Original Article

Efficacy of Intradermal Transaxamic Acid in the Treatment of Melasma: A Retrospective Study of Clinical Cases

Aqsa Naheed[1], Tehseen Naveed[3], Aashi Ahmed[2], Nadia Nisar[2], Anwar Bibi[2] and Javeria Hafeez[3]

ABSTRACT

Objective: To evaluate the efficacy of intradermal transaxamic acid in the treatment of melasma.
Study Design: A Retrospective Study
Place and Duration of Study: This study was conducted at the Dermatology Department of CMH hospital, Peshawar from June 2022 to December 2022.
Materials and Methods: Pregnant and lactating mothers, those who had any medical illness, bleeding disorder, on anticoagulant therapy were not included. Injection Tranexamic acid (TA) in a concentration of 4mg/ml of distilled water in insulin syringe was used for mesotherapy. Treatment comprises of 4 session one month apart and mMASI score (Melasma Area and Severity Index) was used to assess the severity of melasma before and one month after the treatment. Side effects were noted. Patient's level of satisfaction was recorded using 4-point scale.
Results: The mean of MASI I score (before treatment) among the study participants was 12.86+5.6 and the mean MASI II after treatment with Tranexamic acid intradermally was 7.36 + 4.6. On applying the paired t test, a statistically significant difference (P= .000) among the MASI score was observed among study participants.
Conclusion: Intradermal Transaxamic acid can be considered as effective and safe treatment modality for melasma to improve patients social and psychological wellbeing.
Key Words: Transaxamic acid, Melasma, MASI score

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INTRODUCTION

Melasma is a patchy discoloration of skin in the form of patches mostly on cheeks, nose and forehead. Skin type III and IV are more likely to develop melasma as compare to type II, also females are more prone to develop it in reproductive age group when compare with males.[1] Unnatural skin colour variation can be frustrating for females, especially in today's digital age. There is always some degree of psychological lurking below so both should be address at the same time.[2]

Melasma is triggered by multiple factors like sunlight, genetic factors and hormonal changes. Pathogenesis of melasma is diverse and has extended beyond the involvement of melanocytes. Histological features showed wide spectral changes from basement membrane disruption, mast cells involvement, neovascularization and changes in keratinocytes.[2]

Treatment of melasma is challenging due to partial understanding of its pathogenesis, long standing course and high recurrence rate.[3] Management plan includes four main targets like suppressing the activity of melanocytes this prevent worsening of melasma. This includes UV light protection and avoidance of triggering factors.[4,5] Topical therapies that prevent new pigment formation like hydroquinone, azelaic acid, retinoid and vitamin C. There are various procedures done to remove melanin pigment like microdermabrasion and chemical peels. Whereas, melanin pigment is scattered by using lasers treatments.[4]

Use of tranexamic acid in the treatment of melasma is a novel concept. However, exact mechanism of action is still not fully understood. TA is a derivative (synthetic) of amino acid lysine, a plasmin inhibitor and fibrinolysis inhibitor used to control bleeding. TA reversibly block lysine-binding sites on plasminogen molecules which inhibits plasminogen activator from transforming plasminogen into plasmin. Plasminogen is also present in the stratum basale of the epidermis. Anti plasmin activity of TA is mainly responsible for

1. Department of Dermatology / Community Medicine[2], HITEC-IMS (Heavy Industry Taxila Education City Institute of Medical Sciences), Taxila.
3. Department of Dermatology, CMH, Peshawar.

Correspondence: Dr. Aqsa Naheed, Professor Dermatology, HITEC-IMS (Heavy Industry Taxila Education City Institute of Medical Sciences, Taxila.
Contact No: 03236513804
Email: aqsanahid@gmail.com

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hypopigmentation It is thought that it causes shrinkage of dermal vasculature and reduce melanin production by decreasing tyrosine kinase activity, alter interaction between melanocytes and keratinocytes. It can be used both orally as well as in topical form. Various studies have been done in this regard.[6]

Efficacy of oral tranexamic acid injection has been reviewed in some studies. A study done in Iran comparing the efficacy of intra dermal TA with topical hydroquinone cream reported significant improvement with 4mg/ml TA as compare to hydroquinone cream.[7] Similarly, another split face study comparison the efficacy of tranexamic acid mesotherapy versus 0.9% normal Saline for melasma done in Pakistan showed excellent response in 60.7% of patients, good in 56.7%, fair in 33.3% and poor in 3.3% of patients. Studies and trials on the use of intradermal injection of TA in the treatment of melasma are limited. Therefore, the main purpose of this study is to evaluate the safety and efficacy of intradermal tranexamic acid in the treatment of melasma.

