

Clinical Research Progress of Chinese Medicine in the Treatment of Vitiligo

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Abstract: A review of the clinical research literature on the treatment of vitiligo by Chinese medicine in China from 2015 to 2020 showed that the treatment of vitiligo by Chinese medicine is based on the differentiation and typing of the disease, and both internal and external treatment are available, summarizing the various methods of Chinese medicine in the treatment of vitiligo and the current situation of its application, identifying the shortcomings of them, and providing reference for future clinical treatment and research.

1. Introduction

Vitiligo is a primary, limited or generalised pigment loss skin disease. It is easy to diagnose and difficult to treat. In ancient times, most Chinese medicine considered it to belong to the categories of "Bai Biao Feng", "Bai Biao", "Biao Biao" and "Bai Pu". It is believed that the etiology of the disease is a combination of wind and evil and a loss of harmony between qi and blood. In the Treatise on the Origin of the Diseases, it is written that "the wind and the evil fight against the skin, and the blood and energy are not in harmony" [1]. In recent years, Chinese medicine in the inheritance of ancient theory, continue to carry out in-depth research on vitiligo, the etiology of the disease has a deeper discussion of the pathogenesis of the disease. The most important thing is that it is not only a matter of time, but also of time. The prevalence of vitiligo is increasing year by year, according to literature data, the global prevalence of vitiligo is 0.06% to 2.28% [3], and the total prevalence in China is 0.553% [4]. The pathogenesis of vitiligo is complex and has not yet been elucidated. Domestic and international studies have found that it may be related to a variety of factors, such as genetics, autoimmunity, neuropsychiatric, melanocyte self-destruction, trace elements, epidermal oxidative stress, etc [5]. The pathogenesis of vitiligo has not yet been clarified, and Western medicine is facing many challenges in its treatment.

2. Internal treatment with Chinese herbs

2.1 Evidence of Qi and Blood disharmony

In the treatment of vitiligo, Ma Lin et al [6] used the self-prepared formula of Yu Gui Wu Expel White Soup (ingredients of the formula: Angelica sinensis, Su Mu, Fucus, Radix et Rhizoma, Cicada, Tribulus terrestris, Bai Xian Pi, Radix Bupleurum, Radix et Rhizoma chinensis, Cyperus rotundus,

Radix et Rhizoma cocklebur, Radix et Rhizoma groundnut, Radix et Rhizoma saffron, Radix et Rhizoma licorice) to treat vitiligo. 91.84%, compared with the control group (with vitiligo pills), the difference was significant ($P<0.05$). Wang Qi et al [7] treated vitiligo with Ru Yi Black and White San plus reduction (ingredients of the formula: dry lotus grass, dahurica, He Shou Wu, Tribulus terrestris, comfrey, Chonglou, Dan Shen, bitter ginseng, Cang Zhu, sand tribulus) combined with 0.1% tacrolimus ointment for external application, the result: 2 cases were cured, 7 cases were effective, 11 cases were improved and 1 case was invalid in the 20 cases treatment group, the total effective rate was 95.00%. Chen Xiaoyan et al[8] treated vitiligo with the combination of compound Shouwu Tribulus soup (composition of the formula: He Shouwu, dry lotus grass, Fangfeng, Angelica sinensis, chasteberry, fried Tribulus terrestris, Shengdihuang, Wei Lingxian, Fucus, Sha Yuanzi, Cang Erzi, and roasted licorice), the results: 8 cases were cured, 25 cases were effective, 16 cases were improved, and 8 cases were ineffective in the 57 cases observation group, the total effective rate was 85.96%, compared with the 56 cases control group (topical application of compound tincture of Kalizarin). The difference was significant ($P<0.05$) compared with 56 cases in the control group (topical application of compound kalizarin tincture). Liu Xiang et al[9] treated vitiligo for 16 weeks with an in-hospital preparation of purple copper anti-white tincture (ingredients of the formula: walnut, purple grass, purple heliotrope, purple back floating pine, purple danshen, purple copper, safflower, yujin, jujube, chicken blood vine, tribulus terrestris) in combination with 308nm excimer laser, the results: 9 cases were cured, 14 cases showed efficacy, 6 cases improved and 1 case was ineffective in the 30 cases treatment group, with a total effective rate of 76.67%, compared with 30 cases The difference was significant ($P<0.01$) compared with the control group (308nm excimer laser alone).

