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Research Protocol

Dermatology Section

# Efficacy of Tranexamic Acid Mesotherapy using a Novel Device versus Topical Tranexamic Acid in Patients with Melasma: Protocol for a Randomised Clinical Trial

YASH KASHIKAR[1], BHUSHAN MADKE[2], ADARSHLATA SINGH[3], SOHAM MEGHE[4], KAVERI RUSIA[5]




## ABSTRACT

**Introduction:** Melasma is a widely prevalent acquired condition characterised by gray-brown pigmentation with a predilection on the face, affecting the quality of life. Tranexamic Acid (TXA) has been used for managing melasma orally and topically, while mesotherapy is a well known modality in cosmetology.

**Need of the study:** There is a paucity of literature comparing the efficacy of topical and intralesional microinjections of TXA. A novel device (Meso-Ice®) has recently been commercialised for mesotherapy, working on the principle of electroporation technology for drug diffusion, which has not yet been evaluated for managing melasma using TXA.

**Aim:** To compare the efficacy of TXA mesotherapy using the novel device versus topical TXA in patients with melasma.

**Materials and Methods:** This is a randomised clinical trial assessing the comparative efficacy of Group 1: Mesotherapy using the novel device with TXA injection (4 mg/mL) and Group 2: Topical TXA gel (3%) for treating melasma. The severity of melasma will be assessed using the Melasma Area and Severity Index (MASI) at baseline, four weeks, and eight weeks. One-way Analysis of Variance (ANOVA) will be used to compare intra-group variables, and the paired t-test will be used for inter-group comparison. A p-value of <0.05 will be considered significant.


**Keywords:** Antifibrinolytic, Hyperpigmentation, Microneedling

## INTRODUCTION

A typical acquired dermatosis known as melasma is characterised by the development of light-to-dark brown patches and macules on the face and neck. Most frequently, women are affected by this condition [1]. While the exact aetiology of melasma is still unknown, some known risk factors include genetic predisposition, exposure to ultraviolet radiation, pregnancy, sex hormones, contraceptive pills, thyroid disorders, cosmetics, and phototoxic medicines [2].

Melasma is treated using a variety of techniques. These include using sunscreen, hypopigmenting chemicals, glycolic and lactic acid for superficial peeling, and laser therapy [1-3]. Recent research has shown that the haemostatic drug TXA has a hypopigmentary impact on melasma lesions and also inhibits Ultraviolet (UV) induced pigmentation. It has haemostatic effects in addition to having anti-allergic and anti-inflammatory properties. The TXA via systemic or topical route and transdermal via intralesional microinjections has shown promising depigmentation effects [2,4,5].

Mesotherapy is a novel therapeutic modality commonly used in aesthetic dermatology and trending therapy in the management of melasma [6]. Recently, Renewcell Cosmedica LLP, India has launched an advanced needleless mesotherapy device (Meso Ice®) based on the cryo-electroporation technology for drug diffusion [7]. Till date, its efficacy in the management of melasma using TXA has not been evaluated. Hence, the present study comparatively assesses the efficacy of TXA mesotherapy using the novel Meso-Ice device versus topical TXA in patients with melasma.

**Rationale/Need for the study:** Over the last few years, off-label TXA has developed as a potential treatment for melasma. TXA has been used topically, systemically, and by transdermal drug delivery methods like intralesional microinjections. Mesotherapy is a popular novel therapeutic modality commonly used in aesthetic dermatology [2,5,6]. Hence, the present study is needed to comparatively evaluate the effect of topical versus mesotherapy using TXA. According to the available data, it is hypothesised that there is an additional benefit of TXA mesotherapy using the novel device over topical TXA in patients with melasma.

**Objectives:**

1. To evaluate the efficacy of TXA mesotherapy using the novel device on the MASI score of patients with melasma.
2. To evaluate the efficacy of topical TXA on the MASI score of patients with melasma.
3. To compare the efficacy of both modalities on the MASI of patients with melasma.

## REVIEW OF LITERATURE

Lee JH et al., observed a significant decrease in the MASI of 100 women with melasma from baseline to 8 and 12 weeks following intralesional localised microinjection of TA acid (0.05 mL; (4 mg/mL) with no adverse events [2].

Saki N et al., in a split-face controlled trial, on 37 patients with melasma reported that monthly TXA injection (20 mg/mL) was better than daily application of topical hydroquinone (2%) in reducing the melanin value during the first 4 to 3 weeks [4].

Khurana VK et al., in a prospective, randomised, open-label study reported that the oral TXA 250 mg twice a day group showed a significant reduction in MASI score compared to the localised intralesional microinjections (4 mg/mL) of TXA monthly in 64 patients with melasma [5].

## MATERIALS AND METHODS

This randomised clinical trial will be conducted in the outpatient department of Dermatology, Venereology, and Leprosy, Acharya Vinoba Bhave Rural Hospital (AVBRH), DMIHER, Sawangi, Wardha, Maharashtra, India from March 2024 to September 2025. The

Ethical Committee of DMIHER has approved the conduction of this study (IEC no-DMIMS (DU)/IEC/2023/744). The trial has been applied for clinical trial registry (REF/2023/05/067541).

