

Basic and clinical application progression of invigorating blood and dissolving stasis Chinese medicine in ophthalmology

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活血化瘀中药在眼科的基础和临床应用进展

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摘要

活血化瘀法是中医的一种独特疗法,现代对血瘀证及活血化瘀疗法的研究深入,使活血化瘀疗法在眼科临床的应用广泛,并且在西药难以奏效的眼底疾病中,起到了意想不到的作用,提高了眼底疾病的治愈率。从眼睑、结膜、泪囊、眼肌、玻璃体到脉络膜和视网膜、视神经、黄斑,不管疾病位于眼内还是眼外,或病变涉及到炎症、变性、萎缩、增生、坏死纤维组织增生等,都有一定的疗效。本文就近年来活血化瘀中药在眼科的研究基础以及临床应用进展作一总结概述。

关键词:活血化瘀;眼科应用;综述

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Abstract

• Invigorating blood and dissolving stasis method is a kind of unique therapy of Traditional Chinese Medicine (TCM) treatment, which efficacy has become increasingly prominent in the treatment of ophthalmology. With the further studies of blood stasis

and invigorating blood and dissolving stasis therapy, it is widely used in clinical ophthalmology, and get good effects beyond thought, especially when western medicine has no curative effects. It improved the cure rate of fundus oculi disease from the eyelids, conjunctiva, lacrimal sac, vitreous body to the choroid and retina, optic nerve and macula lutea, from surface to fundus, or pathological changes related to inflammation, degeneration, necrosis, atrophy, hyperplasia of fibrous tissue hyperplasia. This paper is aim to explain the definition of invigorating blood and dissolving stasis and make a review of basic research and clinical application about it in several diseases.

• **KEYWORDS:** invigorating blood and dissolving stasis; application in ophthalmology; review

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INTRODUCTION

The Definition of Blood Stasis *Shuo Wen Jie Zi* said "stasis is accumulations of blood", blood stasis produces because of the weakened function of zang-fu, the imbalance of "Qi", blood, fluids, essence, externally-contracted six pathogenic factors, injury and all kinds of bleeding. Qi can carry blood moving together, Qi stagnation and deficiency make blood stasis, then blood stasis blocks zang-fu blood vessels, leading tissue and organ degeneration, poor blood flow, and multiple vascular lesions^[1]. Summarize the modern research results related to blood stasis, which generally include the following aspects: 1) the blood circulation disorders, abnormal hemodynamics, especially abnormal microcirculation disorder; 2) the abnormality of blood coagulation system and platelet function and activity factors; 3) capillary permeability abnormality; 4) the capillary permeability of the macrophage function abnormality; 5) connective tissue metabolism abnormality; 6) the immune system and endocrine function abnormality; 7) endocrine function abnormality. From pathological point of view, the main pathological changes of blood stasis include: 1) local or systemic blood circulation abnormality; 2) vascular

degeneration and exudative lesions, thrombosis, hemorrhage *etc*; 3) inflammatory lesions of various degrees; 4) the hyperplastic lesions (fibrosis, scar stasis, or tumor and tumor like lesions *etc*); 5) the pathological changes of cell degeneration and dysfunction^[2]. The ophthalmic manifestations are aqueous and vitreum hemorrhage, exudation, hemorrhage opacity of the fundus of the elevated intraocular pressure, proptosis, eyelid bruising or swelling scleroma, red eye, coarse choroid mass, ocular bleeding caused by poor circulation^[3], tongue has petechia or ecchymosis, sublingual varicose veins, wiry and choppy pulse.