2.2 Evidence of liver stagnation and qi stagnation

In the treatment of vitiligo, Qin Tao et al. [10] used the combination of liver-depressant and blood-activating soup (ingredients of the formula: Angelica dahurica, Chai Hu, Fang Feng, Bupleurum, Radix Angelicae Sinensis, Radix Rehmanniae Sinensis, Radix Paeoniae Alba, Cinnamomum, Radix Aromaticus, Mudanpi, Citrus aurantium, Peach kernel, Chen Pi, Chuanxiong, Hong Hua, Jinyin Hua, Radix et Rhizoma Glycyrrhiza Uralensis) and tincture of whitening to treat vitiligo, the results: 24 cases were clinically controlled, 21 cases showed efficacy, 11 cases were effective and 5 cases were ineffective in the 61 cases observation group. The total effective rate was 91.8%, and the difference was significant ($P<0.05$) compared with 61 cases in the control group (using the tincture of whitening alone). Qian Yewen et al [11] treated vitiligo with the combination of Astragalus membranaceus, Radix Angelicae Sinensis, Fenfeng, Mudanpi, Panax notoginseng powder, Radix Paeoniae Alba, Radix Aromaticus, Radix Bupleurum, Radix Paeoniae Alba, Citrus aurantium, Radix Bupleurum, Mulberry and Black Soybean. The difference was significant ($P<0.05$) compared with the control group (topical application of Bai Ling tincture). Wang Qi et al [7] treated vitiligo with the combination of 0.1% tacrolimus ointment and topical application (formula ingredients: Chai Hu, Yu Jin, Angelica sinensis, Chuanxiong, Shu Di Huang, Bai Shao, Tribulus terrestris, Shou Wu Vine, Sha Yuan Zi, Chong Lou, He Shou Wu, Hong Hua). The results showed that among the 63 cases in the observation group, 31 cases were cured, 20 cases were effective, 9 cases were improved and 1 case was ineffective. The total effective rate was 80.9%, compared with 63 cases in the control group (0.1% methicillin solution was applied to the affected area, and then irradiated with narrow medium wave ultraviolet 311 narrow spectrum therapy instrument), the difference was significant ($P<0.05$).

2.3 Evidence of weakness of the spleen and stomach

Han Xianwei et al [13] used the in-hospital preparation of Paediatric Anti-whitening Formula I (ingredients: hen's internal gold, jiao malt, Radix et Rhizoma Atractylodis Macrocephalae, Poria,

roasted licorice, roasted astragalus, Chen Pi, black sesame, angelica, honeysuckle, and antifungal. Increase or decrease dosage according to age. (Add or subtract with symptoms: add Yu Li Ren for constipation, add turmeric for white spots on the upper limbs and papaya for white spots on the lower limbs) while treating vitiligo externally with the internal formula. Results: 13 cases were cured, 15 cases were significantly effective, 5 cases were improved and 1 case was invalid in the 34 cases treatment group, with a total effective rate of 97.1%, which was significantly different ($P < 0.05$) compared with the control group (0.03% tacrolimus ointment applied alone). Chen Xiaorong [14] used self-designed spleen whitening soup (Radix et Rhizoma Ginseng, Radix Astragali, Radix Angelicae Sinensis, Poria, Fried Atractylodes Macrocephala, Radix Paeoniae Alba, Fructus Anemarrhenae, Cicada, Jiao Shanzha, Jiao Ma Ma Ye, Pericarpium Citri Reticulatae, Comfrey, Glycyrrhiza Glabra, plus or minus dosage according to age) combined with 308 excimer laser to treat vitiligo in children with a weak spleen and stomach. The difference was significant ($P < 0.05$) compared with the control group (treated with 308 excimer laser alone).

