

Original Research Article

Effectiveness of the external application of Jidesheng snake tablets, trehalose glycerin mud, and hydroquinone cream in the treatment of melisma

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Abstract

Purpose: To determine the effectiveness of the external application of Jidesheng snake tablets, trehalose glycerin mud, and hydroquinone cream in the treatment of melasma.

Methods: The study was conducted on 60 patients with melasma who were treated in the Affiliated Yueqing Hospital of Wenzhou Medical University between January 1, 2021, and January 31, 2022. The patients were randomly but equally assigned to two groups (study and control). The study group received Jidesheng snake medicine, glycerin, boiled water, and trehalose medicinal mud at a 10:4:2:1 combination ratio, applied to the affected parts 12 h a day for 2 - 4 weeks. After cleansing the skin, hydroquinone cream was applied to the affected area. On the other hand, the control group was treated with a similar formulation but without trehalose medicinal mud in the ratio of 10:4:2. Changes in facial melasma of the patients were observed, while the satisfaction, clinical efficacy, incidence of adverse reactions, and recurrence rate were monitored.

Results: Patients in the study group were more satisfied with the treatment than those in the control group (90 vs. 73.3 %, $p < 0.05$). Furthermore, treatment effectiveness was significantly higher in the study group than in the control group (93.3 vs. 70 %, $p < 0.05$).

Conclusion: The external application of Jidesheng medicine + glycerin + cold boiled water + trehalose is a reliable therapeutic strategy for the management of patients with melasma. It is more cost-effective, less prone to adverse reactions, and is associated with a low recurrence rate and high satisfaction.

Keywords: Jidesheng snake medicine, Trehalose, Hydroquinone cream, Melasma

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INTRODUCTION

Melasma, a skin condition characterized by the pigmentation of the face, usually affects women in their middle age. Managing and removing melisma, therefore, has become a tricky clinical problem in the field of skin diseases [1,2]. The

number of patients who suffer from this disease is large, and treatment is complex and expensive. Currently, there is a wide range of treatment methods, none of which are particularly effective and easy to relapse [3]. Laser treatment may be effective, but pigmentation returns within a short time. The use

of antioxidants requires longer treatment sessions and is associated with side effects [4,5]. Previously, *Jidesheng* snake tablets were reported to be effective for removing freckles during clinical trials. Accordingly, the present study was undertaken to investigate the efficacy of *Jidesheng* snake tablets in the treatment of melasma.

METHODS

General patient profile

Sixty female patients with confirmed melasma who were treated at The Affiliated Yueqing Hospital of Wenzhou Medical University between January 2021 and January 2022 were enrolled in the study. They were divided into study and control groups. The study participants were 32 - 49 years with an average age of 42.37 ± 5.01 years. Control participants were aged 30 - 51 years with an average age of 43.15 ± 4.83 years. The distribution of baseline characteristics was well-balanced between the two groups ($p > 0.05$). The experiment was approved by the Affiliated Yueqing Hospital of Wenzhou Medical University Ethics Committee (approval no. WZYQ-2210/7). All subjects gave written informed consent. The study protocol was as per the Declaration of Helsinki [6].

Inclusion criteria

Participants were assessed as eligible if they satisfied the following: Female aged between 20 and 60 years, met the *Clinical Diagnosis and Effectiveness Criteria for melasma* [7], signed the informed consent form voluntarily, received treatment in the hospital throughout the process, and did not drop out from the study mid-way.

Exclusion criteria

Participants were assessed as ineligible if they: were pregnant, lactating, or suffering from mental illness or other infectious diseases. If they had signs of ulceration, pus, and skin damage, had a history of melasma in the family, had received laser, chemical, or oral lightening treatments within the last three months, did not utilize sun protection measures, and were exposed to the sun during the course of the treatment and were allergic to the medication used in the study, they were excluded from the study.

Treatments

The study group received *Jidesheng* snake medicine, glycerin, boiled water, and trehalose medicinal mud externally at a 10:4:2:1

combination ratio, applied to the affected parts 12 h a day for 2 - 4 weeks. After cleansing the skin, hydroquinone cream was applied to the affected area. The control group received *Jidesheng* snake medicine, glycerin, and cold boiled water for external application in the ratio of 10:4:2. The treatment was applied in the same way as for the study group. The study was terminated immediately if allergic reactions were detected in either group.

