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Advances in Traditional Chinese Medicine Prevention and Treatment of Contrast Nephropathy

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Abstract: With the continuous development and wide use of modern imaging technology and the increasing number of interventional procedures, contrast-induced nephropathy (CIN) has become one of the important causes of acquired acute kidney injury, a widespread concern. In recent years, clinical research results show that traditional Chinese medicine also has a certain effect in the prevention and treatment of CIN. This paper summarizes the research progress of traditional Chinese medicine on the prevention and treatment of CIN and provides new research ideas for the further development of traditional Chinese medicine-related drugs for the prevention and treatment of CIN.

With the development and use of modern imaging technology and the increasing number of interventional procedures, contrast-induced nephropathy (CIN) has become one of the important causes of acquired acute kidney injury and has received widespread attention. The diagnostic criteria for CIN are that the serum creatinine (Scr) within 3 days of intravascular use of contrast agents is higher than the baseline value of 44.2 μmol/L (0.5 mg/d L) or 25%, and other causes of renal damage are excluded [1]. Commonly used contrast agents are: iopromide, meglumine, meglumine, iodixanol, etc. [2, 3] （Fig.1）Studies have shown that the risk of CIN in the general population is 1% to 2%, but the risk of CIN in patients with other underlying diseases (such as diabetes, coronary heart disease, etc.) is as high as more than 50% [2]. Most of the clinically common CIN patients have one or more chronic underlying diseases, which lead to increased risk of death and adverse outcomes.(Fig.2)Therefore, how to better prevent and treat CIN has become the focus of clinicians. Traditional Chinese medicine is the traditional medicine of the Chinese nation. In recent years, clinical research results have shown that traditional Chinese medicine also has certain curative effects in the prevention and treatment of CIN. This article mainly reviews the research progress of traditional Chinese medicine in the prevention and treatment of CIN in recent years.

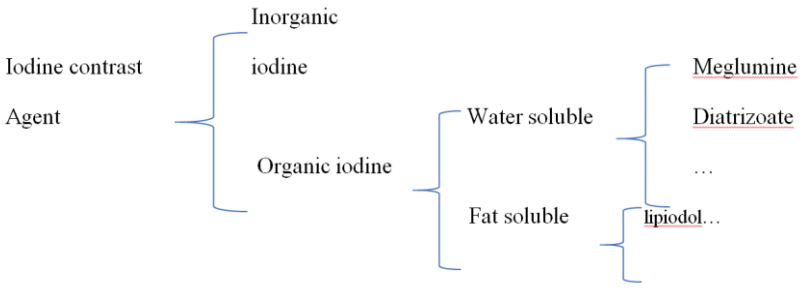

Figure 1: Classification of iodine contrast agents.

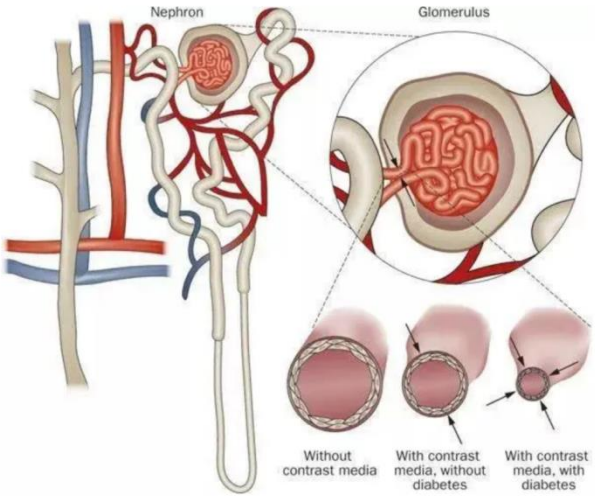

Figure 2: Schematic diagram of the pathology of contrast medium combined with diabetes mellitus.

