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Observation of the Efficacy of Different Administration Routes of Tranexamic Acid in the Treatment of Melasma

Liu Le[1a] & SiTu Fangmin[1b,*]

[1] Jinan University First Affiliated Hospital, Guangzhou 510000, Guangdong, China

[a]15779730290@163.com, [b]situfm@126.com

[*] Corresponding Author

Abstract

Facial hyperpigmentation, commonly known as melasma, primarily affects women of childbearing age. This condition has complex causes, including hormonal imbalances, genetic factors, UV exposure, oxidative stress, local microbial balance, cosmetic use, and psychological stress, all of which greatly impact patients' appearance and mental well-being. Although current treatments for melasma yield limited results, research has indicated that oral tranexamic acid shows some clinical effectiveness in treating melasma. This study aims to explore the therapeutic effects of different administration methods of tranexamic acid on patients with melasma, with the goal of providing new insights for clinical treatment.

Keywords

Tranexamic acid, Different administration routes, Melasma, Treatment efficacy

1. Introduction

Melasma, a common, long-term skin issue associated with hyperpigmentation, has an uncertain etiology. According to recent data, the incidence of melasma varies from 8.8% to 40%, with factors such as UV exposure, hormonal changes, thyroid dysfunction, and medication use contributing to its onset or exacerbation. Typical treatment strategies focus on inhibiting melanin production and reducing the transfer of melanin from producing cells to epidermal cells. Studies suggest that tranexamic acid can block the communication between melanocytes and epidermal cells, thereby preventing melanin production and reversing melasma-related skin abnormalities. Tranexamic acid (also known as TA) was first used to treat melasma in 1979 and has since demonstrated significant efficacy (Konisky, Hailey, et al., 2023). The drug temporarily blocks lysine-binding sites on plasminogen, reducing free arachidonic acid levels and inhibiting prostaglandin synthesis. Since prostaglandins are key activators of tyrosinase, their reduction helps slow melanin production.In a novel prospective, randomized split-face study

involving 40 participants, subjects were randomly assigned to receive microneedling treatment on one side of the face, while the other side served as a control. The procedure involved microneedling on both cheeks, followed by the application of a 10% tranexamic acid solution on the experimental side and purified water on the control side (Behrangi et al., 2022). Clinical responses and satisfaction scores were carefully evaluated. The study concluded that topical tranexamic acid combined with microneedling provided significant clinical benefits in treating melasma. Xing et al. evaluated the efficacy and safety of microneedling with 1.8% liposomal tranexamic acid and 5% tranexamic acid solution in treating melasma. The study recruited 60 melasma patients who were randomly assigned to receive either 1.8% liposomal tranexamic acid treatment twice daily, weekly 5% tranexamic acid solution microneedling, or 2% hydroquinone treatment every night. Results showed that the groups receiving microneedling with tranexamic acid solution and hydroquinone outperformed the liposomal tranexamic acid group in improving melasma. Tranexamic acid can be administered orally, intradermally, or via microneedling. The following section explores the effects of different administration routes of tranexamic acid and its combination with other therapies in treating melasma (Batra et al., 2022).

2. Materials and Methods

2.1 Clinical Data

Participants were dermatology outpatients at the author's medical institution, receiving treatment between March 2021 and February 2022, totaling 96 cases. The 96 patients were randomly divided into two groups: Observation group: 48 members, including 18 males and 30 females, with an average age of 32.7±2.6 years and an average disease duration of 3.6±1.6 years. Control group: 48 participants, including 19 males and 29 females, with an average age of 34.1±3.1 years.There were no significant differences between the groups regarding gender ratio, age, disease classification, disease duration, or lesion severity score (all P values > 0.05).