2.4 Evidence of stagnation of meridians

The treatment should be to regulate qi and activate blood circulation, dispel wind and open the channels; Wang upstream [15] used self-designed peach and red anti-white soup (ingredients of the formula: peach kernel, red flower, Chuanxiong, red peony, Dan Shen, dahurica, dry lotus grass, fried Tribulus terrestris, Astragalus, bone marrow, aromatic herb, cuscuta, turtle nail, tea tree root, marigold silver plate, medicine king tea) with 308 excimer laser irradiation method to treat vitiligo, the results: 53 cases in the treatment group were significantly effective 12 cases, significant effect 20 cases, ineffective 9 cases, total effective rate 60.30%, compared with 53 cases of the control group (internal immunomodulators with 308 excimer laser irradiation), the difference was significant ($P < 0.05$). Shen Fang et al [16] treated vitiligo with NB-UVB irradiation in combination with an in-hospital preparation of compound red flower and tribulus granules (ingredients: red vine, astragalus, astragalus, safflower, tribulus terrestris, boneset (fried in salt water), peach kernel, angelica, salvia, codonopsis, thorny mustard, fangfeng, cang erzi, datura, ling magnet, he shou wu, licorice), the results: of 147 target lesions in the treatment group, 50 were cured, 72 were effective, 15 were improved and 10 were ineffective. The total effective rate was 82.99%, and the difference was significant ($P < 0.01$) compared with 144 target skin lesions in the control group (only with NB-UVB irradiation). Cao Shuli et al [17] used a self-prepared formula (ingredients of the formula: white peony, Chuanxiong, red peony, cuscuta, safflower, raw groundnut, ripe groundnut, peach kernel, prepared heshouwu, angelica, astragalus. (Add cinnamon, tonic bone and wolfberry for patients with kidney yang deficiency; add yellow essence, cyperus and dendrobium for patients with kidney yin deficiency) plus ultraviolet light therapy combined with conventional western medicine (tacrolimus ointment and compound glycyrrhizin tablets) for the treatment of vitiligo, results: in the 50 cases of observation group, there were 14 cases with significant effect, 20 cases with effective effect and 16 cases with ineffective effect, the total effective rate was 68.0%, compared with the control group (ultraviolet light therapy combined with conventional western medicine), the difference was significant ($P < 0.05$). Yuan Jing et al [18] treated vitiligo with an in-hospital preparation of white spot granule I formula (ingredients of the formula: dahurica dahurica, bone marrow, jujube, red flower, peach kernel, fangfeng, red peony, chuanxiong, ginger, onion white, etc.) combined with autologous epidermal transplantation, the results: 25 cases were cured, 5 cases were effective, 2 cases were improved and 1 case was ineffective in the 31 cases treated group, the effectiveness rate was 90.9% and the recurrence rate was 3.0%, compared with the control group (using autologous epidermal transplantation only). The difference was significant ($P < 0.05$) compared with the control group (using only autologous epidermal graft). Li Meihong et al [19] treated blood stasis type vitiligo with Ping

Xiang Pill (composition of the formula: Phyllanthus, Shen Xiang, Radix et Rhizoma, Dan Shen, Safflower, Radix et Rhizoma, Semen Cuscutae, Dan Pi, Tribulus terrestris, etc., batch no.: Shaanxi Pharmaceutical Control No. [2001] No. 0018) orally combined with moxibustion (moxa wool, bone marrow, Tribulus terrestris, Safflower, Angelica dahurica, etc., dried in a stone mortar and pounded repeatedly into the wool, and then glued together with cotton paper rolls). Vitiligo, the results: 9 cases were cured, 8 cases showed efficacy, 10 cases were effective and 1 case was ineffective in 39 cases of treatment group, with an overall effective rate of 34.22%, which was significantly different ($P < 0.01$) compared with 37 cases of control group 1 (using lipid dahurica moxa alone) and control group 2 (taking floating pills alone). Zhan Qingxia et al [20] treated vitiligo with the combination of topical application of 0.1% mometasone furoate cream or 0.1% tacrolimus ointment with the formula of White Spot Granules No.I (ingredients of the formula: safflower, windproof, peach kernel, jujube, Sichuan dome, ginger, onion white, red peony, bone marrow, dahurica dahurica, etc.), the results: 3 cases were cured, 7 cases showed efficacy, 30 cases were effective and 9 cases were ineffective in the 49 cases of the test group, the total effective rate was 81.63%, compared with The difference was significant ($P < 0.05$) compared with 43 cases in the control group (oral transfer factor capsule alone, the rest of the treatment was the same as the test group). Chen Youjun et al [21] treated vitiligo with our preparation of color-enhancing pills (ingredients of the formula: Angelica sinensis, Chuanxiong rhizome, Danshen, henbane and safflower) combined with fire acupuncture and external rubbing of 0.1% tacrolimus ointment, the results: 3 cases were cured, 12 cases showed efficacy, 11 cases were effective, 4 cases were ineffective, the total effective rate was 86.6%, compared with 30 cases in the control group (with fire acupuncture and external rubbing of 0.1% tacrolimus ointment). The difference was significant ($P < 0.05$) compared with the 30 cases in the control group (with fire injection and external rubbing of 0.1% tacrolimus ointment).

