatment plan and a more efficient treatment method.

2. Mechanism

Inflammation plays a key role in the occurrence and development of atherosclerosis. After vascular endothelial cells are damaged, a variety of inflammatory mediators, such as interleukin and tumor necrosis factor, are released to attract inflammatory cells to gather. Monocytes enter the subendometrium and are transformed into macrophages, which further aggravate the inflammatory response by secreting cytokines and reactive oxygen species. Inflammation also promotes the proliferation and migration of smooth muscle cells, thickens the plaque fiber cap, and also affects the stability of plaque. When the inflammatory response is excessive, the plaque fiber cap becomes thin and prone to rupture, triggering thrombosis and acute cardiovascular events.

2.1. Interleukin (IL)

Interleukin plays a complex role in the development of atherosclerosis. The oIL protein family is a class of cytokines secreted by immune cells and other cells, which play a key role in immune response, inflammation and tissue repair. It has a variety of biological activities and can stimulate many cells. IL-1 plays an important role in hormone regulation, for example, IL-1 promotes insulin secretion at low concentration, inhibits insulin secretion at high concentration and induces glucocorticoid production, which is one of the important mechanisms to maintain the dynamic balance of immune response. But not all of this family of proteins have a positive effect on inflammation. Atherosclerosis may be accompanied by acute myocardial infarction, a symptom with a high mortality rate. IL-6 can promote the secretion of inflammatory factors, and the increase of IL-6 and other levels will cause vascular intimal damage, spasm and plaque shedding, promote the narrowing of coronary artery lumen, accelerate the inflammatory response of vascular wall, and then participate in the process of atherosclerosis (Feng&Luo, 1989). In summary, IL-1 plays a pro-inflammatory role in atherosclerosis, blocking the binding of IL-1 to its receptor, inhibiting the activation of inflammatory cells and the release of inflammatory mediators, reducing the damage of vascular endothelial cells, the formation of foam cells, and the abnormal proliferation and migration of smooth muscle cells. Thereby delaying the progression of atherosclerosis and reducing the risk of plaque rupture. IL-6 inhibitors such as tocilizumab have been used in a variety of inflammatory diseases. In terms of atherosclerosis, they can block IL-6-mediated inflammatory signaling pathways, inhibit immune cell activation and inflammatory response, stabilize atherosclerotic plaques, and reduce the risk of cardiovascular events.

2.2. TNF- α

TNF- α can promote the recruitment and activation of inflammatory cells to help clear pathogens, but overexpression can lead to inflammatory diseases. The inflammatory factor TNF- α and IL-6 are essentially the same, and they are both polypeptide cytokines, which directly participate in the systemic inflammatory response, immune response and other processes (Gu, 2017). It can initiate, induce and regulate the body's inflammatory response. TNF- α is secreted by macrophages and increases the permeability of blood vessels (Shen&Dong&Zheng,2024). Its content in serum can reflect the degree of inflammation in the body. TNF- α can play a role in anti-infection, killing tumor cells directly or through regulated immune pathways. However, TNF- α has the function of activating inflammatory cells, causing a large number of white cells to travel to the infarct area, further aggravating myocardial damage. In addition, TNF- α can activate immune cells, such as macrophages,

T cells and B cells, enhance their phagocytosis, killing and secretion functions, and play an important role in the body's resistance to pathogen infection (Yin, 2020).

2.3. TSP-2

Thromboprotein-2 (TSP-2). and TSP-1 both belong to thromboprotein-trimer subgroup a. Although TSP-2 shares a high degree of homology with TSP-1, they do not perform exactly the same functions in the heart. TSP interacts with matrix metalloproteinase-2 to maintain the integrity of the heart matrix. Relevant studies have shown that TSP-2, as a protein expressed in platelets and endothelial cells, has a variety of biological functions such as regulating angiogenesis and inflammatory response. It plays an important role in the regulation of cardiovascular diseases. 2. Its abnormal expression is related to the occurrence and development of atherosclerosis, and may be a potential target for prevention and treatment of this disease.

3. Treatment method

3.1. Therapies targeting the TSP-2 pathway (inhibitors)

A cell called HEK293 can transfect, the process is first seed the HEK293 cell line in a culture dish and allow it to reach a confluence of 70 - 80%. Then mix the expression vector and the target gene with the transfection reagent, and incubate them in the culture medium to form a transfection complex. After that add the transfection complex to the cell culture dish. Determine the optimal transfection conditions and time according to the type of transfection reagent and experimental requirements.

