DOI: 10.53469/jcmp.2026.08(02).06

Discussion on the Pathogenesis and Treatment of Melasma

Tianen Chen, Jianrong Hui*

Shaanxi University of Chinese Medicine, Xianyang 712046, Shanxi, China
**Correspondence Author*

Abstract: ***Melasma is a common skin pigmentation disorder characterized by symmetrical pigmented patches on the face, usually on the forehead, cheekbones, upper lip and chin. Although this disease is not life-threatening, it causes harm to the patient's appearance and mental health, and seriously affects the quality of life of the patient. In recent years, with the increasing emphasis on skin beauty, melasma has become one of the hot topics of research. However, the pathogenesis of melasma and its therapeutic aspects remain many unsolved mysteries, which provides broad space and challenges for our research.***

Keywords: Chloasma, Pathogenesis, Treat.

1. Pathogenesis of Melasma

1.1 Traditional Chinese Medicine Understanding of Melasma

Melasma belongs to the categories of traditional Chinese medicine such as "facial dust", "liver spots", "dark spots", "dark spots", etc., commonly known as "butterfly spots". The earliest record of the etiology and pathogenesis of melasma is found in "Nanjing: Twenty-Four Difficulties": "If the hand Shaoyin qi is cut off, the pulse will be blocked, and if the pulse is blocked, the blood will not flow, and if the blood does not flow, the color will be gone, so the complexion is as dark as dark [1]. "Surgical Authenticity" Volume 11: "Dark spots, water deficiency cannot control fire, blood is weak and cannot smooth flesh, so that fire dryness forms black spots, black withering and not lustrous [2]. It is pointed out that the kidney water is insufficient, the water does not make fire, and the blood deficiency cannot nourish the skin and cause melasma. Modern doctors generally believe that melasma is mainly closely related to the liver, spleen and kidneys, insufficient liver and kidney essence, spleen and stomach transport imbalance, blood loss of transport, and loss of nourishment, thus creating conditions for the generation of melasma.

1.2 Western Medicine's Understanding of Melasma

1.2.1 Genetic factors and ethnic factors

Genetic and ethnic factors play an important role in the pathogenesis of melasma. The study found that all ethnicities were at risk of melasma, but the prevalence was higher among Asians, Indians, Latinos, and African Americans [3]. Some studies have found that individuals with a family history are more likely to develop melasma, with at least one relative in 48% of melasma patients having melasma, of which 97% are first-degree relatives and 3% are second-degree or higher distant relatives. In addition, dark-skinned people are more susceptible to genetic factors, but light-skinned people develop the disease earlier [4].

1.2.2 Hormone regulation

Hormones play an important regulatory role in the development of melasma. Elevated sex hormone levels are considered one of the important factors that promote the formation of melasma. These hormones can affect the production and distribution of melanin, leading to increased skin pigmentation, which can lead to the formation of melasma. Some scholars have shown that estrogen receptor β exist in the skin and most appendages, and may play an important role in the process of skin aging and skin pigmentation. A certain concentration of estrogen can increase the activity of tyrosinase and promote the synthesis of pigment in melanocytes [5]. Zhang Weilong [6] collected blood from 100 melasma patients and 30 women with normal physical examination and centrifuged serum to detect sex hormones such as luteinizing hormone (LH), follicle - stimulating hormone (FSH), and estradiol (E2). The results showed that the serum LH, FSH and E2 levels of melasma patients were higher than those of normal women. It suggests that the serum neutral hormone content in female melasma patients is higher due to endocrine dysfunction and hypothalamic-pituitary-ovarian axis imbalance.

1.2.3 Light exposure

UV radiation produces reactive oxides that cause oxidative stress reactions, and oxidative stress plays a role in the biological effects of UV radiation. As a result, the skin exposed to sunlight is damaged by oxidative stress, causing melanin production. Under chronic UV exposure, the activity of matrix metalloproteinases (MMPs) such as MMP-2 and MMP-9 increases, leading to the degradation of type IV and type VII collagen in the skin, resulting in damage to the basement membrane, which may promote the descent or migration of melanocytes and melanin to the dermis, leading to persistent pigmentation of melasma [7]. The keratinocyte growth factor produced by the skin is able to enter the epidermis to function due to the destruction of the basement membrane. In addition, keratinocyte growth factor (KGF) is upregulated under UV irradiation and stimulates melanocyte production and transfer of melanin as a paracrine factor in the skin [8].

