

Efficacy of Combination of Glycolic Acid Peeling With Topical Regimen in Treatment of Melasma

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ABSTRACT

Background: Various treatment modalities are available for management of melasma, ranging from topical and oral to chemical peeling, but none is promising alone. Very few studies are available regarding efficacy of combination of topical treatment with chemical peeling. Combination of chemical peeling and topical regimen can be a good treatment modality in the management of this recalcitrant disorder.
Objective: To assess the efficacy of combination of topical regimen (2% hydroquinone, 1% hydrocortisone and 0.05% tretinoin) with serial glycolic acid peeling in the treatment of melasma in Indian patients.
Methods: Forty Indian patients of moderate to severe epidermal variety melasma were divided into two groups of 20 each. One Group i.e. peel group received topical regimen (2% hydroquinone, 1% hydrocortisone and 0.05% tretinoin) with serial glycolic acid peeling and other group i.e. control group received topical regimen (2% hydroquinone, 1% hydrocortisone, 0.05% tretinoin).
Results: There was an overall decrease in MASI from baseline in 24 weeks of therapy in both the groups (P value < 0.05). The group receiving the glycolic acid peel with topical regimen showed early and greater improvement than the group which was receiving topical regimen only.
Conclusion: This study concluded that combining topical regimen (2% hydroquinone, 1% hydrocortisone and 0.05% tretinoin) with serial glycolic acid peeling significantly enhances the therapeutic efficacy of glycolic acid peeling. The combination of glycolic acid peeling with the topical regimen is a highly effective, safe and promising therapeutic option in treatment of melasma.

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INTRODUCTION

Melasma is a term derived from the Greek word " melas" meaning black. Melasma is an acquired light or dark brown hyperpigmentation that commonly occurs on the sun exposed areas, most often on the face and arms.[1,2] It is more common in females as compared to males. Males constitute only 10% of the melasma patients.[3] The condition is most commonly seen in persons with Fitzpatrick skin types IV – VI,[4] especially among those living in areas of intense ultraviolet radiation i.e. Asia, Middle East and South America.[5]

Various factors which are proposed in pathogenesis of melasma are genetic factors, UV light exposure, hormonal changes like pregnancy, lactation, ingestion of contraceptive hormones such as estrogen and progesterone, diethylstibesterol, medications such as phototoxic and anti seizure drugs, cosmetics and thyroid dysfunction.[6-10] However, it may be idiopathic also.[5]

Clinical examination of the melasma under Wood's light (wavelength 365nm) helps to determine the location of melanin in the skin as the epidermal form of melasma is enhanced under Wood's light whereas dermal form shows no enhancement.[11] The term mixed and indeterminate are used to denote those forms of melasma that have equivocal enhancement under Wood's light.[12]

Though there is a wide variety of therapeutic options available for this condition, management still remains a challenge. Besides the broad spectrum sunscreens, various topical therapies which are used for the treatment of melasma are hydroquinone in concentration of 2%-5%;[13] topical retinoids in the form of 0.1% tretinoin,[14] 0.05% isotretinoin[15], adapalene 0.1%[16] and topical corticosteroids[17] which are used alone or in combination. In addition, azelaic acid,[18] kojic acid,[19] alpha hydroxy acids like glycolic acid,[20] vitamin C,[21] arbutin[22] and licorice extract[23] are also used. Combination of various topical agents have also been used by many workers for better results which include combination of retinoic acid plus hydroquinone,[24] glycolic acid plus hydroquinone[25] and glycolic acid plus kojic acid.[19] The triple combination of hydroquinone, retinoic acid and topical steroid in various concentrations like hydroquinone 5% plus tretinoin 0.1% plus dexamethasone 0.1% known as Kligman's formula[26] or hydroquinone 2% plus tretinoin 0.05 % plus betamethasone valerate 0.1 %[27] or hydroquinone 4% plus tretinoin 0.05 % plus flucinolone acetonide 0.01%[28] have been shown to enhance the efficacy of treatment in melasma. Oral therapies like oral pycnogenol, grape seed extracts etc. have also been tried in melasma with moderate results.[29,30]

