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Original Article

Comparison between the efficacies of topical tranexamic acid versus intralesional tranexamic acid in treatment of melasma

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Abstract

Objective Melasma is characterized as grey brown patches of pigmentation on photo exposed areas of body, often requiring a multifaceted approach for its management in refractory. Topical tranexamic acid is commonly used but studies claimed that intralesional injection of tranexamic acid was more efficacious. The objective of the study is to compare the efficacy of tranexamic acid intralesional (localized microinjections) versus topical therapy in the treatment of melasma.

Methods This study involved 72 patients of melasma of both genders between 20-50 years, randomly allocated into two treatment groups. Group-A was given topical TXA while Group-B was treated with intradermal injection of TXA. Efficacy was labeled as ≥50% reduction in baseline MASI score after 12 weeks of treatment.

Results The mean age of the patients was 30.53±8.68 years. There were 13 (18.1%) male and 59 (81.9%) female patients. Majority (n=49, 68.1%) of the patients had Fitz-Patrick Type-V skin phototype. Moderate melasma in 47 (65.3%) patients and severe in 25 (34.7%) patients. Melasma was epidermal in 43 (59.7%) patients while dermal and mixed type was noted in 18.1% and 22.2% patient's respectively. The frequency of efficacy was significantly higher in patients treated with intralesional TXA as compared to topical TXA (66.7% vs. 27.8%; p-value=0.001).

Conclusion Intralesional injection of tranexamic acid was found superior to conventional practice of its topical application in the management of patients with melasma regardless of patient's age, gender, marital and educational status, skin type and type, pattern and severity of disease which along with its well established safety profile and convenience of once-weekly dosage advocate the preferred use of this novel approach in the management of such patients in future dermatologic practice.

Key words
Melasma; Topical; Intralesional; Tranexamic acid.

Introduction

Melasma is characterized as grey brown patches of pigmentation mainly over face on sun exposed parts of body.[1] It is observed as a regular cause of facial melanoses occurring in all ethnic groups and populations, however, epidemiological studies reported higher prevalence in Latin Americans, Middle East and

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Asia.[2] Melasma typically affects Indian population. Dermatology clinics in Southeast Asia regularly encounter 0.25 to 4% patients suffering from melasma. It is reported in 41-61% of Brazilian population. The condition is genetic, familial as common in first degree relatives and identical twin sisters. Melasma usually appears at 20-30 years of age and sometimes at 36-40 years.[3]

Exact cause of melasma is yet to be ascertained. Some contributory factors include hormonal imbalance, OCP use, phototoxic drugs, radiation exposure, cosmetics, thyroid dysfunction and genetic factor. Recently interactions between cutaneous vasculature and melanogenesis have been established.[4-6] Familial occurrence found among 30% cases.[7] Melasma usually presents in three clinical forms: malar (the commonest), centrofacial and mandibular.[8] It generally presents in symmetrical fashion. It could be epidermal, dermal type or mixed type depending upon location of melanin deposition in the skin.[9]

The patients of melasma experience significant emotional challenges and social life upsets as evaluated through quality of life scores.[10] Available treatment options include hydroquinone, sunscreens, topical depigmenting agents,[11,12] lightening agents, dermabrasion, laser[13] and chemical peeling[14] but none of the currently used remedies is a permanent solution. Tranexamic acid is basically a plasmin inhibitor which inhibits plasminogen conversion in basal melanocytes into plasmin by inhibiting plasminogen activator, which is generated by keratinocytes and increase the activity of melanocytes.[15,16]

Tranexamic acid is a newer modality which is observed to improve melasma when injected into skin or used in its oral and topical forms.[17] Atefi *et al*; reported that topical tranexamic acid improved melasma as evaluated by through improved MASI score and patient satisfaction.[18] TXA emulsion had shown upto 80% improvement in the pigmentation as reported by Kondou *et al*.[19]

Similarly Kim *et al*; had also observed brilliant results with 2% topical TXA with significant reduction in modified MASI score and Fontana-Masson staining by reduction in melanin content of epidermis.[20]

