Efficacy of Glycolic Acid Peels in the Treatment of Melasma

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Background: Melasma is an acquired hypermelanosis that is often recalcitrant to treatment with hypopigmenting agents.

Objective: To assess the efficacy of 4% hydroquinone cream vs 4% hydroquinone cream combined with glycolic acid peels as treatment for melasma.

Methods: Twenty-one Hispanic women with bilateral epidermal and mixed melasma were enrolled in a split-faced prospective trial lasting 8 weeks. Patients underwent 20% to 30% glycolic acid peels every 2 weeks to one side of the face only in addition to twice-daily full-face application of 4% hydroquinone cream and sun protective factor 25 UV-B sunscreen each morning. Pigmentation was measured objectively using a mexameter and the Melasma Area and Severity Index and subjectively using a linear analog scale and physician and patient global evaluation.

Results: Hydroquinone treatment alone and treatment with the combination of hydroquinone and glycolic acid had a significant effect in reducing skin pigmentation compared with baseline ($P<.001$). However, no significant difference was found using combination therapy compared with hydroquinone alone ($P=.75$).

Conclusions: Use of 4% hydroquinone and a daily sunscreen is effective in the treatment of melasma; however, the addition of 4 glycolic acid peels did not enhance the hypopigmenting effect of hydroquinone treatment alone.

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MELASMA IS a common pigmentary disorder characterized by the development of slowly enlarging tan-brown macules and patches. The condition is seen most commonly on the face of women with Fitzpatrick skin types IV to VI, especially among those living in areas of intense UV radiation. The cause of melasma is multifactorial and includes pregnancy, sunlight exposure, hormone therapy, cosmetic use, and racial or genetic effects. Conventional treatment for melasma includes elimination of any possible causative factors coupled with use of a sunscreen and hypopigmenting agent, often in combination with other therapies, such as tretinoin, topical corticosteroids, or superficial peeling agents. Despite these measures, treatment of this recalcitrant disorder is often difficult and frustrating for the patient and the clinician.

Hydroquinone (HQ) inhibits conversion of dopa to melanin by inhibiting tyrosinase in melanocytes; it is one of the most effective agents in the treatment of melasma. The combination of HQ with other compounds has been reported to enhance its efficacy. Glycolic acid has also been reported to interfere with melanin production and to enhance the treatment of melasma, particularly when administered as part of a hypopigmenting program that includes HQ. Previous trials using glycolic acid for melasma have used subjective measures of clinical improvement, lacked standard photography, studied patients from different racial backgrounds, or yielded results that are not statistically significant. The purpose of this study is to evaluate the efficacy of using 4% HQ cream alone or as part of a glycolic acid peel program in the treatment of epidermal melasma in Hispanic women. We chose only Hispanic women for this study because of the high frequency of melasma in this population and to study a uniform population. We sought to assess the clinical response objectively by evaluating patients on a split-faced basis using standard color and UV photography, a mexameter (Courage & Khazaka Electronic, Cologne, Germany), and the Melasma Area and Severity Index (MASI) and subjectively using a linear analog scale and physician and patient global evaluation.

METHODS

Patients were eligible for the study if they were Hispanic women, aged 18 to 65 years, with Fitzpatrick skin types IV and V and with moderate to severe bilateral and symmetrical epidermal or mixed melasma, confirmed by noting...
enhancement of lesions with a Wood lamp. The study was performed with the approval of the University of Texas southwestern Medical Center institutional review board. Exclusionary criteria included pregnancy, use of HQ within 3 months of the study, or history of chemical peels, microdermabrasion, or facial laser treatment within 9 months of the study. Use of oral contraceptives was permitted; however, such medications were not introduced during the study.

After gentle cleansing with cleanser (Gly Derm cleanser; ICN Pharmaceuticals Inc, Costa Mesa, Calif), the degree of pigmentation on both sides of the face was assessed using the Mexameter and recorded. A third reading was taken from the suprasternal notch, which is exposed to light but not to study treatments, as a control. The Mexameter provides reproducible, objective measurement of pigment (melanin) based on the absorption spectra of light and has an accuracy of ±5%. Mexameter readings range from 1 to 1000, with 1 representing white and 1000 representing black. Mexameter readings were obtained, and a linear analog scale was marked at baseline and at weeks 2, 4, 6, and 8.

