Research Progress on the Prevention and Treatment of Rheumatoid Arthritis (RA)

Yutianle Piao

Suzhou Scienece & Technology Town Foreign Language High School, Jiangsu, China

piaoyutianle0611@outlook.com

Abstract. Rheumatoid arthritis (RA) is an autoimmune disease linked to group A type B haemolytic streptococcus infection, characterized by acute fever and migratory joint pain, mainly affecting large joints. Its pathogenesis involves genetics, environmental factors, infections, and immune dysfunction, with symptoms fluctuating due to weather changes. Recent advances in RA treatment include targeted therapy and biological agents, alongside research on immune abnormalities, genetic predisposition, and environmental triggers. Efforts are being made to develop sensitive biomarkers and imaging tools for early diagnosis, as well as promoting multidisciplinary and patient-centered treatment models. However, studies on pediatric RA remain limited, particularly regarding early diagnosis and age-specific treatment strategies. Key findings from literature include: 1) Certain HLA and MHC genes are strongly associated with RA susceptibility; 2) Smoking, air pollution, alcohol, caffeine, and humid-cold environments contribute to RA risk; 3) ESR, CRP, anti-CCP, anti-cyclo-citrulline IgM antibodies, and MRI aid early diagnosis; 4) Adalimumab is effective both alone and in combination with other drugs; 5) Physical therapies like hot/cold compresses and electrotherapy help relieve symptoms. Future research should focus on cost reduction and treatment simplification to improve accessibility and patient outcomes.

Keywords: Rheumatoid arthritis, interleukin, tumour necrosis factor α.

1. Introduction

Rheumatoid arthritis (RA) is a typical autoimmune disease with complex and diverse causes, involving genetic factors, environmental factors and abnormal activation of the immune system. Studies have found that there are a variety of inflammatory mediators in the body of RA patients, such as tumour necrosis factor α (TNF-α), interleukin-1 (IL-1) and interleukin-6 (IL-6). These factors lead to synovial proliferation and joint destruction by regulating immune response and inflammation. Among the clinical manifestations of the patient, joint lesions are the main ones. The early symptoms are morning stiffness, swelling and pain of the joints. With the development of the disease, they develop into joint deformity, affecting the normal joint function of the patient. Some patients will also have systemic symptoms, such as fever, fatigue and weakness.

Genetic research further reveals the association between the susceptibility of RA and the polymorphism of specific genes, such as the important role of HLA-DRB1*04 alleles in the pathogenesis of RA. Environmental factors such as cold, dampness, smoking and stress are also considered to be important factors that trigger RA. In addition, the incidence of RA is also closely related to the abnormality of the immune system, such as the abnormal activation of B cells and T cells and the production of autoantibodies. Although the aetiology of RA has not been fully clarified, its pathological characteristics and clinical manifestations have provided important direction and guidance for future research. For example, synovitis is the core pathological feature of RA, and the regulatory mechanism of proliferation and death of synovial cells is one of the focuses of current research.

In addition, the degree of joint disfunction and disability of RA patients is also affected by long-term inflammation, which makes prevention, early diagnosis and treatment particularly important.

In recent years, the research on the pathogenesis of RA has also made important breakthroughs. For example, the importance of synosis cells in RA and the role of NLRP3 inflammatory bodies in RA inflammatory response. These studies provide a theoretical basis for the development of new treatments for synovial cells and inflammatory bodies. Not only the pathogenesis of RA, but also its

diagnostic methods have become more diversified with the progress of molecular biology and immunology technologies.

As for the treatment strategy of RA, it has evolved from traditional drugs to biological agents to emerging therapies. Traditional drugs such as methotrexate (MTX) and glucocorticoids play an important role in alleviating symptoms and inhibiting the progression of disease. In recent years, the application of biological agents such as anti-TNF-α antibody and anti-IL-6 receptor antibody has significantly improved the prognosis of patients.

The combined treatment of traditional Chinese and Western medicine has also achieved certain results in RA management. For example, traditional Chinese medicine preparations such as Leigong vine polysaccharide tablets, acupuncture, hot compress and other therapies have shown unique advantages in alleviating symptoms and improving the quality of life of patients.

