The Combination of Glycolic Acid Peels With a Topical Regimen in the Treatment of Melasma in Dark-Skinned Patients: A Comparative Study

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BACKGROUND. Melasma continues to be a difficult condition to treat, especially in dark-skinned patients, although various topical modalities including hydroquinone, tretinoin, and/or topical steroids have been used singly or in combination with variable results.

OBJECTIVE. To determine if serial glycolic acid peels provide additional improvement when combined with a time-tested topical regimen, a modification of Kligman’s formula (hydroquinone 5%, tretinoin 0.05%, hydrocortisone acetate 1% in a cream base). All cases had epidermal melasma as detected by Wood’s light examination.

METHODS. Forty Indian melasma patients were divided into two groups of 20 each. One group received serial glycolic acid peel combined with a topical regimen, modified Kligman’s formula. The other, a control group, received only modified Kligman’s formula. The results were evaluated by a clinical investigator both subjectively and with photographs taken at baseline, 12 (before the fourth peel), and 21 (3 weeks after the sixth peel) weeks. For clinical evaluation, the Melasma Area and Severity Index (MASI) was used.

RESULTS. A significant decrease in the MASI score from baseline to 21 weeks was observed in both groups (P < .001). The group receiving the glycolic acid peels showed a trend toward more rapid and greater improvement, with statistically significant results (P < .001). Only a few side effects were observed in the peel group.

CONCLUSION. This study demonstrates that serial glycolic acid peels provide an additional effect to a topical regimen which is a modification of the time-tested Kligman’s regimen for treating melasma in dark-complexioned individuals if used judiciously and under supervision. It demonstrates that superficial chemical peels are beneficial in the treatment of melasma.

MELASMA IS a common, acquired, symmetric hypermelanosis characterized by irregular light to dark brown macules and patches involving sun-exposed areas of the skin, the common sites being the cheeks, forehead, upper lip, nose, and chin. It causes considerable cosmetic disfigurement, and remains a difficult condition to treat. Melasma is seen in both sexes and all races, but women of childbearing age are most commonly affected. The exact incidence and prevalence of melasma is unknown, but it is probably more prevalent in darkly pigmented races, especially Asians, where the treatment is generally unsatisfactory. The treatment options are hydroquinone, tretinoin, topical corticosteroids, various combinations of these, or laser surgery. Combinations of hydroquinone with topical steroids and tretinoin have been reported to be effective and relatively safe in the treatment of melasma; the best-known combination being Kligman’s formula (tretinoin 0.1%, hydroquinone 5%, and dexamethasone 1% in hydrophilic ointment). There are other variations of Kligman’s formula which have been adapted for dark-skinned persons with melasma.

Chemical peels have become an increasingly popular method for treating a myriad of benign skin disorders, including melasma. Superficial and medium-depth chemical peels, especially glycolic acid, have been found to be especially beneficial in this condition. Deep peels are generally not used, as they are associated with various complications such as hypopigmentation, hyperpigmentation, scarring, and keloid formation. Glycolic acid is an α-hydroxy acid that has an epidermal discohesive effect at low concentrations, but causes epidermolysis at high concentrations. Recent studies have shown that treatment of melasma and postinflammatory hyperpigmentation with chemical peels in conjunction with tretinoin and hydroquinone daily in patients of different skin types is beneficial. 

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skin types produces satisfactory results. These studies suggest that the improvement of melasma can be hastened by removal of the superficial layers of the epidermis by chemical peeling agents, because treatment of melasma by other agents, such as tretinoin, can require as long as 10 months.

There is a paucity of controlled trials demonstrating the effectiveness of chemical peels either alone or in conjunction with tretinoin, hydroquinone, and topical steroids in darker racial/ethnic groups, where melasma is extremely common, and can cause emotional distress to the patient because of cosmetic disfigurement. This prompted us to compare the effectiveness and safety of a topical regimen that was a modification of Kligman’s formula (MKF) combined with serial chemical peels with glycolic acid versus only the topical regimen (MKF), which acted as control, in Indian patients. Our goal was to determine if serial glycolic acid peels added any additional improvement to the topical regimen for the treatment of melasma in dark-complexioned individuals.