2.5 Liver and kidney deficiency

The treatment is to nourish the liver and kidney, nourish blood and invigorate blood; Hu Wentao et al [22] used the self-prepared formula for tonifying the kidney No.1 (ingredients: bone marrow, bone crushed tonic, angelica, Chuanxiong, black sesame, he shou wu, mulberry leaf, cuscuta, Zhi Mu, Mo dry lotus, chasteberry and comfrey) to treat vitiligo, the result: 2 cases were cured, 5 cases were effective, 16 cases were effective and 7 cases were ineffective in the 30 cases treatment group, the total effective rate was 76.66%, compared with 30 cases in the control group (given vitiligo pill orally). The total effective rate was 76.66%, compared with 30 cases in the control group (given vitiligo pills for oral administration). The difference was significant ($P < 0.05$) when compared with 30 cases in the control group (given vitiligo pills orally. Drug ingredients: Radix Bupleuri, Radix Angelicae Sinensis, Radix et Rhizoma Dioscoreae, Tribulus Terrestris). In the treatment of vitiligo, Rong Guanghui et al [23] used an in-hospital preparation of color-enhancing pills (ingredients of the formula: composed of Sha Yuan Zi, Cuscuta, Zi He Che, Boneset, Dry Lotus Grass, Mulberry, Prepared Shou Wu, Black Sesame, Astragalus, Ganoderma Lucidum, Bai Zhi, Tribulus Terrestris, Licorice, etc.), the results: 10 cases were cured, 9 cases were significantly effective, 4 cases were improved and 7 cases were ineffective in the 30 cases observation group, with a total effective rate of 63.33%, compared with the 30 cases control group (using Bai Ling tablets alone). The difference was significant ($P < 0.05$) compared with 30 cases of the control group (Bai Ling tablets alone). Wang Qi et al [7] used consistent decoction (formula ingredients: Bei Sha Shen, Mai Dong, Angelica, Mulberry, Sheng Di, Wolfberry, Neem) combined with 0.1% tacrolimus ointment for the treatment of vitiligo, the results: 0 cases were cured, 0 cases were effective, 6 cases were effective, 3 cases were ineffective in the 9 cases treatment group, the total effective rate was 66.67%. The results showed that 12 cases were cured, 9 cases showed efficacy, 4 cases were effective and 5 cases were ineffective in the 30 cases treatment group,

