

# *Mechanism and Research Progress of Danqu Capsule in the Treatment of Maintenance Hemodialysis Complicated with Cardiovascular Disease*

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**Abstract:** There are many Cardiovascular risk factors in patients with maintenance hemodialysis (MHD), which is a high risk population of Cardiovascular disease (CVD) and an important cause of death in MHD patients. Danqu capsule is a traditional Chinese medicine compound preparation made by Shaanxi Hospital of Traditional Chinese Medicine. It has been found in the preliminary clinical observation that Danqu capsule can significantly improve the clinical symptoms of patients with coronary heart disease angina pectoris syndrome of phlegm-stasis interaction type, and improve the quality of life of patients. Through literature review, the pathogenesis of MHD combined with CVD in Traditional Chinese and western medicine was reviewed, and the mechanism of danqu capsule in the treatment of MHD combined with CVD was elaborated, in order to provide reference for clinical research and treatment promotion of MHD combined with CVD.

## 1. Introduction

End-stage renal disease (ESRD) is a common disease that seriously endangers life and health, and the incidence is increasing year by year. MHD is one of the main renal replacement therapies for ESRD patients. Patients with Chronic renal failure (CRF) receive hemodialysis to maintain life, prolong life cycle and improve life quality. There are many complications in hemodialysis, among which MHD patients have cardiovascular risk factors, and they are the high-risk group suffering from cardiovascular diseases with a higher prevalence than normal people. According to studies, central vascular events account for about 50% of death causes in hemodialysis patients <sup>[1]</sup>. Zhang Xiaohua et al. <sup>[2]</sup> found that the survival rate of hemodialysis patients decreased significantly year by year, and the 10-year survival rate was only 16.4%, among which CVD was the primary cause of death in MHD patients. Therefore, it is of great significance for long-term survival of hemodialysis patients to reduce the incidence of cardiovascular events, prevent and cure the cardiovascular complications of chronic

renal failure, and improve dialysis and life quality. Danqu capsule is a traditional Chinese medicine master Lei Zhongyi in the research and development of Dan Lou tablet based on the summary of the study of the formula, is currently made in shaanxi Province hospital of Traditional Chinese medicine a hospital preparation. Fan Hong et al.<sup>[3]</sup> found that Danqu Formula has the effects of cleansing phlegm and removing turbidity, promoting blood circulation and removing blood stasis, clearing heat and detoxifying, and has the effects of anti-embolism, anti-inflammation, regulating lipid and preventing spots. It is safe and effective to treat angina pectoris of coronary heart disease with phlegm and stasis interaction, which can significantly improve clinical symptoms such as palpitation, chest tightness and chest pain. Through preliminary clinical observation and study, Dan qu capsule can significantly reduce phlegm and blood stasis mutual junction in patients with maintenance hemodialysis hs-CRP levels, blood lipid, inhibit the expression of homocysteine, platelet aggregation and reduce the risk of cardiovascular events, improve the overall quality of life of patients, and no obvious adverse reaction, it has certain clinical value<sup>[4]</sup>. This article reviews the mechanism and research progress of Danqu capsule in the treatment of maintenance hemodialysis complicated with cardiovascular disease.

## 2. MHD Combined with CVD Risk Factors

MHD merger CVD is caused by a variety of risk factors, according to the present study can be classified into traditional factors (such as smoking, diabetes, high blood pressure, lipid metabolic abnormalities, etc.), blood flow dynamics (anemia, atherosclerosis, etc.) and metabolic factors (lipid metabolic disorders, inflammation, oxidative stress and high homocysteine levels, etc.) three types of factors<sup>[5]</sup>. Epidemiological investigation shows that hypertension causes a high risk of cardiovascular disease in PATIENTS with CRF, so blood pressure control is the most important method to reduce the incidence of cardiovascular events and mortality in patients with CRF. In MHD patients with CVD, angina pectoris is partly caused by anemia and increased oxygen consumption, and oxidative stress exists in CRF, which is also an important factor for atherosclerosis<sup>[6]</sup>. Zhao Q, Et al.<sup>[7]</sup> found that inflammatory mediators in plasma of MHD patients are related to the occurrence of cardiovascular disease, and increased levels of AIP, CRP, TNF- $\alpha$  and IL-6 in MHD patients are risk factors for the occurrence of cardiovascular disease, and AIP, as an indicator to predict lipid metabolism disorders, is related to the occurrence of CVD in MHD patients. MHD combined with CVD has a high incidence of vascular calcification and a high level of microinflammatory factors<sup>[8]</sup>. Hyperlipidemia is also one of the high risk factors for MHD combined with CVD. Li Kangling et al.<sup>[9]</sup> found through clinical studies that MHD patients have a higher risk of hyperhomocysteinemia than non-MHD patients and an increased risk of atherosclerosis.

