ORIGINAL ARTICLE

SPLIT-FACE COMPARATIVE ANALYSIS OF MICRO-NEEDLING WITH TRANEXAMIC ACID VS VITAMIN C SERUM IN MELASMA

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Background: Melasma is a very common skin problem that is much more prevalent in women. In our society, it results in many psycho-social implications and eventually leads to an impaired quality of life. Many treatment modalities have been developed for it. However, in recent years resistant forms of melasma have emerged that are unresponsive to the usual first line treatment options. Thus, this study is being conducted to explore new treatment modalities for this disease by using micro-needling with vitamin C and tranexamic acid. **Methods:** Thirty patients participated in this non-randomized clinical trial including 11 males and 19 females. All patients received Tranexamic acid via micro-needling on right side of the face and Vitamin C on the left side. A total of three biweekly sessions were performed. Patients' response was evaluated at week 2, 4 and 6 on the basis of Physician Global Assessment, Patient Global Assessment, modified Melasma Area Severity Index and clinical assessment. Paired sample t-tests were used to calculate the difference in the means of two groups at 2, 4 and 6 weeks and *p*-value of <0.05 was considered significant. **Results:** After first session, there was more improvement observed with tranexamic acid. At the end of 6 weeks, modified Melasma Area Severity Index, Physician Global Assessment and Patient Global Assessment showed significant improvement with both tranexamic acid and vitamin C. However, the difference between them was not statistically significant ($p>0.05$). **Conclusion:** Both Tranexamic acid and Vitamin C are potent therapies for melasma as an adjuvant to micro-needling.

Keywords: Melasma; Micro needling; Tranexamic acid; Vitamin C

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INTRODUCTION

Melasma is one of the commonest disorders of pigmentation affecting millions of people around the world.[1] The exact pathogenesis of this frustrating condition eludes us; however sun exposure, family history, hormonal contraception and pregnancy are the four main factors found to be responsible.[2] It presents as tan or brown macules and patches primarily over the sun-exposed areas of face.[3] The disorder has profound psychological effects, leading to an impaired quality of life, decreased confidence and lowered self-esteem.[4]

Numerous treatment options are available for the management of melasma. These include depigmenting agents, physical therapies, oral drugs as well as lasers. Topical treatments such as fixed triple combinations (hydroquinone, retinoids, and corticosteroid) are considered first line.[5] Alternative treatments include single agents such as 4% hydroquinone, 20% azelaic acid, glycolic acid along with lasers and light based therapies in non-responsive patients.[6] Tranexamic acid (TXA) has also been used for treatment of recalcitrant melasma in various formulations such as a topical cream, intradermal injection and orally with good results.[7] Vitamin C (ascorbic acid) is an excellent agent for the treatment of pigmentation however, its efficacy is compromised due to its lack of skin penetration and unstable molecular nature. Therefore, procedures such as iontophoresis and micro needling have been done to increase its effectiveness.[8,9] Since melasma affects an overwhelming majority of the patients in our population, not all treatments lead to satisfactory results. Hence, the need for new treatment modalities remains. We conducted this study to evaluate the effect of topical TXA versus vitamin C in conjugation with micro needling. These options are safe and if found effective may be used widely in the future.

MATERIAL AND METHODS

Our study was conducted over a period of 7 months, from May to November 2020. This non-randomized clinical trial was conducted after taking approval from the hospital administration. Non-probability consecutive sampling technique was employed. Patients with melasma that presented to the outpatient department were approached and the study was explained to them in depth. After taking informed consent, 30 patients participated in the trial. Our research had a strict inclusion criterion that comprised of patients ranging from 20–55 years and presence of melasma on the face that is both bilateral as well as symmetrical. Patients with any type of bleeding diathesis, systemic diseases, and those on any form of hormonal contraceptives were not included in our study. Patients underwent a detailed examination and parameters such as duration of disease, skin type, extent of sun

exposure, family history and presence of iron deficiency were documented. The modified Melasma Area Severity index (mMASI)[10] was used in the study for patient evaluation. It is calculated as:

mMASI total score= 0.3xA (forehead) x D(forehead)+ 0.3xA (left malar) x D (left malar) + 0.3xA (right malar) xD (right malar) + 0.1xA(chin) x D(chin)

