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Research Progress on the Pathogenesis and Integrated Traditional Chinese and Western Medicine Treatment of Gout

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Abstract: ***Gout is a common inflammatory metabolic rheumatic disease caused by persistent hyperuricemia and monosodium urate (MSU) crystal deposition in joints and soft tissues. With the continuous update of global dietary structure and lifestyle, the incidence of gout has shown a sustained upward trend and tends to occur at younger age, bringing heavy economic and social burdens to patients and society. Modern Western medicine has formed a mature diagnostic and treatment system for gout, focusing on rapid anti-inflammatory analgesia and long-term urate-lowering therapy, but there are obvious limitations such as single target of action, adverse drug reactions, and easy recurrence after drug withdrawal. Traditional Chinese medicine (TCM) has unique advantages in the treatment of gout based on syndrome differentiation and treatment, multi-target intervention, and holistic regulation, which can effectively improve clinical symptoms, reduce serum uric acid level, reduce recurrence rate, and improve patients' quality of life. Based on the latest domestic and foreign research literature in recent five years, this review systematically summarizes the modern pathogenesis of gout, the latest progress of Western medicine treatment, the TCM etiology and pathogenesis characteristics, as well as the clinical and experimental research status of single Chinese medicine, compound prescriptions, acupuncture and comprehensive TCM intervention. Meanwhile, it analyzes the existing problems in current research and puts forward future research directions, aiming to provide theoretical reference and novel perspectives for standardized clinical treatment and translational basic research of integrated traditional Chinese and Western medicine for gout.***

Keywords: Gout, Hyperuricemia, Integrated traditional Chinese and Western medicine, Pathogenesis, Therapeutic progress, Syndrome differentiation.

1. Introduction

Gout is a heterogeneous metabolic rheumatic disease characterized by recurrent acute arthritis, presenting with joint redness, swelling, heat, and pain, and may progress to tophi, joint deformity, or renal damage in severe cases. Globally, the prevalence of hyperuricemia and gout has risen steadily, with China witnessing a rapid increase over the past decade, particularly among middle-aged and young adults. Modern research identifies MSU crystal-induced NLRP3 inflammasome activation and purine metabolic disturbances as core pathogenic mechanisms, involving genetic susceptibility, gut dysbiosis, and immune inflammation.

Current Western medical therapies—including xanthine oxidase inhibitors, uricosurics, and anti-inflammatory agents — are effective in managing acute flares and lowering uric acid. However, long-term use carries risks of hepatorenal toxicity, gastrointestinal irritation, and poor prognosis in patients with metabolic comorbidities or renal impairment. As a complementary therapy, TCM addresses gout through holistic regulation of zang-fu organs, qi-blood balance, and elimination of damp-heat and blood stasis, showing advantages in improving metabolic status, reducing recurrence, and minimizing side effects. Recent advances in network pharmacology, metabolomics, and molecular biology have progressively elucidated the active constituents and mechanisms of TCM, providing a scientific basis for its clinical application. This review synthesizes current progress in gout pathogenesis and integrated TCM-Western medicine treatment, while critically examining existing limitations and future directions to inform standardized practice and translational research.

2. Modern Pathogenesis of Gout

2.1 Abnormal Purine Metabolism and Hyperuricemia

Hyperuricemia is the prerequisite pathological basis for the occurrence of gout. Human uric acid is the final metabolite of purine compounds, and its metabolic balance depends on the dynamic balance of endogenous synthesis and exogenous intake and renal excretion [1-2]. Modern studies have confirmed that the occurrence of hyperuricemia is mainly divided into two mechanisms: excessive uric acid production and reduced uric acid excretion. The excessive activation of xanthine oxidase (XO) is the key enzyme leading to increased uric acid synthesis, which can catalyze xanthine and hypoxanthine to produce a large amount of uric acid [3]. Renal uric acid excretion disorder is closely related to the abnormal expression of renal tubular urate transporters, including the up-regulation of reabsorption transporters such as URAT1 and GLUT9, and the down-regulation of excretion transporters such as OAT1 and OAT3, resulting in reduced renal uric acid clearance and elevated serum uric acid levels [4].

2.2 MSU Crystal-Mediated Immune Inflammatory Response

Persistent hyperuricemia leads to the deposition of supersaturated urate in the form of MSU crystals in joints and surrounding soft tissues. MSU crystals are recognized as danger-associated molecular patterns (DAMPs) by innate immune cells such as macrophages and neutrophils, which can specifically activate the NLRP3 inflammasome [5-7]. The activated NLRP3 inflammasome promotes the maturation and

release of inflammatory cytokines such as interleukin-1β (IL-1β), interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α), triggering a cascade of inflammatory reactions, resulting in acute joint inflammatory injury [8-10]. This is the core molecular mechanism of acute gouty arthritis attacks. In addition, long-term chronic inflammatory stimulation can induce synovial hyperplasia, cartilage destruction and tophi formation, and further progress into chronic gouty arthritis [11-12].

