

# Research Progress of Chinese and Western Medicine in Treatment of Rheumatoid Arthritis

Guifu Tian<sup>1</sup> & Zhibin Li<sup>2</sup>

<sup>1</sup> Graduate Student of Class 2021, Shaanxi University of Chinese Medicine, Xianyang 712046, China

<sup>2</sup> Joint Ward, Bone Injury Hospital, Affiliated Hospital of Shaanxi University of Chinese Medicine, Xianyang 712000, China

Correspondence: Zhibin Li, Joint Ward, Bone Injury Hospital, Affiliated Hospital of Shaanxi University of Chinese Medicine, Xianyang 712000, China.

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## Abstract

At present, the etiology of rheumatoid arthritis (RA) is not clear, and its pathogenesis has not been clarified. For this, in clinic can only make corresponding treatment for the onset period and sequelae of the disease. Through reviewing relevant literature in recent years, it is found that the combined use of traditional Chinese and western medicine has great advantages in the treatment of rheumatoid arthritis. This paper will analyze and summarize the current treatment status and medication rules of traditional Chinese and western medicine for rheumatoid arthritis, hoping to provide reference for clinical treatment plans, so as to further improve clinical efficacy and improve treatment plans.

**Keywords:** rheumatoid arthritis, pathogenesis, medication, clinical effect

## 1. Understanding of Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a connective tissue disease of unknown etiology that can be influenced by genetics, environment, hormone levels, and neurological conditions (Wu Shasha, Wang Yan, Xu Ting, et al., 2022). The main clinical manifestations of this disease are symmetrical and persistent pain in the small joints of both hands and wrists, multi-joint swelling and pain of the whole body and the dysfunction of the affected joints. Generally, rheumatoid factor (RF) and other positive indicators can be detected in serum (Ge Gaoyue & Zheng Xinchun, 2021). Epidemiological investigation shows that this disease is most common in middle-aged and elderly women, and the global incidence is about 1% (Jiang Quan, 2020). Currently, the adult prevalence of RA in our country is about 0.3%-0.4%, with a higher incidence in females and an incidence 2-3 times higher than that in males (Rheumatology Branch of Chinese Medical Association, 2018). At present, there is no drug to cure this disease in clinic, and there is no specific drug. The treatment of RA has become a worldwide problem, and the long-term side effects of western medicine cannot be ignored (Xing Shasha, Pang Yuzhou, Chen Qiuxia, et al., 2019).

Rheumatoid arthritis (RA) is classified by traditional Chinese medicine as “arthralgia” and “WP”. There is a saying in: “Wind, cold, wet three qi mixed to the combination of Bi also.” It is pointed out that Bi syndrome is mainly caused by external evil invading the human body, weak body and lack of healthy qi, and internal transmission of viscera, resulting in Bi (Yuan Lin, Wu Jinyu, Zhang Zhiyan, et al., 2020). *The Complete Book of Jingyue* said: “But Qi and blood are not filled, the wind cold can enter... the big end of the pain of Bi also. This indicates that Bi syndrome is caused by Qi and blood deficiency and external evil spirits coming in (Pan Hui, Wang Yuan & Chen Lei, 2016). Modern physician Zhou Zhongying (Zhou Shenghua, Zhou Jichun & Liu Long, 2014) believed that its pathogenesis was based on deficiency of Qi and blood, interlocking of phlegm and blood stasis, and resistance of wind, cold and moisture. The pain, swelling and stiffness of multiple small joints in the

limbs are caused by the poor operation of Qi and blood. It can be known that the disease is located in the muscles and bones of the joint, the basic rules of its treatment for early dispelling wind and dehumidification, promoting blood circulation and removing blood stasis, dredging collages and relieving pain; In the middle and late period, the liver and kidney should be toned and the spleen and stomach should be emphasized (Mu Xiaorui & Jiang Quan, 2015). It has been repeatedly verified that traditional Chinese medicine has significant efficacy, high safety and fewer adverse reactions in the treatment of RA, and has obvious advantages compared with Western medicine in alleviating symptoms and controlling the course of the disease (Liu Jijia, Wang Yuan, Chen Lei, et al., 2018).