The range of the total score is 0 to 24. Area (A) and darkness(D) are scored as follows:

Area of involvement: 0 = absent, 1 = <10%, 2 = 10–29%, 3 = 30–49%, 4 = 50–69%, 5 = 70–89%, and 6 = 90–100%;

Darkness: 0=absent, 1=slight, 2=mild, 3=marked and 4=severe.

The affected malar area was washed, followed by application of topical anaesthetic cream for 30-40 minutes. TXA is available as a 500 mg/5 ml ampoule. 1 to 2 ml of TXA was used on the right side of face and 20% Vitamin C serum on the left side during micro-needling. Dr Pen A6 device was used with 36 needle tip and needle depth set at 0.5 mm. After the procedure, cooling was done with ice and strict avoidance of sunlight was advised. Sessions were done on day 0 and then at two weekly intervals on week 2 and 4. Patients were assessed at week 2, 4 and 6 using clinical assessment, modified Melasma Area Severity Index (mMASI) scoring, Physician Global Assessment (PGA), and Patient Global Assessment (PtGA). In order to properly categorize improvement, the following subgroups were devised: Poor= 0–25% improvement, Fair= 25−50% improvement, Good= 50−75% improvement, Excellent= >75% improvement. SPSS software was used for analysing the data. Quantitative data was depicted as means with standard deviations whereas qualitative data was illustrated in the form of frequencies and percentages. Paired sample statistics (t-tests) were run between the first recorded values of modified melasma area severity index, i.e., mMASI of right and left side of the face at the initial visit, and subsequent follow-ups.

RESULTS

This study included a total of 30 patients from various age groups comprising of 19 females and 11 male patients. A maximum of around 87% patients belonged to the Fitz Patrick Type 4 skin classification. Almost 75% of all the patients fell in the age group of 20–40 years. No statistically significant difference was observed between the left and right side regarding overall melasma severity before treatment commenced (p>0.05). Patients received an initial session and mMASI was calculated upon their follow-up after 2 weeks. Patients right side of face which received TXA therapy had an excellent response which was demonstrated by the fact that approximately 27% of the patients had a remarkable decrease in the severity of melasma (p<0.05) (Figure-1 and 2). On the other hand, treatment with vitamin C on the left side of face led to a decrease in severity of melasma in only 15% of patients. After the second session of micro-needling, both the right and left side showed an excellent response. It illustrated that further 20% patients could now be classified into the category of lowest mMASI score (Figure-3 and 4) (Table-1). After the 3rd session, it was noted that there was an overall significant improvement in mMASI ultimately, regardless of the agent used (p<0.01). Physician and patient global assessments mean percentage of the left side showed that approximately 13% patients had an excellent response, 43% had a good response and 30% had a fair improvement after the first session with vitamin C. In contrast to this, the right side treated with TXA showed that around 16% patients had an excellent response, 40% had a good outcome and around 26% showed a mild improvement. It was seen that the patients who suffered from widespread deep dermal melasma of comparatively more severity did not yield to either therapy even after multiple sessions. A very mild response was observed and they largely remained unaffected with the mMASI scores improving negligibly.

