SHORT REPORT

Intradermal application of tranexamic acid (TA) as treatment of melasma in the out-patients department of a public sector hospital: A pilot study

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Abstract

The effect of intradermal TA on melasma was evaluated as a possible treatment modality on all of the 11 patients (fitting the inclusion criteria) presenting in the out-patient department of the Benazir Bhutto Hospital, Rawalpindi during Sep 2019 to Mar 2020. Their pre- and post-interventional results were evaluated after being injected with 4 mg/ml of TA on the lesions once weekly for 6 weeks, using Wilcoxon signed rank test in SPSS v 24.

The average duration of melasma in our patients was 25.3±7.6 in months. The mean modified MASI score rating was 12.2 (2.3) and 5.1 (1.4) before and after intervention with intradermal TA respectively. The largest difference obtained in the mMASI scores of the patients was 10.8.

TA has a distinctive effect as a treatment modality for melasma, as it is easily employable with very few side effects.

Keywords: Melasma, Tranexamic acid, TA, intradermal TA, mMASI.

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Introduction

Melasma is considered an acquired chronic skin condition, which manifests in the form of hyperpigmentation in areas predominantly exposed to sun, affecting mainly the forehead, cheeks, nasal bridge and sublabial region. Although it is found in all skin types, it is relatively common in people of Asian, Hispanic and African descent.[1] It is most commonly linked to pregnancy or alterations in uterine and ovarian hormones; however, it may have a number of potential triggers, including cosmetic use, photosensitivity and use of oral drugs such as contraceptives (OCP's), steroids etc.[2]

Melasma, apart from being a chronic skin condition, can also cause a significant social and psychological effect thereby decreasing one's quality of life. In a study conducted to evaluate the quality of life of melasma patients, the majority reported to be depressed, frustrated and embarrassed about their skin condition.[3] Considering this, the main objective of an acceptable treatment should be the improvement of hyperpigmentation, ultimately impacting the quality of life.[1] For a long time, a number of treatments have been employed including photo protection, skin bleaching techniques, chemical peels, laser, dermabrasion etc but unfortunately, they have not proven to be very effective remedies. However, studies have supported the effectiveness of tranexamic acid (TA) as a treatment for melasma in various forms (i.e., oral, topical and localised intradermal microinjections).[4]

Nonetheless due to a lack of adequate data no definitive consensus on the use of TA for melasma currently exists, which indicates the need for a large-scale RCT.[4,5] This study was conducted as a pilot study to assess the effect of intradermal TA on melasma as a possible treatment for out-patients, however, we plan to conduct an even larger RCT to assess further effects of this possible treatment modality in the near future.

Patients and methods

This pilot study was conducted at Benazir Bhutto Hospital (BBH), Rawalpindi, from September 2019 to March 2020 and consisted of patients from both genders, presenting in the out-patient department of the hospital. Ethical approval was obtained from the Institution Research Forum and the Research & Ethical Committee (REC) of Rawalpindi Medical University and BBH. A sample of 11 subjects were inducted using consecutive sampling, after a well-informed verbal and written consent where they were explained the entire procedure. A pre-formed Performa was employed to record the patient demographic data, including age, gender, disease duration, and past family history of melasma.

The patients included in the study had no previous history of needle phobia, any chronic systemic disease. Exclusion criteria were patients actively using any form of topical, oral or any interventional melasma treatment in last 4 weeks including bleaching agents, steroids, glutathione, LASERS, micro-needling, PRP and peeling agents, having a history of coagulation and thrombotic disorder, history of use of anticoagulants, allergy to TA, undergoing treatment for melasma within six months prior to the study, and history

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of herpes simplex lesions on the face. Patients using OCP's, pregnant or lactating within the prior 12 months were also excluded. The patients were assessed by a panel of two dermatologists and a consensus was made on the modified MASI (mMASI) score of each participant, which is a score ranging from 0-24 (with 0 being the least severe to 24 being the most).[6]

The subjects were asked to apply a topical anaesthetic cream on the face for 45 minutes under occlusion, then wash it off before treatment. They were given 4 mg of TA diluted in 1 ml of distilled water intradermally using a 1CC Becton Dickinson insulin syringe having 6mm X 31 G needle, on the lesions both peripherally and centrally, covering as much area as possible. The patients were recommended to use a broad-spectrum sunscreen with a sun protection factor (SPF) of 50, when going outdoors in the sun and were prohibited from using any whitening creams. The patients were followed up weekly and were injected TA intradermally as mentioned previously. After 6 weeks the patients were evaluated again under the same protocols.

The data was analysed using a SPSS v 24. A p-value of less than 0.05 was considered statistically significant. Wilcoxon-signed rank test was used to analyse the difference in the mMASI scores of the melasma patients before and after the TA treatment.

Results

Among the 11 patients, 7 (63.6%) were males whereas 4 (36.4%) were females with a female to male ratio of 1:1.14. The mean age of the participants was 24.6±6.10 years. (Table) The average duration of melasma in our patients was 25.3±7.6 months. None of the patients reported any underlying diseases. Sunlight exposure was the most common precipitating factor among our participants.