Intradermal injection of tranexamic acid was used by Shetty and coworkers and good clinical response was noted and patients were satisfied.[21] Intralesional administration of TXA was reported to be effective way of treatment for melasma with minimum risk of adverse effects for epidermal and mixed type of melasma.[22] A study was undertaken by Steiner and teammates to compare the efficacy and safety of topical versus localized microinjections of TXA, which showed significant improvement in both comparison groups, on objective basis but subjective clinical evaluation revealed superiority of injectable TXA (4 mg/ml) over topical preparation. Hence, TXA is a promising new therapeutic option for melasma.[23]

Numerous studies mostly debated the use of topical or oral tranexamic acid in melasma treatment. The outcome of the topical tranexamic acid is satisfactory in comparison with oral tranexamic acid because of fewer side effects. Tranexamic acid is, so far, cheap and easily available drug so convenient to use for melasma. There are a few studies available worldwide that compared the efficacy of topical tranexamic acid versus intralesional tranexamic acid in the treatment of melasma, therefore, it is pertinent to conduct a study regarding this topic.

Hypothesis

It was constructed as "intralesional tranexamic acid is more efficacious than topical tranexamic acid in the treatment of melasma".

Methods

It was a randomized controlled trial carried out at Department of Dermatology Sir Ganga Ram Hospital, Lahore for a Duration of 6 months with formal permission a from institutional review board on 72 patients (36 patients in each group A & B) were selected by Non-Probability, Consecutive Sampling suffering from Melasma: of epidermal and dermal types diagnosed clinically and through Wood's lamp examination of moderate to severe variety with MASI score >16 were included in the study. Adult patients, both genders, between 20 to 50 years, Fitzpatrick's types 3-5, not on any topical/ systemic treatment for last 3 months were included. While Pregnant or lactating mothers, on hormonal therapy or oral contraceptives, taking any anti-coagulant, history of bleeding disorders, allergic to drug or having any associated medical illness like chronic liver/ kidney disease were excluded. All demographic details were noted on a structured proforma like name, gender, education, socioeconomic and marital statuses. Enrolled patients were given guidance not to apply any other agent for melasma except sunblock SPF 60 every four hourly. Group A was advised to use topical tranexamic acid 5% cream twice daily at home. Group B was called once a week for application of intradermally tranexamic acid 0.05ml (4mg/ml) in each cm square of melasma affected area, after application of topical anaesthesia. A maximum quantity of 2ml was injected to any patient in one session. Patients were assessed for MASI score. Melasma Area and Severity Index (MASI) Score decrease: Calculated as baseline and after 12 weeks of treatment. Post treatment value subtracted from baseline and percentage decrease was calculated as: Baseline MASI-After treatment MASI/ Baseline MASIxl00. Outcome variables were recorded as per operational definition. Efficacy was labeled if the response of tranexamic acid to reduce the MASI score was 50% or more after 12 weeks treatment period. Grading of response: was assessed as shown in **Table 1**.

Table 1 Grading of response.

Grades of response		*Reduction of MASI score*
Go	No response	No reduction
G1	Mild	<25%
G2	Moderate	25%-50%
G3	Good	51 %-75%
G4	Very	Good >75%

All the collected data was entered and analyzed through SPSS version 20.0. Numerical variables i.e. age, MASI score at baseline and follow-up and change and percent reduction in MASI score have been presented by mean±SD. Categorical variables i.e. gender, skin type, marital and educational status and type, pattern and severity of disease and efficacy of treatment have been presented as frequency and percentage. Chi-square test has been applied for comparison of efficacy of treatment between the study groups taking p-value ≤0.05 as statistically significant. Data has been stratified for age, gender, skin type, marital and educational status and type, pattern and severity of disease to address effect modifiers and post-stratification chi-square test has been applied taking p-value ≤0.05 as statistically significant.

Results

The age of the patients ranged from 20 years to 50 years with a mean of 30.53±8.68 years. There were 13 (18.1%) male and 59 (81.9%) female patients with a male to female ratio of 1:4.5. 16 (22.2%) patients were unmarried. 17 (23.6%) patients were illiterate, 33 (45.8%) patients were under matric and 22 (30.6%) patients had matriculation or above degree. Majority (n=49, 68.1%) of the patients had Fitz-Patrick Type-V skin phototype while 23 (31.9%) patient had Type-IV phototype skin. It was moderate melasma in 47 (65.3%) patients and severe in 25 (34.7%) patients. Melasma was epidermal in 43

