Clinical Experience

Whitening Efficacy of Tranexamic Acid Cataplasm on Melasma in Chinese Women

Jun Lu    Lili Yang    Ping Xu    Fenghua Bian    Huimin Zhang

Department of Dermatology, Shu-guang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai, China

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Abstract

**Background/Aims:** Oral tranexamic acid (TXA) has been reported to be effective for treating melasma. However, the effect of topical TXA on melasma remains controversial. The aim of this study was to assess the effects of topical TXA cataplasm on melasma. **Methods:** Eighty-four patients with melasma were randomly assigned to a treatment group or a separate control group. They were instructed to apply 2 pieces of cataplasm with or without TXA. The melasma area severity index (MASI), skin color tone scale (SCTS), and area score were evaluated by dermatologists blinded to the treatment. **Results:** A significant decrease in the MASI and SCTS was observed on either or both sides of the face by the end of 8 weeks compared to the control group \( (p < 0.05) \). The area score was also significantly reduced on both tested sides compared to the control group \( (p < 0.05) \). **Conclusion:** Based on these results, we believe that localized cataplasm of TXA may be used as a potentially new, effective, and safe therapeutic modality for treating melasma.
Introduction

Melasma is a common acquired pigmentary disorder that occurs usually in women, especially in Asia. The prevalence of melasma is around 13% and can seriously affect the appearance and quality of life of the women it affects [1]. Oral tranexamic acid (TXA) treatment is regarded as the preferred method for curing melasma in some countries [2]. However, oral TXA treatment of melasma, which requires a long treatment period, has the side effect of menstrual reduction in some patients [3]. Therefore, topical TXA treatment of melasma has received much more attention. Nowadays, TXA is added to some cosmetics, but there is no consensus on the clinical effect yet.

Cataplasm is also called gel patch or poultice and has a special hydrophilic polymer structure. It was suggested that cataplasm can improve the transdermal absorption rate. Cataplasm, as a remarkable drug carrier, has been used for a long time in Japan and China [4].

The present study was conducted in Chinese females with melasma to investigate the efficacy and safety of topical TXA treatment.

Materials and Methods

Materials

Cataplasm (containing 2.5% TXA or no TXA) was produced by Anssure Pharmaceutical Co., Ltd. (Tianjin, China). Cataplasm forms a special hydrophilic polymer structure through sodium and aluminum ion-connecting technology. The drug (TXA) is then mixed with a hydrophilic polymer matrix coated on a backing material. The polymer structure contains 50–60% of water and can increase the concentration of drugs and release drugs into the skin more quickly than other drug delivery routes, retaining a sufficient amount of moisture for more than 12 h [5] (Fig. 1).

The skin color tone scale (SCTS) bars were obtained from Inforward, Inc. (Tokyo, Japan). The planimetry was purchased from Xinan Science Instrument Co., Ltd. (Jiangsu, China).

Methods

Study Design

The study was a simple randomized trial (with computer-generated random numbers), and patients and dermatologists were blinded to the treatment. A total of 84 patients with melasma were recruited for the study. The study was carried out according to the principles of the Declaration of Helsinki and was approved by the Shanghai University of Traditional Chinese Medicine Ethics Committee. Informed consent was obtained from all patients. All patients with Fitzpatrick skin types III or IV and with moderate to severe facial melasma were enrolled based on guidelines for clinical trials in melasma [6]. Patients’ age ranged from 23 to 58 years (median, 43 years), and the duration of melasma varied from 1 to 7 years (median, 4 years). They were randomly assigned to a treatment group and a separate control group. Pregnant or nursing women, patients taking whitening drugs and being treated within 3 months prior to enrolment, and patients with a history of thrombosis, thrombophilia, serious liver and kidney dysfunction, or cardiovascular or respiratory disease were excluded. The therapeutic process was as follows: 2 pieces of cataplasm containing TXA or no TXA were applied to the treatment group or the control group for approximately 7 h per day. During this 8-week period, all patients were asked to visit the hospital in weeks 2, 4, 6, and 8. The patients were advised to avoid excessive sun exposure and to apply the same broad-spectrum sunscreen with a sun protection factor 30.
Evaluation of Efficacy

As mentioned in the guidelines for clinical trials on melasma [6], a blinded dermatologist quantified the melasma area and severity index (MASI) [7]. As objective evaluation techniques, SCTS score [8] and area score were assessed in this study. Skin pigment was measured by SCTS according to Konishi et al. [8]. Briefly, the SCTS bar is composed of 5 different-hue plastic bars. Nineteen kinds of value color charts from 4.0 to 8.5 with increments of 0.25 were attached to each bar. The value (V) was recorded before treatment and after treatment. The difference in V from pretreatment (ΔV) was calculated. The difference in V in the SCTS compared to pretreatment was rated as follows: marked improvement (ΔV ≥1.5), general improvement (ΔV ≥0.75), slight change (ΔV ≥0.26), unchanged (ΔV 0–0.25), and deterioration (ΔV <0). The areas of the pigmented patches were depicted by a piece of transparent paper. The area scores were measured by planimetry to calculate the total pigmented area.

Statistical Analysis

The values (MASI, SCTS, and area score) were recorded before treatment and at 2, 4, 6, and 8 weeks after treatment. The data were analyzed using analysis of variance and the Student t test. A p value of <0.05 was considered significant. Data are presented as means ± standard deviations.

Results

Of the 84 patients, 81 completed the study, while the remaining 3 patients failed to finish the study. One lost patient belonged to the treatment group, and the other 2 were from the control group. A 48-year-old woman in the treatment arm failed to complete the trial because of moving to another city during the treatment. In the control group, a 42-year-old woman...
and a patient aged 52 years lost touch with us before the end of the treatment. The means of the MASI, SCTS, and area scores before treatment were not statistically different between the 2 groups (data not shown).