Table: The comparative analysis of mMASI values before and after administration of intradermal TA. The table shows the mean, standard deviations and the *p*-value.

	mMASI Scores		*p*-value
	Before	After	
Mean±SD	12.4±2.3	5.1±1.4	0.003

A Wilcoxon signed-rank test produced a non-normally distributed outcome which showed that a six week, once weekly intradermal TA treatment course elicited a statistically significant change in the melasma pattern of the individuals (Z=-2.9, *p*= 0.003). The mean modified MASI score rating was 12.4 (2.3) and 5.1 (1.4) before and after intervention with intradermal TA respectively. The largest difference obtained in the mMASI scores of the patients was 10.8. The mMASI scores of all the patients showed a decrease in the score post treatment. These changes in the mMASI scores were statistically significant with a *p*-value of 0.003. All of the patients were satisfied with the treatment, and showed improvement as depicted by Figure.

Conclusion

Pakistan is an Asian country with a predominantly darker skin complexion. Unfortunately, it is a widely known fact

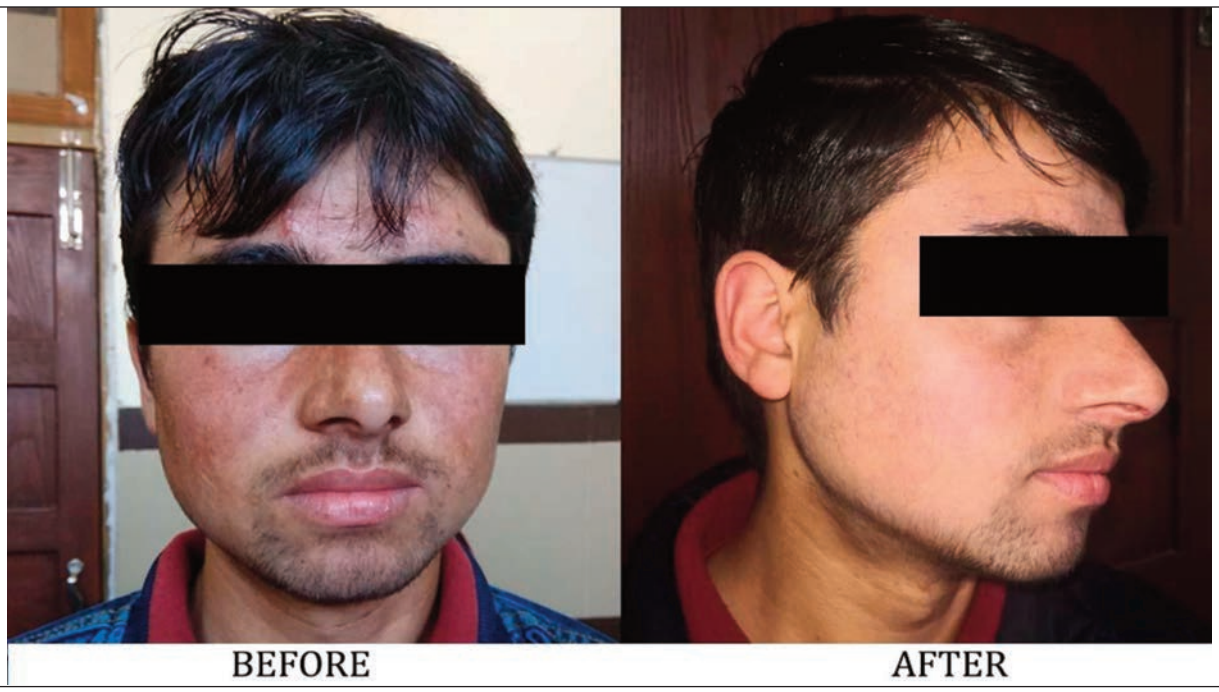

Figure: The effect on the condition of melasma before and after intervention with TA.

that even now, none of the treatments especially topical have been found to be suitable in the long-term for a darker skin type. These treatments mainly include topical bleaching agents that can irritate the skin, produce hyperpigmentation owing to post inflammatory reactions, or in most cases, need a rather long period to achieve lightening,[7] which brings us to a new option recently explored as a possible treatment modality for melasma.

Following a pilot study 6 of 4-mg/mL intradermal TA injection, there was a decrease of 31.8% in the mMASI score at 8 weeks, and 42.7% after 12 weeks of treatment. In another study, the researchers observed a reduction of 24.1% in 8 weeks and 31.5% in 12 weeks. 8. In our study however, we found a mean difference of 7.2 among the pre- and post-intervention mMASI scores, which makes a mean score reduction by a staggering 58.1% under just six weeks of treatment. In both of these studies, there was a decrease in the mMASI scores at 8th and 12th week, but our study generated results at the 6th week.

Study subjects did not report any precarious side effects apart from a mild local discomfort (because of the injection itself), burning sensation and local erythema (redness) that manifested transiently.[2,7] However, studies did report a recurrence pattern in melasma using intradermal TA at 24th week.[8] Unfortunately, in our case, we could not take the follow-ups in our study that far, owing to the closure of the OPD's following the official COVID-19 pandemic protocol.

Melasma treatment is a challenge for dermatologists, as no gold-standard exists and recurrence is common.[9] Therefore, being demonstrated to be as consistently satisfactory; TA could be recommended as a combination treatment paired with other topical and laser therapies, or maintenance therapy to decrease the relapse rate of melasma.

Our study, although the first of its kind in the region, was unable to achieve its aspired goals owing to the small number of patients and lack of a control group. Nonetheless, we observed that TA has a distinctive effect as a treatment modality of melasma, with very few counter-effects. It is a safe and easily employable procedure in the out-patient department. Therefore, additional large, double-blinded, controlled trials succeeding this pilot study are needed to accurately find out more about TA as a suitably dependable treatment.

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Conflict of interest: None.

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