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COMPARATIVE EVALUATION OF MICRONEEDLING WITH MESO SOLUTION VERSUS MICRONEEDLING ALONE IN TREATMENT OF RECALCITRANT MELASMA: A SPLIT FACE STUDY.

Dermatology

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ABSTRACT

Melasma is a common yet difficult condition to treat. In current study, we compared the efficacy and safety of microneedling with mesosolution (glutathione, ascorbic acid and pyruvic acid) and microneedling alone in fifty cases of recalcitrant melasma. The sides of face were randomly assigned to Side A and B. On Side A, only microneedling was done and over side B, patients were treated with microneedling along with mesosolution. On side A, mean percentage reduction in MASI score from baseline was 17.81%, 22.01% and 19.58 % at 4, 12 and 20 weeks respectively. While on side B, there was 23.98%, 33.98% and 34.22% reduction (p value = 0.001). Addition of mesosolution along with microneedling resulted in significantly superior results.

KEYWORDS

Recalcitrant melasma, microneedling, mesotherapy, MASI score

INTRODUCTION

Melasma is a term derived from the Greek word "melas" meaning black. It is an acquired pigmentary disorder characterized by more or less symmetrically distributed, medium to dark brown macules with well defined geographic borders, affecting sun exposed areas.[1] It is frequently seen in women in third and fourth decade, especially in Asians. The development of melasma is multifactorial, and the exact etiology is not clear. It's triggering can be attributed to various factors like ultraviolet radiation (UVR), pregnancy, oral contraceptive pills (OCPs), cosmetics application, use of photosensitizing drugs, hormone replacement therapy (HRT), stress, different procedures and inflammatory reactions of the skin.[2,3]

The aim of treatment is to target melanocytes activity, proliferation, associated signalling pathways, and tissue damage due to photoaging.[4] The transdermal delivery of active agents helps to achieve effective stratum corneum layer permeability and enhance penetration of topical agents. Various methods have been used in the past. Recently, microneedling (MN) has been proposed as a new physical method to enhance transdermal drug delivery.[5] In the present study we compared the efficacy of MN with mesosolution (MS) (glutathione 20%, ascorbic acid 10% and pyruvic acid 10%) and MN alone in cases of recalcitrant melasma in a split face design.

MATERIALS AND METHODS

Fifty patients of recalcitrant melasma were enrolled from the Out Patient Department of Skin and STD Department, Government Medical College, Amritsar, after approval from the Institutional Ethics Committee.

Inclusion Criteria:

- Adults between 18 and 60 years of age with moderate to severe recalcitrant melasma that is more than five year of evolution and relapses to more than three attempts to treatment.

Exclusion Criteria:

- Presence of active skin infections or inflammatory dermatoses. Patients on immunosuppressive therapy or oral contraceptives.
- Pregnancy and lactation.
- History of keloid scarring, diabetes, bleeding disorder, collagen vascular disease, anticoagulant therapy, presence of skin cancers, solar keratosis.

PROCEDURE:

Patients with recalcitrant facial melasma were enrolled after clinical & baseline assessment. Dermoscopic and Wood's lamp examination was done to classify the type of melasma (epidermal, dermal, or mixed). A pre-informed written consent was taken and recorded before the study. In each patient, the sides of face were randomly assigned to Side A or Side B. On Side A, only microneedling was done and over side B, patients were treated with combined microneedling and mesosolution. Mesosolution is available in 10 ml vial containing Glutahione 20%, Ascorbic acid 10% and Pyruvic acid 10%. 0.5 to 1 ml of the solution was used in each session. After gentle cleansing, topical EMLA cream was applied to lesional areas under occlusion for 45 to 60 minutes. On side A, skin was stretched with one hand and microneedling was done with dermapen with needle depth of 1-2 mm with the other hand until the uniform pin-point bleeding point appears. Similar steps were followed over side B and after microneedling, the mesosolution was poured over the area and the procedure was repeated. Patients were instructed to follow strict photo protective measures. The procedure was done thrice at monthly intervals (0, 4 and 8 weeks) and patients were followed up for further 3 months. MASI score, physician global assessment (PGA), and patient global assessment (PtGA) were calculated at baseline, 4th, 8th, 12th, 16th and 20th week to assess clinical response.[6] Any adverse events and complications were recorded.

The data was filed and processed using Microsoft Excel software, 2007 version. The statistical analysis was performed using IBM SPSS Statistics version 22.0. Descriptive analysis was used for the baseline characteristics. Difference between the sides was analysed using chi square and t – test. A □-value less than 0.05 was considered to be statistically significant.