In addition to drug treatment and combined treatment of traditional Chinese and Western medicine, physical therapy such as ultrasonic drug penetration technology has also shown good results in the treatment of pain related to knee osteoarthritis.

The study of RA not only helps to reveal its complex pathological mechanism, but also provides a scientific basis for clinical treatment. The development of early diagnosis technology also helps to achieve early intervention in disease, thus reducing the risk of joint damage and disability. The emergence of new therapies such as biological agents and stem cell therapy provides more options for RA patients and is expected to improve long-term prognosis. The popularisation of the combined treatment model of traditional Chinese and Western medicine has also provided a more comprehensive health management plan for patients. Therefore, this article will introduce RA from the aspects of disease prevention, drug treatment, traditional Chinese medicine treatment and physical therapy, further analyse the treatment method of RA and its principle and effect, aiming to summarise the pathogenesis of RA and its treatment method.

2. Prevention

2.1. Risk factors

2.1.1 Genetic factors

Genetic factors play an important role in the pathogenesis of RA, but they are not the only determining factor. Genetic research shows that RA has a certain family aggregation. Epidemiological surveys show that the genetic susceptibility of RA is about 20% to 60%, which means that genetic factors play an important role in the susceptibility of RA [1]. Specifically, some specific HLA (human leukocyte antigen) genes are closely related to the susceptibility of RA, such as the HLA-DRB1 allele. These genes are located in the main histocompatibility complex (MHC) region on chromosome 6, which is an important genetic marker of the onset of RA [2]. In addition to the HLA gene, there are also many non-MHC-related genes related to the susceptibility of RA. For example, the polymorphism of genes such as PTPN22, STAT4 and PADI4 is also found to be related to the risk of developing RA [3]. These genes involve the regulation of the immune system, inflammatory response and cytokine production, which further supports the complex role of genetic factors in the pathogenesis of RA.

2.1.2 Environmental factors

Although genetic factors increase the risk of developing RA, they are not a decisive factor. Environmental factors such as smoking, air pollution, diet and socio-economic factors can also affect the incidence of RA. Data shows that the risk of RA in smokers is significantly increased, and the condition of smokers is usually more serious. Smoking will increase the level of inflammation in the body, resulting in aggravating joint damage [4]. Pollutants such as particulate matter, fine particles (PM2.5) and inhalable particles in the air may activate the immune system and promote inflammatory reactions, thus increasing the risk of RA. These pollutants can activate macrophages in the lungs, produce pro-inflammatory cytokines, and further aggravate arthritis. Some ingredients in the diet,

such as caffeine and alcohol, may be associated with the onset of RA. For example, excessive caffeine intake may increase the risk of RA, while alcohol intake may aggravate the disease by affecting metabolism and immune function [5]. Low socio-economic status may be related to the increased risk of RA. This may be related to bad living habits, poor medical conditions and high stress levels [6].

2.2. Preventive methods

2.2.1 Early diagnosis

The early diagnosis of RA requires a variety of methods, including clinical symptoms, laboratory examination and imaging examination. First of all, clinical symptoms are an important basis for early diagnosis. Patients usually have joint pain, swelling and stiffness, especially small joints such as fingers, wrists and palm joints. The morning stiffness time usually exceeds 1 hour and is symmetrically distributed, which helps to make a preliminary judgement of whether it is RA. Laboratory examination plays a key role in early diagnosis. The elevation of blood sedimentation (ESR) and C-reactive protein (CRP) levels suggests inflammatory activity, but these indicators are not specific and need to be comprehensively evaluated in combination with other test results. The detection of anti-cyclic citrulline antibody (anti-CCP) and anti-cyclic cycylline IgM antibody is highly specific, especially in the case of anti-RA33 antibody negative [7]. Based on the above methods, doctors can diagnose rheumatoid arthritis more accurately. For example, according to the classification criteria of the American Society of Rheumatology/European Anti-Rheumatic Alliance (ACR/EULAR) in 2010, patients need to meet one of the following conditions: morning stiffness for more than 30 minutes, RF positive, anti-CCP antibody positive, etc. In addition, pathological examinations and synovial fluid examinations can also provide important information, but these methods are usually used to rule out other diseases or further confirm.