MATERIALS AND METHODS

This Retrospective cohort study was done in Dermatology Department of CMH Peshawar from June 2022 to December 2022. Sample size was calculated[8]

$$\text{Sample size} = \frac{2SD^2(Z_{a/2} + Z_{\beta})^2}{d^2}$$

Sample size calculated was 41 taking difference in mMASI score 1.83 and Standard deviation 2.94. Anticipating loss to follow up (attrition problem) we enrolled 70 patients in our study, we had complete data of 63 females between 18-50 years with melasma fulfilling the inclusion criteria and willing to participate were consecutively enrolled in the study. Pregnant and lactating mothers or those who used topical treatment for melasma in last 2 months, those who had any medical illness, bleeding disorder, on anticoagulant therapy were not included. All patients were explained the purpose of research, procedure and number of sessions before taking written informed consent.

Each patient was diagnosed and examined by Consultant Dermatologist. Complete history and physical examination was done and noted on a preformed proforma. Color photographs were taken before sessions. mMASI score (Melasma Area and Severity Index) was used to assess the severity of melasma. Its range is 0-24, <8 is considered Mild, 8-16 is Moderate and >16 is Severe.

Injection Tranexamic acid (TA) is available in 5ml ampoule having 500mg of transaxamic acid. In order to prepare a concentration of 4mg/ml, 4 IU of TA /96 IU of distilled water in insulin syringe was used for mesotherapy. Alcohol swab was used for cleaning of face then local anesthetic, Lignocain cream was applied for 35-45 minutes. Injection TA was injected intradermally 1cm apart in the patch of melasma. Sunblock was advised for use at home. Side effects were noted at each visit. We repeated the session after 4 weeks (i.e 0,4,8 and12). mMASI was again calcutated 4 weeks after last session. Patients level of satisfaction at the end of study was noted as, Poor = 0-25%, Fair = 25-50%, Good=50-75%, Excellent =75-100%.

Data was analyzed using Statistical Package for the Social Sciences SPSS Statistics ver.26.0. Categorical data were described in frequencies and percentages while numerical data were analyzed by means and standard deviation. The difference in means of mMasi score before and after the intervention for each patient was analyzed by paired t-test. $P<0.05$ was taken as significant.

RESULTS

Out of total 70 participants of the study, complete data regarding the MASI II scores was obtained from total 63 participants. Therefore, the analysis was performed on total 63 participants of the study. Age of the study participants ranged from 22-48 years. The mean age of the participants was 33.03 years with a standard deviation of 5.8 years (33.03+5.8). Out of total 63 participants, 61 (96.8%) were married and only 2 (3.2%) were unmarried. Skin type III was the most observed type among 58.7% (n=37) participants followed by skin type IV 36.5% (n=23). Only 2 participants (4.8%) had skin type II. The duration of melasma among study participants ranged from 1-18 years. The mean duration of melasma among the study participants was 4.31 years with a standard deviation of 3.4 years. (4.31+3.4).

The range of MASI I score (before starting ITA) among the study participants ranged from 5-23, with a mean score of 12.86 and SD= +5.6. After injecting Tranexamic acid intradermally for treatment of melasma the MASI II score among the study participants lowered to 1-23, with a mean MASI II Score of 7.36 + 4.6. On applying the paired t test to determine the significance of the difference in MASI score after treatment, a statistically significant difference (P= .000) among the MASI score was observed among study participants indicating the effectiveness of intradermal transaxamic acid (ITA) for treatment of melasma.

Table.No. 1: Before and After MASI Score among study participants

SCORE	N	Mean	Std. deviation	P value
MASI I Score	63	12.86	5.69	.000
MASI II Score	63	7.36	4.69	

Regarding the side effects of the treatment, 31.7% (n=20) participants experience no side effect. Erythema was the most experience side effect followed by pain and bleb formation.

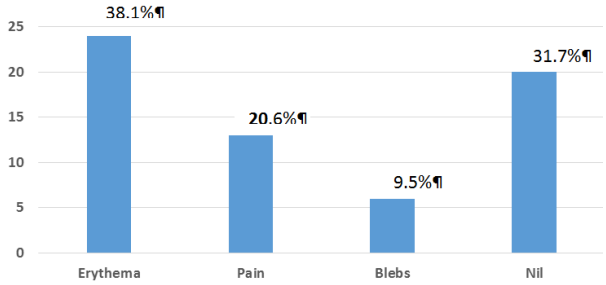

Figure No. 1: Frequency of side effects of intradermal transexamic acid among study participants

Table No. 2: Patients level of satisfaction at the end of study

Patients level of satisfaction	Poor	Fair	Good	Excellent
No. of Patients (N=63)	15 (23.8%)	25 (39.7%)	16 (25.4%)	7 (11.1%)