Chemical peeling has now become an established technique for the treatment of melasma. Depending upon the depth of peeling, the chemical peeling agents are classified into very superficial, superficial, medium and deep peels.[31] In dark skinned individuals, deep chemical peels should not be used as it may result in post inflammatory hyperpigmentation.[31] In Indian pa-

tients, very superficial or superficial chemical peels are more commonly used due to lower risk of post inflammatory hyperpigmentation[31] as the skin is usually dark colored. Among these peels, Glycolic acid is the most commonly used agent.[32] It is considered a very versatile peeling agent as it has good penetration of the skin because of lower molecular weight, increased bio- availability, gets easily neutralized and its effect is usually superficial. Hence, is safe with very few post peel complications.[33] It is available in concentrations ranging from 20% to 70%. Glycolic acid peeling has been shown to be efficacious and well tolerated in melasma[34, 35] in various studies.

"This study demonstrated that combining topical regimen of hydroquinone plus tretinoin plus hydrocortisone acetate to serial glycolic acid peeling is better than topical regimen alone for treatment of melasma in dark complexioned individuals."

Some studies have been done combining glycolic acid peeling with various topical agents like azelaic acid 20% plus adapalene gel 0.1%;[36] hydroquinone 4%;[37] glycolic acid cream 10% plus hydroquinone 4%[38] to enhance the efficacy of treatment and have shown better results. Sarkar et al, studied the glycolic acid peeling in combination with topical application of 5% hydroquinone plus 0.05% tretinoin plus 1% hydrocortisone in a cream base ie, modified Kligman's formula and concluded that this combination therapy gives additional benefit with rapid and greater improvement in melisma.[39] This is of considerable importance because this combination therapy, with its higher efficacy and minimal untoward effects, may prove to be an important line of therapy in melasma which is a therapeutic challenge for the clinician and is an emotional stress to the patient due to cosmetic disfigurement.

Paucity of controlled trials demonstrating the effectiveness of glycolic acid peels either alone or in conjunction with tretinoin, hydroquinone and topical steroids in darker racial/ethnic groups, where melasma is extremely common prompted us to undertake a clinical trial to study the efficacy and safety of serial glycolic acid peeling combined with topical regimen of 2% hydroquinone, 1% hydrocortisone and 0.05% tretinoin in the treatment of melasma.

METHODS

Forty Indian patients with Fitzpatricks skin type III-V with moderate to severe melasma of epidermal variety were included in this study. Study was conducted between June 2007 to Jan 2009. Patients were followed for atleast 24 weeks.

Inclusion Criteria

1. Every patient with facial melasma seeking medical treatment voluntarily in Department of Dermatology, Pt. BD, Sharma PGIMS, Rohtak, India.
2. Epidermal variety of melasma on Wood's lamp examination.
3. Interest to participate in research.

Exclusion Criteria

1. Pregnant and lactating women
2. Hypersensivity to formulation used in the study
3. Patients on oral contraceptives, hormonal replacement therapy, oral retinoids or any other concurrent medications.
4. Active or recurrent herpes simplex infection
5. Facial warts or molluscum contagiosum
6. Keloidal tendencies
7. Unrealistic expectations
8. Active dermatosis of atopic, seborrheic or other eczematous type.

All patients were explained about the risk of the procedure and written informed consent was obtained prior to the procedure. Detailed history of all the patients was taken to rule out all exclusion criteria and history of all precipitating factors or initiating factors was recorded. Patients were then subjected to complete dermatological examination including Wood's light examination and Melasma area severity index (MASI)[40] scoring was done. Patients with only epidermal variety of melasma were chosen for the study. Forty patients were taken for the study and were randomly divided into two groups of 20 each. Written informed consent was obtained from each patient. All patients were advised to apply topical sunscreen of SPF 15 or more.

