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Research Article

Assessment of response of microdermabrasion with 2% kojic acid in melasma

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ABSTRACT

Background: Melasma is an acquired disorder of hypermelanosis and several therapeutic modalities is in use to treat melasma. Kojic acid is a popular depigmenting agent, but its hydrophilic nature limits its transepidermal penetration. Microdermabrasion has been reported to increase the penetration of topical preparations. The objective of the study was to compare the efficacy of daily kojic acid (2%) gel along with biweekly microdermabrasion versus daily kojic acid (2%) gel alone in Indian patients.
Methods: This study was carried out in 60 patients with melasma which were randomised into 2 groups of 30 patients each. The group I patients were treated with kojic acid 2% gel along with biweekly microdermabrasion, and group II patients were treated with kojic acid 2% gel alone. The results were assessed and compared after 12 weeks.
Results: Both objective assessment and subjective assessment did not reveal a statistically significant difference in the treatment efficacy of two groups. However, the patients who received biweekly microdermabrasion were significantly more satisfied than those who did not.
Conclusions: Microdermabrasion does not appear to have any synergistic effect with kojic acid in decreasing pigmentation in melasma. However, it does have a placebo effect on the patient.

Keywords: Melasma, Microdermabrasion, Kojic acid

INTRODUCTION

Melasma is an acquired disorder of hypermelanosis of great psychosocial concern. It is characterized by irregular light brown to dark muddy brown macules and patches involving sun-exposed areas of the face (i.e., cheeks, forehead, nose, upper lip and chin). It affects millions of people worldwide and is found most commonly in women with Fitzpatrick skin phototypes III-VI. The common contributing factors are genetic predisposition, pregnancy, oral contraceptives, endocrine dysfunction, hormonal treatments, drugs containing phototoxic agents, and stress. Exposure to ultraviolet light is a major aggravating factor for melasma.[1] Tyrosinase is a key enzyme that is responsible for melanogenesis and consequently pigmentation. The inhibition of tyrosinase greatly affects the melanogenesis process and melanin production, and is therefore the therapeutic target of many depigmenting agents.[2] Several therapeutic modalities are being used to treat melasma, which include numerous topical agents, chemical peels and a variety of lasers and light-based devices.[1] However, most treatment options have been disappointing with relatively frequent failures and relapses.

Kojic acid is a well-known antityrosinase agent widely used to treat melasma and is used, alone or in combination, in many depigmenting preparations. It is a natural antibiotic produced by various bacterial or fungal strains such as *Aspergillusoryzae*, *Penicillium or Acetrobacter* species.[3-5] It is a slow binding inhibitor of

the diphenolase activity of tyrosinase enzyme, due to the ability of chelating copper ion at the active site, resulting in antimelanogenic action.[6] A study also suggested that the pharmacological mechanism of kojic acid is associated with the IL-6 production in keratinocytes.[7]

Microdermabrasion was first introduced in 1985. It is simple, safe and one of the least invasive office cosmetic procedure. Microdermabrasion has been utilized for a variety of indications such as photoaging and resurfacing including acne scars and stretch marks. It has also been reported that microdermabrasion causes changes in skin's pigmentation pattern, leading to clinical improvements in dyschromia.[8] It is a popular choice as there is little recovery time and the adverse effects are uncommon and transient. Despite its popularity, microdermabrasion alone is a mild therapy as compared to the more aggressive therapies such as chemical peels or laser resurfacing. However, the synergistic effects of microdermabrasion in combination with other therapies such as Q switched Nd:YAG laser and glycolic acid and retinoic acid chemical peels have been reported.[9,10,11]

Skin preferentially allows low molecular weight, lipophilic molecules, to penetrate intact skin as compared to hydrophilic molecules and macromolecules.[12] The hydrophilic nature of kojic acid limits its ability to penetrate through the stratum corneum, thereby hindering the delivery of the drug to melanocytes which are localized to the basal layer.[2,13] Microdermabrasion has been shown to improve the skin penetration of topical preparations, especially hydrophilic molecules.[14] This ability can theoretically be useful to enhance the therapeutic effects of kojic acid. The objective of the study was to compare the efficacy of daily kojic acid (2%) gel along with biweekly microdermabrasion versus daily kojic acid (2%) gel alone in Indian patients.

METHODS

Approval of the study design was taken from the institutional ethical committee. Melasma patients attending the outpatient department of a tertiary care hospital in south-west Rajasthan were considered for the study. The following inclusion and exclusion criteria were followed:

Inclusion criteria

- Patients willing to give informed consent and agreeing for regular follow up.
- Treatment naïve patients or patients not on any topical or systemic treatment for melasma for the last 3 months.