## 2. Stage of Rheumatoid Arthritis

The pathogenesis of this disease can be divided into four stages (Xie Zhaohu, Xie Jing, Wu Jingjin, et al., 2020):

The first stage: acute activity. These patients may present with morning stiffness, pain, swelling and significant dysfunction. Some patients have low or high fever. The results of three rheumatism tests were positive and the titration degree was high.

The second stage is subacute activity. The above situation is more obvious. At this stage, the rheumatoid factor test results were positive but the titration degree was low.

The third stage is chronic migration delay. Bone destruction, this part of patients in the current clinical account for the majority. This part of patients to the hospital for medical treatment on its damage, make the corresponding treatment.

The bone damage is irreversible.

The fourth stage is the stable period. The clinical symptoms of these patients are not obvious, but their joints are deformed and accompanied by different degrees of dysfunction. Only for its sequelae do the corresponding treatment. Control the incidence degree and improve the quality of life of these patients.

## 3. The Treatment of Rheumatoid Arthritis with Traditional Chinese Medicine

### 3.1 TCM Classification Treatment

#### 3.1.1 Rheumatic Heat Obstruction Meridians

Patients mainly due to physical deficiency or overwork or internal injuries caused by Qi and blood camp Wei is insufficient, Wei is not solid, rheumatic fever toxic evil enters, leaving joints, meridians or meridians, so that Qi and blood in the obstruction, stasis, this syndrome is mostly manifested as the affected joint swelling heat pain; Tongue image: red tongue, yellow and greasy moss; Pulse: the number of sliding or floating pulses (Yuan Lin, Wu Jinyu, Zhang Zhiyan, et al., 2020). Treatment options are often to clear heat and dehumidify, dispel wind and dredge collars. Bai Zengchun (2019) observed 100 patients with damp-heat bi type RA, 50 patients in the control group were treated with oral methotrexate tablets, and 50 patients in the observation group were treated with Angeli Juanbi Decoction combined with methotrexate tablets. The results showed that the clinical symptoms of patients in the observation group were significantly relieved, the pain was relieved and the bone structure was improved, indicating that Danggui Juanbi Decoction had an effect on damp-heat arthralgia type RA. For example, the study found that 100 cases of damp-heat bi RA patients selected in the control group (50 cases) were treated with moxibustion, and the observation group (50 cases) were treated with Simiaoyong An decoction on the basis of the control group. The statistical results showed that the total effective rate of the treatment in the observation group was 90%, higher than 74% in the control group, the difference was statistically significant ( $P < 0.05$ ). It has been proved that Simiaoyong An Decoction has a good therapeutic effect on RA, which can relieve joint swelling and pain, shorten the time of morning stiffness, and reduce inflammation with good safety (Bayan Aikeheti & Gujie Naitehan Bailim, 2022).

#### 3.1.2 Wind, Cold and Damp Obstruction of Meridians

Due to insufficient Yang Qi or long living in a cold and wet place, Yang qi and other Yin evil causes Yang qi depletion, Yang qi deficiency leads to endogenous deficiency heat, cold and wet heat or cold and heat interleaving, obstructing Qi and blood in the joint, obstructing joint movement, aggravating in cold, and reducing heat pain. The tongue is light, the tongue coating is thin and white or greasy, and the pulse floats tightly or slowly (Hu Yong & Xing Yurui, 2018). The treatment should focus on dispelling wind and cold, dredging collagories and relieving pain, helping Yang and dehumidifying. Many studies have proved that Coix Seed Decoction is effective in the treatment of this type. For example, through the analysis of Coix Seed Soup in the treatment of RAMeta, it was found that Coix Seed Soup had high efficacy and safety in the treatment of cold and dampness arthralgia RA (Yang Xue, Li Suhua, Cong Shan, et al., 2022). For example, Zhang Wenfu (2021) analyzed the effects of Shao Gan Fuzi Decoction on inflammatory response and joint activity of RA patients with cold and damp bi. The observation group was treated with Shao Gan Fuzi decoction on the basis of conventional treatment, and the observation group had more obvious effect than the control group. It indicates

that combined Shao Gan Fu Zi Decoction can effectively relieve clinical symptoms of RA.