In Group 1 (Peel group) serial glycolic acid peeling with topical regimen (2% hydroquinone, 1% hydrocortisone and 0.05% tretinoin) was used. A post auricular test peel was performed and left for 15-20 minutes for detection of any hypersensitivity to the ingredients of the peeling agent. All patients in peel group were given serial glycolic acid peel sessions. Total 8 sessions were performed at 3 weekly interval. In first session 30% glycolic acid was used for 1 to 2 minutes, in 2nd session 30% glycolic acid was used for 3 minutes, in 3rd session 30% glycolic acid was used for 4 minutes, in 4th session 40% glycolic acid was used for 1 to 2 minutes, in 5th session 40% glycolic acid was used for 3 minutes, in 6th session 40% glycolic acid was used for 4minutes,

in 7th session 50% glycolic acid was used for 1-2 minutes and in 8th session 50% glycolic acid was used for 3 minutes. Before performing the peeling procedure patients were advised to stop topical regimen 2 days prior to the session, avoid extensive sun exposure, stop any cosmetic procedures like waxing, depilators, electrolysis, masks, loofahs, other sponges, hair dying, permanent wavening, straightening treatment and other resurfacing and exfoliating treatments one week prior to the treatment. Patients were asked to come with a fully cleansed face, with no makeup or aftershave. Male patients were advised to avoid shaving on the day of peel. Peeling was done and after the procedure patients were instructed to take strict photoprotective measures and apply sunscreen , not to use abrasives or exfoliating sponges on the treated areas. Patients were strictly advised not to peel, scratch, pick or scrape the skin and not to use masks on the skin and start the topical regimen after 3 days of session.

In Group 2 (Control Group) the triple combination of topical regimens ie, 2% hydroquinone, 1% hydrocortisone and 0.05% tretinoin cream was used at night time for total 24 weeks duration and broad spectrum sunscreen of SPF 15 or more regularly in day time. Follow up was done at 3 weekly interval.The results were evaluated by comparing the changes in the MASI scoring of the patients in the two groups by the following formula

Total MASI score = Forehead 0.3 (D+H) A + Right malar 0.3 (D+H) A + left malar0.3 (D+H) A + chin 0.1 (D+H) A

MASI score was calculated before treatment as baseline and after every two successive sessions for 24 weeks. Clinical photographs were taken at baseline and after two sessions at 6 weekly intervals. Front, right and left view of each patient was photographed. All photographs were taken using a Sony digital still camera of model DSCW70. A high MASI score correlates well with severe hyperpigmentation.The results were tabulated and evaluated using statistical analysis using student's t –test and paired t – test.

RESULTS

Forty Indian patients of melasma were included in the study. Majority of patients were in age range of 21 – 40 years and the mean age of patients was 34 years. There were 38 females and 2 males (male: female 1:19), indicating female preponderance. The duration of disease varied from 6 months to 5-6 years. The mean duration of disease was 3.12 ± 1.57 years.

Mean MASI scoring of the group 1 (peel group) and group 2 (control group) patients at various intervals are compared in Table 1 and Figure 1.

Mean percentage decrease in MASI scoring of the group 1 patients (peel group) group 2 patients at various intervals are compared in Table 2 and Figure 2. The percentage decrease in MASI scoring in group 1 (peel group) was significantly higher than group 2 (control group).

TABLE 1.

MASI SCORING of Group 1 & Group 2 at Various Time Intervals

Time interval	Group 1 Peel group Mean ± Standard Deviation	Group 2 Control group Mean ± Standard Deviation	*P* value
Baseline	17.01 ± 3.33	16.55 ± 3.42	< 0.05
6weeks	12.07 ± 3.03	14.46 ± 2.68	< 0.05
12weeks	8.52 ± 2.91	12.64 ± 2.57	< 0.05
18weeks	5.75 ± 2.89	10.97 ± 2.39	< 0.05
24weeks	4.61 ± 2.28	9.28 ± 2.46	< 0.05

FIGURE 1. Mean of the MASI scores from Baseline to 24 weeks of therapy.

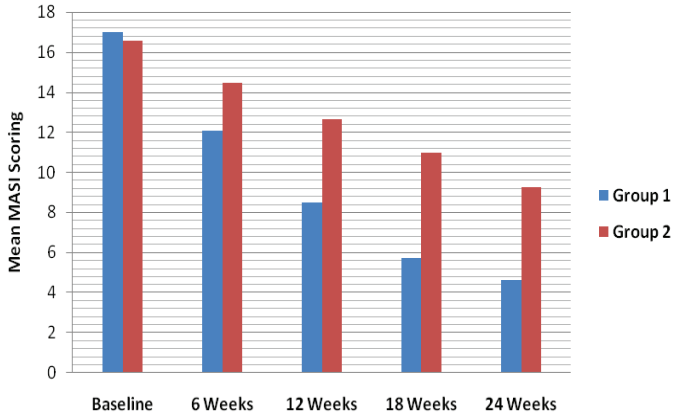


TABLE 2.