RESULTS

The results were collected; tabulated (Table1-3) and following conclusions were made.

Table 1 : Table showing age and sex wise distribution of cases

Age group (years)	*Number of cases*		
	Male (%)	*Female (%)*	*Total (%)*
<30	6 (100%)	13 (29.55%)	19 (38%)
31-40	0	22 (50%)	22(44%)
41-50	0	9 (20.45%)	9(18%)
Total	6 (100%)	44 (100%)	50(100%)

Table 2 : Table showing demographic data and predisposing factors

Characteristics	*Summary Statistics*	
Marital status	Married	34 (68%)
	Unmarried	16 (32%)
Occupation	Homemaker	29 (58%)
	Indoor workers	14 (28%)
	Unemployed and students	7 (14%)
Family history	Present	18 (36%)
	Absent	32 (64%)
History in previous pregnancy	Present	17 (34%)
	Absent	18 (36%);NA =15 (30%)

Use of cosmetics	Present	28 (56%)
	Absent	22 (44%)
Use of home remedies/ any oil etc	Present	2 (4%)
	Absent	48 (96%)
Features of hormonal imbalance	Present	9 (18%)
	Absent	41 (82%)
Drugs	Present	10 (20%)
	Absent	40 (80%)
Anaemia	Present	25 (50%)
	Absent	25 (50%)
Sun exposure (hours/day)	None or mild (0-2)	44 (88%)
	Moderate (2-4)	5 (10%)
	Severe (4-6)	1 (2%)
Fitzpatrick Skin Type	III	9 (18%)
	IV	38 (76%)
	V	3 (6%)

Table 3 : Table showing specific characteristics of melasma

Age of patient at the onset of disease (years)	≤20	6 (12%)
	20-30	30 (60%)
	31-40	11 (22%)
	>40	3 (6%)
Seasonal variation	Summer	19 (38%)
	Winter	7 (14%)
	None	24 (48%)
Color of pigmentation	Light brown	19 (38%)
	Dark brown	17 (34%)
	Mixed	14 (28%)
Pattern of pigmentation	Uniform	15 (30%)
	Non uniform	35 (70%)
Progression of disease	Progressive	29 (58%)
	Non progressive	21 (42%)
Clinical pattern	Centrofacial	29 (58%)
	Malar	20 (40%)
	Mandibular	1 (2%)

MASI score

The mean MASI scores of side A and B at baseline were 5.088 (± 2.353) and 4.980 (± 2.384). No significant difference was noted (p value = 0.344). The mean MASI score of side A at the end of 4, 8, 12, 16 and 20 weeks was 4.182 (±2.323), 4.026(±2.321), 3.968(±2.253), 4.062(±2.432) and 4.092(±2.428). The mean MASI score on side B at the end of 4, 8, 12, 16 and 20 weeks was 3.786 (±2.119), 3.246(±2.099), 3.288(±2.177), 3.276(±2.177) and 3.276(±2.177). On side A, statistically significant reduction in MASI score in comparison to baseline value was noted from 8 weeks while on side B, it was seen from 4 weeks onwards (p value <0.0 5). (Figure 1)

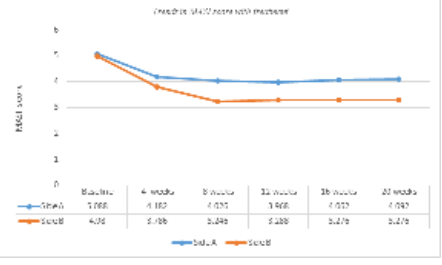

Figure 1 : Graph showing trends in MASI score with treatment

Statistically significant difference in grades of therapeutic improvement was noted between both the sides (p= 0.003). (Figure 2)

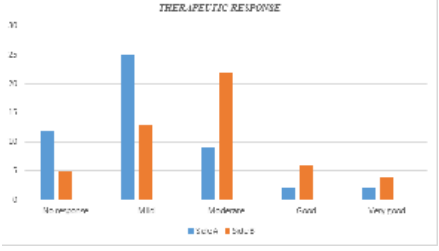

Figure 2 : Graph showing therapeutic response

Patient global assessment score is the improvement of hyperpig mentation on visual analogue scale from 0 to 10 with 0 as no improvement and 10 as the best possible improvement. In our study, mean PGA was 3.800 ± 1.678 after 4 weeks of treatment which increased to 4.600 ± 2.356 at the end of follow up period (20 weeks) (p=0.932). The mean Physician global assessment score was 3.920 ± 0.396 after 4 weeks of treatment which increased to 3.720±0.858 at the end of follow up period (20 weeks). Mild to moderate clearance was seen on global assessment of lesions on both sides. There was no significant difference when compared with baseline (p=1.000).