And for the protein expression, it through 48 - 72 hours after transfection, first collect the cells into centrifuge tubes. Then, rinse the cells with sterile washing solutions such as PBS (phosphate - buffered saline). or normal saline to remove the residual culture medium and cell debris in the culture dish. TSP-2 has a potential role in maintaining the stability of the extracellular matrix of the vascular wall, and its abnormal expression may be related to the occurrence and development of atherosclerosis. By regulating the TSP-2 pathway, it is possible to stabilize the extracellular matrix of the blood vessel wall and delay the atherosclerosis process. However, at present, the relevant researches are mostly in the basic experimental stage, and there is no mature clinical treatment method. TSP-2 may be involved in regulating the proliferation and migration of vascular smooth muscle cells and the deposition of extracellular matrix during the repair process after vascular injury. The study of the TSP-2 pathway may provide a theoretical basis for the development of treatment methods to promote the repair of vascular injury and reduce the complications of vascular restenosis (Zhang&Zhu, 2019).

3.2. Therapy targeting IL pathway

IL-1 comes in two forms, IL-1 α and IL-1 β , which activate inflammatory signaling pathways by binding to IL-1 receptors. Therapy targeting IL-1 mainly reduces inflammation by inhibiting IL-1 from binding to receptors or blocking its downstream signaling. For IL-17, therapies targeting IL-17 inhibit inflammatory cell recruitment and the release of inflammatory mediators by neutralizing IL-17 or blocking its receptor, IL-17R. IL-6 can activate JAK-STAT and other signaling pathways, promote B cell differentiation, T cell activation and acute phase protein synthesis. The treatment targeting IL-6 is mainly aimed at IL-6 or its receptor IL-6R, blocking its signaling, inhibiting inflammatory response and immune cell activation (Gu, 2017; Ma et al,2024; Zhang&Li, 2024).

4. Discussion

4.1. Negative effects of drugs

Currently on the market there are anti-pressure drugs, anti-platelet drugs and so on. Antiplatelet drugs can affect clotting, so it takes longer for the wound to clot after taking anticoagulant drugs.

Antistress medications can cause low blood pressure and dehydration, and some patients may experience fatigue, drowsiness, depression and other symptoms. Some drugs that regulate blood lipids will also have an impact on kidney function, so you must be careful when choosing drugs.

4.2. Effective drugs

Studies have shown that Guizhi Poria pills in traditional Chinese medicine is the agent of eliminating signs and removing blood stasis. It is used for female patients with abdominal pain who refuse to press due to signs or blood stasis in the abdomen. In recent years, doctors have recommended the use of Guizhi Poria pills to promote blood stasis and treat carotid atherosclerosis. Guizhi Poria pills can reduce the release of inflammatory factors in the serum of patients with CAS, and can play a role in reducing the number and size of carotid plaque and the thickness of carotid intima (Li et al., 2025). The other is probiotics, which may inhibit the occurrence and development of atherosclerosis by inhibiting inflammatory response. Studies have shown that probiotics combined intervention can significantly inhibit the occurrence and development of atherosclerosis, and may play an inhibitory role by inhibiting the expression of inflammatory factors and enhancing the expression of cholesterol transport molecules (Li, et al., 2024).

4.3. How to Prevent

On how to prevent atherosclerosis, in terms of life, it is needed to eat a reasonable diet, such as controlling fat intake Increase the intake of fruits and vegetables to reduce fat accumulation. Proper exercise can help increase metabolic rate and strengthen muscles. Regular physical examinations are beneficial for monitoring blood sugar, blood fat, and blood pressure. Additionally, appropriate supplementation of antioxidants can help reduce the damage of free radicals to the blood vessel walls.

5. Conclusion

To sum up, atherosclerosis is the main pathological basis of cardiovascular diseases, and its pathogenesis driven by inflammation has received extensive attention. IL-1, IL-6, TNF- α , TSP-2 and other inflammation-related factors in interleukin participate in the occurrence and development of atherosclerosis through complex biological processes. It opens up new avenues for the treatment of atherosclerosis. Although the current clinical application is limited, but the prospect is broad. In the actual treatment, the existing drugs have many drawbacks, but the natural or traditional drugs such as Guizhi Poria pills and probiotics show unique advantages. In addition, the prevention of atherosclerosis needs to start from the intervention of lifestyle, reasonable diet, proper exercise, regular physical examination and other measures are crucial. Future research should focus on optimizing existing treatments and developing safer and more effective drugs. According to the individual situation of patients, personalized treatment plans are formulated to achieve accurate prevention and control of atherosclerosis and provide better treatment plans for patients.

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