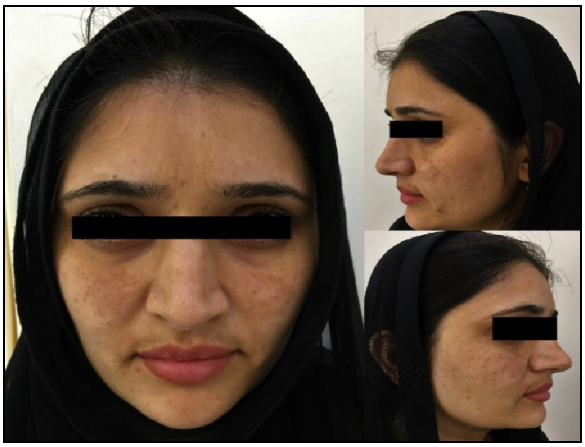

Figure-1: mMASI Score- Right side= 4.1, Left Side=4.1 (DAY-0)

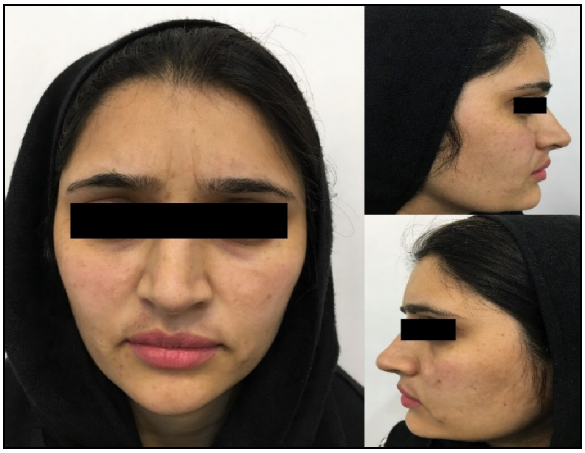

Figure-2: mMASI Score Right Side= 1.05, Left Side= 1.3 (DAY-14)

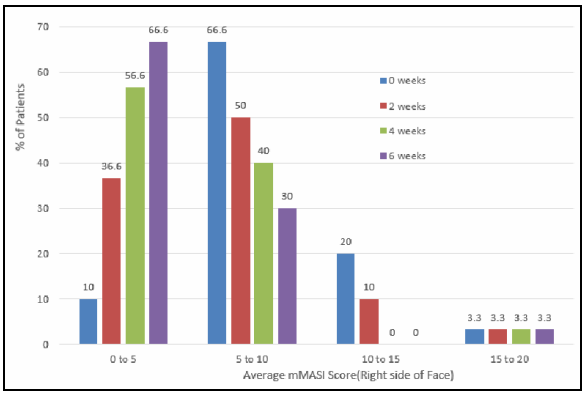

Figure-3: Average mMASI score- Right side of Face

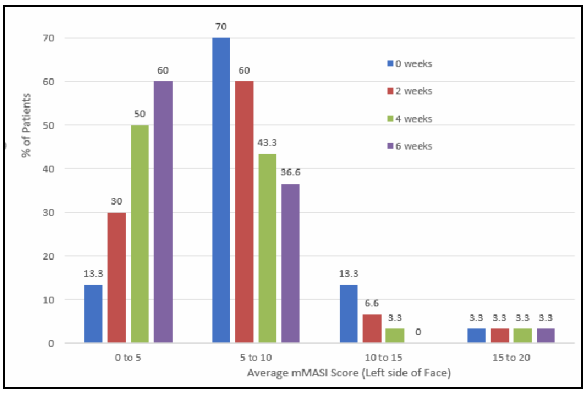

Figure-4: Average mMASI score -Left side of Face

Table-1: Mean mMASI of both left and right side of face at 2, 4, and 6 weeks

Parameters	Day 0	Day 14	Day 28	Day 42
Mean mMASI -Right Side of Face	7.98±2.94	6.50±3.13	5.19±3.22	4.81±3.25
Mean mMASI -Left side of face	8.02±2.87	6.63±3.11	5.45±3.16	5.12±3.08
Physician Global Assessment -Right Side of Face		2.30±0.95	1.97±1.0	1.5±0.78
Physician Global Assessment -Left Side of Face		2.33±0.92	2.17±1.02	1.70±0.88
Patient Global Assessment -Right Side of Face		2.53±0.94	2.20±0.96	1.77±0.93
Patient Global Assessment -Left Side of Face		2.57±0.89	2.47±0.94	1.97±0.93