## 3. Understanding of TCM Pathogenesis of MHD Complicated with CVD

The etiology and pathogenesis of chronic renal failure are complex. At present, many doctors think that the pathogenesis is based on the virtual standard. Renal damage of pixu (spleen deficient), has no right to pixu (spleen deficient) operation, and the opening and closing of kidney loss, deferment, long qi and Yang Yang and Yin, and eventually lead to kidney failure, can't distinguish secrete turbidity, turbid poison indicates lag, from the heart, can cause a better mousetrap stasis, alongwith thread, and blood stasis block, block qi activity, causing blood perform poorly, blood stasis and qi stagnation, qi and blood stasis cycles, and blood stasis resistance disease such as heart arteries and veins can appear obstruction of heartache. In general, chronic renal failure is based on deficiency of spleen and kidney and marked by dampness, turbidness, stasis and toxin. The basic pathogenesis of chronic renal failure is deficiency of spleen and kidney, deficiency of qi and blood, interaction of phlegm and stasis, and damage of kidney collaterals by poison. MHD combined with CVD is a further development on the

basis of chronic renal failure. From the perspective of traditional Chinese medicine (TCM), the deficiency of heart and kidney and deficiency of qi and Yin are the main symptoms of MHD combined with CVD. Zhang Xichun in the *Intergrating Chinese and Western Medicine of Phlegm drink prescription* believes that heart and kidney disease affects the transport of water and eventually leads to the formation of phlegm. Kidney Yin deficit Yin essence can not bear, hyperthyroidism, is caused by the kidney to the heart and disease, heart fire downward consumption of kidney Yin, kidney loss, heart and kidney do not cross, hot fluid coagulation, phlegm and saliva obstruction. On the treatment of the kidney to treat the heart, the heart kidney with the treatment, only the heart kidney water and fire phase, Yin Pingyang secret, the spirit is to treat<sup>[12]</sup>.

#### 4. Study on the Mechanism of Danqu Capsule in the Treatment of MHD and CVD

Dan qu capsule is a master in national physician LeiZhongYi in research and development on the basis of fructus tablet further summed up the research, by Salvia Miltiorrhiza, Red Kojic, Red Peony Root, Cortex Moutan, Broiled Astragalus Root, Pinellia, Pericarpium trichosanthis, Leeches, Puerarin, Ginkgo biloba leaves, Notoginseng, Rhizoma Coptidis, Allium macrostemon 13 herbs, with xuan bi fights, blood detoxification as the method, used in the treatment of sputum silt exchanged junction obstruction of heartache. Professor Lei believed that chest pain was mainly due to insufficiency of kidney Yang and phlegm turbidized blood block as the criteria. Phlegm turbidized blood turbidized poison condensation was the key to the pathogenesis<sup>[13]</sup>, which also confirmed that treating heart with kidney was the basis of MHD combined with CVD. Prescription with salvia miltiorrhizae broken blood, fill new blood, tongjing pain, red koji into the camp broken blood, spleen digestion, the two groups are king medicine; Notoginseng blood dispersing pain, Red Peony clearing heat cool blood, heat dispersing, blood stagnation; Ginkgo biloba leaves promote blood circulation, relieve pain, reduce turbidity and lipid; Leeches break blood to relieve menstruation and eliminate stasis; Pericarpium trichosanthis wide chest li Qi, Allium macrostemon Tongyang Sanjie, Pinellia ternata dissipates phlegm and distension, Coptis can clear away heat and remove fire to detoxify, all drugs combined for the minister medicine; Pueraria shengyang, channeling meridian activating collaterals, Astragalus qi nourishing Yin, Cortex Moutan cool blood and blood, Removing heat from blood, the three are adjuvant; The combination of all drugs, played huoxue huayu, yiqi tongluo, tongbi Sanjie.