### 3.1.3 Blood Stasis Phlegm Turbidity Obstruction Meridians

Due to the lack of positive qi, evil qi external attack caused Qi and blood deficiency, viscera Qi machinery disorder, Qi and blood and body fluid running obstacles. Blood deficiency is weak, blood stasis endogenous, water valley does not turn into phlegm turbidities, phlegm stasis mutual obstruction of joint meridians, resulting in joint enlargement and disease. Joint qi and blood obstruction, stasis, not general pain, the clinical manifestations of joint swelling pain, joint activity disorder. The tongue is dark purple or has ecchymosis, the tongue coating is white and greasy, and the pulse string is astringent (Ma Xiaoran & Li Wuyin, 2018). For this type of syndrome can promote blood circulation and remove stasis, Shu Jing and activate collaterals treatment. Zhang Qian et al. (Zhang Qian & Chen Jinchun, 2021) observed the clinical efficacy of patients with phlegm-yubi obstruction type, and used Buyang Huanwu decoction in the treatment group and methotrexate tablets in the control group. The results showed that the effective rate of the treatment group was significantly higher than that of the control group, and the treatment group had fewer adverse reactions and high application safety. In addition, Zhang Jian et al. (2018) proved that the self-designed Quyu, phlegm-removing and phlegm-removing activating Luo prescription has achieved good efficacy in treating RA with phlegm-stasis obstruction. This prescription fully embodies the good treatment of Bi syndrome based on phlegm and blood stasis, dispelling phlegm and turbidification and strengthening the liver and kidney as well as strengthening the muscles and bones, and highlights the characteristics of the combination of commonly used classical traditional Chinese medicine prescriptions. More refined and effective targeted treatment, TCM syndromes have been significantly improved, which is obviously superior to western medicine treatment alone.

### 3.1.4 Deficiency of Liver and Kidney and Loss of Meridians

The patient suffers from Qi and blood deficiency, so that the essence and blood do not melt, the muscles and bones lose their health, and the liver and kidney deficiency accompanied by bone impotence and the muscles lose in the care, resulting in joint pain and weakness, poor joint flexion and extension, and then joint deformity, accompanied by waist and knee tenderness and five heart heat. The tongue is red, moss is scarce, and the pulse is heavy and fine (Liu Shasha, 2018). Therefore, in the treatment of tonifying liver and kidney, as well as dispelling rheumatism, strengthening muscles and bones, Shu Jin Tongluo stop bi pain. Tian Ying et al. (Tian Ying, Ge Zijing, 2022) randomly divided 130 patients with deficiency of liver and kidney into observation group (65 cases) and control group (65 cases). After 4 weeks, the total effective rate of the observation group was 96.92%, higher than 80.00% of the control group ( $P < 0.05$ ), so the effect of tonifying liver and kidney soup was more ideal and could improve the symptoms of patients. Inhibit the expression of inflammatory factors. Chen Xialin (Chen Xialin, Yin Zhijun & Wang Huajie, 2020) proved that the treatment with Duhuo Zhizhi Decoction was more effective than the western drug leflunomide, and the symptoms and inflammatory indicators of the patients were significantly improved.

## 3.2 Treatment of Rheumatoid Arthritis with Minority Drugs

Mongolian medicine believed that the disease occurred because of improper diet, improper living conditions and other factors. The treatment principles are mainly to promote blood circulation and relieve jin, clear heat, dry yellow water, regulate human body's three root hormones and treat syndrome differentiation. Dong Qiumei (Guo Jie, Dong Qiumei & Liu Jun, 2021) 's team found that Mongolian medicine Zhongluna Decoction had good clinical effect in treating RA, and could alleviate the symptoms of RA in the active period. Tibetan medicine calls it true cloth; Many folk Tibetan doctors have found the curative effect to be exact. Its characteristic drugs are Sanhuangshui prescriptions (Pega, Huangkuizi, Cassia) (Liu Zixuan, Luo Jie, Deluo, et al., 2021), and RA is the dominant disease in the treatment of Sanhuangshui prescriptions. In the treatment of rheumatoid arthritis (RA), there are few characteristic drugs and almost no representative drugs. At present, the commonly used traditional Chinese medicines of Uyghur are pseudogentian, mallet fructus, maidenhair fern, ragwort papyrus and seedless grape (Maimaitijiang Wusman & Ainiwal Abra, 2017). Rheumatoid arthritis (RA), named "Runke" in Zhuang medicine, is one of the dominant diseases in the treatment of Zhuang medicine, and its most representative prescription is Longzuantongbi formula (Huang Lan, Lin Jiyong & Liang Fengzhen, 2018). In addition, there are some commonly used folk zhuang medicines, such as Wuzhufeng, triangle maple, octagonal maple, chicken poop Teng, etc. (Huang An, Xu Jing, Chen Xiaoyue, et al., 2016)