Parameters evaluated

Patient satisfaction assessment

The patient's satisfaction (SR) with the treatment was recorded after the completion of treatment cycles. The formula of satisfaction was calculated using Eq 1.

$$SR = (S_n/T_n)100 \dots\dots\dots (1)$$

where S_n = satisfied number, and T_n = total number.

Clinical efficacy/effectiveness

The treatment outcomes were classified into 3 grades. Grade A - cured: spots have completely disappeared; grade B - improved: spots have become significantly lighter; grade C: spots have faded slightly; grade D: spots have not changed; grade E: discontinuation due to allergic reaction. Efficacy/effectiveness (E) was calculated using Eq 2.

$$E = (nP/T_n)100 \dots\dots\dots (2)$$

where nP = number of changes in pigmentation.

Statistical analysis

The statistical analysis was carried out using SPSS 3.0 statistical software. The measurement data were expressed as mean \pm standard deviation (SD) and analyzed using *t*-test. The count data were expressed as a percentage (%) and analyzed using the chi-square test. GraphPad Prism 8 was used for graphics rendering. Significant differences were set at $p < 0.05$.

RESULTS

Baseline characteristics of patients

The distribution of baseline characteristics was well-balanced between the two groups ($p > 0.05$, Table 1).

Table 1: Comparison of general data between the two groups (n = 30; mean \pm SD)

Group	Age (year)	Disease course (year)	Skin area (cm ²)
Study	42.37 \pm 5.01	4.27 \pm 2.73	8.19 \pm 3.45
Control	43.15 \pm 4.83	5.04 \pm 3.11	7.32 \pm 3.60
<i>t</i>	0.722	1.306	0.625
<i>P</i> -value	0.65	0.145	0.517

Patient satisfaction

In both groups, after four weeks of continuous treatment, there was no obvious discomfort or allergic response. There were 27 individuals in the study group satisfied with the treatment, and 22 individuals in the control group were satisfied with the treatment. The patients in the study group were more satisfied with the treatment than those in the control group (90 vs. 73.3 %) ($\chi^2 = 8.319$, $p = 0.025$).

Clinical effectiveness

The effectiveness rate of the study group was significantly higher than that of the control group (93.33 vs. 70 %) ($\chi^2 = 5.455$, $p = 0.02$).

Table 2: Comparison of clinical effects between the two groups (n = 30)

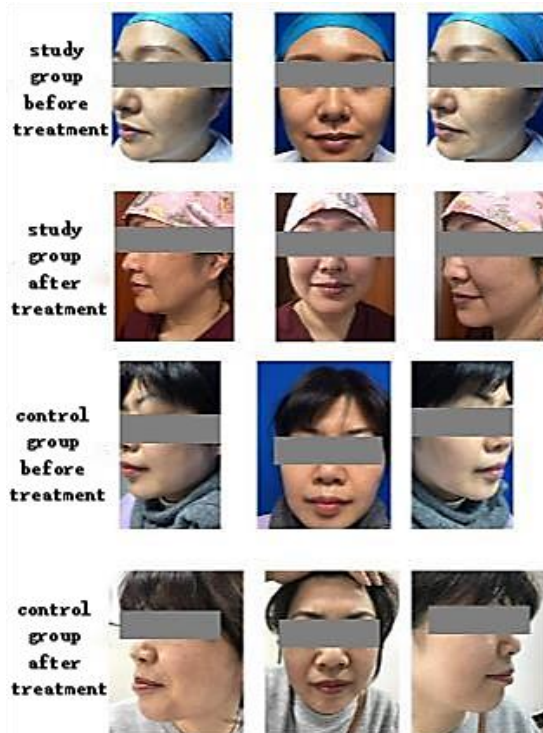
Group	A	B	C	D	E	Overall effectiveness (%)
Study	8	15	5	2	0	28(93.33)
Control	5	12	4	9	0	21(70.00)
χ^2						5.455
<i>P</i> -value						0.02

Recurrence and incidence of adverse reaction

The incidence of adverse reactions was not significantly different between the two groups ($p > 0.05$). As shown in Table 3, the recurrence rate in the study group was significantly lower than that in the control group ($p < 0.05$).