Clinical diagnosis followed the guidelines issued by the Dermatology and Venereology Committee of the Chinese Society of Integrated Traditional Chinese and Western Medicine in 2003. Inclusion criteria were patients aged 18-60 years who met the diagnostic criteria. The exclusion criteria were: (1) Pregnant or lactating women; (2) Patients with bleeding tendencies or abnormal coagulation mechanisms in initial laboratory tests (Sahu et al., 2020); (3) Individuals with major diseases such as liver or heart disease, or a history of thrombosis or cerebral ischemia; (4) Women who had given birth within six months or had used contraceptives within the past six months; (5) Individuals who had used other treatments for melasma or taken other medications within the last three months; (6) Patients who stopped treatment or changed medications during the course of treatment; (7) Individuals whose incomplete information prevented accurate efficacy evaluation or who withdrew from the study early during the observation period. Given the potential risk of increased blood clotting from long-term tranexamic acid use, coagulation function and hemorheology parameters were assessed before and after

treatment, and menstrual cycle lengths were recorded for female patients (Wang et al., 2023).

2.2 Methods

Observation group: Patients took oral tranexamic acid tablets (product name: Trasamin, approval number: H20080034) produced by Daiichi Sankyo Co., Ltd., Japan, at a dosage of 0.5 g twice daily. Additionally, they applied 4% hydroquinone cream (approval number: H04001040) provided by the Pharmacy Department of the Chinese Academy of Medical Sciences Dermatology Hospital every night for 12 weeks of combined treatment (Bhattacharjee et al., 2023).

Control group: Patients took 1.2 g of vitamin C tablets daily, produced by Nanjing Baijingyu Pharmaceutical Co., Ltd., along with nightly application of 4% hydroquinone cream for 12 weeks. Treatment efficacy was evaluated at the end of treatment, as well as at 12 weeks and 24 weeks post-treatment (Ebrahim, Mustafa, & Saba, 2020).

2.3 Efficacy Evaluation Criteria

Cure: ≥90% reduction in melasma area, and near-complete color fading.Marked improvement: 60%-89% reduction in area, with significant lightening of color. Improvement: 30%-59% reduction in area, with moderate color fading. No effect: <30% reduction in area, with minimal or no color change. Effectiveness rate is defined as the sum of the cure and marked improvement rates.

Patient satisfaction was classified as "very satisfied," "satisfied," or "unsatisfied," with overall satisfaction calculated as the proportion of "very satisfied" and "satisfied" responses (Agamia et al., 2021).

Skin condition was assessed by measuring the melasma area and severity index (MASI), which ranges from 0 to 48, with higher scores indicating more severe skin damage. Specific color scoring criteria were as follows: 0 = normal skin color, 1 = light brown, 2 = brown, 3 = dark brown. Area scoring criteria were as follows: 0 = no lesion, 1 = <2 cm^2, 2 = 2-4 cm^2, 3 = >4 cm^2. Higher scores indicate more severe skin damage.

2.4 Statistical Methods

Data were processed using SPSS 21.0 software, with measurement data expressed as (x±s) and t-tests performed. Count data were expressed as percentages and analyzed using the $\chi 2$ test. $P<0.05$ was considered statistically significant. (Maeda, 2022)

3. Results

3.1 Comparison of the Effectiveness rates of Patients after Receiving Relevant Treatments

The effectiveness rate of the observation group was higher than that of the control group, with a statistically significant difference ($p<0.05$), as shown in Table 1.

Table 1. Comparison of the Effectiveness Rates of Patients after Receiving Relevant Treatments (n, %)

Group	Cases	Cured		Significant effect		Effective		Ineffective		Effectiveness rate (%)
		Treatment end	6 months after treatment	Treatment end	6 months after treatment	Treatment end	6 months after treatment	Treatment end	6 months after treatment	
Observation group	48	21	30	13	15	9	2	5	1	47（97.91%）
Control group	48	13	16	10	14	8	5	17	15	33（68.75%）
χ^2										14.7000
P										0.0001

3.2 Comparison of Patient Satisfaction after Receiving Relevant Treatments

The satisfaction rate in the observation group was higher than in the control group, with a statistically significant difference ($p<0.05$), as shown in Table 2.