with a total effective rate of 83.3%, compared with the 30 control group. (The difference was significant ($P<0.05$) compared with the 30 control group (internal administration of anti-white babuji tablets combined with topical application of compound kali ziran tincture). Liu Desen[25] treated vitiligo of liver and kidney deficiency type with Wu Qu Qua anti-white soup (ingredients of the formula: Tribulus terrestris, Licorice, Huang Cen, Radix et Rhizoma Ligustrum, Cuscuta, Bupleurum, Safflower, Prepared He Shou Wu, Comfrey), the results: 21 cases were cured, 10 cases showed efficacy, 6 cases were effective and 2 cases were invalid in the 39 cases of treatment group, the total effective rate was 94.87%, compared with 39 cases of control group (treatment with compound glycyrrhizin tablets and application of Mometasone furoate cream was applied and light massage was performed), the difference was significant ($P<0.05$). Yin Xin et al [26] treated vitiligo with wu qua anti-white soup (ingredients of the formula: Boneset, Prepared He Shou Wu, Female chasteberry, Dry lotus grass, Cuscuta, Dan Shen, Red peony, Perilla leaf, Comfrey, Safflower, Scutellaria, Tribulus terrestris, Glycyrrhiza) and applied a water decoction solution externally to the affected area, and then applied mometasone furoate cream to the affected area with light massage, the results: 2 cases were cured, 10 cases were significantly effective, 13 cases were effective and invalid in the 29 cases treatment group 4 cases, total effective rate 86.21%, compared with 28 cases of control group (compound glycyrrhizin tablets orally, the rest of the treatment as the treatment group), the difference is significant ($P<0.05$). Xia Zhihua et al[27] treated vitiligo with the self-prepared Chinese herbal remedy, "Ginseng, Astragalus, Radix Rehmanniae, Radix Shou Wu, Radix chasteberry, Fructus Lycii, Radix Paeoniae Alba 12g, Tribulus terrestris, Radix Angelicae Sinensis, Rhizoma Ligustici, Radix et Rhizoma Ligustici, Radix et Rhizoma Blood, Peach kernel, Safflower, Salviae Miltiorrhizae, Radix Pinosylvae), the results: 15 cases were cured, 20 cases showed efficacy, 4 cases were effective, 1 case was ineffective, the total effective rate was 97.5%. 97.5%, compared with 40 cases in the control group (methoxsalen tablets taken orally), the difference was significant ($P<0.05$). In the treatment of vitiligo, Du Wenqi[28] formulated his own formula of Boneset Soup with addition and subtraction (ingredients of the formula: Boneset, Cuscuta, He Shou Wu, Radix et Rhizoma Pinelliae, Mercurial Lotus, Tribulus terrestris, Angelica dahuricae, Wu Mei, Shu Di Huang, Angelicae Sinensis, Chicken Blood Vine, Tao Ren, Roasted Licorice, Red Flower), the results were: 37 cases were cured, 2 cases showed efficacy, 3 cases were effective, and 1 case was ineffective in the 43 cases treatment group, with an overall effective rate of 97.67%, compared with 43 cases in the control group (methicillin hydrochloride tablets taken orally). The difference was significant ($P<0.05$) compared with 43 cases of the control group (levamisole hydrochloride tablets taken orally).

3. Topical Chinese medicine treatment

The external treatment of Chinese medicine is also of great significance in the treatment of vitiligo. The "source of medical unification" cloud: "the evidence of surgery is most important external treatment". In clinical practice, on the basis of TCM diagnosis and treatment, the combination of TCM external treatment can give full play to the advantages and characteristics of TCM, with more significant efficacy. Fang Zhaogun et al [29] treated vitiligo with compound dahurica tincture after NB-UVB irradiation for 24 weeks, the results: 2 cases were cured, 19 cases were effective, 13 cases were improved and 1 case was invalid in the combined group of 35 cases, the total effective rate was 97.14%, compared with the conventional group of 35 cases (halomethasone cream was first given externally, followed by NB-UVB irradiation), the difference was significant ($P<0.05$). Zhou Xiangnan [30] treated vitiligo with tincture of bai bao (made from tincture of boneset, dahurica dahurica, horseradish, soaked in 50% alcohol 200mL, sealed away from light and soaked for 1 week) combined with NB-UVB phototherapy instrument. The difference was significant ($P<0.05$) compared with 27 cases in the control group (treated with NB-UVB irradiation alone). Han Chunlei et al [31]

used topical application of compound tincture of *Sophora flavescens* and Boneset (100mL of "Baixian tincture" mixed with 20mL of alcoholic extract of *Sophora flavescens* and *Phellodendron* spp. 10,000mL soak for 2 weeks, take the tincture for external use), oral vitamin B complex, followed by external application of 0.05% fluticasone propionate cream (2 times a day, stop after 2 months), combined with NB-UVB treatment for vitiligo, 6 months, results: 97 cases of observation group, 44 cases cured, 37 cases with significant effect, 15 cases improved, 1 case invalid, total effective rate The difference was significant ($P<0.01$) compared with 93 cases in the control group (compound *Sophora* tincture was replaced by Baixiao tincture, and the rest of the treatment was the same as the observation group). Chen Ting [32] treated vitiligo with topical application of compound Bai Zhi tincture combined with 308nm excimer light, the results: 29 cases were cured, 31 cases were effective, 5 cases were improved and 1 case was invalid in the 66 cases observation group, the total effective rate was 90.9%, compared with 66 cases control group (treated with 308nm excimer light alone), the difference was significant ($P<0.05$). Tan Xin et al [33] treated vitiligo with homemade tincture of Chinese medicine (ingredients: Boneset, Dry Lotus Grass, He Shou Wu, Bai Xian Pi, White Flower and Snake Tongue Grass, *Tribulus terrestris*, Xi Cao, Xuan Shen and Safflower soaked in 75% ethanol for 7d and then diluted by removing the dregs) combined with NB-UVB phototherapy instrument, the results: 10 cases were cured, 10 cases were effective, 6 cases were improved and 4 cases were ineffective in the 30 cases treatment group. The total effective rate was 86.67%, compared with 30 cases of control group (irradiated with NB-UVB phototherapy instrument), the difference was significant ($P<0.05$). Chang Zheng et al [34] treated vitiligo with whitening tincture combined with 308nm excimer phototherapy system, the results: 31 cured, 55 effective, 20 improved and 13 invalid in the treatment group with 119 target lesions, the total effective rate was 72.3%, compared with the control group with 112 target lesions (treated with 308nm excimer light alone), the difference was significant ($p<0.05$).