Table 3: Comparison of recurrence rates and incidence of adverse reaction rates between the two groups of patients (n = 30)

Group	Itchy skin	Redness/burning	Incidence	Total recurrence
Study	0	1	1(3.33)	3(10.00)
Control	0	2	2(6.67)	7(23.33)
χ^2			1.937	4.772
<i>P</i> -value			0.083	0.031

**Figure 1:** Comparison of the study group and the control group before and after treatment

DISCUSSION

Melasma is a yellowish-brown pigmented spot on the face that is not a separate disease but rather a subtype of cutaneous melanosis [8,9]. Despite the lack of a clear etiology, melasma is believed to be caused by a multiplicity of factors, among which genetic susceptibility, sun exposure (ultraviolet rays), and changes in hormone levels are important predisposing factors [10]. It is attributed to a defect in the melanin metabolism in the skin, an impaired epidermal permeability barrier function, and a local inflammatory response [11,12]. As such, this process is related to estrogen and progesterone. It is known that estrogen can stimulate melanocytes to secrete melanin, and progesterone facilitates the transport and diffusion of melanin granules [13].

As previously reported, melasma is also associated with depression and anxiety, both of which are risk factors for the disease [14]. To maintain beauty, some women use cosmetics to cover the spots, but this leads to the further development of melasma [15]. Presently, the primary treatment is the joint use of oral and topical drugs with laser therapy as a complement [8]. However, it should be noted that all these are associated with recurrence, long treatment duration, and high cost. The major pharmaceutical companies around the world are striving to develop the best treatment plan, and

hydroquinone cream in combination with Jidesheng snake medicine and trehalose glycerin mud for external application to treat melasma is a breakthrough in the history of melasma treatment worldwide [16].

Jidesheng snake medicine is a traditional Chinese patent medicine used primarily for treating snake bites, and it also has produced useful benefits in dermatitis, cellulitis, abscesses, pharyngitis, non-specific encephalitis, and phlebitis with drug extravasation [17,18]. Prior to the development of antivenom, Jidesheng snake pills were the most effective remedies for treating snake venom in the world. Hydroquinone cream works by inhibiting the metabolism of melanocytes and causing reversible fading of the skin and is prescribed for the treatment of melasma and freckles [19]. Furthermore, it affects the pigmentation of the skin caused by inflammation. Under severe environmental conditions, such as extreme temperatures (high and low), high osmotic pressure, drying, and dehydration, trehalose forms a protective film on the surface of cells that can effectively protect protein molecules from denaturation and inactivation, thereby maintaining the biological characteristics of the cells [20]. The major functions of polyphenols in cosmetics are moisturizing, anti-radiation, adapting to the environment, stabilizing antioxidants, and resisting skin aging. In pharmaceuticals, polyphenols function as active biological protectants of protein drugs, enzymes, vaccines, and blood products [21,22].

The findings of this present study showed that the patients in the study group were more satisfied with the treatment than those in the control group (90 vs. 73.3 %), and the effectiveness rates were significantly higher in the study group than the control group, with a good safety profile. It indicates that trehalose can be used as the additive of Jidesheng snake medicine, which maintains the performance of the medicine making it stable, keeps moist, and resists oxidation. After the medicinal mud is applied to the face, it often dries within half an hour, and it is not easy to keep moist. After adding glycerin, it can effectively lock the water and achieve the purpose of moisturizing.

CONCLUSION

The external application of *Jidesheng* medicine + glycerin + cold boiled water + trehalose in a hydroquinone cream base is a reliable strategy for treating patients with melasma. It is more cost-effective, less prone to adverse reactions, and associated with a low recurrence rate and

high satisfaction than than the application without trehalose. However, the number of cases reported in this paper is few and hence further investigations are required to validate these findings.

DECLARATIONS

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Ethical approval

This was approved by the Affiliated Yueqing Hospital of Wenzhou Medical University Ethics Committee (approval no. WZYQ-2210/7).

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

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