Burning was the most common complaint experienced by 48 (96%) cases followed by redness in 46 (92%) cases. However, these side effects were tolerable and subsided within 24-48 hours period in all the patients. Post inflammatory hyperpigmentation (PIH) was seen in 4 (8%) of the study cases who belonged to FST V (1), IV (2) and III (1). Hence, both the sides i.e. microneedling alone and combined microneedling with meso solution (containing Glutahione 20%, Ascorbic acid 10% and Pyruvic acid 10%) showed significant improvement in MASI score with minimal side effects.

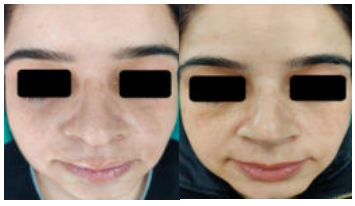

Figure 3 (A & B) : Photo of patient at baseline & at 20 weeks (Side A = Left ; Side B = Right)

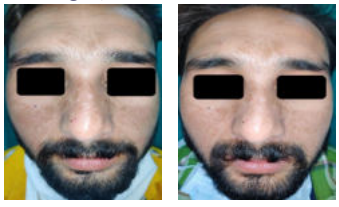

Figure 4 (A & B): Photo of patient at baseline & at 20 weeks (Side A = Right ; Side B = Left)

DISCUSSION

Management of melasma, often requires toilsome effort, attributed to its chronic and relapsing nature. Multiple treatment options are available, which includes topical, oral, procedural, and combination therapy. Despite the availability of a huge number of depigmenting agents, the treatment of melasma is long and complicated, mainly due to ineffective penetration of these agents. Indeed, the stratum corneum, is the main obstacle to the drugs' percutaneous absorption because its barrier function significantly restricts the drugs' transdermal delivery.[5] Transdermal delivery of active substances, has come out to be an advanced approach in treatment of various skin conditions. Recently, many techniques have been developed to enhance skin penetration of topical agents, like electroporation, sonophoresis, and iontophoresis, among others. Skin microneedling has been introduced as a new physical method to improve transdermal delivery of agents. Mesotherapy is a non-surgical technique of drug delivery that uses multiple microinjections of minute doses of a mixture of compounds, injected in a minimally invasive way.[7]

Microneedling offers a minimally invasive and painless route of drug delivery. This method involves the creation of micron-sized channels in the skin, thus allowing the passage of a variety of therapeutic molecules which would not otherwise cross the intact skin.[8] Based on the literature, it has been considered for multiple indications such as a delivery system for active principles in rejuvenation, as an isolated stimulus in the rejuvenation of the face, improving colour, texture, and brightness of the skin in wrinkles, acne scars and post burn scars.

There is lack of evidence on the exact mechanism of skin lightening by microneedling itself. It has been proposed that microneedling can restore upper dermal and basal membrane damage in melasma by stimulating proliferation of fibroblasts and dermal collagenesis, disfavouring the contact of melanocytes with melanogenic stimuli released from dermis such as endothelin, stem cell factor and hepatocyte growth factor. Thick epidermis can also provide additional protection from UVR.[9,10]

Glutathione as a depigmenting agent has been used recently in topical, oral as well as intravenous forms. There are limited published studies about effect and method of glutathione use for melasma treatment. Vitamin C is widely used for the treatment of melasma due to its anti melanogenic property. But topical vitamin C has limited stability, permeability, and may cause irritation and allergy. It is frequently used in mesotherapy formulations but there is lack of data on the efficacy and safety of vitamin C mesotherapy for the treatment for melasma. PA was also found to be an effective and safe peeling agent that can improve skin texture and skin colour and hyperpigmented lesions. Above mentioned agents have been used in past either individually or with other chemicals.[11-15] But, the studies conducted on the efficacy and safety of these agents in mesotherapy are few. And, no study had been done to compare results of microneedling with mesosolution (glutathione 20%, ascorbic acid 10% and pyruvic acid 10%) and microneedling alone in cases of recalcitrant melasma to the best of our knowledge.