Percentage Decrease in MASI Scoring Between Group 1 and Group 2 at Various Time Intervals

Time interval	Percentage decrease in MASI Score Group1 Peel group Mean ± Standard Deviation	Percentage decrease in MASI Score Group2 Control group Mean ± Standard Deviation	*P* value
6 weeks	29.6 ± 0.09%	11.93 ± 0.08%	<0.05
12 weeks	50.71 ± 0.09%	23.15 ±0.09%	<0.05
18 weeks	67.42 ± 0.11%	32.82 ±0.12%	<0.05
24 weeks	73.69 ± 0.08%	42.33 ± 0.1%	<0.05
24 weeks	4.61 ± 2.28	9.28 ± 2.46	< 0.05

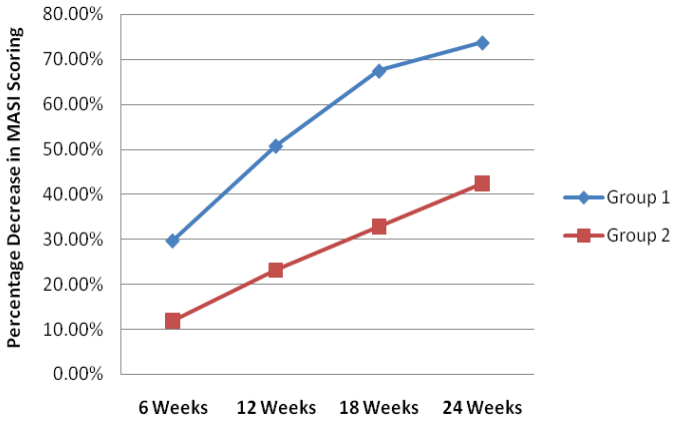
In group 1 (peel group) four patients showed post peel

Erythema, three had post inflammatory hyperpigmentation which resolved after appplication of 1% hydrocortisone cream, one had hypertrichosis at the end of 24 weeks of therapy, which resolved after stopping the topical regimen and four had burning and stinging sensation for which ice cooling was done and calamine lotion was applied. In group 2 (control group) three

TABLE 3.

Side Effects		
Side Effects	Group 1 Peel Group (Topical regimen + Peel)	Group 2 Control Group (Topical regimen)
Erythema	4	-
Post Inflammatory Hyperpigmentation	3	-
Hypertrichosis	1	-
Burning and Stinging Sensation	9	3

FIGURE 2. Percentage Decrease in the MASI Score from baseline.



patients had burning and stinging sensation for which ice cooling was done and calamine lotion was applied (Table 3). None of the patients in either of the groups experienced any severe and persistent side effects.

DISCUSSION

This study demonstrated that combining topical regimen of hydroquinone plus tretinoin plus hydrocortisone acetate to serial glycolic acid peeling is better than topical regimen alone for treatment of melasma in dark complexioned individuals. Very few side effects were encountered and none was severe and persistent. This might be because all the three components of the topical regimen have unique importance when used with glycolic acid peeling. Hydroquinone acts as a priming agent and also decreases the post inflammatory hyperpigmentation especially in Indian skin ie, Fitzpatricks type III –V which has more tendency towards post inflammatory hyperpigmentation.[31] Tretinoin also acts as a priming agent which increases the penetration of hydroquinone and glycolic acid,[35] thereby making peel more effective and protects from the side effects of topical steroids like atrophy. The third component ie, hydrocortisone decreases the chance of post peel hyperpigmentation due to its anti inflammatory action.

This study demonstrated that the combination of serial glycolic acid peeling with topical regimen of 2% hydroquinone plus 0.05% tretinoin plus 1% hydrocortisone is a well-tolerated and highly effective treatment stratergy for melasma.

DISCLOSURES

None of the authors have disclosed any relevant conflicts of interest.

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