(59.7%) patients while dermal and mixed type was noted in 18.1% and 22.2% patients respectively. The disease pattern was centrofacial in 29 (40.3%) patients followed by mandibular (36.1%) and malar (23.6%) patterns .Both the study groups were comparable in terms of mean age (p-value=0.936) and distribution of various groups based on patient's age (p-value=0.800), gender (p-value=0.759), marital status (p-value=0.571), educational status (p-value=0.956), skin phototype (p-value=0.800), type (p-value=0.839), pattern (p-value=0.954) and severity (p-value=0.804) of melasma as shown in **Table 1**. The mean MASI score was comparable in patients receiving injections versus topical TXA at baseline (27.75±9.07 vs. 27.86±9.79; p-value=0.960).

Table 1 Baseline Characteristics of Study Groups.

Characteristics	*Intralesional TXA n=36*	*Topical TXA n=36*	*P-value*
Age (years)	30.44±7.91	30.61±9.49	0.936
20-34 years	25 (69.4%)	24 (66.7%)	0.800
35-50 years	11 (30.6%)	12 (33.3%)	
Gender			
Male	6 (16.7%)	7 (19.4%)	0.759
Female	30 (83.3%)	29 (80.6%)	
Marital Status			
Un-Married	9 (25.0%)	7 (19.4%)	0.571
Married	27 (75.0%)	29 (80.6%)	
Educational Status			
Illiterate	9 (25.0%)	8 (22.2%)	
Under Matric	16 (44.4%)	17 (47.2%)	0.956
Matric and above	11 (30.6%)	11 (30.6%)	
Skin Phototype			
Fitz-Patrick IV	12 (33.3%)	11 (30.6%)	0.800
Fitz-Patrick V	24 (66.7%)	25 (69.4%)	
Severity of Melasma			
Moderate	24 (66.7%)	23 (63.9%)	0.804
Severe	12 (33.3%)	13 (36.1%)	
Type of Melasma			
Epidermal	21 (58.3%)	22 (61.1%)	
Dermal	6 (16.7%)	7 (19.4%)	0.839
Mixed	9 (25.0%)	7 (19.4%)	
Pattern of Melasma			
Centrofacial	15 (41.7%)	14 (38.9%)	
Malar	8 (22.2%)	9 (25.0%)	0.954
Mandibular	13 (36.1%)	13 (36.1%)	

Chi-square test and Independent sample t-test, observed difference was statistically insignificant

Table 2 Comparison of efficacy between the study groups.

Efficacy	*Intralesional TXA n=36*	*Topical TXA n=36*	*P-value*
Yes	24 (66.7%)	10 (27.8%)	0.001*
No	12 (33.3%)	26 (72.2%)	
Total	36 (100.0%)	36 (100.0%)	

*Chi-square test, * observed difference was statistically significant*

The mean MASI score decreased significantly from baseline in both the groups; TXA injections (27.75±9.07 to 11.03±5.29; p-value<0.001) and topical TXA (27.86±9.79 to 14.95±7.03; p-value<0.001). The follow-up mean MASI score was significantly lower in patients receiving injections versus topical TXA (11.03±5.29 vs. 14.95±7.03; p-value=0.009). The mean change in MASI score (16.72±7.85 vs. 12.92±4.52; p-value=0.014) and mean of percent reduction in MASI score (59.67±15.46 vs. 47.81±12.78%; p-value=0.001) were significantly higher in patients receiving injections versus topical TXA. Treatment was effective in 34 (47.2%) patients. The frequency of efficacy was significantly higher in patients treated with intralesional TXA as compared to topical TXA (66.7% vs. 27.8%; p-value=0.001) **Table 2**. Similar variations were recorded among the groups and across various subgroups based on patient's age, gender, skin type, marital and educational status and type, pattern and severity of disease **Table 3.**

Discussion

Melasma is an acquired pigmentation disorder mainly over sunexpoed areas.[1] Among all available options, treatment remains challenging.[1,2,7]

Tranexamic acid (TXA), is a plasminogen activator inhibitor.[11,16] Tyrosinase activity is reduced and it results in reduction of melasma, ultraviolet‑induced hyperpigmentation, and other post-inflammatory hyperpigmentation.[16]

Table 3 Comparison of efficacy between the study groups across various subgroups.