Table 2. Comparison of Patient Satisfaction after Receiving Relevant Treatments (n, %)

Group	Cases	Very satisfied	Satisfied	Unsatisfied	Satisfaction rate (%)
Observation group	48	34	12	2	46 (96.66%)
Control group	48	27	10	11	37 (73.33%)
χ^2					7.2067
P					0.0072

3.3 Comparison of the Incidence of Adverse Events after Receiving Relevant Ttreatments

The incidence of adverse events in the observation group was lower than that in the control group, with a statistically significant difference ($p<0.05$), as shown in Table 3.

Table 3. Comparison of the Incidence of Adverse Events after Receiving Relevant Treatments (n, %)

Group	Cases	Diarrhea	Nausea	Vomiting	Incidence of adverse events (%)
Observation group	48	35	12	1	47 (96.66%)
Control group	48	32	6	10	38 (73.33%)
$\chi 2$					8.3166
P					0.0039

3.4 Comparison of Skin-related Scores before and after Treatment in the Two Groups

The skin-related scores of the observation group were better than those of the control group, with a statistically significant difference (P<0.05). The specific results are shown in Table 4.

Table 4. Comparison of Skin-related Scores before and after Treatment in the Two Goups (x±s)

Group	Cases	MASI Score		Lesion Color Score		Lesion Area Score	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	48	12.32±1.21	8.75±1.91	2.24±0.81	1.98±0.11	2.55±0.21	1.43±0.34
Observation group	48	12.65±1.54	6.43±1.02	2.25±0.12	1.43±0.32	2.65±0.58	0.74±0.17
t		1.1674	7.4232	0.0846	11.2611	1.1232	12.5758
P		0.2460	0.0000	0.9328	0.0000	0.2642	0.0000

3.5 Comparison of Laboratory Indicators between the two Groups

The laboratory indicators of the observation group were better than those of the control group, with a statistically significant difference (P<0.05) (Feng et al., 2022). The specific results are shown in Table 5.

Table 5. Comparison of Laboratory Indicators between the Two Groups (x±s)

Group	Cases	α-MSH(μg/L)		SOD(U/ml)		MDA(nmol/ml)		Nr2(ng/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	48	38.32±1.21	31.75±1.91	42.24±2.81	55.38±3.91	5.35±1.21	4.43±1.34	195.35±7.13	252.34±7.43
Observation group	48	38.65±1.54	24.43±1.02	42.41±2.12	68.53±2.32	5.45±1.98	3.14±0.37	196.45±7.61	285.43±8.04
t		1.1674	23.4215	0.3346	20.0388	0.2986	6.4291	0.7308	20.9414
P		0.2460	0.0000	0.7387	0.0000	0.7659	0.0000	0.4667	0.0000

4. Discussion

Melasma is a common condition of hyperpigmentation, characterized by light to dark brown patches on the skin that are usually symmetrical and do not cause noticeable discomfort, such as redness or peeling. Its causes are diverse, including genetic predisposition, UV exposure, pregnancy, contraceptive use, thyroid dysfunction, cosmetic product use, and medication effects. Current treatment options include vitamin supplements, skin-lightening creams, chemical peels, and laser or light therapies (Kuster, et al., 2021). While these treatments have varying degrees of efficacy, they also have limitations. Tranexamic acid (TA), an antifibrinolytic agent, is widely used in the clinical treatment of various bleeding disorders. It works by inhibiting the lysine binding sites on plasminogen, preventing fibrinolysis without increasing prothrombin activity or affecting coagulation. It can be administered orally or intravenously. Studies have shown that in the treatment of melasma, TA's mechanism of action may involve improvements in dermal changes. As a fibrinolytic inhibitor, TA can prevent angiogenesis, reduce erythema and vascular density, and decrease the number and activity of mast cells (Abd, Israa, Zakaria, & Ibrahim, 2023).