Exclusion criteria

- Patients on oral contraceptives or on hormone replacement therapy.
- Patients having history of herpes simplex infection.

A total of 60 patients were enrolled in the study and were randomized into two groups of 30 patients each. Relevant history taking and clinical examination were performed. The profiles of patients of the two groups have been outlined in Table 1.

Table 1: Profiles of patients in the two treatment groups.

Feature	Group I (n=30)	Group II (n=30)
Female:male ratio	20:10	21:9
Treatment naïve patients	8	9
Epidermal/dermal/mixed	8/6/16	7/7/16
Pattern		
Centrofacial	14	15
Malar	6	4
Mandibular	5	6

The severity of melasma of each patient was assessed by melasma area severity index and clinical photographs.[21] Patients of both groups applied a physical sunscreen (25% zinc oxide) in the morning and kojic acid 2% gel regularly at night. Additionally, patients of group I underwent microdermabrasion every two weeks. For microdermabrasion, the patient was rested in a comfortable position and the face was cleaned and degreased with alcohol. Microdermabrasion was performed using aluminium oxide crystals of size 100 microns and three passes were given, followed by sunscreen application. At scheduled visits, the possible adverse effects such as erythema, burning, pain, peeling, edema, petechiae, or post inflammatory pigmentary changes were assessed on the basis of history and examination were recorded. This protocol was followed for a total of 12 weeks, after which the results of the two groups were evaluated.

Objective assessment

The objective assessment was done on the basis of pre and post treatment melasma area severity index (MASI) scores.

Subjective assessment

Subjective assessment was done by an independent observer by evaluating the pre and post treatment clinical photographs of patients.

Patient satisfaction

At the end of the study period, the patients were questioned about their satisfaction with the treatment provided. Both subjective assessment and patient satisfaction was graded using a 4 point scale as follows:

1. Poor (0-25% clearing).
2. Fair (26-50% clearing).
3. Good (51-75% clearing).

4. Excellent (> 75% clearing).

RESULTS

Out of the total 60 patients, 10 patients were lost to follow up (5 patients from each group). Results of the 25 patients in each group who completed the follow up were evaluated. On objective assessment, the pre-treatment and post-treatment mean MASI scores for the two groups have been outlined in Table 2. There was no statistical difference in the pre-treatment MASI scores for the two groups on applying the student's t-test (unpaired). Similarly, there was no statistical difference in the post-treatment MASI scores for the two groups. However, both the groups revealed statistically significant differences when their pre and post-treatment MASI scores were evaluated using paired t-test (Table 3) (Figure 1, Figure 2).

Table 2: Comparison and statistical evaluation of MASI scores between the two groups.

	Group I mean MASI	Group II mean MASI	t-value	p-value	Statistical significance
Pre-tmt	15.83	15.51	0.358	0.360	Not significant
Post tmt	9.02	9.98	-1.03	0.15	Not significant

Tmt= Treatment.

Table 3: Comparison and statistical evaluation of difference between pre-treatment and post-treatment MASI scores in the two groups.

Group	Mean difference in MASI (pre and post tmt)	t-value	p-value	Statistical significance
I	-6.81	-12.08	<0.00001	Significant
II	-5.52	-27.69	<0.00001	Significant

The results of subjective assessment by an independent observer have been tabulated in Table 4. The chi-square statistic for subjective assessment was found to be 0.35, and the p-value was 0.94 (not significant at p <0.05). Patient evaluation revealed greater satisfaction rates in Group I (Table 5). The chi-square statistic was found to be 9.79, and the p-value was 0.02 (significant at p <0.05).

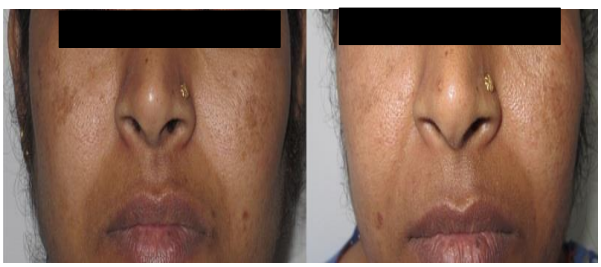

Figure 1: Pre and post treatment image of group I.