Materials and Methods

Forty Indian patients with Fitzpatrick skin types III–V with moderate to severe melasma were recruited into the study. We used an open pilot study that lasted 21 weeks. The exclusion criteria included pregnant or nursing women, patients with hypersensitivity to the formulations, patients on any concurrent therapy, concurrent illness, active or recurrent herpes labialis, keloidal tendencies, unrealistic expectations, and women on oral contraceptives. All patients were told the risks of the procedure and a written informed consent was obtained from all prior to the procedure. Prior to study entry, patients must not have used topical steroids or any skin bleaching agents for 2 weeks and systemic steroids for 1 month.

Detailed clinical histories including the duration of the disease, precipitating or aggravating factors, any associated illness, and previous treatments were taken and are shown in Table 1. Clinical examination, including the pattern of melasma, was noted in each patient. A Wood’s light examination was done prior to treatment and the type of melasma was noted. Patients with only the epidermal variety of melasma were chosen for the study.

Twenty patients each were recruited into two groups, one receiving modified Kligman’s formula (MKF) and second receiving a combination of glycolic acid peels with MKF. All patients had to use a broad-spectrum SPF 15 sunscreen. Prior to application, written informed consent was obtained from each patient. A postauricular test peel was performed and left for 15–20 minutes to determine any hypersensitivity to the ingredients of the peeling agent. All patients in the peel group were given a maintenance regimen (MKF) with 0.05% tretinoin cream, 2% hydroquinone, and 1% hydrocortisone cream for 2 weeks before the chemical peels for the purpose of testing their sensitivity to hydroquinone. A mild soap and emollient were also provided. One group received MKF throughout the treatment period.

The peel group used MKF daily and received six serial glycolic acid peels at 3-week intervals. For this group, the MKF region was discontinued 2 days prior to receiving a peel and restarted 3 days after the peel. Before performing the peel, the patient was advised to wash his/her face with soap and water. After patting the face dry, cleansing was done with methyl alcohol and acetone-soaked gauze scrubs to remove cutaneous oils. The first three peels were 30% glycolic acid applied with cotton gauze with mild strokes to remove cutaneous oils. The first three peels were at 40% glycolic acid, with the time of contact increased in a similar way to the first three peels. The second three peels were done with methyl alcohol and acetone-soaked gauze scrubs to remove cutaneous oils. The first three peels were 30% glycolic acid applied with cotton gauze with mild strokes and a contact time of 1–2 minutes, depending on the patient’s tolerance, gradually increasing by 40–60 seconds at every peel, depending on the patient tolerance. The next three peels were at 40% glycolic acid, with the time of contact increased in a similar way to the first three peels. The maximum time of contact was 3 minutes. The face was then rinsed in cool water. Patients were advised to use only a sunscreen, a mild soap, and petrolatum for 3 days after the peel. After three days, the peel group of patients was again started on MKF in a similar manner.

Evaluation of melasma severity was performed at baseline and at weeks 12 and 21 based on three measures: the first was a subjective measure based on the area and severity of hyperpigmentation—the Melasma Area and Severity Index (MASI)—determined by Kinbrough-Green et al. According to the MASI score, the face is divided into four areas: forehead, right malar, left malar, and chin—that corresponds to 30%, 30%, 30%, and 10% of the total face area, respectively. The melasma in each of these areas was graded on three variables: percentage of total area involved, on a scale of 0 (no involvement) to 6 (90–100% involvement); darkness, on a scale of 0 (absent) to 4 (severe); and

### Table 1. Characteristics of Dark-Complexioned Melasma Patients

<table>
<thead>
<tr>
<th>General data</th>
<th>Chemical peel group</th>
<th>Topical regimen (MKF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>31.45 (19–44)</td>
<td>31.05 (21–45)</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>18/22</td>
<td>18/22</td>
</tr>
<tr>
<td>Duration (years)</td>
<td>2.08 (0.50–6)</td>
<td>2.18 (0.50–4)</td>
</tr>
<tr>
<td>Patients on previous therapy</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>Precipitating factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnancy</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Sunlight</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Oral contraceptives</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Baseline MASI score (0–48)</td>
<td>19.12 ± 6.71</td>
<td>18.85 ± 5.43</td>
</tr>
<tr>
<td>12-week MASI score (0–48)</td>
<td>10.17 ± 4.30&lt;sup&gt;b,c&lt;/sup&gt;</td>
<td>12.52 ± 3.94&lt;sup&gt;b,c&lt;/sup&gt;</td>
</tr>
<tr>
<td>21-week MASI score (0–48)</td>
<td>3.93 ± 2.42&lt;sup&gt;b,c&lt;/sup&gt;</td>
<td>6.97 ± 2.58&lt;sup&gt;b,c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Values are expressed as mean (range).<br><sup>b</sup>Statistically significant difference between the peel and topical regimen group by Student’s t-test, P < .001.<br><sup>c</sup>Statistically significant difference between the peel and topical regimen group by Student’s t-test, P < .05.
homogeneity, on a scale of 0 (absent) to 4 (maximum). The MASI was then calculated by the following equation:

\[
\text{MASI} = 0.3(DF + HF)AF + 0.3(DMR + HMR) AMR + 0.3(DML + HML) AML + 0.1(DC + HC) AC,
\]

where D is darkness, H is homogeneity, A is area, F is forehead, MR is right malar, ML is left malar, C is chin, and the values 0.3, 0.3, 0.3 and 0.1 are respective percentages of total facial area.

A high MASI score correlates with severe hyperpigmentation. The results were tabulated using statistical analysis using Student’s t-tests and paired t-tests. After the third peel and before the fourth peel (12 weeks) and 3 weeks after the sixth peel (21 weeks), the patients were asked to give their subjective assessment of their clinical response to the peels as excellent, good, fair, or poor. Photographs were taken in a standardized position at baseline, week 12, and week 21. However, some patients did not have their photographs taken on the last visit.

Results

Forty melasma patients completed the study. Patients’ ages ranged from 19 to 44 years (mean 31.45 years). There were 22 women and 18 men (male:female ratio 1:1.2). The duration of melasma ranged from 6 months to 6 years (mean 2.08 years). The demographic features of the patients are given in Table 1. Their final evaluation was at 21 weeks (3 weeks after receiving the sixth chemical peel). Both groups experienced significant overall lightening of the melasma, both by the MASI score, subjective evaluation, and by photography.

The mean MASI score for the peel group decreased from 19.12 ± 6.71 at baseline to 10.17 at 12 weeks and 3.93 at 21 weeks (Table 1). This represents a percentage change of 45.89% at week 12 and 79.99% at week 21 (Figures 1–4), which is highly significant (\( P < .001 \)). In the control group, the mean MASI score at baseline was 18.85 ± 5.43 which decreased to 12.52 at week 12 and 6.97 at week 21, representing a 33.16% and 63.14% change in pigment intensity, respectively, which was highly significant (\( P < .001 \)). The difference between the two groups was also found to be significant both at week 12 and week 21 (\( P < .01 \)), with a better response in the form of lightening of melasma being experienced in the group receiving the chemical peels. The photographs were also in agreement with these results.

At the end of the study, a subjective improvement was noticed by most of the patients. In the peel group, 80% of the patients graded their improvement as excellent, 10% as good, and 10% as fair. In the control (MKF) group, 60% of the patients graded improvement in their melasma as excellent, 20% as good, and 20% as fair.

The adverse effects were minimal in both patient groups. Nearly all patients in the peel group and eight patients in the control (MKF) group experienced mild cutaneous erythema and superficial desquamation, which was treated with emollients, and no further intervention was required. One patient had herpes labialis at the end of treatment (six chemical peels) and was treated with 5% acyclovir ointment. The patients in the peel group experienced focal erythema and mild burning during the peels. Two patients in the peel group developed focal superficial vesiculation which left behind postinflammatory hyperpigmentation that subsided with the regular application of betamethasone dipropionate 0.05% cream twice a day. In the control (MKF) group, four patients had acneiform eruptions and were treated with benzoyl peroxide 0.5% locally at night while the MKF regimen was stopped for a few days. A persistent erythema was observed in two patients in the peel group and the patients were asked to use sunscreens and topical corticosteroids.

Discussion

This study demonstrates that serial glycolic acid peels can enhance the efficacy of a topical regimen when treating melasma in dark-complexioned persons. The findings were significant in both the chemical peel and the MKF group, but the trend was definitely toward a more rapid and greater overall response in the peel group. The treatments were tolerated well and most patients were satisfied with the treatment regimen and therapeutic results, which was greater in the peel group.