## 4. Treatment of Rheumatoid Arthritis with Modern Drugs

### 4.1 Methotrexate

This drug is a common anti-rheumatic drug, which has a particularly good effect on the control of the disease. However, this kind of patients need to take this drug for a long time, and withdrawal of the drug can lead to the recurrence of the disease. Such patients also need to pay attention to lifestyle, weight control, avoid joint weight bearing, regular check-ups, and keep the body and mind relaxed. The dosage is 5mg-25mg per week, which can

be combined with folic acid (Du Siying & Ouyang Hua, 2021). In addition, studies have found that the use of high-dose methotrexate in the acute active stage of RA, namely 25mg once a week, should be combined with folic acid, 5mg once a week, can further improve the efficacy without increasing the side effects of drugs (Jiang Wei, Zhao Yi, Jiang Hong, et al., 2021).

#### 4.2 Leflunomide

The drug is a specific immunomodulator with an oral dose of 50mg per day. The maintenance dose was 10mg-20mg. When the dose is too large or toxic reactions occur, immediately stop the drug and seek medical attention for regular observation. The mechanism of leflunomide is to block the transmission of inflammatory response of macrophages in synovial membrane, thereby reducing the absorption of the affected joints and bone, and effectively controlling the progression of the disease (Hu Yanwei, 2020). Xie Jun et al. (Xie Jun, Huang Liyan & Li Shengfei, 2019) selected 90 cases of patients with rheumatic immunity, 45 cases of the control group (hormone therapy) and 45 cases of the experimental group (leflunomide treatment on the basis of the control group). The results showed that after treatment, indicators such as ESR and CRP in the experimental group decreased and were better than those in the control group.

#### 4.3 Hydroxychloroquine

The usual dose is 250mg/ day, 5 times a week. Hydroxychloroquine is the main antirheumatic drug used in the treatment of RA, which generally takes effect after 2-3 months (Bian Zhengqiao, 2018). Hydroxychloroquine (HCQ), as one of the traditional anti-rheumatic drugs, has a certain effect on chronic prolonged RA, and has good safety and tolerance (Xie Wenhui & Zhang Zhuoli, 2019). Hydroxychloroquine is suitable for the treatment of mild RA alone, and in combination with other immunosuppressive agents for acute active RA. Ren Zhanfen et al. (Ren Zhanfen, Zheng Xuejun, Luo Huan, et al., 2021) randomly divided 180 RA patients into control group (90 cases) and treatment group (90 cases). In addition to methotrexate in both groups, the treatment group was given hydroxychloroquine tablets, and the treatment cycle was half a year. Results the total effective rate of the treatment group was 81.11%, which was significantly higher than that of the control group (66.67%) ( $P < 0.05$ ). It is proved that hydroxychloroquine combined with methotrexate can improve the bone metabolism of patients and reduce the inflammatory response level of the body.

#### 4.4 Cyclophosphamide

The drug is an immunosuppressant. 100mg each time, once a day, generally take the drug after one and a half months can take effect. Side effects include hepatotoxicity and digestive tract reaction, and in severe cases, alopecia, amenorrhea, hemorrhagic cystitis, etc. (Wang Yunping, 2016). In addition, the study found that cyclophosphamide shock therapy had a significant effect on refractory and acute active RA. Wenling Ma (2017) collected 60 patients with refractory RA for observation, 30 patients in the control group were treated with methotrexate, and 30 patients in the observation group were treated with high-dose cyclophosphamide shock therapy. The final statistics showed that morning stiffness time, the number of joint swelling, CRP and ESR indexes in the observation group were significantly lower than those before treatment, and the difference was statistically significant ( $P < 0.05$ ).