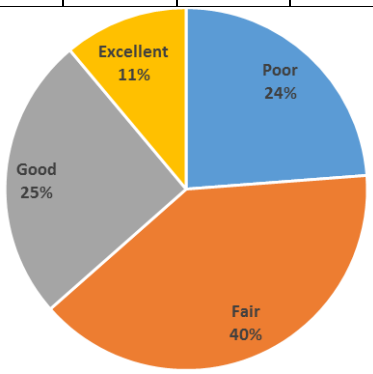

Figure No. 2: Patients level of satisfaction at the end of study

DISCUSSION

Melasma is a common, difficult to treat hypermelanotic condition with a great tendency to relapse. In this study the age of female participants ranged from 22 to 48 years with a mean age of 33.03+5.8. The mean MASI score significantly (P<.0001) reduced from 12.86 + 5.69 to 7.36 + 4.69 after monthly intradermal transexemic acid treatment for 5 months. The study done by Verma YR et al, reported a decrease in the mean MASI score from baseline (week-0) of 8.42±5.63 to 6.71±4.65 at a follow up after 4 weeks. MASI score subsequently reduced to 5.09±3.59 and 3.41±3.06 at the follow up on week 8 and 12 respectively showing a statistically significant reduction from 8th week onwards (p value <0.001).[9] In contrast to the results reposted by Verma YR et al, a statistically significant reduction in MASI score was observed in our study over a long period of time (5 months). This longer duration of treatment to observe significant reduction in MASI score might be due to initial high MASI score of 12.86 + 5.69 in our study as compared to starting MASI score of 8.42±5.63 in study conducted by Verma YR et al.

In a study conducted by Komal S, comparing the efficacy of intradermal tranexamic acid (ITA) with topical 20% azelaic acid in the treatment of melasma the mean age of participants was 34.15 ± 3.64 years. Out of total 58 participants receiving ITA, 54 (93.1%) were married and 4 (6.9%) were un-married. The demographic profile of study participants reported in this study are similar to that of ours. In our study the mean age of study participants was 33.03+5.8 and out of total 63 participants, 61 (96.8%) were married and only 2 (3.2%) were unmarried. The mean duration of illness reported by Komal S, was 3.96 ± 1.93 years, which is much shorter than observed in our study that is 4.31+3.4 years. The mean MASI score in patients receiving ITA before and after 6 weeks of treatment was 7.10 ± 2.94 and 5.27 ± 2.44, respectively reported by Komal S.[12] Contrary to this finding, a decrease in MASI score from12.86 + 5.69 to 7.36 + 4.69 over a period of five months was observed in present study. This can be attributed to difference in disease duration and to low initial MASI scores (7.10 ± 2.94) among the patients enrolled by Komal S as compared to ours where this range of MASI score was achieved at end of five months, starting from a high zero MASI scores at beginning of study.

In our study all 63 participants were female with a mean age of 33.03+5.8 years (range22-48 years). Most frequent skin type was III (58.7%, n=37) followed by skin type IV (36.5%, n=23). Another study was conducted by Samanthula H, among 21 females and 9 males aged 25-40 years having skin type IV or V in India. A statistically significant (p<.001) reduction in mean MASI score from 7.766 to post treatment MASI score of 2.686 was reported after six weeks of treatment.[10] The same study reported the reoccurrence of the melasma showing a rise of mean MASI score from 2.68 to 3.27 after 3 months of follow up. Again, these findings contradict the high initial pretreatment and post treatment MASI scores of our study that was12.86 + 5.69 and 7.36 + 4.69 respectively. However, all the patients experienced pain at injection site and blebs formation that lasted for 3-4 hours after treatment. Inconsistent to this, erythema was the most frequent side effect in our study.

In a study conducted by Muneeb B, including one hundred and seventy participants of both genders with a mean age of 35.46±8.00 years, results showed improvement in melasma after 4 weeks of Intradermal transexemic acid treatment. According to this study effectiveness after treatment for 4 and 8 weeks and 4 to 12 weeks was statistically significant p <0.05. Whereas, the comparison of effectiveness after treatment for 8 and 12 weeks was statistically insignificant (p= 0.06), indicating the reoccurrence of the melasma. Contradictory to our high MASI scores at beginning of

study, the MASI zero score before start of treatment in study by Muneeb B, was 2.73±1.07 at week zero and 1.17±0.82 at week 12 respectively.[11]

CONCLUSION

Intra dermal Transaxamic acid can be considered as effective and safe treatment modality for melasma to improve patients social and psychological wellbeing. Moreover, the administration can be directly observed and so enhances the compliance specially for resistant and chronic melasma not respond to topical creams. Sample size was not large and follow up was short are the limitation of this study. However, studies with large sample size can be done to further evaluate the efficacy of transaxamic acid mesotherapy in the treatment of melasma.

Author's Contribution:

Concept & Design of Study:	Aqsa Naheed
Drafting:	Tehseen Naveed, Aashi Ahmed
Data Analysis:	Nadia Nisar, Anwar Bibi, Javeria Hafeez
Revisiting Critically:	Aqsa Naheed, Tehseen Naveed
Final Approval of version:	Aqsa Naheed

Conflict of Interest: The study has no conflict of interest to declare by any author.

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