2.2.2 Environmental prevention

There are many ways to prevent rheumatoid arthritis from the environmental aspect. Among them, it is especially important to avoid cold and humid environments. Cold and humid environments are easy to induce rheumatoid arthritis, so keep warm, especially in the joints. The living environment should be kept dry and warm, and avoid staying in a humid environment for a long time. At the same time, it is necessary to avoid some bad living habits, quit smoking and limit alcohol. Smoking and excessive drinking can weaken physical function and increase the risk of disease. Control blood sugar levels. High blood sugar will increase the risk of RA.

3. Drug treatment

3.1. Single antibody

3.1.1 Principle

Adalimumab is a biological agent mainly used to treat autoimmune diseases such as RA. First of all, in terms of targeted tumour necrosis factor (TNF), adamumab is an anti-TNF antibody that can bind to TNF molecules and block the interaction between TNF and its receptors (such as p55 and p75). TNF is a pro-inflammatory cytokine, which plays a central role in the pathogenesis of RA. By inhibiting TNF, adalimab can reduce the inflammatory response, thus reducing joint pain and swelling [8]. In addition, adamusumab has a good performance in reducing inflammation and joint damage. Adamumab reduces the release of inflammatory mediators by blocking TNF, thus reducing arthritis and synovis proliferation. Studies show that adamumab can significantly reduce joint structural damage, improve bone mineral density, and regulate bone metabolism [9]. In addition, adalimab can also reduce the level of inflammatory markers in serum, CRP) and ESR, which are important biomarkers for evaluating RA activity [10]. Adamumab not only excels in alleviating symptoms, but also improves patients' joint function and quality of life. For example, in one study, patients in the adalimab treatment group were similar to those of the placebo group in maintaining clinical and functional improvement, and were consistently effective [11]. In addition, adalimab has also been

shown to reduce joint damage and improve patients' daily mobility. Finally, about the combined use of adalimab with other drugs. Adamusamine is often used in combination with other drugs (such as methotrexate) to enhance the therapeutic effect. Studies have shown that the combined use of adalimum and methotrexate can significantly improve the therapeutic effect, especially in patients with poor efficacy of traditional DMARDs (such as methotrexate) [12].

3.1.2 Effects and side effects

Adamumab has a significant effect on the treatment of RA. Adamumab has shown remarkable effects in improving the DAS28-ESR score of RA patients. The study showed that after 6 months of treatment with adalimab, the DAS28 score dropped from the baseline of 2.71±4.60 to 3.23±4.60, and continued to improve during treatment. In a study in Japan, 38.3% of patients treated with adalimumab achieved clinical remission, and 42.4% of patients achieved low disease activity [13]. Compared with other biological agents (such as infliximab), adalimamab has a similar or better effect in improving the health assessment questionnaire (HAQ) score. In patients who had been using adalimab for a long time (more than 5 years), the DAS28 score continued to decline, and there was no significant deterioration during treatment. In a seven-year study, the treatment of patients with rheumatoid arthritis in children with adalimumab showed long-term safety and effectiveness, which can significantly improve the quality of life of patients [14]. When used in combination with methotrexate (MTX), the therapeutic effect can be significantly improved, especially in patients who do not respond well to MTX monotherapy. In patients who continue to use adalimab after discontinuing MTX, the disease activity score (DAS28-ESR) decreased significantly, and the pain visual simulation score also decreased significantly [15].

Of course, Adamumab will also have some side effects. Common side effects include pain, redness and itching at the injection site. In addition, there are some mild to moderate side effects, including headache, cough, gastrointestinal discomfort, etc [16]. And the risk of fever and infection: Adamumab may increase the risk of infection, especially severe infection and sepsis. It can also cause neurological diseases such as multiple sclerosis (MS). The immunogenicity of adamumab may affect its efficacy. Research shows that the production of anti-drug antibodies is closely related to drug concentration and clinical response [17]. Patients who are positive for antibodies may need higher doses of drugs or replace other biological agents.