Currently, several laser technologies are available for treating melasma. Some patients have achieved significant results using combinations of different laser and phototherapy methods. Additionally, there is ongoing research into combining laser therapy with medication to enhance treatment efficacy, and TA has gradually become a promising treatment option. While the exact cause and mechanism of melasma remain unclear, it is generally believed to be associated with factors such as endocrine system disorders, emotional fluctuations, UV exposure, genetic predisposition, medication use, and cosmetic application (Cassiano et al., 2022). The pathological features of melasma mainly include increased melanin content in the epidermis. It is believed that the number of melanocytes does not increase; rather, their size and

synaptic activity become more pronounced, indicating increased melanocyte activity (Otb et al., 2022). Despite various traditional treatments, results are often unsatisfactory. The topical agent 4% hydroquinone, a common depigmenting agent, inhibits tyrosinase activity, thereby blocking the conversion of dopa to melanin. TA has become a commonly used drug for melasma treatment, with its mechanism possibly linked to tyrosinase inhibition. Research has shown that TA can reduce tyrosinase activity by preventing the conversion of plasminogen to plasmin, thereby reducing interactions between melanocytes and keratinocytes, leading to decreased melanin production. In animal models of melasma, when TA was injected into the lesion site, no significant change in melanocyte numbers was observed, but melanin content decreased. This suggests that TA does not affect the number of melanocytes but may regulate their function to inhibit melanin synthesis, providing experimental support for melasma treatment (Donovan, 2005).

The side effects of TA mainly include thromboembolism, gastrointestinal reactions (such as diarrhea, nausea, and vomiting), and menstrual discomfort due to blood clotting during menstruation. A comparison of coagulation indices and hemorheology data before and after treatment, along with an analysis of the menstrual cycle lengths of female patients, revealed no significant changes in these parameters. As an antifibrinolytic agent targeting the fibrinolytic system, TA primarily prevents fibrin dissolution by inhibiting plasmin activity, thus achieving its hemostatic effect. Oral administration of TA does not interfere with coagulation or fibrinolysis and does not affect the menstrual cycle. This study demonstrated that daily oral administration of 1.0 grams of TA for melasma treatment is safe.Recent studies have shown that using low-power 1064 nm laser technology to treat melasma is effective. When combined with oral TA, the results are even more significant. TA requires only a small oral dose to be effective in treating melasma and can be used alone or in combination with other treatments, such as oral medications, topical agents, or laser therapy. The duration of treatment significantly impacts the efficacy, with results typically appearing 1-2 months after starting the medication. The longer the treatment period, the better the results. TA is relatively safe, with its main side effects being gastrointestinal issues, such as nausea, vomiting, diarrhea, and menstrual reduction. Glycolic acid, an organic compound found in sugarcane and various fruits, promotes the renewal of skin surface cells and stimulates collagen production in the dermis. An Indian study evaluated the efficacy, safety, and improvement in quality of life index of 30% glycolic acid and 5% arbutin solution in the topical treatment of epidermal melasma. Once ingested, the drug can penetrate deep into the skin through the bloodstream, directly affecting melanocytes, reducing tyrosinase activity, and thus effectively decreasing melanin production and discharge. The drug's low side effects accelerate melanin degradation, producing a cumulative effect that helps eliminate melasma and reduce recurrence. α-MSH, a peptide hormone, stimulates melanin production and release, while MDA, a product of lipid peroxidation in cell membranes, is closely related to cell damage and oxidative stress. Research found that the combined topical treatment of 30% glycolic acid and arbutin had a similar efficacy, safety, and improvement level compared to glycolic acid alone.Long-term follow-up studies have shown that

taking 250 mg of TA twice daily for 6 to 15 months has significant safety and efficacy in treating melasma. Further research has shown that combining TA with reduced glutathione yields even better treatment results for melasma. In this study, patients took 1.0 grams of TA orally daily for 12 weeks, supplemented by topical hydroquinone. The results demonstrated significant efficacy in melasma treatment. More importantly, patients maintained good results even 12 weeks after discontinuing the medication, with minimal side effects. This finding offers a safe and effective new method for treating melasma in clinical practice.

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