1. Basic Overview of CIN

At present, with the more extensive clinical application of contrast media, the frequency of use of contrast media is also increasing. Contrast media nephropathy, also known as contrast media nephropathy, refers to the new acute kidney damage or the original kidney after the application of contrast media. The damage is aggravated, and renal dysfunction caused by other reasons is excluded [4]; contrast nephropathy often occurs 24-72 hours after the use of contrast agents, sometimes accompanied by oliguria, and abnormal urine tests to varying degrees appear 24-48 hours after contrast media. Creatinine rises and begins to fall within 3 to 7 days. (Fig.3)

In terms of treatment, Sun Yiqi [5] and others compared 15 domestic and foreign guidelines for contrast nephropathy. The study showed that the preventive measure commonly recommended in the guidelines for contrast nephropathy is intravenous hydration therapy, and the recommendations for hydration fluids are relatively uniform, such as isotonic saline (0.9%) and isotonic sodium bicarbonate can be used, but the choice of duration and infusion rate is difficult to unify; and it is believed that nephrotoxic drugs, such as non-steroidal anti-inflammatory drugs, Diuretics, methotrexate, etc. Currently, renal replacement therapy is not recommended as the routine prevention of CIN. It can be seen that intravenous hydration is still the only proven and generally accepted measure to prevent contrast nephropathy[6].

Figure 3: Renal arteriography.

2. TCM's Understanding of CIN.

There is no CIN disease name in traditional Chinese medicine diagnostics, but its clinical manifestations, such as abnormal renal function, oliguria and anuria, and edema, can be classified as "long closure", "drowning poison", "edema" and "close". Grid" and other categories. From the perspective of traditional Chinese medicine, the contrast agent belongs to the category of "exogenous evil". There are six qi in nature. If it hurts the human body, it is called the six evils in TCM theory. , contrast agent is easy to invade the human body, block the qi machine, the qi machine does not run smoothly, and the qi is the commander of the blood, which leads to the obstruction of the blood supply of the human body, the blood flow speed is slowed down, and the renal tubular filtration rate decreases, and the glomerular perfusion decreases. Symptoms such as decreased creatinine clearance and decreased creatinine clearance; the existing TCM theories believe that the pathogenesis of contrast nephropathy is a deficiency and deficiency. The distribution law and correlation of syndrome types. The results show that the TCM syndrome types of these patients are mainly yang deficiency, and the deficiency of Yang qi and yang deficiency of the heart and kidney are highly correlated with the occurrence of CIN. Evil, easy to damage yang characteristics. Traditional Chinese medicine believes that the contrast agent, as a cult poison, enters the interior to transform heat, damp heat accumulates in the spleen, and the spleen cannot transport and transform water, resulting in edema due to the water staying under the skin. "Toxin and blood stasis are the main factors. (Figure 4)" Gong Xuezhong [7] believes that "toxin is the forerunner, and poison and blood stasis are intertwined" is the main pathogenesis of contrast agent nephropathy. To clear the stasis and dissipate heat. From this point of view, expelling pathogens should be the main focus in the early stage, while strengthening the righteousness in the later stage, which can accelerate the excretion of contrast agents in each stage of the development of the disease and achieve the purpose of treatment [8].

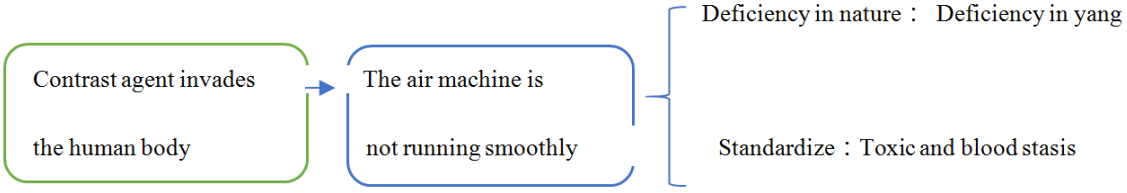

Figure 4: Diagram of the pathogenesis of contrast-induced nephropathy

3. Research Progress of Traditional Chinese Medicine Related Drugs in CIN

3.1. Traditional Chinese Medicine Injections

3.1.1. Danhong Injection

Danhong injection is a compound preparation made from safflower and danshen, two traditional Chinese medicines. The content is unclear; its mechanism of action is to reduce the damage of renal tubular epithelial cells on the basis of hydration, reduce the generation of oxygen free radicals, accelerate the scavenging of free radicals, and reduce the protective effect of hs-CPR on the kidneys in patients. Relevant studies [9, 10] show that Danhong injection has a definite effect on reducing the damage to renal function caused by contrast media and improving renal function; and compared with simple hydration, Danhong injection is effective in patients with blood stasis type congestive heart failure. The incidence of CIAKI may have a certain preventive effect; hydration increases the risk of exacerbating heart failure, and Danhong injection dilates blood vessels, which may have a certain protective effect on cardiac function. (Fig. 5)