3.2. Traditional Chinese Medicine

Traditional Chinese medicine treatment is the core method of traditional Chinese medicine to treat rheumatoid arthritis. Commonly used drugs include osmanthus, safflower, Sichuan astragalus, ox knee, etc., which have the effect of warming and invigorating blood, dispelling wind and dehumidifying. Among them, Duhuo Parasitic Soup can be used to dispel wind and dehumidify, dispel cold and pass the channels; King Kongzhi Dilong formula has the effect of invigorating blood and opening channels, warming meridians and dispelling moisture; Guizhiwu medicine soup can dispel wind, dispel cold and dehumidifying; Wet and hot Biqing Pill is conducive to clearing heat and moisturising, and is suitable for wet and heat retention rheumatoid arthritis. Acupuncture stimulates specific acupoints, adjusts qi and blood circulation, promotes joint blood circulation, and relieves pain and swelling. Among them, acupuncture and suspension moxibustion have shown good effects in the treatment of rheumatoid arthritis.

4. Physical therapy

4.1. Hot compress and cold compress

Cold compress is suitable for acute inflammation or when the disease is serious, which can effectively reduce the inflammatory reaction and swelling, and relieve pain. For example, during the acute attack of gouty arthritis, cold compresses can quickly reduce the local temperature and reduce the exudation of inflammatory mediators, thus relieving pain. Hot compress is suitable for chronic

inflammation or long-term joint stiffness, which can promote blood circulation, relieve muscle tension and reduce pain. For example, when the symptoms of morning stiffness are obvious, hot compress can effectively improve joint flexibility and range of movement. For some patients, alternate use of hot and cold compresses can achieve better results. For example, cold compresses are used to relieve inflammation during acute inflammation, and hot compresses are used to promote blood circulation and restore function after symptoms are relieved [18].

4.2. Electrotherapy

Electrotherapy stimulates the affected area through electric current, regulates nerve and muscle function, and promotes blood circulation, so as to achieve the effect of relieving pain, anti-inflammatory and improving joint function. Specific mechanisms include promoting blood circulation, relieving pain, anti-inflammatory, and improving joint function. Electrotherapy can stimulate peripheral blood vessels, increase blood flow, improve the metabolism of local tissues, help inflammation absorption and tissue repair, and interfere with the transmission of pain signals by stimulating nerve fibres, thus reducing joint pain. At the same time, electrotherapy can reduce the release of inflammatory factors, such as interleukin-1β (IL-1β) and tumour necrosis factor-α (TNF-α), thus reducing the inflammatory reaction. In addition to the above functions, electrotherapy can enhance muscle strength, improve joint stability, and reduce joint stiffness. Of course, electrotherapy also has certain limitations. Electrotherapy cannot cure rheumatoid arthritis, but can only be used as an auxiliary treatment. And for patients with severe arthritis, electrotherapy may not provide sufficient pain relief or function improvement [19].

5. Conclusion

After reading a large number of research literature on RA, this paper studies the genetic and environmental factors of RA, the principle and side effects of diagnostic methods and environmental prevention methods, monoantibody drug treatment, traditional Chinese medicine treatment, cold compress, hot compress and electrotherapy. The onset of RA is influenced by both genetic and environmental factors, among which genetic factors play an important role. Early diagnosis and comprehensive treatment are the keys to improving the quality of life of patients. As an effective biological agent, adamumab has shown remarkable efficacy in the treatment of RA, and the effect will be more effective when combined with other drugs, but attention should be paid to its potential side effects. Traditional Chinese medicine also plays an important auxiliary role in the treatment of RA, but there is a lack of sufficient research data. Future research should further explore more effective treatments for RA and more ranged and low-cost drugs for use in remote or low-economic areas.

References

[1] ABUL KHAIR AHMEDULLAH, SHAMIM AHMED, MD. ABU SHAHIN, MD. ARIFUL ISLAM. Roles of Genes in the Susceptibility to and Severity of Rheumatoid Arthritis [J]. 2012, 13: 51-54.

[2] Liu Wei, Wu Xin, Xu Huji. Research progress on the genetic background of susceptible genes in rheumatoid arthritis [J]. Theory and Practice of Diagnostics, 2018, 17 (3): 347-351.

[3] Yasuto Araki, Toshihide Mimural. The Mechanisms Underlying Chronic Inflammation in Rheumatoid Arthritis from the Perspective of the Epigenetic Landscape [J]. Journal of Immunology Research, 2016.

[4] R. S. Nithyashree, R. Deveswaran. A Comprehensive Review on Rheumatoid Arthritis [J]. Journal of Pharmaceutical Research International, 2020, 32 (12):18-32.