Subgroups	*Efficacy of Treatment (%)*		*P-value*
	Intralesional TXA n=36	*Topical TXA n=36*	
Age (years)			
20-34 years	17/25 (68.0%)	8/24 (33.3%)	0.015*
35-50 years	7/11 (63.6%)	2/12 (16.7%)	0.021*
Gender			
Male	4/6 (66.7%)	2/7 (28.6%)	0.170
Female	20/30 (66.7%)	8/29 (27.6%)	0.003*
Marital Status			
Un-Married	6/9 (66.7%)	2/7 (28.6%)	0.131*
Married	18/27 (66.7%)	8/29 (27.6%)	0.003*
Educational Status			
Illiterate	6/9 (66.7%)	2/8 (25.0%)	0.086
Under Matric	11/16 (68.8%)	5/17 (29.4%)	0.024*
Matric and above	7/11 (63.6%)	3/11 (27.3%)	0.087
Skin Phototype			
Fitz-Patrick IV	8/12 (66.7%)	3/11 (27.3%)	0.059
Fitz-Patrick V	16/24 (66.7%)	7/25 (28.0%)	0.007*
Severity of Melasma			
Moderate	17/24 (70.8%)	7/23 (30.4%)	0.006*
Severe	7/12 (58.3%)	3/13 (23.1%)	0.072
Type of Melasma			
Epidermal	14/21 (66.7%)	6/22 (27.3%)	0.010*
Dermal	4/6 (66.7%)	2/7 (28.6%)	0.170
Mixed	6/9 (66.7%)	2/7 (28.6%)	0.131
Pattern of Melasma			
Centrofacial	10/15 (66.7%)	4/14 (28.6%)	0.040*
Malar	5/8 (62.5%)	2/9 (22.2%)	0.092
Mandibular	9/13 (69.2%)	4/13 (30.8%)	0.050*

*Chi-square test, * observed difference was statistically significant*.

Multiple routes of administration and dosages of TXA have been trialed with topical route being more convenient for patient to apply.[18-23] Intralesional injection (microinjections) of tranexamic acid are relatively newer and being claimed more efficacious.[23]

In the present study, among 72 patients the mean age of the patients was 30.53±8.68 years which is similar to the observation of Ejaz *et al*., (30.4±5.8) at Combined Military Hospital, Karachi.[24] and Aman *et al*., (30.4±9.2) at Services Hospital, Lahore.[25] While Ali *et al*; had observed relatively younger (29.9±4.2) patients of melasma it to be at Mayo Hospital, Lahore.[26] Likewise Desale *et al*; (28.8±6.5) had noted the same mean age among their Indian patients.[27] Melasma is more common in female as evident from our study results (1:4.5 male to female) and Ejaz *et al*; also noted same 1:5.8.[23] Divya *et al*;[28] (1:6.3) and Desale *et al*;[27] (1:7.3) had noted female predominance even in higher ratios. A similar trend was noted in Nepalese population (1:5.8) by Kakru.[29]

We had classified our study population according to Fitzpatrick skin phototype and majority (68.1%) of the patients had Type-V and rest had 31.9% Type-IV (31.9%) skin. Similarly Bari *et al*; had noted Type-IV(25.0%) and Type-V (75.0%) skin at Military Hospital, Rawalpindi.[30] While Ejaz *et al*. reported even higher percentage of Type-V (80.7%) than Type-IV (19.3%) in local population.[24] Budamakuntla *et al*; in Indian patients reported Type-IV 36.7% and Type-V 63.3% melasma

patients.[31] We suggest that over all the majority skin phototype in our region is type V and these people suffer from melasma more than other skin phototypes.