Theoretical Basis of Invigorating Blood and Dissolving Stasis Medicine

Invigorating blood and dissolving stasis is treatment rule for blood stasis, it is a method to remove blood stasis, dredge blood vessels, the basic pharmacological effect can be summarized as follows: 1) improvement of hemodynamics; 2) improvement of blood rheology and thrombosis; 3) improvement of the microcirculation *etc*^[4]. Invigorating blood and dissolving stasis comes from the theory of blood stasis. "Extravasated blood", "blood coagulation", "blood bi" are early recorded in *Huangdi Neijing*, and referred to the methods of "dredging blood vessels", "breaking up blood", "dissipating masses". There is discussion "blood stasis fills in eyes is due to coagulation and stagnation" in *Shen Shi Yao Han*. Zhong - Jing Zhang proposed "blood stasis", "blood amassment", "dry blood" in *Treatise on Febrile Diseases* and *Synopsis of the Golden Chamber*, and narrated pattern differentiation and treatment of invigorating blood and dissolving stasis. There are much development of Blood Stasis Theory after the Sui Dynasty such as "Source", *Thousand Golden Prescriptions*, *Wai Tai Mi Yao* of the Sui and Tang Dynasties, *Esoteric Yanke Longmu Theory* of Song Dynasty, *Compendium of Materia Medica* of the Ming Dynasty, *Mujing Dacheng* of the Qing Dynasty, the books all did complement and innovation to principles, methods, formulas, and medicinals of invigorating blood and dissolving stasis. The Qing Dynasty had appeared some summarized systemic monographs, taking example of *Errors in Medicine Corrected* written by Qin - Ren Wang which centered on invigorating blood and dissolving stasis and create 33 formulas. At the end of the Qing Dynasty, Rong - Chuan Tang's *Blood Syndrome Theory* advocated that to treat blood disease should pay attention to the principle of dissolving stasis to create fresh blood, which thought that all blood out of vessels are stasis. So dissolve stasis to create fresh blood, if not, there was no source of fresh blood.

In recent years, research on invigorating blood and dissolving stasis has new development, and it has been widely used in clinical departments. Traditional Chinese Medicine (TCM) theory think that the eye is an important organ of the human body, its physiological and pathological processes are closely linked with the body organs. Through main and collateral channels, Qi and blood in zang-fu, the eye contacts with various tissues and organs. Systemic zang-fu dysfunction, can be reflected in the eye and eye diseases can be reflected through the channels and zang-fu. Thus the diagnosis and treatment

of ophthalmic diseases can also be treated by systemic medication, invigorating blood and dissolving stasis is widely used in the diagnosis and treatment of ophthalmic diseases.

CLINICAL APPLICATION OF INVIGORATING BLOOD AND DISSOLVING STASIS CHINESE MEDICINE IN OPHTHALMIC DISEASES

Traumatic Hyphema Traumatic hyphema is because of the eye that suddenly being hit by the external force, the anterior chamber pressure surge, the iris ciliary body blood vessel rupture caused by aqueous humor pounding the surrounding tissue, whose principles of treatment are stop bleeding, promote blood absorption, prevent bleeding and reduce complications. Wen *et al*^[5] treated 112 traumatic hyphema cases with compound "Xueshuantong" capsule and "Yunnan Baiyao" capsule together with local corticosteroids, the hyphema of all patients were absorbed. Song^[6] used invigorating blood and dissolving stasis together with fortifying the spleen and promoting urination to treat traumatic hyphema, got good curative effect, short treatment period, less side effect, avoiding patient's pain caused by operation, and reduced intraocular tissue damage caused by surgery.

Fundus Hemorrhage Fundus hemorrhage belongs to the sudden blindness and blurring vision of TCM, which mainly caused by emotion, internal damage such as damaging the YIN-blood, deficiency fire stirring internally or excess heat in the liver channel, exuberant fire and Qi counter flow. Blood heat is the main reason, which causing blood flows outside the vessels and becomes blood stasis. So using invigorating blood and dissolving stasis to treat ophthalmic blood syndrome obtained satisfactory curative effect. "Ding Xinyan" think fundus hemorrhage according to the specific characteristics of different stages of bleeding can be divided into early, middle and late phases to do pattern differentiation and treatment^[7]. Early bleeding or recurrent bleeding tendency should be cooling blood to stop bleeding, combined with invigorating blood and dissolving stasis, using Pollen Typhae Decoction. The middle phase without fresh bleeding should invigorate blood and dissolve stasis, combined with moving Qi and stanching bleeding, using Peach Kernel and Carthamus Four Substances Decoction. At late phase most fundus hemorrhage was absorpt, edema and effusion regression, or exists black blood stasis, organization focus, hard exudate, it should enrich yin and supplement kidney, combined with invigorating blood and dissolving stasis, using Zhujing Pill. Zhou *et al*^[8] put forward different treatment according to the differentiation characteristics of different periods: a period of bleeding period (less than 15d), for first period should cool the blood and stanch bleeding; second period (15-45d), should invigorate blood and dissolve stasis; third period is the blood of dead period (45-75d) should break up blood stasis combined with soften hardness and dissipate masses; fourth period is dry blood stage (more than 75d) should break up blood and expel stasis, soften hardness and dissipate masses combined with reinforcing healthy Qi and consolidate Promordial Qi. All patients of different periods were given Pollen Typhae Decoction, Peach Kernel and Carthamus Four Substances Decoction, Blood Mansion Stasis - Expelling Decoction,