#### 4.5 Adalimumab

Adalimumab, a tumor necrosis factor (TNF) - $\alpha$  antagonist, belongs to the class of biological agents. Anti-tnf- $\alpha$  mainly acts on osteoclasts and chondrocytes to eliminate inflammation and relieve symptoms (Wang Xia & Xia Guangtao, 2018). Adalimumab is a new type of anti-rheumatic drug, its clinical effect is very significant, and the price is reasonable, for the majority of patients. Studies have found that adalimumab combined with methotrexate can significantly improve joint dysfunction, and has high tolerance and safety (Wang Lei & Yao Hongwei, 2021). Jiang Xiaoxu et al. (Jiang Xiaoxu, Xu Wei, He Nannan, et al., 2022) treated 86 patients with active RA with adalimumab. After 12 weeks, 16 (18.60%) of the 86 patients were ineffective and 70 (81.40%) were effective. These results indicated that adalimumab could effectively reduce the levels of serum IL-8 and hs-CRP.

### 5. Chinese Medicine Extract

#### 5.1 *Tripterygium Glycosides*

At present, tripterygium wilfordii polyglycoside tablets 10mg, 3 times a day, taken after meals, can reduce clinical symptoms, reduce ESR, rheumatoid factor titer or turn negative. Adverse reactions can lead to irregular menstruation in women and decreased reproductive function, abdominal pain and diarrhea in men. Generally, the symptoms can be eliminated after stopping the medication. Studies have found that tripterygium wilfordii polyglycoside tablets can effectively reduce the immune inflammatory indicators of RA patients, and tripterygium wilfordii polyglycoside tablets combined with traditional Chinese medicine decoction are significantly better than oral tripterygium wilfordii polyglycoside tablets alone in improving symptoms and

reducing liver and kidney function damage in RA patients (Dong Wenzhe, Liu Jian, Xin Ling, et al., 2019). Tripterygium wilfordii polyglycoside tablets have a strong clinical effect by treating RA with multiple targets and multiple pathways. The latest drug guidelines show that the adverse reactions are proportional to the dose and time of drug use, and strict control of the dose and time of drug use can minimize the adverse reactions (Lin Na, Jiang Quan, Liu Wei, et al., 2020). Among the 80 elderly RA patients collected by Li Xuyan (2021), the control group was only treated with methotrexate tablets, while the observation group was treated with methotrexate combined with tripterygium glycoside tablets. Finally, the total effective rate of treatment in the observation group was significantly higher than that in the control group. Therefore, for senile RA, it is recommended to combine tripterygium wilfordii polyglycoside tablets to further enhance clinical efficacy.

### 5.2 Total Glucoside of *Paeony*

The dosage of this drug is 0.6g/ time, 2-3 times/day. It has anti-inflammatory, swelling and analgesic, bidirectional immune regulation and other pharmacological effects, and began to take effect after two courses of treatment. The main components of total glucosides of paeonia lactiflora are glucosides, which can inhibit the autoimmune inflammatory reaction in various ways and have a definite effect on the treatment of RA (Qi Wenxia, Wang Gang, Yan Yanfeng, et al., 2020). The adverse reactions included increased frequency of stool, abdominal pain and other gastrointestinal reactions. Wenjing Yu et al. (Yu Wenjing, Xu Jing, Liang Yi, et al., 2018) designed the control group: methotrexate + leflunomide, and the observation group: total glucoside of paeoniflora alba + methotrexate + leflunomide. After 4 weeks, the total effective rate of the observation group was 83.33%, which was significantly higher than that of the control group 68.42%. In conclusion, total glucoside of paeoniae alba combined with other antirheumatic drugs has definite curative effect on RA.