2.3 Genetic and Microenvironmental Regulatory Mechanisms

Genome-wide association studies (GWAS) have confirmed that multiple gene loci are associated with the susceptibility of gout and hyperuricemia, mainly involving urate transport and purine metabolism-related genes, and there are significant ethnic and regional differences in genetic susceptibility. Intestinal flora imbalance is also an important auxiliary pathogenesis of gout [13-15]. Abnormal proliferation of purine-degrading bacteria and reduction of beneficial bacteria in the intestine will lead to increased purine absorption and inflammatory intestinal microenvironment, aggravating hyperuricemia and systemic inflammatory response [16]. In addition, obesity, hyperglycemia, dyslipidemia and other metabolic disorders are closely correlated with gout, forming a mutual promotion pathological relationship [17].

3. Current Status of Western Medicine Treatment for Gout

3.1 Acute Attack Stage: Anti-Inflammatory and Analgesic Treatment

The core goal of Western medicine treatment in acute gout attack stage is to quickly control inflammation and relieve joint pain and swelling. The first-line clinical drugs include non-steroidal anti-inflammatory drugs (NSAIDs), colchicine and glucocorticoids [18-20]. NSAIDs such as etoricoxib and indomethacin exert anti-inflammatory and analgesic effects by inhibiting cyclooxygenase and reducing prostaglandin synthesis, which are suitable for most patients with acute attacks, but long-term use may cause gastrointestinal mucosal damage and renal function injury [21]. Low-dose colchicine is the classic drug for the treatment of acute gout, with definite curative effect, but it is easy to cause adverse reactions such as diarrhea and nausea, and has certain myelosuppression toxicity [22]. For patients with poor efficacy or contraindications to the above two types of drugs, short-term low-dose glucocorticoids can be used for emergency anti-inflammatory treatment, but sudden drug withdrawal can easily cause inflammatory rebound [23].

3.2 Remission Stage: Standardized Urate-Lowering Therapy

Long-term standardized urate-lowering therapy is the key to prevent gout recurrence and delay disease progression. At present, clinical urate-lowering drugs are mainly divided into three categories. First, XO inhibitors represented by allopurinol and febuxostat, which inhibit uric acid synthesis by blocking XO activity, and are suitable for patients with excessive uric acid production. Among them, febuxostat has high selectivity and strong efficacy, but it needs to be alert to cardiovascular adverse reactions in long-term application [24-26]. Second, uricosuric drugs such as benzbromarone and dotinurad, which promote renal uric acid excretion by inhibiting URAT1 transporter activity, and are suitable for patients with reduced uric acid excretion, but patients with renal insufficiency and urinary tract stones need to use them cautiously [27-28]. Third, urate oxidase preparations such as pegloticase, which are mainly used for refractory severe gout patients with poor response to conventional drugs [29].

3.3 Limitations of Western Medicine Treatment

Although Western medicine has rapid and accurate effects in controlling acute symptoms and reducing blood uric acid, it has obvious clinical limitations. First of all, Western medicine treatment is single-target intervention, which only focuses on the regulation of uric acid metabolism and inflammatory indicators, and lacks holistic regulation of the patient's metabolic state and immune microenvironment. Secondly, long-term medication is accompanied by multiple adverse reactions, which reduces patient compliance. In addition, after standardized urate-lowering drug withdrawal, the serum uric acid level is easy to rebound, and the recurrence rate of gout is high, which cannot fundamentally improve the patient's physical condition.

4. TCM Understanding and Research Progress of Gout

4.1 TCM Etiology and Pathogenesis

Gout belongs to the categories of "bi syndrome", "gout wind", "white tiger wind" in TCM. Modern TCM scholars have summarized the core pathogenesis of gout based on traditional theories and clinical practice [30]. The disease is located in the joints and meridians, and is closely related to the dysfunction of spleen, kidney and liver. The basic etiology is congenital insufficiency of spleen and kidney, improper diet, overeating greasy and sweet food, leading to spleen dysfunction, damp-heat endogenous, long-term damp-heat stagnation, qi stagnation and blood stasis, phlegm-stasis blocking meridians and joints, resulting in joint swelling and pain. In the acute stage, damp-heat stagnation and blood stasis blocking collaterals are the main excess syndromes; in the chronic remission stage, spleen and kidney deficiency, phlegm-stasis lingering are the main deficiency-excess mixed syndromes [31]. The pathological characteristics of "dampness, heat, phlegm, stasis and deficiency" run through the whole course of gout, which provides the theoretical basis for TCM syndrome differentiation and treatment [32].