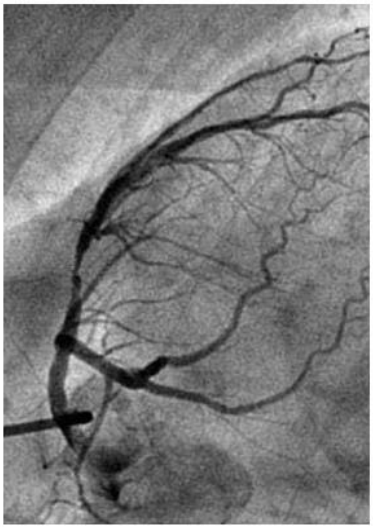

Figure 5: Coronary angiography.

3.1.2. Shenkang Injection

Shenkang injection is a compound preparation made from rhubarb, astragalus, saliva and safflower, which can effectively inhibit the changes of renal function indicators such as creatinine and urea nitrogen caused by contrast agents. Effectively remove poisonous silt, replenish the deficiency and release the excess, to achieve the effect of preventing and treating CIN. Liu Dong [11] et al selected 60 patients with lower extremity arteriosclerosis obliterans admitted to the Department of Vascular Surgery of Wangjing Hospital, Chinese Academy of Chinese Medical Sciences to discuss the safety and efficacy of Shenkang injection. The occurrence of postoperative CIN has a certain preventive effect, and its curative effect is better than that of simple hydration therapy [12, 13].

3.1.3. Ligustrazine Injection

The main component of ligustrazine injection is ligustrazine hydrochloride, the chemical name is tetramethylpyrazine, which is a biologically active base obtained from Ligusticum chuanxiong, has a variety of effective pharmacological effects on the body, and has obvious blood-activating and

qi-transforming effects. Its effect on renal tissue is mainly by regulating the balance of renal tissue and plasma thromboxane/prostaglandin ratio, inhibiting the proliferation of mesangial cells, epithelial cells, endothelial cells, etc., reducing or scavenging free radicals, to alleviate the pathological damage of the glomerulus, reduce the production of urine protein, and achieve the effect of protecting the kidney. The finished drug injection has the best curative effect [14].

3.1.4. Shenmai Injection

Shenmai injection is composed of red ginseng and Ophiopogon japonicus. The main active ingredients are ginsenosides, Ophiopogon, saponins, etc. The red ginseng in the prescription is strong, warm, and dry, and can best invigorate vitality; Ophiopogon japonicus can nourish yin and moisten the lungs, benefit invigorating the stomach, clearing the heart and eliminating vexation. Modern pharmacological experiments have confirmed that Shenmai injection has anti-inflammatory, improves microcirculation, antioxidative stress effects, and can exert therapeutic effects through multiple pathways such as immune regulation. The red ginseng in Shenmai injection has various effects such as dilating blood vessels, enhancing coronary blood flow, improving myocardial ischemia, improving microcirculation, and anticoagulation. Function Shenmai injection has a definite effect in preventing the occurrence of CIN after PCI [15].

3.2. Classic Formula

Xiaoyu Xiezhuo Decoction was made by Li Xueming, a national famous Chinese medicine doctor, according to the prescription "Buyang Huanwu Decoction" by Wang Qingren, a famous doctor in the Qing Dynasty. It was originally mainly used to treat chronic kidney disease with Qi deficiency and blood stasis syndrome. It has a good effect in terms of [16], and the formulations include Junhuang, peach kernel, Achyranthes, Dilong, raw astragalus, and plantain. The symptoms include long disease course, backache and fatigue, foamy urine, increased nocturia, poor stool, thin and astringent pulses, pale tongue, thin and greasy fur, etc. Recent studies[17] found that oral stasis relieving based on hydration, the increase of Scr, BUN, and decrease of eGFR in the treatment group of Xiezhuoyin at 48 hours after PCI were smaller than those of simple hydration treatment, and the incidence of CIN in the treatment group after PCI was significantly lower than that in the control group, suggesting that Xiaoyu Xiezhuo Compared with simple hydration therapy, drinking combined with hydration therapy can further reduce the damage to renal function caused by contrast media.