**MASI of Patients with Melasma before and after Treatment**

Clinical manifestations revealed that the color and area of the skin lesions had improved significantly after treatment (Fig. 2). In weeks 4, 6, and 8, the mean MASI of the treatment group was significantly decreased \( (p < 0.01) \) (Table 1). However, the mean MASI scores of the control group were virtually unchanged \( (p > 0.05) \) (Fig. 3a).

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**Table 1. Melasma area and severity index of patients with melasma**

|                  | 0 week | 2 weeks | 4 weeks | 6 weeks | 8 weeks |
|------------------|--------|---------|---------|---------|---------|
| Treatment group  | 9.08±3.46 | 8.25±2.84 | 7.56±2.58∗ | 6.53±2.57∗ | 3.82±2.76∗ |
| Control group    | 14.52±3.64 | 15.04±3.05 | 14.82±2.45∗ | 15.12±2.26∗ | 15.25±2.08∗ |

* \( p < 0.01 \).

**Table 2. Skin color tone scale score of patients with melasma**

|                  | 0 week | 2 weeks | 4 weeks | 6 weeks | 8 weeks |
|------------------|--------|---------|---------|---------|---------|
| Treatment group  | 6.53±0.52 | 6.24±0.42 | 6.33±0.42 | 6.42±0.54 | 6.51±0.51∗ |
| Control group    | 5.44±0.54 | 5.24±0.46 | 5.53±0.44 | 5.22±0.53 | 5.13±0.42∗ |

* \( p < 0.05 \).

**Table 3. Area score (mm²) of patients with melasma**

|                  | 0 week | 2 weeks | 4 weeks | 6 weeks | 8 weeks |
|------------------|--------|---------|---------|---------|---------|
| Treatment group  | 5,402±1,550 | 4,605±1,150 | 4,015±1,025 | 3,508±804 | 3,006±752∗ |
| Control group    | 6,750±1,400 | 6,210±824 | 6,409±506 | 6,002±505 | 6,020±750∗ |

* \( p < 0.05 \).
**SCTS of Patients with Melasma before and after Treatment**

The mean ΔV of the treatment group changed obviously from the 2nd week \((p < 0.05)\) (Table 2). After 8 weeks of treatment, the mean ΔV of the treatment group was 0.76 ± 0.27, indicating moderate to marked improvement \((p < 0.05)\) (Fig. 3b).

**Area Score of Patients with Melasma before and after Treatment**

The area score of the treatment group decreased after 8 weeks of treatment compared to the control group \((p < 0.05)\) (Fig. 3c). Patients in the treatment group exhibited a 60–70% improvement after treatment (Table 3).

**Relationship between Lesion Location and Efficacy**

With respect to the distribution of lesions, malar melasma was the most common (43 cases, 54%) in our study. Eyelid, perioral, and cheek melasma were present in 16, 9, and 21% of the patients, respectively. No difference in the improvement rate (%) of MASI (63.2 vs. 67.5%), SCTS (17.1 vs. 15.6%), and area score (61.7 vs. 65.4%) was observed between malar melasma and nonmalar melasma \((p > 0.05)\).
Safety

No side effects, such as allergy symptoms, erythema, papula, or pruritus, were observed.

Discussion

Integrative medicine (IM) is a patient-centered, healing-oriented clinical paradigm that explicitly includes all appropriate therapeutic approaches whether they originate in conventional or complementary medicine. While there is some evidence for the clinical and cost-effectiveness of IM practice models, the existing evidence base for IM depends largely on studies of individual complementary medicine therapies. Topical TXA cataplasm on melasma is a good example of IM [9].

TXA was discovered in 1962 by Utako Okamoto [10]; it is a synthetic derivative of the amino acid lysine and has been used to prevent abnormal fibrinolysis to reduce blood loss. The side effects of TXA include changes in color vision, blood dots, and allergic reactions. Nijo [11] (1970) first reported on the efficacy of oral TXA in the treatment of melasma in Japan. It inhibits UV-induced plasmin activity in keratinocytes and decreases melanocyte tyrosinase activity. In recent years, in order to avoid the side effects of oral TXA, researchers began to use TXA topically in the treatment of melasma. TXA cataplasm is a promising alternative among topical preparations.

Cataplasm is a special transdermal drug carrier. Kanikkannan et al. [12] reported that the concentrations of drugs in the serum and tissue (skin and muscle) after application of the cataplasm in rats also increased with an increase in the content of the drug. Drugs can be absorbed in proportion to its contents. Our results of the present study suggested significant improvements in MASI, SCTS score, and area score in the treatment group, which may be closely related to the high absorption rate of drugs by cataplasm. By the way, the oral dosage of treatment for melasma is usually 0.75–1.0 g per day [13]. Only 0.1 g of topical TXA cataplasm was used per day in our study. Therefore, the risk associated with TXA, which can cause some side effects, is probably reduced.

A recent study reported that TXA can accelerate skin barrier recovery and upregulate occludin induced by physicochemical damage to human skin [14]. It stimulates antioxidant activity, eliminates pigmentation disorder, protects the skin from the environment, slows down aging, makes the skin more elastic, and promotes moisture retention. This is of great importance for the treatment of melasma.

In conclusion, our preliminary study indicates that TXA cataplasm seems to be a potentially new and promising therapeutic option. However, a large-scale and multicenter study will be needed to define its long-term benefits and any potential additional adverse effects.

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