According to type of melasma, we had observed epidermal type in 43 (59.7%) patients while dermal and mixed type were noted in 18.1% and 22.2% patient's respectively. Again the most common type was epidermal (61.5%) as seen by Aamir *et al*; than dermal (15.5%) and mixed (23.0%) at Sheikh Zayed Hospital, Lahore.[8] In Nepalese patients Kakru *et al*; observed the same frequency with majority falling into epidermal (61.2%) category as compared to dermal (16.6%) and mixed (22.2%) variety.[29]

The most common pattern of melasma we had observed was centrofacial in 29 (40.3%) patients followed by mandibular (36.1%) and malar (23.6%) patterns. This is in line with observations of many like Amir *et al*., who reported centrofacial (43.7%) being the commonest at Mayo Hospital, Lahore.[8] And in Indian patients also centrofacial (41.7%) was the commonest pattern as compared to mandibular (31.6%) and malar (26.7%) melasma.[30] In Nepalese patients Kakru *et al*., again noted centrofacial (51.1%) pattern being the commonest.[29]

We observed that the frequency of efficacy was significantly higher in patients treated with intralesional TXA as compared to topical TXA (66.7% vs. 27.8%; p-value=0.001). This higher efficacy when stratified among various subgroups like patient's age, gender, skin type, marital and educational status and type, pattern and severity of disease, efficacy was higher in patients who received intralesional TXA. Our results are in line with the previously published research where Steiner *et al*. (2009) also observed similar significantly higher efficacy of intralesional injection of TXA (66.7% vs. 12.5%; p-value <0.05) as compared to conventional practice of topical application.[23]

The present study is first of its kind in local population and adds to the limited already published international research evidence on the topic. A very strong limitation to the present study was that we didn't compare various side effects between the two approaches particularly hemorrhage and disturbance of coagulation profile as well as patients convenience and satisfaction which are very important concern in dermatological practice and reason for poor patient's compliance and treatment drop outs. Such a study is highly recommended in future research.

Conclusion

In the present study, intralesional injection of tranexamic acid was found superior to conventional practice of its topical application in the management of patients and convenience of once-weekly dosage advocate the preferred use of this novel approach in the management of such patients in future dermatologic practice.

References

1. A review of treatments for melasma, British Journal of Dermatology, Volume 187, Issue 3, 1 September 2022, Page e135, https://doi.org/10.1111/bjd.21725
2. Christopher EM. Griffith's MD Acquired pigmentary disorders, melasma, Rook's textbook of Dermatology, 9th edition. 2016; 88: 10-12.
3. Majid I, Aleem S, Melasma: Update on Epedemiology, Clinical Presentation, Assesment, and Scoring. *J Skin Stem Cell*. 2021;**8(4)**:e120283. doi: 10.5812/jssc.120283
4. Espósito ACC, Cassiano DP, da Silva CN, Lima PB, Dias JAF, Hassun K, Bagatin E, Miot LDB, Miot HA. Update on Melasma-Part I: Pathogenesis. *Dermatol Ther (Heidelb)*. 2022;**12(9)**:1967-88. doi: 10.1007/s13555-022-00779-x. Epub 2022