##### 4.1 Anti-inflammatory and antioxidant effects

Modern pharmacological studies have found that salvia miltiorrhiza has anti-lipid peroxidation, antibacterial and anti-inflammatory effects<sup>[14]</sup>, and can also improve the symptoms of renal failure and uremia in model rats, thereby improving renal function<sup>[15]</sup>. Red peony root contains tannins, flavonoids, volatile oil and other active components, with anti-inflammatory, antioxidant and other pharmacological effects<sup>[16,17]</sup>. Paeonol significantly reduced the level of renal fibrosis in unilateral ureteral ligation mice, decreased the expressions of CD68, CD11b and pro-apoptotic factors in renal tissues, increased the content of anti-apoptotic factor Bcl-2, regulated and inhibited the apoptosis of inflammatory factors, and played an anti-fibrosis role<sup>[18]</sup>. The active ingredients of leeches play a role in the treatment of cardiovascular and cerebrovascular diseases mainly through anti-inflammatory, antioxidant, inhibition of vascular endothelial injury, reduction of platelet activation, anti-apoptosis and other mechanisms<sup>[19]</sup>. Studies in experimental animals have shown that Panax notoginseng and its active ingredients can delay the progression of renal fibrosis and chronic kidney disease by reducing the aggregation of inflammatory cells, inhibiting the expression of renal fibrosis related factors and the proliferation of renal interstitial fibroblasts<sup>[20]</sup>. Animal experimental studies have found that the mechanism of action in treating rats with CHD syndrome of phlegm-stasis interaction may

be to inhibit EGFR and MMP9 expression levels by regulating glycerophospholipid metabolism and energy metabolism, and affect the expression of inflammatory factors and oxidative stress-related effector indicators, thus exerting anti-inflammatory and antioxidant effects [21].

#### 4.2 Anti-platelet aggregation effect

Ellagic acid in *Radix paeoniae lactiflora* can inhibit the expression of pro-inflammatory cytokines, and total glycosides in *Radix paeoniae lactiflora* have the effects of anti-coagulation, anti-platelet aggregation and improvement of hemorheology [22]. *Astragalus* can regulate immunity, inhibit platelet aggregation, improve coagulation state, correct abnormal protein and lipid metabolism, fight oxidation and protect kidney tissue [23]. *Astragalus membranaceus* can reduce blood pressure of essential hypertension model rats, increase the content of natriuretic peptide, reduce the levels of total cholesterol and triglyceride in hyperlipidemia model mice, and prevent thrombosis [24].

#### 4.3 Antihypertensive and lipid-lowering effects

Red kojic rice with step-down, hypolipidemic, hypoglycemic, anti-inflammatory, prevention and treatment of osteoporosis [25], *Dan lou* piece can effectively treat CIH causes of dyslipidemia and atherosclerosis [26], has a protective effect of combined with hyperlipidemia rats and its mechanism may be related to reduce blood lipid levels, reduce the cell inflammation infiltration on [27]. As a key drug for chest obstruction, *trichosanthes* also improved micro-circulation and reduced serum cholesterol in modern pharmacological studies [28]. *Ginkgo biloba* leaves can effectively improve blood lipids and inhibit the formation of atherosclerosis, thus playing a role in lowering blood pressure [29]. Active substances extracted from *Ginkgo biloba* leaf can relieve arteriolar spasm, dilate arterioles and increase local blood supply [30]. Studies have found that *ginkgo biloba* extract can regulate the distribution of polyunsaturated fatty acids in hyperlipidemia rats, inhibit HMG-COA reductase, reduce the absorption of cholesterol, reduce plasma and liver sterols, and achieve the effect of lipid regulation. *Pueraria* root contains isoflavones, glucosides, coumarins, polysaccharides and other components, which have biological activities such as cardio-cerebrovascular protection and lowering blood lipids [31]. The study also found that *puerarin* can protect kidney by reducing oxidative stress, inhibiting non-enzymatic glycosylation of protein, lowering blood glucose, reducing urinary protein and improving hemodynamics. At the same time, *puerarin* can effectively reduce the content of serum creatinine and uric acid, inhibit the apoptosis of glomerular cells and improve renal function [32].

