

Research Progress of Pathogenesis of Gout and Corresponding Treatment by Chinese Herbs

Mei Zhong

Infirmary of Xichang University

Xichang University

Xichang, China

84536683@qq.com

Abstract—Pathogenesis of gout is explained from the standpoints of traditional Chinese and western medicine, and recent research progress related to treatment of gout is summed by Chinese medicine of unilateral potion and polypragmasy. Methods: analyzing, organizing document and abroad documents. Conclusion: polypragmasy shows small side effect and significant effect in gout treatment, while more aspects need deep research and improvement. Based on existing Chinese herbs and polypragmasy therapeutic mechanism for gout treatment, more innovating Chinese herbs and proved recipe beneficial for gout treatment may be developed, which contributes more in expanding Chinese medicine.

Keywords—Gout, Chinese medicine, Individual herbs, Compound medicines

I. INTRODUCTION

Resulted by disturbance of purine metabolism and decrease of uric acid excretion, gout is a kind of crystal-induced arthritis. High uric acid, deposition of urate crystal in joint tissue such as articular capsule, cartilage, synovial and bone. Gout brings pathological lesion and inflammatory reaction to synovial and surrounding tissue and potential urate nephrosis, lithangiuria or even severe joint deformity and renal insufficiency[1]. Recently, with the improvement of living standard, gout incidence rate has been increasing, and covered more young patients. The newest epidemiology shows gout incidence rate in European and American area falls in 0. 20%~1. 70%, and it is obvious high in Asia. In China, it shows 1. 26%~1. 59% for male and 0. 30%~0. 36% for female[2].

II. PATHOGENESIS OF GOUT

A. Theory of Traditional Chinese Medicine

The first record for gout is “Mingyi Bielu” by TAO Hong-jing. According to “Hezhi Yulun, gout” by ZHU Dan-xi in Yuan dynasty, gout is always caused by catching cold from cool water, wet floor or cool wind after over heat in blood. As the inner heat meets outer chill, dirty and bitter, thus may cause pain, especially at night, circle in Yin. “Huangdi Neijing” in the Warring States Period explains paralysis like this:wind-cold-dampness to be arthralgia, such as migratory arthralgia, arthralgia aggravated by cold, arthralgia mainly due to dampness. Which is the famous pathogenic from exterior reason theory in traditional Chinese medicine. “Zhangshi Yitong, gout” in Qing dynasty by ZHANG Lu still believes gout is caused by cold in meridian, and slowing down of blood circulation.

Based on former research, modern Chinese medical doctors have obtained further knowledge for gout. WU Sheng-yuan points that the etiology of gout lies in sputum, moisture and stagnate of blood, and the basic pathogenesis is Spleen Dysfunction due to dampness and accumulation of damp heat[3]. Professor QIAN Xian points out that gout is the combined result of internal and external evil with essential pathogenesis of efficiency of liver and kidney and superficial of wind, cold, heat pathogen and meridian impatency from phlegm or blood stasis[4]. Director TANG Xiao-hu believes that gout is a primary asthenia-secondary sthenia syndrome, patients with spleen-kidney-yang deficiency and sick body suffer meridian restraint from moisture, heat, phlegm and stasis certification, which results in weak Qi and blood circulation and pain[5]. Professor XIAO Wan-ze considers the main cause of gout is endogenous dampness, early function damage of spleen, stomach and kidney results in body fluid accumulation in middle burner, both activating blood and separating the clear is bad, which brings abnormal distribution of body fluid. Long accumulation of damp generates phlegm, the evil results blood stasis move slowly around tendons and condyles in four limbs while the evil stays in blood and can not be discharged, gout is brought by staying of these evil in joints in outer edge of limbs[6]. Professor ZHANG thinks from the standpoint of Chinese medicine, gout may be explained as long damp accumulation around points, which brings blockage of Qi and blood, qi stagnation and blood stasis. Dampness pathogen is etiological factor of gout, venation restraint is the basic pathogenesis, and interaction of damp and stasis are the final pathological products[7].

B. Theory of Western Medicine

1) Uric acid metabolism: 80% uric acid in human body comes from catabolism of nucleotide, and uric acid is the final metabolite of purine. Too much uric synthesis may be caused by high purine food and much nucleic acid decomposition. 70% uric in human body is discharged through kidney and the other is break up into small molecule materials such as ammonia, carbon dioxide etc. in gut cavity. Uric excretion in kidney is controlled through glomerulus filtration, reabsorption before secretion, initiative secretion by renal tubule and reabsorption after secretion (major route). urate is a kind of polar molecule, which means ion channels are necessary to make it pass through epithelium cell membrane in renal tubule. human urate-anion exchanger(hURAT1)is the most critical ion channel, which promotes the reabsorption of uric acid by renal tubule, therefore

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influence extent of uric acid discharge from kidney. 80%-85% patients suffer gout for inadequate excretion of uric acid[8]. Thus too much uric acid syntheses and less excretion may cause high concentration of uric acid.

2) *Deposition of urate crystal:* With sustain increase of concentration of uric acid, needle point shaped single sodium urate crystal brought by supersaturation may deposited in joint tissue located in articular capsule, cartilage, synovial membrane and bone. Urate crystal has a feature of WBC migration, which is easily identified and devoured by WBC in soft tissue, and hydrolytic enzyme is released to bring damage to WBC, therefor gout is generated for pathological lesion and inflammatory reaction appeared in synovial as well as surrounding tissue. Urate crystal was found within gout patient body by Alfred Baring Garrod, who believed it had direct relation to gout clinical symptoms[9]. McGill group proved the relation between urate crystal and acute gouty arthritis by confirmation of higher crystallization ability of articular cavity synovial fluid from gout patients[10].