The age of the 50 study cases ranged from 22-50 years with majority of the cases i.e. 22 (44%) from 31-40 years of age group. This may be due to the fact that young people are more involved in outdoor activities. Further, pregnancy and the usage of OCP are likely in the reproductive age group (18-45 years). The female to male ratio was approximately 7.3 : 1, thus showing the preponderance of females over males. Gender difference has been reported in incidence of hyperpigmentary disorders.[16-18] In our study, that 36 (68%) cases were married, while 16 (32%) of them were unmarried indicating higher incidence of melasma in married subjects. This may be attributed to the role of hormonal influences, pregnancy, use of oral contraceptives in the etiopathogenesis of melasma.[19] Even though sun exposure aggravates melasma, housewives who do not have much photo exposure constituted a majority i.e. 29 (58%) of our patients which probably indicates the importance of a hormonal influence in the etiology of melasma. Another explanation for higher prevalence of melasma in females engaged in household work could be due to exposure to chronic infrared radiations by working in front of gas/stove which can act as an aggravating factor. Since most of the cases in our study were housewives and maximum i.e. 44 (88%) reported only mild sun exposure. So, factors other than sunlight must be responsible for the disease in our study cases.

On side A, statistically significant reduction in MASI score in comparison to baseline value was noted from eight weeks (p value = 0.025) onwards. While on side B, it was noted from four weeks (p value = 0.001) onwards. The mean percentage reduction in MASI score from baseline on side A was 17.81% , 22.01% and 19.58 % at 4, 12 and 20 weeks respectively. Whereas on side B, there was 23.98%, 33.98% and 34.22% reduction at 4, 12 and 20 weeks respectively. There was statistically significant difference in percentage reduction in MASI score between the two sides when compared (p value = 0.001). Our findings on side A, showed consistency with study by Lima et al (2017), in which they showed that Microneedling alone, without the addition of any active medication resulted in lightening of skin lesions in cases of recalcitrant melasma. There was significant reduction of MASI score (-70%) after two sessions of microneedling ($p < 0.03$).[10] Though microneedling achieved significant reduction in MASI score but percentage reduction in MASI score was higher on side B as compared to side A in our study.

Similarly in other studies, better outcomes were noticed with mesotherapy. In a study by Fabbrocini G et al (2011), reduction in the baseline mean MASI score was more in the microneedling + serum group (9.9 points) as compared to serum only group (7.1 Points) 2 months post treatment.[20] Balevi et al in 2017 reported decrease in MASI score by 68.11% in group A (SA peel and vitamin c mesotherapy) and 13.17% in group B (SA peel). This study showed that the effect of SA peel was increased when combined with vitamin C mesotherapy.[21]

In a split face study by Iraji et al in 2018, showed appropriate outcomes with use of combination mesotherapy in treatment of melasma irrespective of type of agents used. However, glutathione containing cocktail (TA 4 mg/mL; vitamin C 3% and glutathione 2%) showed significantly more reduction (1.28 ± 0.64) of mMASI score as compared to cocktail containing tranexamic acid and vitamin C without glutathione.[22] Similar results were seen also seen in a study by Puri et al (2020) on efficacy of mesotherapy using glutathione and vitamin C, where the author noticed 42.38% and 53.84% reduction in MASI score at 12 weeks and 6 months of treatment respectively.[23]

Although asymptomatic, melasma negatively impacts the quality of life and self esteem of the affected individuals. The results of previous studies are difficult to compare due to the use of different modalities and agents in the evaluation of efficacy of mesotherapy in melasma.

CONCLUSION

Comparison of two sides showed that addition of mesosolution on side B along with microneedling resulted in significant superior results than what was seen on side A. Therefore, we suggest that combining mesotherapy with microneedling is better and effective approach than microneedling alone in the treatment of melasma. Microneedling is safe, office based procedure with mild adverse effects and minimal or no downtime.

However, further research with a larger sample size is required to identify the ideal modality, agent, formulation, and duration of therapy to treat melasma effectively.

LIMITATIONS OF THE STUDY

- It was not a blinded study.
- The study did not include controls.
- There is a possibility of observer's bias as MASI score is a subjective assessment tool.

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CONFLICTS OF INTEREST: Nil.