4.2 Clinical Application of TCM Single Herb

A variety of traditional Chinese medicines have definite effects on lowering uric acid and anti-gout inflammation, with the characteristics of multi-target and low toxicity [33]. Common single herbs include Smilax glabra, Plantago asiatica, Coix seed, Lonicera japonica, Salvia miltiorrhiza and so on [34-36]. Modern pharmacological studies have confirmed that the active ingredients of Smilax glabra can inhibit XO activity, reduce uric acid synthesis, and inhibit NLRP3 inflammasome activation to reduce inflammatory

cytokine release [37]. Plantago asiatica and Coix seed can promote uric acid excretion by regulating renal urate transporters, and have the effects of invigorating spleen and eliminating dampness. Salvia miltiorrhiza and Panax notoginseng can improve microcirculation, eliminate blood stasis and unblock collaterals, and relieve joint inflammatory edema and pain [38-42].

4.3 Clinical Efficacy of TCM Compound Prescriptions

Guided by syndrome differentiation, TCM compound prescriptions provide tailored interventions for different gout stages and patterns, achieving better outcomes than single herbs. For acute damp-heat stasis gout, modified Simiao Powder and Ermiao Powder clear heat, drain dampness, activate blood, and dredge collaterals for rapid symptom relief. For chronic gout with spleen-kidney deficiency and phlegm-stasis, modified Buzhong Yiqi Decoction and Shenqi Pill strengthen the spleen, tonify the kidney, resolve phlegm, and dispel stasis, steadily lowering uric acid and reducing recurrence [43]. Network pharmacology confirms that these compounds synergistically target NLRP3, IL-1β, and TNF-α to co-regulate uric acid metabolism and inflammation, demonstrating unique multi-target advantages.

4.4 Acupuncture and Comprehensive TCM Intervention

Acupuncture, moxibustion, cupping and other external TCM therapies are important auxiliary methods for gout treatment. Acupuncture can dredge meridians, regulate qi and blood, inhibit local inflammatory response, and has a rapid analgesic effect on acute gout joint pain. Clinical studies have shown that acupuncture combined with herbal medicine can significantly improve the clinical efficacy, reduce the dosage of Western medicine, and reduce the incidence of adverse reactions. In addition, TCM dietary conditioning, acupoint application and other comprehensive intervention measures can regulate the patient's physical condition from multiple dimensions, improve metabolic level, and effectively prevent gout recurrence [44].

5. Research Deficiencies and Future Prospects

5.1 Existing Research Deficiencies

Current TCM research on gout faces three key barriers to clinical translation. First, clinical evidence is weak—most trials are small-scale, lack multicenter validation, and suffer from non-standardized diagnostic criteria and inconsistent endpoints. Second, mechanistic studies remain shallow, focusing on surface biomarkers like uric acid while failing to clarify TCM's multi-target molecular networks. Third, standardized protocols and long-term follow-up data are insufficient, leaving the sustained safety and efficacy of TCM therapies unproven [45].

5.2 Future Research Directions

Future research on integrated traditional Chinese and Western medicine for gout should focus on three aspects. First, high-quality clinical studies are needed to establish unified TCM diagnostic standards and treatment protocols, and to define the efficacy and suitable patients for different TCM therapies. Second, modern omics technologies should be used to identify active ingredients and key mechanisms of TCM compounds, particularly their multi-target regulation of uric acid metabolism, inflammation, and gut microbiota [46]. Third, optimal combination regimens should be explored to maximize the complementary benefits of Western medicine in rapid inflammation control and TCM in systemic regulation, thereby reducing side effects, improving long-term prognosis, and facilitating precise individualized treatment.

6. Conclusion

Gout is a refractory chronic metabolic rheumatic disease with complex pathogenesis and high recurrence. Western medicine controls acute inflammation and lowers uric acid effectively, but has limitations like single target, adverse effects, and relapse after withdrawal. TCM, based on holistic regulation and syndrome differentiation, offers advantages in metabolic balance, immune modulation, recurrence reduction, and quality of life. The integrated model combines their strengths for better efficacy. However, current evidence and mechanistic research remain insufficient. Future studies should focus on high-quality trials and mechanistic explorations to standardize TCM protocols, promote modernization, and provide safer, more effective treatments for gout patients.

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