Jul 29. PMID: 35904706; PMCID: PMC9464278.
5. Kim EH, Kim YC, Lee ES, Kang HY. The vascular characteristics of melasma. *J Dermatol Sci*. 2007;**46(2)**:111-6.
6. Aishwarya K, Bhagwat PV, John N. Current concepts in melasma - A review article. *J Skin Sex Transm Dis*. 2020;**2(1)**:13-7.
7. Aamir S, Naseem R. Oral tranexamic acid in treatment of melasma in Pakistani population: a pilot study. *J Pak Assoc Dermatol*. 2014;**24(3)**:198-203.
8. Sarkar SK, Sen KG, Mostofa MK, Das AR, Saha SK, Islam MS. The role of triple combination topical agents in the treatment of facial melasma. *Faridpur Med Coll J*. 2017;**12(2)**:68-70.
9. Freitag FM, Cestari TF, Leopoldo LR, Paludo P. Boza JC. Effect of melasma on quality of life in a sample of women living in southern Brazil. *J Eur Acad Dermatol Venereol*. 2008;**22**:655-62.
10. Gupta AK, Gover MD, Nouri K, Taylor S. The treatment of melasma: a review of clinical trials. *J Am Acad Dermatol*. 2006;**55**:1048-65.
11. Bentley-Phillips B, Bayles MA. Cutaneous reactions to topical application of hydroquinone. Results of a 6-year investigation. *S Afr Med J*. 1975;**49**:1391-5.
12. Li YH, Chen JZ, Wei HC, Wu Y, Liu M, Xu YY, *et al*. Efficacy and safety of intense pulsed light in treatment of melasma in Chinese patients. *Dermatol Surg*. 2008;**34**:693-700.
13. Hurley ME, Guervara IL, Gonzales RM, Pandya AG. Efficacy of glycolic acid peels in the treatment of melasma. *Arch Dermatol*. 2002;**138**:1578-82.
14. Lee JH, Park JG, Lim SH, Kim JY, Ahn KY, Kim MY, *et al*. Localized intradermal microinjection of tranexamic acid for treatment of melasma in Asian patients: a preliminary clinical trial. *Dermatol Surg*. 2006;**32**:626-31.
15. Maeda K, Tomita Y. Mechanism of the inhibitory effect of tranexamic acid in melanogenesis in cultured human melanocytes in the presence of keratinocytes-conditioned medium. *J Health Sci*. 2007;**53(4)**:389-96.
16. Khurana VK, Misri RR, Agarwal S, Thole AV, Kumar S, Anand T. A randomized, open-label, comparative study of oral tranexamic acid and tranexamic acid microinjections in patients with melasma. *Indian J Dermatol Venereol Leprol*. 2019;**85**:39-43.
17. Atefi N, Dalvand B, Ghassemi M, Mehran G, Hevdarian A. Therapeutic effects of topical tranexamic acid in comparison with hydroquinone in treatment of women with melasma. *Dermatol Ther*. 2017;**7(3)**:417-24.
18. Kondou S, Okada Y, Tomita Y. Clinical study of effect of tranexamic acid emulsion on melasma and freckles. *Skin Res*. 2007;**6**:309-15.
19. Kim S J, Park JY, Kang HY. Efficacy and possible mechanism of topical tranexamic acid in melasma. *Clin Exp Dermatol*. 2016;**41(5)**:1-9.
20. Shetty VH, Shetty M. Comparative study of localized intradermal microinjection of tranexamic acid and oral tranexamic acid for the treatment of melasma. *Int J Res Dermatol*. 2018;**4**:363-7.
21. Veggalam V, Perumalla N. Intralesional tranexamic acid: safe and effective way of treatment for melasma. *Indian J Drugs Dermatol*. 2017;**3**:81-3.
22. Steiner D, Feola C, Bialeski N, de Morais e Silva FA, Antiori ACP, Addor FASA, *et al*. Study evaluating the efficacy of topical and injected tranexamic acid in treatment of melasma. *Surg Cosmet Dermatol*. 2009;**1(4)**:174-7.
23. Ejaz A, Raza N, Iftikhar N, Muzzafar F. Comparison of 30% salicylic acid with Jessner's solution for superficial chemical peeling in epidermal melasma. *J Coll Physicians Surg Pak*. 2008;18:205-8.
24. Aman S, Nadeem M, Mahmood K, Ghafoor MB. Pattern of skin diseases among patients attending a tertiary care hospital in Lahore, Pakistan. *J Taibah Uni Med Sci*. 2017;**12(5)**:392-6.
25. Ali R, Aman S, Nadeem M, Kazmi AH. Quality of life in patients of melasma. *J Pak Assoc Dermatol*. 2013;**23(2)**:143-8.
26. SDesale SP, Gugle AS, Kote R, Jadhav VM. Comparative study of efficacy of glycolic acid peel and intense pulsed light in the treatment of melasma. *MVP J Med Sci*. 2015;**2(1)**:39-48.
27. Divya KG, Narasimhan M, Rajagopalan V, Parveen B. Efficacy and safety of 70% glycolic acid versus q switched ND: YAG laser in the treatment of melasma: a comparative study. *Int J Res Dermatol*. 2017;**3(1)**:1-6.

28. Kakru SN, Raihan M, Beg MA, Kakroo B. Efficacy of oral tranexamic acid in the treatment of melasma: a pilot study. *Int Arch BioMed Clin Res*. 2017;**3(4)**:93-6.
29. Bari AU, Iqbal Z, Rahman SB. Tolerance and safety of superficial chemical peeling with salicylic acid in various facial dermatoses. *Indian J Dermatol Venereol Leprol*. 2005;**71(2)**:87-90.
30. Budamakuntla L, Loganathan E, Suresh D, Shanmugam S, Dongare A, Prabhu N, *et al*. A randomised, open-label, comparative study of tranexamic acid microinjections and tranexamic acid with microneedling in patients with melasma. *J Cutan Aesthet Surg*. 2013;**6(3)**:139.