1.2.4 Oxygen radical damage

Reactive oxygen species (ROS) are chemically active oxygen-containing atoms or groups of atoms. Under normal physiological conditions, ROS production and clearance were

in a dynamic equilibrium state. In the pathological state, the imbalance of ROS production and clearance can lead to oxidative stress, and excessive ROS accumulation is not removed in time, resulting in oxidative damage to proteins, lipids, nucleic acids, and other substances, resulting in a variety of diseases [9]. If the excess ROS is not removed in time, the structure and function of the biofilm will be damaged, the peroxide products will increase, and the further decomposition will form malondialdehyde (MDA), which is highly oxidizing, and then destroy and damage the body [10]. Superoxide dismutase (SOD) is an important component of the body's antioxidant system and is the main enzyme that scavenges free radicals by converting superoxide anions into hydrogen peroxide and oxygen. In addition, glutathione peroxidase (GSH-PX) can convert hydrogen peroxide into oxygen and water, thereby attenuating the oxidative stress of hydrogen peroxide and causing tissue damage. Li Yaoyao [11] treated 66 patients with melasma with Yurong Xiaoban Decoction and measured serum malondialdehyde (MDA), lipid peroxide (LPO), and superoxide dismutase (SOD) levels. The experimental results showed that the serum MDA and LPO levels in the treatment group were significantly lower than those before treatment, and the SOD levels were significantly higher after treatment than before treatment, which suggested that the MDA and LPO in melasma patients were higher than those in normal people, while SOD was lower than that in normal people, indicating that oxidative stress can damage skin cells and tissues, leading to pigmentation.

1.2.5 Inflammatory response

Chronic inflammatory responses are also involved in the pathogenesis of melasma. The release of inflammatory factors can affect the function and distribution of melanocytes, leading to increased pigmentation. When the skin is damaged by ultraviolet rays, the number of mast cells increases, the melanocytoine level is regulated, and the white blood cell infiltration and vasodilation are obvious. Histological analysis showed that melasma is caused by cellular interactions between melanocytes, keratinocytes, mast cells, fibroblasts, and skin tissue, and its characteristics are similar to those of chronic sun injury. Levels of interleukin (IL-17) and pro-inflammatory mediator cyclooxygenase (COX-2) were significantly increased in damaged skin compared to healthy skin. Interleukin (IL-17) is one of the main mediators of tissue inflammation and is involved in recurrent skin diseases such as psoriasis and melasma. Cyclooxygenase (COX-2) can induce keratinocytes to secrete prostaglandins involved in epidermal pigmentation, which is related to the pathogenesis of post-inflammatory pigmentation [12].

2. Treatment of Melasma

2.1 Laser Treatment

The principle of laser treatment for melasma is to use specific wavelengths of laser energy to dispel pigmentation in the targeted pigmentation area. The energy of the laser is absorbed by these melanin particles, allowing them to break down and be excreted with the skin's natural metabolism, resulting in a lightening effect on spots. Ding Gao [13] treated 90 patients with melasma and divided them into three groups: group A was treated with tranexamic acid microneedling alone, group B was treated with C6 large spot low-energy laser therapy alone, and group C was treated with tranexamic acid microneedling combined with C6 large spot low-energy laser therapy. The results showed that the effective rate of group C (47.6%) was higher than that of group A (16.1%) and group B (26.3%), and the effective rate of group C was higher than that of group A, and the difference was statistically significant. Huang Sun [14] selected 126 patients with melasma to be treated with Q-switched Nd: YAG laser, followed up 12 months after treatment, and divided the patients into recurrence group (37 cases) and non-recurrence group (89 cases) according to the survey results. According to the follow-up results after 12 months of treatment, there were 37 patients with recurrence and pigmentation, with a recurrence rate of 29.37%; There were 89 patients without recurrence, with a non-recurrence rate of 70.63%. It suggests that there are certain defects in laser treatment of melasma, but the overall non-recurrence rate is much greater than the recurrence rate, so laser can be used to treat melasma clinically, and the effect is better.

2.2 Tranexamic Acid

Tranexamic Acid (TXA) is an antifibrinolytic drug that has been widely used in recent years to treat melasma. Tranexamic acid works by inhibiting the activity of plasmin. Plasmin plays an important role in the inflammatory response, activating tyrosinase and promoting melanin production. By inhibiting plasmin activity, tranexamic acid reduces melanin production, thereby reducing pigmentation. Qi Zhifeng [15] treated 120 patients with melasma and randomly divided them into 3 groups of 40 patients in each group. Group C received oral vitamin C tablets, vitamin E softgels, and qi yellow oral liquid; Group B was introduced with 5% tranexamic acid solution with a needle roller at the same time on the basis of group C, 2 times/month; The group was simultaneously introduced with 10% tranexamic acid solution on the basis of group C, 2 times/month; The course of treatment in all three groups was 3 months. The results showed that the total effective rate of group A was 87.5%, group B was 67.5%, and group C was 52.5%, and the difference between the three groups was statistically significant. Wang Xianfen [16] selected 92 patients with melasma to receive tranexamic acid combined with laser therapy, the control group received Q-switched 1064nm laser treatment for 6 months, and the observation group received tranexamic acid topical treatment for 6 months on the basis of the control group. After the end of treatment, the results showed that the total effective number of people in the control group was 29, with a total effective rate of 63.04%, and the total effective number of people in the experimental group was 38, with a total effective rate of 82.61%, indicating that tranexamic acid had a certain effect on the treatment of melasma, and the treatment effect of laser combined with tranexamic acid was better.