3.3. Chinese Medicines and Chinese Medicine Extracts

3.3.1. Salvia Polyphenolate

Salvia polyphenolate is a water-soluble salvia extract, the main component is salvianolic acid. Studies have shown that salvianolic acid A can improve renal hypoxia, promote the survival of renal tubular cells, and improve renal function, thereby preventing the occurrence of CIN. The meta-analysis of Xi Yuantang et al. [18] included 2 186 patients who underwent coronary angiography or PCI to evaluate the efficacy and safety of salvianolate combined with hydration in the prevention of contrast nephropathy. The results show that the intravenous drip of salvianolate combined with hydration has a good clinical effect on the prevention of contrast agent nephropathy; it can reduce the incidence of CIN, and its mechanism may be related to the scavenging of oxygen free radicals, anti-inflammatory, improving related to microcirculation. Saliva polyphenolate combined with conventional hydration has a definite clinical effect in the prevention of contrast agent nephropathy.

3.3.2. Jiahua Tablet

Jiahua Tablet is an in-hospital preparation of Jiangsu Provincial Hospital of Traditional Chinese Medicine. It is refined from hollyhocks. It has the effect of invigorating the kidney, clearing the swelling, and detoxification. Symptoms such as edema, hematuria, and proteinuria. Wu Qiang[19] believed that Jiahua Tablets can significantly reduce the levels of Scr, BUN, Cys C, NAG, GAL, hsCRP, IL-6, and IL-8 in patients after coronary angiography or coronary stent implantation, increase eGFR, reduce The occurrence of CIN can better protect renal function. Xu Zhongchi[20] believed that hollyhock flower extract from Jiahua tablets can inhibit the activation of ROS-ASK1-MAPKs pathway signal transduction induced by iopromide, reduce the occurrence of apoptosis, and thus achieve the effect of preventing and treating contrast agent nephropathy. Modern pharmacological studies have shown that hollyhocks have anti-inflammatory, antibacterial, anti-platelet aggregation, anti-oxidation and elimination of oxygen free radicals, regulation of immune function, diuresis, protection of glomeruli and renal tubules and so on.

3.3.3. Yam - Rhizoma Imperatae Pair

Chinese yam has the effects of invigorating the spleen and nourishing the stomach, invigorating the lungs, invigorating the kidney, and astringent essence, and has the functions of lowering blood sugar, regulating blood lipids, improving digestive function, anti-oxidation, and anti-tumor [21, 22]; The effect of clearing heat and diuresis is mostly used to treat diseases such as edema, hematuria, hemorrhage, and stranguria [23, 24]. Ding Rui[25] explored whether the yam-imperial root drug pair could reduce the renal damage of rats caused by the contrast agent through an experimental study on 48 rats. Function and renal structure damage up-regulate the expression of Bcl-2 protein, down-regulate the expression of caspase-3 protein, and reduce the apoptosis of renal tubular epithelial cells, thereby protecting the kidney and preventing renal damage caused by contrast media.

4. Summary

Regarding the prevention and treatment of CIN, Western medicine is mainly used clinically, and the prevention and treatment methods of traditional Chinese medicine are less used. However, there are also unique prevention and treatment methods in traditional Chinese medicine. In addition to the prescriptions listed in this article, external treatment methods with TCM characteristics also have certain curative effects on contrast agent nephropathy, but they are all in their infancy. At present, there are few clinical studies on the prevention and treatment of contrast agent nephropathy with traditional Chinese medicine, and the basis for medication cannot be unified. In addition, the pathogenesis of contrast-induced nephropathy is still incomplete. Therefore, further research is needed in the future to clarify the pathogenesis of CIN, to unify medication standards, and to rationally select preventive measures.

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