**Inclusion criteria:** Systemically healthy patients with clinically diagnosed melasma based on subjective assessment of hyperpigmented lesions over the face and belonging to the age group of 18 to 60 years will be included in this study.

**Exclusion criteria:** Patients suffering from significant systemic illness, a history of using topical or systemic depigmenting agents or photosensitising drugs like tetracyclines, phenytoin, carbamazepine, and spironolactone or anticoagulants, and those on drugs which could interact with the metabolism of TXA such as anticoagulants, drugs that prevent bleeding, oestrogens, hormonal birth control, tibolone, tretinoin; any other pre-existing facial dermatoses, pregnant and lactating women will be excluded from this study [2,4,5].

**Sample size estimation:** The sample size was calculated using the software, OpenEpi sample size calculator, using the formula n=DEFF*Np(1-p)/(d/Z-α/2*(N-1)+p*(1-p) wherein DEFF (Design Effect)=1, p (estimated prevalence)=0.19, d (Desired precision)=0.57, α (margin of error)=0.05, Z (Critical value of the normal distribution at the required confidence level)=1.96, and N (population size)=200.

The inputs entered were a 19% population having melasma [8] and considering the improvement in MASI score by microinjection of TXA as 5.75 as per the previous study [2] and a 5% precision, and a confidence level of 95%. These inputs generated a sample size of atleast 16 participants per group. Considering a 10% dropout rate, a final sample size of 40 (20 per group) was considered significant.

### Procedure

**Assignment of interventions (for controlled trials):** The participants will be enrolled by evaluating their skin type using the Fitzpatrick classification (Type I to Type VI) and classifying the type of melasma according to the area involved (malar, mandibular, or centrofacial), and the depth of pigmentation (epidermal and mixed) will be determined by a wood's lamp examination [9].

The severity of melasma will be gauged by calculating MASI, which is a validated scale used to measure the extent of facial hyperpigmentation. This is a numeric score calculated as an area-weighted score of pigmentation and homogeneity located on the forehead, chin, right, and left malar cheek.

The score is calculated based on the formula: 0.3×A (forehead)×(D+H) (forehead)+0.3×A (left malar)×(D+H) (left malar)+0.3×A (right malar)×(D+H) (right malar)+0.1×A (chin)×(D+H) (chin) wherein A denotes the area of involvement, D represents darkness, and H represents homogeneity. The MASI score ranges from 0 to 48, with 48 being the most severe [10].

**Patient allocation:** The patients will be randomly allocated to two groups. Patients in Group 1 will be managed by mesotherapy using TXA injection (4 mg/mL) [11], while patients in Group 2 will be managed by topical TXA gel (3%).

**Blinding:** The patients will be blinded to the intervention they will receive.

**Intervention:** In Group 1: Mesotherapy will be done once every 4 weeks using the MESO-ICE device™ as per the manufacturer's guidelines (consisting of three probes viz., thermal, electroporation, and cryo). Initially, the thermal probe of the device will be applied for 10 minutes, followed by electroporation of one ampoule of TXA (500 mg, Injection Pause; Emcure Pharmaceuticals, India) for 10 minutes over the affected area [11]. The Cryo Probe will be used at the end for 10 minutes. Patients will be instructed to maintain sun protection using sunscreen (SPF 30 or higher) in the morning, with re-application of the sunscreen every three hours.

**In Group 2:** TXA gel (3%, Tranesma Gel, Acumentis Healthcare Ltd., India) [12] will be given to the patients. Patients will be advised to apply the gel over the pigmented area once a day before sleep and to be kept overnight followed by wash using normal water. Patients will be instructed to maintain sun protection using sunscreen (SPF 30 or higher) in the morning, with re-application of the sunscreen every three hours. The outcome will be assessed at baseline, 4 weeks, and 8 weeks.

**Outcome measure:** Reduction of MASI scores by TXA mesotherapy using the novel device in comparison to topical application at four weeks and eight weeks.

**Participant timeline:** The outcome will be assessed at Baseline, 4 weeks, and 8 weeks.

## STATISTICAL ANALYSIS

Demographic variables will be expressed as mean and frequency distribution. Reduction in MASI scores over the timeline in individual groups will be analysed using One-way Variance (ANOVA). At each time interval, the comparison between the two groups will be done using a paired t-test. Categorical variables will be analysed using the chi-square test. A p-value of less than 0.05 will be considered significant.

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**PARTICULARS OF CONTRIBUTORS:**
1. Resident, Department of Dermatology, Jawaharlal Nehru Medical College, Wardha, Maharashtra, India.
2. Professor, Department of Dermatology, Jawaharlal Nehru Medical College, Wardha, Maharashtra, India.
3. Professor, Department of Dermatology, Jawaharlal Nehru Medical College, Wardha, Maharashtra, India.
4. Resident, Department of Dermatology, Jawaharlal Nehru Medical College, Wardha, Maharashtra, India.
5. Resident, Department of Dermatology, Jawaharlal Nehru Medical College, Wardha, Maharashtra, India.

**NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:**
Dr Yash Kashikar,
DMIHER, Sawangi (Meghe), Wardha-442107, Maharashtra, India.
E-mail: yash.kashikar@gmail.com

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