2.3 Acupuncture Treatment

Acupuncture, as a traditional Chinese medicine treatment, is also used to treat melasma. By stimulating specific acupuncture points, it regulates the qi and blood function of the internal organs and improves the body's endocrine disorders, so as to achieve the effect of lightening dark spots.

Acupuncture for the clinical treatment of melasma is often combined with traditional Chinese medicine and traditional Chinese and Western medicine. Huang Yahua [17] randomly divided 108 melasma patients into two groups: tranexamic acid group with oral tranexamic acid tablets 0.25g twice a day for 6 months, and facial microneedling acupuncture on the basis of tranexamic acid group once every 2 weeks for 6 months. The results showed that the total effective rate of treatment in the combination treatment group (94.44%) was higher than that in the tranexamic acid group (72.22%). After 2, 4 and 6 months of treatment, the MASI score of the two groups decreased compared with that before treatment, and the combined treatment group was lower than that of the tranexamic acid group. Zhao Jing [18] selected 50 female melasma patients and randomly divided them into control group and observation group. The control group was treated with tranexamic acid, and the observation group was treated with acupuncture combined with tranexamic acid, and the total effective rate and lesion scores before and after treatment were compared between the two groups, and the levels of estradiol (E2), luteinizing hormone (LH) and follicle - stimulating hormone (FSH) were compared. The results showed that the total effective rate of treatment in the observation group (96.00%) was higher than that in the control group (76.00%), and the difference was statistically significant. Before treatment, the skin lesion scores of the two groups were similar, and the levels of E2, FSH and LH were similar. After treatment, the skin lesion scores, E2, FSH and LH levels decreased in the two groups, and the observation group was better than the control group.

2.4 Traditional Chinese Medicine Treatment

Traditional Chinese medicine believes that the formation of melasma is related to factors such as visceral disorders, qi and blood disharmony, emotional disorders, and improper diet. Therefore, the treatment of melasma with traditional Chinese medicine mainly improves the symptoms by regulating the internal organs, relieving the liver and regulating qi, promoting blood circulation and removing blood stasis, nourishing blood and moisturizing the skin. Zhou Lanhua [19] randomly divided 69 female patients with melasma renal ischemia and blood stasis syndrome into experimental group and positive control group, with 34 people in the experimental group taking deer fetal salvia white peony granules and 35 people in the positive control group taking tranexamic acid tablets for 60 days. The results showed that the MASI score, pigmentation area, color, TCM syndrome score, and quality of life score of the experimental group and the positive control group were significantly improved after treatment. Liu Juan [20] used a random number table method to randomly divide 200 melasma patients into a control group treated with laser therapy and an experimental group treated with laser combined with Huoxue Hua Yu Fang treatment, with 100 cases in each group. After 2 courses of treatment, the clinical efficacy, melanin index, erythema index, transepidermal water loss (TEWL), satisfaction, and type I collagen levels were compared between the two groups. The results showed that the total clinical effective rate of the experimental group after treatment was 82.00% and that of the control group was 62.00%, and the experimental group was higher than that of the control group. The melanin index in the experimental group was lower than that in the control group, and the type I collagen index in the experimental group was higher than that in the control group. The TEWL and erythema index in the experimental group were lower than those in the control group. The total clinical satisfaction rate of the experimental group was 84.00%, that of the control group was 64.00%, and that of the experimental group was higher than that of the control group. The results showed that the formula was effective in the treatment of melasma, and the effect was better with laser treatment.

3. Summary

In summary, melasma is a cosmetic disease with complex pathogenesis and diverse treatments. Single causes such as genetics, race, and light can cause melasma. Usually, various causes interact to control the occurrence and development of melasma. Individualized and comprehensive treatment measures are often better in the treatment of melasma, which can improve patient satisfaction while ensuring the treatment effect. Future research needs to delve deeper into the pathogenesis of melasma, especially in terms of genetics, epigenetics, and microenvironmental changes. Understanding these mechanisms may lead to the development of more effective treatments. With the advancement of science and technology, new molecular target-based treatments, new laser technologies, and comprehensive treatment options combining drugs and physical therapy may continue to emerge, and future treatment methods will be more diverse and precise.

References

[1] LI Yang, GAO Mingzhou, WANG Jieqiong, et al. Research progress on the treatment of melasma in traditional Chinese medicine [J]. Shizhen Traditional Chinese Medicine, 2022, 33(05):1191-1193.