DISCUSSION

The underlying pathology of melasma involves a collection of complex mechanisms and therefore, till this day, its treatment remains a challenge. Inventive therapies remain the ultimate objective in the management of melasma. There are several different ways to treat melasma comprising oral and topical drugs, laser and light therapies, chemical peels and micro-needling using various kinds of substances. One such is Tranexamic acid (TXA) which is basically an anti-fibrinolytic agent. TXA inhibits the intracellular synthesis of melanin by means of interrupting the interaction of melanocytes with keratinocytes through the inhibition of the plasminogen/plasmin system. Plasmin has been known to carry melanogenic potential.[11,12]

On the other hand, Vitamin C is a potent antioxidant; it acts as a Reactive Oxygen Species (ROS) scavenger having a wide variety of uses in the treatment of melasma as well as other hyperpigmentation disorders.[13] The act of micro-needling itself induces matrix metalloproteinase which are thought to reduce hyperpigmentation[14] thereby causing a marked decrease in the production of melanin. This improvement was noted in a case series after microneedling.[15]

A study conducted by Ebrahim *et al* evaluated the efficacy of TXA via intra-dermal injection vs TXA via micro-needling. TXA was administered in the form of an intra-dermal injection on one half of the face whereas on the other half, micro needling was used to deliver TXA. Effectiveness of treatment was evaluated through mMASI scores at the baseline and after treatment. There was significant reduction in melasma from baseline in both the sides but greater patient satisfaction was reported on the side treated with micro-needling. Our study illustrated the fact that micro-needling is complimented by the use of both TXA and vitamin C however, TXA was shown to have a slightly expeditious result. No significant side effects occurred in both the studies. Overall, the importance of micro-needling in melasma cannot be denied.[16]

A study comprising 30 women having melasma on the face that was bilaterally symmetrical were studied. In this research, the application of micro needling versus fractional CO_2 laser for administration of TXA was assessed. Patients received six biweekly micro-needling sessions on one half of the face, and CO_2 laser on the other half. TXA was topically applied subsequent to the laser therapy. The mean±SD baseline mMASI showed an average reduction of 57.73% in the side that was treated via micro-needling and a 55.82% decrease in the half that received CO_2 laser therapy.[17] This was almost similar to our study where the mean mMASI showed an improvement of around 60% on the half of the face which received TXA via micro-needling.

In another study, a dermoscopic evaluation was performed on 30 female patients, where right side of the face was treated via micro-needling + TXA and left side via micro-needling + vitamin C for 5 sittings after every two weeks. Noteworthy decrease in dark fine granules was evident bilaterally (p-value < .001), a significant

decrease in homogeneous pigmentation (p-value = .005) as well as pseudo reticular brown network (p-value = .028). Improvement in telangiectasia was observed on the half which received TXA (p = .002). This emphasizes the fact that micro-needling acts as an adjunct to Vitamin-C and TXA and is significantly efficacious in melasma, a finding that is further substantiated by our study.[18] Meanwhile another study compared the effectiveness of transdermal injections of TXA versus vitamin C using Myjet. At the conclusion of their study, it was seen that both the topical agents had a similar efficacy which led to a significant improvement in the mMASI scores when compared to the baseline.[19] Our study depicted a comparable result where the side treated with TXA was found to have a speedy outcome initially however with the passage of time, the difference in results between the sides treated with TXA and vitamin C became indistinguishable.

Limitations of our study are the small sample size and selecting face side randomly. Nonetheless results are useful to contribute to existing body of knowledge.

CONCLUSION

Therefore, we conclude that both Tranexamic acid and Vitamin C are potent therapies in the management of melasma when used in combination with micro-needling and a lot of patients can benefit from these safe therapies.

AUTHORS' CONTRIBUTION

MHR: Conceptualization of idea, Study design, Sample collection, Literature search, Data entry. NI, AAM: Proof reading. AA: Literature search, Discussion, Proof reading. MABH, ST: Drafting of manuscript, Analysis and Interpretation of Data, Derivation of Results, Critical Revision, Grammar check.

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