#### 4.4 Influence on atherosclerosis

The main components of *Pinellia ternata* are alkaloids, organic acids, volatile oils, flavonoids, etc. [33]. *Pinellia ternata* has anti-emetic, anti-inflammatory and anti-arteriosclerosis effects [34]. *Coptis* has high medicinal value, including hypoglycemic, anti-inflammatory, anti-tumor and other pharmacological effects, anti-arrhythmia, anti-hypertensive, improvement of myocardial ischemia, and anti-platelet aggregation [35, 36]. *Allium macrostemon* and its extracts have anti-atherosclerosis and anti-tumor effects [37]. At the same time, *allium macrostemon* is widely used in the treatment of angina pectoris, coronary heart disease, hyperlipemia, myocardial ischemia and other diseases, and is also effective in improving clinical symptoms such as chest pain and tightness. *Paeonol* can inhibit the inflammatory response of vascular endothelial cells and regulate the functions of vascular smooth muscle cells and macrophages to achieve the effect of anti-atherosclerosis [38].

The modern pharmacological studies of these danqu capsules showed that the main ingredients of Danqu capsules have the functions of protecting kidney and cardiovascular system, anti-inflammation, anti-oxidation, anti-platelet aggregation, lipid-lowering, antihypertensive and anti-atherosclerosis. By

animal experimental study, Dan capsules can improve the state of the rat model of myocardial ischemia, myocardial cells of the division of the mitochondria of myocardial ischemia-reperfusion injury of mitochondria has certain protective effect<sup>[39]</sup>, and hold on the model rats with step-down, reduce the role of cardiac muscle tension time index, and security is higher, it is safe and effective for patients with coronary heart disease complicated with hypertension and tachycardia<sup>[40]</sup>.

## 5. Summary and outlook

With the aging society in China, the prevalence and fatality rate of CKD are increasing year by year, which is recognized as a major global public health problem. CVD is the primary cause of death in MHD patients. It is of great significance for long-term survival of hemodialysis patients to reduce the incidence of cardiovascular events, prevent and cure the cardiovascular complications of chronic renal failure, and improve dialysis and life quality. Danqu capsule is composed of 13 herbs including salvia miltiorrhiza, red koji, peony root, cortex moutan, Astragalus, Pinellia trichosanthes, pericarpium trichosanthes, leech, radix puerariae, Ginkgo leaf, panax notoginseng, rhizoma coptidis and allium macrostemon. It has the effect of xuanbi sanjie, removing blood stasis and detoxification. The research results show that danqu capsule can effectively reduce blood lipid, hs-CRP, HCY and other inflammatory indicators, protect kidney and cardiovascular, inhibit inflammatory factors, and significantly improve the clinical symptoms of MHD patients such as chest tightness and chest pain. Based on this, it can be further explored to promote clinical use. Traditional Chinese medicine has the advantages of multiple targets, multiple systems, multiple pathways and small toxic and side effects. Based on the guiding principles of TCM theories such as "syndrome differentiation and treatment" and "holistic concept", TCM compound can effectively improve the clinical symptoms of patients, delay the progression of the disease and improve the quality of life. Modern medical treatment of cardiovascular diseases mainly focuses on the control of traditional cardiovascular risk factors, and there is no effective strategy for the treatment of CKD-CVD, so the benefits of patients are not obvious. Current research Dan qu capsule in the treatment of MHD merger direct action mechanism of CVD is not enough in-depth, clinical observation of sample size is little, lack the support of the experimental data in a follow-up study, should also need large sample, multi-center clinical research data and further experiment data, to demonstrate Dan qu capsule can effectively treat MHD merger CVD relieve clinical symptoms, Delay the progress of cardiac renal failure, improve the long-term efficacy, provide objective scientific basis.

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