[2] Chang Shuchen. The effectiveness of adding and subtracting the combination of body acupuncture and acupuncture in the treatment of melasma (liver depression and kidney deficiency type) [D]. Nanjing University of Traditional Chinese Medicine, 2018, 53-54.

[3] Wu Jiahui, Liu Zhichao. Journal of Shandong First Medical University (Shandong Academy of Medical Sciences), 2021, 42(06):471-475.

[4] Xu Qingfang, Ouyang Mengting. Research progress on the pathogenesis of melasma [J]. Journal of Dermatology and Venereology Diagnosis and Treatment, 2023, 30(06): 524-528.

[5] Tang Nan, Wu Yanhua, Li Qilin, et al. Research status of melasma etiology and pathogenesis [J]. Journal of Dermatology and Venereology Diagnosis and Treatment, 2013, 20(04): 302-304.

[6] ZHANG Weilong, XIE Guolie, LI Xiaohua, et al. Correlation analysis between sex hormone and SOD levels and melasma in women [J]. China Medical Innovation, 2017, 14(15):107-110.

[7] Torres-Álvarez B, Mesa-Garza IG, Castanedo-Cázares JP, et al. Histochemical and immunohistochemical study in melasma: evidence of damage in the basal membrane. Am J Dermatopathol. 2011; 33(3):291-295.

[8] Hasegawa K, Fujiwara R, Sato K, et al. Possible Involvement of Keratinocyte Growth Factor in the

Persistence of Hyperpigmentation in both Human Facial Solar Lentigines and Melasma. Ann Dermatol. 2015; 27(5): 626-629.
[9] Ulan Toya, Li Ruiya. Inner Mongolia Medical Journal, 2018, 50(11):1299-1301.
[10] Xiang Qiantong, Cui Wei, Zhang Hui. Efficacy of oral tranexamic acid combined with supramolecular salicylic acid peel in the treatment of melasma and its effect on serum MDA and E2 [J]. Chinese Journal of Aesthetic Medicine, 2024, 33(01):95-98.
[11] LI Yaoyao, CHEN Zhiwei, WANG Yang, et al. Yurong Xiaoban Decoction for the treatment of melasma with qi stagnation and blood stasis and its effect on serum MDA, LPO and SOD levels [J]. Chinese Journal of Integrative Dermatology and Venereology, 2020, 19(03):249-251.
[12] Rodríguez-Arámbula A, Torres-Álvarez B, Cortés-García D, et al. CD4, IL-17, and COX-2 Are Associated With Subclinical Inflammation in Malar Melasma. Am J Dermatopathol. 2015; 37(10):761-766.
[13] Ding Gao, Wei Yun, Sun Lan. Clinical study on tranexamic acid microneedling combined with C6 large spot laser in the treatment of melasma [J]. Journal of Clinical Dermatology, 2024, 53(07):413-415.
[14] Huang Sun. Research on the influencing factors of recurrence and pigmentation after laser treatment of melasma [J]. Anhui Journal of Medical College, 2024, 23(03): 50-52.
[15] Qi Zhifeng, Jiang Yanan, Chen Liyun, et al. Evaluation of the efficacy of tranexamic acid solution combined with different concentrations of tranexamic acid solution in the treatment of melasma in women based on the method of nourishing water and condensing wood [J]. Journal of Yan'an University (Medical Science Edition), 2024, 22(01):34-38.
[16] Wang Xianfen. Evaluation of the effect of tranexamic acid topical combined with Q-switched 1064nm laser to improve the degree of skin lesions in melasma patients [J]. Electronic Journal of Modern Medicine and Health Research, 2024, 8(04):46-49.
[17] Huang Yahua, Ye Xiangyang. Clinical efficacy of tranexamic acid combined with microneedling and acupuncture in the treatment of melasma [J]. Jiangsu Medicine, 2019, 45(10):1044-1047.
[18] Zhao Jing, Xu Xiaoshuang, Yan Yan. The efficacy of acupuncture combined with tranexamic acid in the treatment of melasma in women and its effect on the level of sex hormones in patients [J]. Chinese Journal of Aesthetic Medicine, 2020, 29(08):108-111.
[19] Zhou Lanhua, Lv Meiyu, Zhao Rui, et al. Clinical observation of deer fetal salvia and white peony granules to remove melasma [J]. Chinese Journal of Basic Medicine of Traditional Chinese Medicine, 2024, 30(06): 1045-1047.
[20] Liu Juan, Zhang Qian, Ding Hongqing, et al. The effect of adjuvant laser on the treatment of melasma with blood stasis and blood stasis and its effect on type I collagen [J]. Chinese Journal of Dermatology and Venereology, 2024, 38(07): 761-767.