### 5.3 Sinomenine

The usual clinical dose of sinomenine is 40-60mg/ time, 2-3 times/day; It has anti-inflammatory, analgesic, immunomodulatory and other pharmacological effects, which can inhibit synovial hyperplasia and reduce bone damage (Zhou Yingying, Liu Yuling, Lin Longfei, et al., 2021). Side effects can include a rash, a decrease in white blood cells, and possibly nausea and vomiting, but this can go away when the drug is discontinued. CAI Qiang (2019) observed the efficacy of sinomenine combined with methotrexate in the treatment of 68 patients with early-stage RA with cold-dampness blocking collaterals. The control group took methotrexate, and the treatment group took methotrexate combined with sinomenine. Statistically, it was found that clinical symptoms were relieved more significantly in the treatment group than in the control group, which proved that sinomenine combined with antirheumatic drugs could effectively improve clinical symptoms.

## 6. Treatment of Rheumatoid Arthritis with the Combination of Traditional Chinese and Western Medicine

The pathogenesis of rheumatoid arthritis (RA) is complex and changeable. Single drug therapy is often difficult to control the disease effectively due to the problems of the body's target. Studies have found that the combined use of Chinese and Western medicines can reduce the disability rate and improve the clinical efficacy, which may be related to the synergistic action of Chinese medicines on multiple sites and targets (Xie Zhaohu, Xie Jing, Wu Jingjin, et al., 2020). The combination of traditional Chinese and western medicine breaks the limitation of pharmacological action of Chinese and western medicine, and the combination of traditional Chinese and western medicine is the best treatment plan for RA. If Sanhan Dehumidification (Liu Mao, Liu Hongqiong, Wu Peng, et al., 2021) prescription combined with conventional Western medicine treatment can improve the clinical symptoms of patients with cold and dampness Bi and control the development of the disease. Deng Yunming (Deng Yunming & Xie Caini, 2022) observed the effect of Duhuo Zhishi Decoction combined with Western medicine in the treatment of cold and wet RA, and finally proved that the treatment of Duhuo Zhishi decoction combined with eramod and hydroxychloroquine could effectively improve patients' symptoms and clinical effects, with fewer adverse reactions. It can be seen that the current combined treatment of traditional Chinese and western medicine can enhance strengths and avoid weaknesses and complement each other's strengths. It can meet the advantages of anti-rheumatism drugs, non-steroidal anti-inflammatory drugs or biological agents combined with traditional Chinese medicine for disease differentiation and treatment based on syndrome differentiation of traditional Chinese medicine at the same time. According to the patient's symptoms and syndrome differentiation, disease differentiation and syndrome differentiation can be combined to achieve rapid and effective clinical relief (Tang Jie, 2017).

## 7. Deficiencies and Prospects

To sum up, the clinical treatment of RA is often combined with two or more drugs, not limited to one class of drugs or one therapy. In recent years, a large amount of literature shows that the combination of traditional Chinese medicine and western medicine is obviously superior to the treatment of traditional Chinese medicine or western medicine alone. It not only improves the clinical efficacy, but also reduces the toxic and side effects of western medicine. Its advantages can quickly control the disease, improve joint function and prognosis (Wei

Zhiping, Hong Fangfang & Yang Shulong, 2017); But in the course of treatment, we should pay attention to early diagnosis, early treatment, combined medication and individualized treatment. In addition, the combination of traditional Chinese medicine and western medicine is effective, improving the quality of life of patients, and does not increase the economic burden of patients (Fu Ling, Zhou Xueping, Li Guochun, et al., 2016). Based on the combination of traditional Chinese and western medicine, combined with external application of traditional Chinese medicine, fumigation and washing of traditional Chinese medicine, acupuncture (Zhao Juan, 2011) and other therapies are expected to achieve more ideal clinical effects, which has broad prospects. Therefore, for the treatment of RA, one or two drugs should not be restricted clinically in the future, and multiple drugs or Chinese and Western medicines should be used together; Traditional Chinese medicine treatment has great advantages, we need to further explore. Of course, there are still shortcomings in the treatment of traditional Chinese medicine and western medicine: (1) Some clinical workers are unable to achieve the treatment based on syndrome differentiation when they carry out traditional Chinese medicine treatment, and blindly choose “proven and special prescriptions”, which leads to a decline in clinical efficacy and makes patients lose confidence in the treatment of integrated traditional Chinese medicine and western medicine. (2) At present, there is no standard for the combination of traditional Chinese and western medicine for RA, and there is a lack of further research at a higher level and the recognition of domestic and foreign experts, which is not convincing.

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