dissolve stasis and dissipate masses tablets, and Yishi tablets.

Retinal Vein Occlusion Central retinal vein or its branch vein occlusion is a ocular disease caused by a variety of reasons characterized by retinal vein dilation, inconvenienced retinal hemorrhage, exudant, hydnocus^[9]. Li^[10] divided 116 cases of retinal vein occlusion randomly into treatment group and control group of 58 cases each, treatment group was treated with TCM invigorating blood and dissolving stasis treatment based on syndrome differentiation, the control group was given Mai Ling oral liquid, the total effective rate was 76% in treatment group and 53.9% in the control group. The total effective rate of branch vein occlusion in treatment group was 93.9%, which was significantly higher than that of control group (59.4%). Qin and Zhang^[11] used TCM treatment of boosting Qi, invigorating blood and dissolving stasis method combined with laser therapy to treat retinal vein occlusion patients got significant curative effects; boosting Qi, invigorating blood and dissolving stasis method adjust the patient's blood capillary, resulting in intravascular pressure decrease, alleviate edema reaction of patients, the prescription of red peony root, safflower, peach *etc.* It has function of breaking up blood stasis, for rhizoma Chuanxiong soothes the liver and resolves constraint, moves Qi and blood, Radix Angelicae Sinensis nourishes blood and enrichs yin, Cortex Moutan cools the blood and stanchs bleeding; the interaction of drugs can give full play to invigorate blood and move Qi, combined with laser it can effectively improve retinal hypoxia and reduced angiogenesis rate.

Retinal Arterial Occlusion Retinal arterial occlusion is due to thrombosis, embolization, arterial spasm causing central retinal artery interruption, then leading retinal ischemia, hypoxia, edema, optic cells die rapidly, resulting in a serious decline in visual acuity, or even permanent eye damage^[12]. Chen *et al*^[13] using unblock the orifices and Blood-moving Decoction in the treatment of 36 retinal artery occlusion patients with western medicine, 7d for 1 course, count effect after 3 courses of treatment, results: 9 cases were cured, 11 cases markedly effective, 10 cases improved, 6 cases ineffective, the total efficiency is 83.3%. Zhang^[14] used unblocking the orifices and moving blood method for treatment of retinal artery occlusion in 35 cases with good results.

Diabetic Retinopathy Diabetic retinopathy (DR) is the most common microvascular complications of diabetes, is the main cause of blindness in adults^[15]. The mainly pathogenesis including the disorder of the polyol pathway, protein kinase C pathway of polyol pathway activation and growth factor expression and advanced glycation end products accumulation, oxidative stress, renin angiotensin system activation. According to the severity of fundus lesions, DR can be divided into non-proliferative retinopathy (NPDR) and proliferative retinopathy (PDR). Numerous studies have suggested that blood stasis exists in every stage^[16], and with the progress of the disease, it is becoming more and more serious, invigorating blood and dissolving stasis therapy is one of the most commonly methods^[17]. Shen *et al*^[18] divided 76 patients (82 eyes) with DR into two groups, using self-made