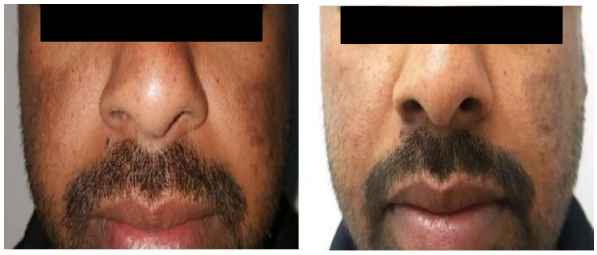

Figure 2: Pre and post treatment image of group II.

No relation of treatment response to age, duration, pattern or depth of pigmentation of melasma could be established in this study. No significant adverse effects were noted due to microdermabrasion in our patients.

Table 4: Results of subjective assessment by an independent observer.

Group	0-25% (poor)	26-50% (fair)	51-75% (good)	76-100% (excellent)
I	5	8	9	3
II	6	7	8	4

Table 5: Results of patient satisfaction with the treatment in the two groups.

Group	0-25% (poor)	26-50% (fair)	51-75% (good)	76-100% (excellent)
I	2	6	9	8
II	9	9	5	2

DISCUSSION

Traditionally, topical drugs have been the mainstay of treatment in melasma. The main barrier to transdermal transport of topical drugs is stratum corneum, which is the outer 10-15 µm layer of skin. The viable epidermal and dermal layers beneath the stratum corneum typically offer much less resistance to drug transport. The stratum corneum is composed of non-viable corneocytes that are surrounded by a lipid extracellular matrix. Consequently, skin preferentially allows transdermal transport of lipophilic molecules as compared to hydrophilic molecules.[12] Kojic acid, being a hydrophilic molecule, encounters greater resistance by the cutaneous barrier. Many strategies have been employed to enhance transdermal delivery of hydrophilic drugs. These include the use of permeation enhancers, employing vesicular drug delivery systems, delivering hydrophilic drugs using microneedles, or augmenting transdermal flux using laser systems.[15-24] Microdermabrasion, which involves blowing of aluminum oxide crystals or other abrasive substances onto the face and then vacuuming them off, 24peels the stratum corneum, leading to better penetration of topical preparations. Using microdermabrasion various researchers have shown increased permeability of freshly excised animal skin to very low molecular weight

compound (<300Da) recording a 10 to 20 fold flux enhancement of estradiol, vitamin-C and 5-minolevulinic acid.[25-27] These properties, along with the ability of microdermabrasion to increase the penetration of hydrophilic molecules, makes it a possibly useful adjunct to kojic acid.

Melasma of the skin is a very common problem and can be the source of significant psychological distress for patients. It is one of the common causes of facial hypermelanosis which is characterized by symmetrical hyperpigmented macules, which may be blotchy, irregular, arcuate, or polycyclic and rarely have a linear or a starburst distribution. The exact etiology of melasma is not known but several factors have been implicated. Ultraviolet (UV) radiation (UVA and UVB) and visible light causes peroxidation of lipids in cellular membrane, leading to generation of free radicals, which stimulate melanogenesis.[5]

Kojic acid has shown good results in combination with glycolic acid and both glycolic acid and hydroquinone.[28,29] Glycolic acid is a superficial peeling agent and also works by improving the penetration of other agents (similar to microdermabrasion). Similarly, microdermabrasion has also been shown to have synergistic effects when used along with Q switched Nd: YAG laser, glycolic acid and topical retinoids.[9,10,11] Despite these studies based on similar principles, we could not find any study which evaluated the synergistic effects of kojic acid and microdermabrasion as compared to kojic acid alone.

In our present study, we compared the effect of microdermabrasion combined with topical kojic acid 2% gel versus kojic acid 2% gel alone. We found that on objective assessment, both groups (kojic acid along with microdermabrasion and kojic acid alone) had a statistically significant improvement in MASI scores at the end of study period. However, there was no statistically significant difference in the post treatment MASI scores of the two groups, implying no additional benefit of microdermabrasion. Similarly, subjective assessment by an independent observer revealed no statistical difference in the results of the two groups. However, the patient satisfaction was significantly higher in the group additionally treated with microdermabrasion. Our study differs from previous studies in the fact that we did not find any additional therapeutic benefit from microdermabrasion.

CONCLUSION

This study indicates that kojic acid is an effective treatment in the management of melasma, but its combination with microdermabrasion does not provide any additional therapeutic benefit. However, the patients are satisfied more when microdermabrasion is done, indicating the placebo effect of the procedure. More studies with larger sample size are desirable for deriving conclusions on the role of microdermabrasion in enhancing the efficacy of topical preparations.

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