4. Discussion

The overall pathogenesis of vitiligo is caused by the external sensation of six perversions, internal injury to the seven emotions and dysfunction of the internal organs, so the clinical treatment is based on the dialectic treatment of Qi and blood disharmony, liver depression and qi stagnation, meridian stasis, spleen and stomach weakness and liver and kidney deficiency. From the clinical research in the last five years and a large amount of literature, it can be seen that Chinese medicine currently has good efficacy and advantages in the treatment of vitiligo, and the clinical combination of modern medicine as well as physical science has greater efficacy on this disease. Although Chinese medicine has a long history of treatment of this disease and has remarkable efficacy, medical practitioners have had their own different opinions on its etiology and dialectical use of medicine over the ages and have adopted a variety of treatment methods, which has brought many challenges to modern scientific research and promotion of Chinese medicine. Firstly, many of the clinical drugs used are prepared in-hospital and should be sourced from authentic herbs and produced in a pollution-free manner to ensure basic efficacy in order to enhance the quality of the medicine. Secondly, there are many shortcomings in the design of the experiments. The lack of a large number of clinical samples, the failure of the experimental design of some clinical studies to be randomised, controlled and double-blind, as well as the lack of uniform criteria for inclusion, exclusion, assessment of efficacy, experimental drug use, and the lack of evidence from basic experiments and pharmacological studies, make the accuracy of the experimental results insufficient. In some cases, there is no specific pathological staging and vitiligo typing. Thirdly, the available clinical experimental research results provide strong support for clinical treatment and more ideas and directions for research in TCM, but there is a large gap compared to Western medicine in terms of the number, scope and results of both

clinical and basic experimental research reports. Due to the lack of basic research in clinical application, the current research found that Chinese medicine can activate tyrosinase, promote melanin synthesis, promote the proliferation and migration of melanocytes, promote melanin synthesis, but its mechanism of action is single, Chinese medicine components and each Chinese medicine components at the same level of vitiligo treatment is not clear, pending in-depth research. The clinical experiments are mostly using several methods of integrated treatment at the same time, so much so that the efficacy of each method is not easy to detect and evaluate. Not only is there a need to study its mechanism of action through modern medicine, but there is also a need for more evidence-based evidence. An in-depth evidence-based meta-analysis of vitiligo treatment options can be conducted in order to obtain more efficient and reliable treatment options. These shortcomings are key to the limitations of research development in Chinese medicine for vitiligo, but also provide a direction for future research development.

Vitiligo has a great negative impact on the physical and psychological health of patients. We should establish a more rigorous, scientific and systematic research program under the knowledge of evidence-based medicine. On the basis of carrying forward traditional medicine, we should optimise the dialectical rotation of traditional Chinese medicine and strengthen the combination of theories, methods, prescriptions and medicines with modern medical research, so that traditional medicine can be innovated and developed. We will cultivate interdisciplinary talents who understand both modern technology and Chinese medicine, deepen clinical applied basic research, draw on the strengths of various schools of thought, use modern disciplines such as molecular biology, cell biology, artificial intelligence and big data to promote interdisciplinary research collaboration and in-depth analysis of the pathogenesis of vitiligo and the pharmacological effects of Chinese medicine. On this basis, we expect to obtain more effective and reliable treatment solutions.

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