REFERENCES

1. Bandyopadhyay, D. (2009). Topical treatment of melasma. *Indian J Dermatol*, 54, 303-309.
2. Ogbechie-Godec, O. A., & Elbuluk, N. (2017). Melasma: an Up-to-Date Comprehensive Review. *Dermatology and therapy*, *7*(3), 305–318.
3. Miot, L. D., Miot, H. A., Silva, M. G., & Marques, M. E. (2009). Fisiopatologia do melasma [Physiopathology of melasma]. *Anais brasileiros de dermatologia*, *84*(6), 623–635.
4. Sarkar, R., Bansal, A., Ailawadi, P. (2020). Future therapies in melasma: What lies ahead? *Indian J Dermatol Venereol Leprol*, 86, 8-17.
5. Konda, D., Thappa, D. M. (2013) Mesotherapy: What is new? *Indian J Dermatol Venereol Leprol,* 79, 127-134.
6. Pandya, A., Berneburg, M., Ortonne, J. P., Picardo, M. (2006) Guidelines for clinical trials in melasma: Pigmentation disorders academy. *Br J Dermatol*, 156, 21-28.
7. Vedamurthy, M. (2007) Mesotherapy. *Indian J Dermatol Venereol Leprol*, 73, 60-62.
8. Singh, A., Yadav, S. (2016) Microneedling: Advances and widening horizons. *Indian Dermatol Online J*, 7(4), 244-54.
9. Lima, E.V. & Lima, M. & Takano, D.. (2013). Microneedling experimental study and classification of the resulting injury. Surgical and Cosmetic Dermatology. 5. 110-114.
10. Lima, E.V.A., Lima, M.M.D.A., Paixão, M.P. Miot, H. A. (2017). Assessment of the effects of skin microneedling as adjuvant therapy for facial melasma: a pilot study. *BMC Dermatol* ,17(1), 14.
11. Sheth, V. M., & Pandya, A. G. (2011). Melasma: a comprehensive update: part II. *Journal of the American Academy of Dermatology*, *65*(4), 699–714.
12. Sonthalia, S., Daulatabad, D., Sarkar, R. (2016). Glutathione as a skin whitening agent: Facts, myths, evidence and controversies. *Indian J Dermatol Venereol Leprol*, 82, 262-72.
13. Telang, P. S. (2013). Vitamin C in dermatology. *Indian Dermatol Online J*, 4(2), 143-146.
14. Menon, A., Eram, H., Kamath, P.R., Goel, S., Babu, A. M. (2019). A Split Face Comparative Study of Safety and Efficacy of Microneedling with Tranexamic Acid versus Microneedling with Vitamin C in the Treatment of Melasma. *Indian Dermatol Online J*, 11(1), 41-45.
15. Berardesca, E., Cameli, N., Primavera, G., Carrera, M. (2006). Clinical and Instrumental Evaluation of Skin Improvement after Treatment with a New 50% Pyruvic Acid Peel. *Dermatol Surg,* 32, 526–531.
16. Achar, A., Rathi, S. K. (2011). Melasma: a clinico-epidemiological study of 312 cases. Indian J Dermatol, 56, 380–382.
17. Tamega, A., Miot, L. D., Bonfietti, C., Gige, T. C., Marques, M. E., & Miot, H. A. (2013). Clinical patterns and epidemiological characteristics of facial melasma in Brazilian women. *Journal of the European Academy of Dermatology and Venereology : JEADV*, *27*(2), 151–156.
18. Hexsel, D., Lacerda, D. A., Cavalcante, A. S., Machado Filho, C. A., Kalil, C. L., Ayres, E. L., Azulay-Abulafia, L., Weber, M. B., Serra, M. S., Lopes, N. F., & Cestari, T. F. (2014). Epidemiology of melasma in Brazilian patients: a multicenter study. *International journal of dermatology*, *53*(4), 440–444.
19. Miot, L. D., Miot, H. A., Silva, M. G., & Marques, M. E. (2009). Physiopathology of melasma. *Anais brasileiros de dermatologia*, *84*(6), 623–635.
20. Fabbrocini, G., De Vita, V., Fardella, N., Pastore, F., Annunziata, M. C., Mauriello, M. C., Monfrecola, A., & Cameli, N. (2011). Skin needling to enhance depigmenting serum penetration in the treatment of melasma. *Plastic surgery international*, *2011*, 158241.
21. Balevi, A., Ustuner, P., & Özdemir, M. (2017). Salicylic acid peeling combined with vitamin C mesotherapy versus salicylic acid peeling alone in the treatment of mixed type melasma: A comparative study. *Journal of cosmetic and laser therapy : official publication of the European Society for Laser Dermatology*, *19*(5), 294–299.
22. Iraji, F., Nasimi, M., Asilian, A., Faghihi, G., Mozafarpoor, S., & Hafezi, H. (2019). Efficacy of mesotherapy with tranexamic acid and ascorbic acid with and without glutathione in treatment of melasma: A split face comparative trial. *Journal of cosmetic dermatology*, 10.1111/jocd.12874. Advance online publication. https://doi.org/10.1111/jocd.12874
23. Puri, N. (2020). A Study on the Efficacy of Mesotherapy using Glutathione and Vitamin C for the Treatment of Melasma. *J Clinic Exper Cosme Derma*, 3, 5.