As can be seen in Figure 1, the group receiving the chemical peel had a more rapid initial improvement as compared to the group receiving the topical regimen. At 21 weeks, a greater beneficial effect in the form of clinical lightening of the melasma was seen in the peel group as compared to the topical regimen. A greater subjective improvement noted by the patients in the peel group could be due to a significant placebo effect. Previous studies have demonstrated that superficial chemical peels enhance the effects of topical therapy in melasma and postinflammatory hyperpigmentation.\(^ {11,13} \)

However, these studies combined the use of superficial chemical peel with topical tretinoin and hydroquinone between peels. Kligman’s regimen and its various modifications give satisfactory results in recalcitrant cases and also when a rapid response is desired.\(^ {6–8} \) Hence a study combining the beneficial effects of topical tretinoin, hydroquinone, and hydrocortisone acetate with
Chemical peels may be of great benefit to dark-complexioned melasma patients, as can be seen in the present study. We used 0.05% tretinoin in MKF, as this percentage is easy for dark-complexioned patients to tolerate and prevents the development of retinoid dermatitis, and hydrocortisone acetate, because the treatment had to be continued for 20 weeks. This modified topical regimen was well tolerated by the patients.

The adverse effects noted from the application of superficial glycolic acid peels in the few previous studies in melasma patients are irritant reaction, extensive epidermolysis, postinflammatory hyperpigmentation, hypopigmentation, and persistent erythema. In the present study we noted focal superficial vesiculation in two patients, postinflammatory hyperpigmentation in one, persistent erythema in two, and herpes labialis in one in the peel group, which is in agreement with other studies, and none of these merited the stoppage of treatment. Glycolic acid chemical peels are generally well tolerated by melasma patients if used prudently.

Moy et al. suggested that the use of superficial glycolic acid peels and 2% hydroquinone in the treatment of melasma is beneficial. Other authors have also studied the combination of tretinoin and hydroquinone with superficial glycolic acid peels in melasma. By and large, there is a dearth of published data regarding the efficacy and safety of chemical peels in darker racial/ethnic groups. Also, there are very few controlled clinical trials evaluating the efficacy of combined peel and topical therapy. Our study was a paired comparison trial that has a greater statistical power than the results of a randomized treatment study and demonstrates that a combination of superficial glycolic acid peel with a topical regimen of a modified Kligman’s regimen would be of great benefit in the treatment of melasma in dark-complexioned persons.
We conclude that superficial glycolic acid peels are a good adjunct to topical therapy in melasma in dark-complexioned patients, as they accelerate the clinical response and are well tolerated if used with topical combination therapy. However, they must be used judiciously and under supervision. Contributions to the scientific use of glycolic acid are meaningful because of the excessive marketing of these products. It has been suggested that studies like these may contribute to the standard of dermatology use of glycolic acid and that dermatologists should continue to keep a higher standard of care in the use of glycolic acid based on our basic skin and skin physiology knowledge.

References

Commentary
The ideal methodology for a peel study is a split treatment design. In the case of melasma, one would use one therapy on half of the face and the other therapy on the other half. The problems with a randomized design (as was done in this peel study) is that you cannot correct for the individual variation between patient response. Some patients with melasma respond fairly rapidly to therapy of any sort, and others respond more slowly and less completely. One cannot correct for the possibility that those randomized to the peel group might have had inherently better response to topical therapy only. Another point about the basic design of this study is that it would have benefited from an objective measure of pigment reduction, such as colorimeter analysis. In site of these issues the study does strengthen the evidence that peels lead to more rapid and complete improvement of melasma when combined with topicals in darker skin types, which be recalcitrant to topicals alone.

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Commentary
This excellent article reaffirms the ability of glycolic acid peels to assist in the penetration of hydroquinone. The authors go a step further than previous investigations and compare the peels to a control with modified Kligman’s bleach alone as well as utilizing a large series of dark-skinned patients.

The final paragraph, though, gives greatest insight. This article demonstrates the science of medicine in treating difficult pigment problems in dark-skinned individuals. Even low-strength glycolic acid in concert with higher-strength bleaches that irritate the skin can result in dyspigmentation, persistent erythema, and herpes simplex. This reinforces that the treatment of this medical condition should be administered by a dermatologist for patient safety.

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