invigorating blood and dissolving stasis Chinese medicine, through observing the clinical curative effect, blood sugar control, after exam the vitreous body of the eye bleeding and central retinal artery hemodynamics with color Doppler flow imaging(CDFI). The total effective rate of Chinese medicine group was 90.2%, significantly higher than 72.1% in the control group. After treatment, the 2-hour blood glucose and resistance index in Chinese medicine group were lower than the control group, the retinal artery peak systolic velocity, diastolic blood flow rate is higher than the maximum central control group, and the differences were statistically significant. Zhou *et al*^[19] thought the basic pathogenesis of the early Xiaoke eye disease is blood stasis and flows slowly, and the scolopendra goes into the liver channel and eye orifices, invigorating blood and dissolving stasis, directly to the focus, getting good curative effects.

Optic Nerve Diseases Except hemorrhagic disease, invigorating blood and dissolving stasis medicine can also be used for non-bleeding optic nerve diseases, such as Liao^[20] used invigorating blood and dissolving stasis medicine ginaton, breviscapine injection to treat nonarteritic anterior ischemic optic neuropathy, confirmed that breviscapine and ginaton were equal slightly higher to the control group. Zhang^[21] used invigorating blood and dissolving stasis medicine combined with puerarin intravenous infusion in the treatment of optic atrophy, making the body to adjust the body function, dilation of blood vessels, dredge collaterals, improve microcirculation, improve eyesight, expand the horizons of clinical efficacy.

Primary Glaucoma Invigorating blood and dissolving stasis medicine are also applied in primary glaucoma to adjust the body function, expand blood vessels, dredge collaterals, improve microcirculation, improve vision, expand the clinical efficacy of vision. Wang *et al*^[22], according to different methods of treatment, divided 50 patients with primary glaucoma into routine treatment group (33 eyes) and invigorating blood and dissolving stasis group (27 eyes). The routine treatment group were given severity of routine hypotensive drugs and surgical treatment. The invigorating blood and dissolving stasis group were added invigorating blood and dissolving stasis medicine in the conventional treatment, then observed and summarize the changes of visual acuity of primary glaucoma in 32 cases (60 eyes) before and after the treatment. The visual acuity was improved in 8 eyes in the conventional treatment group (24.24%), and 16 eyes in the invigorating blood and dissolving stasis group after treatment, and the difference between the two groups was significant. Sun and Guo^[23] according to the different treatment methods divided patients into routine treatment group 21 cases (42 eyes) and invigorating blood and dissolving stasis group 20 cases(40 eyes). The routine group according to the severity were given routine hypotensive drugs and surgical treatment, invigorating blood and dissolving stasis group were added invigorating blood and dissolving stasis medicine on the basic treatment of routine group. After treatment, visual function of 6 cases (12 eyes) has improved significantly in routine group, 13 cases (26 eyes) improved

significantly in the other group, there was significant difference between the two groups.

Ophthalmic Postoperative Complications Modern ophthalmic surgery is one of the main methods for the treatment of eye diseases, but patients still can appear seriously or not postoperative complications, such as eye irritation, conjunctiva or corneal edema, reaction of iridocyclitis and so on. Zhang and Li^[24] applied invigorating blood and dissolving stasis method to postoperation to relieving the ophthalmic surgery reaction, preventing and controlling complications' occurrence and development, promoting the rehabilitation of visual function, and improve the curative effect of ophthalmic perioperative period. Invigorating blood and dissolving stasis Chinese medicine can also be used in the treatment of eyelid and conjunctiva hyperemia, swelling, nodules, pterygium, corneal ulcer, pannus, clouds, keratic precipitates and exudation, aqueous and vitreous body hemorrhage, turbid, elevated intraocular pressure, exophthalmos, eye inflammation, contusion. Invigorating blood and dissolving stasis Chinese medicine have antibiosis function to some extent, can enhance immune function, which are applied to the treatment of retinal vein occlusion, retinal periphlebitis, papillitis, ocular trauma, blood stasis, eye contusion, scleritis, vitreous body cloudy, tobacco amblyopia, chronic uveitis and retinitis pigmentosa^[25-27].

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