[5] Nithyashree, Deveswaran. A Comprehensive Review on Rheumatoid Arthritis [J]. JPRI, 2020, 32 (12): 18-32. DOI: 10.9734/JPRI/2020/v32i1230377.

[6] Jangampalli Adi Pradeepkiran. Insights of rheumatoid arthritis risk factors and associations [J]. Journal of Translational Autoimmunity, 2019, 2: 100012.

[7] Mahin Lashkari, Akram Noori, Fatemeh Hajiimanouchehri, Sonia Oveisi, Amir Mohammad Kazemifar. Determination of Specificity and Sensitivity of Anti-RA 33 in Diagnosis of Early Rheumatoid Arthritis [J]. Global Journal of Health Science, 2014, 6 (4).

[8] Giuseppe Murdaca, Francesca Spanò, Francesco Puppo. Long-term treatment of rheumatoid arthritis with adalimumab [J]. Open Access Rheumatology: Research and Reviews, 2013.

[9] Mélanie Auréal, Irma Machuca-Gayet, Fabienne Coury. Rheumatoid Arthritis in the View of Osteoimmunology [J]. Biomolecules.

[10] M. Victoria Hernández, Silvia Vidaf, Raimon Sanmarti. Analysis of the Mechanism of Action of Biological Therapies in Monotherapy in Patients with Rheumatoid Arthritis: Beyond the ADACTA Study [J]. Advances in Pharmacoepidemiology & Drug Safety, 2013.

[11] Désirée van der Heijde, Joachim Sieper, Walter P. Maksymowych, et al. Clinical and MRI remission in patients with nonradiographic axial spondyloarthritis who received long-term open-label adalimumab treatment: 3-year results of the ABILITY-1 trial [J]. Arthritis Research & Therapy, 2018, 20: 61. DOI: 10.1186/s13075-018-1556-5.

[12] Josef S. Smolen, Robert B. M. Landewé, Johannes W. J. Bijlsma, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update [J]. Annals of the Rheumatic Diseases, 2019.

[13] Tsutomu Takeuchi, Yoshiya Tanaka, Yuko Kaneko, et al. Effectiveness and safety of adalimumab in Japanese patients with rheumatoid arthritis: retrospective analyses of data collected during the first year of adalimumab treatment in routine clinical practice (HARMONY study) [J]. Modern Rheumatology, 2012, 22: 327-338.

[14] Daniel J. Lovell, Nicolino Ruperto, Richard Mouy, et al. Long-Term Safety, Efficacy, and Quality of Life in Patients with Juvenile Idiopathic Arthritis Treated with Intravenous Abatacept for Up to Seven Years [J]. Arthritis & Rheumatology, 2015, 67 (10).

[15] Calenzi, Marco Marucci Erinic, Clodoveo Turi, et al. Etanercept maintains the clinical benefit achieved by infliximab in patients with rheumatoid arthritis who discontinued infliximab because of side effects [J]. Annals of the Rheumatic Diseases, 2007, 66: 249-252. DOI: 10.1136/ard.2006.058776.

[16] Louis Bessette, Majed Khraishi, Alan J. Kivitz, et al. Single-Arm Study of Etanercept in Adult Patients with Moderate to Severe Rheumatoid Arthritis Who Failed Adalimumab Treatment [J]. Rheumatology and Therapy, 2017, 4: 391-404. DOI: 10.1007/s40744-017-0079-x.

[17] Martin Perry, Andrew McGucken. The potential value of blood monitoring of biologic drugs used in the treatment of rheumatoid arthritis [J]. Therapeutic Advances in Musculoskeletal Disease, 2020, 12: 1-13.

[18] Syamsudin, Arti Dwi Astuti. Literature Review: Pengaruh Simplisia Jahe terhadap Penurunan Nyeri Rheumatoid Arthritis [J]. Jurnal Keperawatan, 2021, 7 (2): 37-48.

[19] Tianhong Liu, Zhaojun Song, Shenchen Qiu. The effect of transdermal acupoint electrical stimulation on the expression level of peripheral opioid peptide in rheumatoid arthritis rats [J]. Shanghai Journal of Acupuncture and Moxibustion, 2021.