III. TREATMENT OF GOUT BY CHINESE MEDICINE

There are abundant traditional Chinese medicine resources in China, much has been researched fully for efficacy of treatment of gout. Traditional Chinese medicine has exploited a new way for tout treatment by Chinese herbs with lower cost and less toxic and side effect. Several major Chinese herbs are analyzed as follow.

A. Individual Herbs

Statistics from HE Jia-li group shows that 18 kinds of Chinese herbs are used in treatment of gout over 900 times, including earthworm, papaya, glycrhiza uralensis, coix seed, amur cork tree bark, achyranthes bidentata, atractylodes lancea, glabrous greenbrier rhizome, alisma plantago-aquatica, Japanese honeysuckle stem, red paeony root, clematis root, angelica sinensis, gentiana macrophylla, wolfiporia extensa, poison yam, radix stephaniae and plantain seed. Which are classified into treatment of activating meridians to stoop pain, removing dampness and discharging evil, clearing heat and drying damp for detoxication and strengthen spleen[11,12]. Glabrous greenbrier rhizome, longhairy antenorion herb and plantain seed have obvious diuretic action and promote excretion of uric acid, urea and chloride[13]. LIU Guo-jie, a famous herbalist doctor, stands for more usage of glabrous greenbrier rhizome in gout treatment, the significant effect has been proved in practice[14].

Rhubarb, famous for its yellow outlook, is one kind of traditional medicine belonging into polygonaceae plants. The active ingredient including anthraquinones, ketone, rhubarb polysaccharide and tannin makes rhubarb act as a kind of Chinese medicine[15]. Purine metabolism speed is influenced by negative feedback control from many substrates, including IMP, 5-phosphoric acid-1-pyrophosphoric acid, adenylic acid, glutamine and guanylic acid. XOD plays an important part in uric acid generation, and the variation may accelerate the rising of uric acid for its catalytic action to hypoxanthine and xanthine. Therefore hyperuricemia may be treated through restraining the activity of XOD, thus the conversion from xanthine to uric acid

may be prevented to low down uric acid level[16,17]. Rheum emodin has the function of restraining the activity of XOD. Some pharmacological study and clinical application of treatment of gout with rhubarb have been made by many domestic experts. Ginger and Wu rhubarb are used by ZHOU Jiu-fang in experiment of hyperuricemia treatment in mice, the result shows that UA, BUN and the activity of XOD existing in Cr and liver may be reduced by extract for rhubarb[18]. GUO Yan-fang's research of using rhubarb+vinegar in external application of acute gouty arthritis shows that symptom of joint heat, swelling and pain in treatment group is obviously improved compared to control group($P<0.05$)[19].

B. Compound Medicines

Based on integrate treatment of liver, spleen and kidney Chinese medicine of gout mixture is a experience compound prescription focus on dispelling wind-evil and removing dampness, devoicing stasis-toxin and activating blood. Gout mixture(Japanese honeysuckle stem, Japanese knotweed, clematis root, carthamus, achyranthes root) made by Affiliated Hospital of Qingdao University Medical College is used by WABG Yan-gang group to make experiment on mice with gouty arthritis in acute attack. The result shows: Medium and high dose gout mixture has positive effect on reducing joint swell of the mice, while dose-dependent fashion may generate. High dose gout mixture has stable efficacy as colchicine, which may be explained as its inhibiting effect on collection of leukocyte to local inflammation and secretion of interleukin 1 β , an important inflammatory mediator in pathological process of gouty arthritis[20]. Clinical research on patients in acute phase of gout by LI Cong-rong group with compound gout capsule (atractylodes lancea, amur cork tree bark, angelica sinensis, cyathula officinalis, seed of jobs tears, glabrous greenbrier rhizome, caulis spatholobi, red paeony root, poison yam, fuculæ bombycæ, leech, earthworm etc.), the result shows that the pain and swelling of patients' joint may be reduced by this capsule, meanwhile it is still effective in lowering uric acid, erythrocyte sedimentation rate and C-reactive protein level. Compound gout capsule may greatly reduce uric acid of mice with hyperuricemia in experiment, and has obvious analgesic effect to pain from heat[21]. Effect of Anti-inflammation and analgesia and anti-gouty arthritis from compound Wefu particle (atractylodes lancea, achyranthes bidentata, glabrous greenbrier rhizome, glabrous sarcandra herb, peach seed, carthamus, clematis root etc.) is studied by HUANG LI-zhen group through animal experiment, the effect of anti-inflammation and analgesia and gout efficacy has been proved[22]. The effect of compound Sihuang liquid (scutellaria baicalensis, coptis chinensis, Japanese knotweed, amur cork tree bark, forsythia etc.) to acute gouty arthritis as well as its influence to inflammatory indexes are investigated by CHEN Hai-hong group through a clinical research on 72 samples with acute gouty arthritis, the significant effect on improving clinical symptoms and inflammatory reaction has been proved[23].

IV. SUMMARY

Increasing incidence rate of gout brought negative effect to people's health. Current western medicine for gout treatment aims at relieving pain and reducing uric acid. While most patients have adverse drug reaction such as nausea, vomit and

diarrhea, even function lesion of liver and kidney, dermatitis exfoliativa and bone marrow suppression. Relapse often happens after drug withdrawal, while many patients can not stick to it for high price. Compound Chinese medicine focus on observation of biochemical indexes as uric acid, and does less in further research on mechanism of uric acid treatment. Therefore it is necessary to make deeper research on mechanism of Chinese medicine proved to be effective in gout treatment, and provide theory basis for innovative drug for gout target treatment.

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