Standard and UV photographs and the MASI score for the clinical examination were recorded at baseline and at week 8. The MASI is an index devised to more accurately quantify the severity of melasma and changes during therapy. The index was modified by Kimbrough-Green et al,10 who based it on a similar scoring system devised for psoriasis. The MASI is calculated based on the area (A) of involvement, the darkness (D) of melasma, and the homogeneity (H) of the hyperpigmentation. The right forehead (rf), right malar region (rm), and right chin (rc) correspond to 13%, 30%, and 5% of the total face, respectively. The same regions are measured on the left side, giving a total facial surface area of 100%. The area of involvement in each of these 6 areas is given a numerical value of 0 to 6 (0 indicates no involvement; 1, 0%-9%; 2, 10%-29%; 3, 30%-49%; 4, 50%-69%; 5, 70%-89%; and 6, 90%-100%). The severity of melasma is also determined by measuring 2 additional variables: darkness (D) and homogeneity (H), rated on a scale from 1 to 4 (0 indicates absent; 1, slight; 2, mild; 3, marked; and 4, maximum). The MASI score is calculated by adding the sum of the severity ratings for darkness and homogeneity, multiplied by the value of the area of involvement, for each of the 6 facial areas. The values for each side are then totaled; for example, MASI right = 0.15 [D(rf)+H(rf)] A(rf) + 0.3 [D(rm)+H(rm)] A(rm) + 0.05 [D(rc) + H(rc)] A(rc). The score for each side is 0 to 24.

The patient underwent a 20% glycolic acid peel (Gly Derm glycolic acid pads; ICN Pharmaceuticals Inc) to one half of the face, which was performed by the nonmasking study nurse (R.M.G.). The side to be peeled was determined by a computer-generated randomization code. Other than the gentle cleansing mentioned previously, no further degreasing was performed. The duration of the peel varied from 3 to 5 minutes, depending on the patient's degree of erythema and discomfort. The patient was given a supply of 4% HQ cream (Eldoquin Forte; ICN Pharmaceuticals Inc), with instructions for bilateral application at night at least 45 minutes after applying the HQ cream; and sun protective creams (Hydrotone Lite; ICN Pharmaceuticals) to apply in the morning and evening on both sides of the face.

The other data sets were analyzed using a paired t test. All tests were 1-sided because improvement is directional in nature.

Twenty-one patients were enrolled in the study. Two patients did not follow the protocol completely, and 1 patient was excluded from data analysis because of equipment malfunction. The average duration of the glycolic acid peels was 3 minutes in 6 patients, 4 minutes in 9 patients, and 5 minutes in 3 patients. As stated previously, the duration varied, depending on the patient's degree of erythema and discomfort during the peel.

Demographic data are given in Table 1. The average age of the patients was 40 years (range, 23-56 years), and the average time melasma was present before study entry was 11 years (range, 2-26 years). For each participant, the visit 5 mexameter readings for the sides treated with HQ alone and HQ plus peels were compared with the corresponding readings for the same area at baseline. The P<.001 (observed significance) in both sides indicates a statistically significant treatment effect. The values from the treated areas were compared with the control values obtained from the suprasternal notch at the same visit. The control values did not vary significantly from the main values, indicating that there was no effect from tanning or other factors that might have altered the results. For improvement on the nonpeeled and peeled sides of the face compared with control values, P<.001, indicating a significant treatment effect compared with control values. Thus, treatment with HQ alone and with HQ plus peels reduces skin pigmentation.

For each participant, the improvement in the area treated with HQ alone was subtracted from the corre-
The use of alpha hydroxy acids, particularly glycolic acid, has expanded dramatically during the past decade for the treatment of skin disorders, including hyperpigmentation. Because of their relative safety profile compared with stronger agents such as trichloracetic acid, glycolic acid peels are often used by dermatologists, plastic surgeons, aestheticians, and other skin care specialists. Indeed, because most of the world’s population is brown or dark skinned, a great deal of effort and expense for the performance of peels is being dedicated to the treatment of disorders of hyperpigmentation, particularly melasma. Hydroquinone has been shown to be safe and effective in the treatment of melasma and other types of hyperpigmentation. Studies evaluating the efficacy of glycolic acid peels for melasma thus far have been uncontrolled trials, have been too small to yield statistically significant results, have used subjective methods of evaluation, or have not studied a uniform patient population.\(^2\)\(^,\)\(^3\)

We sought to perform a randomized, controlled, investigator-masked, split-faced prospective trial using a uniform population and recently developed objective methods of evaluation to determine whether glycolic acid peels hasten improvement of melasma with concomitant use of HQ. Our study demonstrated statistically significant improvement on both sides of the face from baseline, with no significant difference on the side that was peeled. This improvement was also noted on subjective analysis, as physician and patient global evaluations revealed that most patients had at least moderate improvement. We controlled for sun exposure by using the patient as her own control, measuring pigmentation at the suprasternal notch, a sun-exposed but untreated site. The measurement taken at the suprasternal notch revealed no significant difference in pigmentation throughout the study.

The results of the linear analog scale correlated with the other findings in that there was no significant difference in the degree of improvement using HQ alone versus combination therapy with HQ and glycolic acid peels. Furthermore, physician global evaluation results supported these findings in that the treatment-masked investigator could not detect a greater degree of improvement on either side of the face. The patient global evaluation, however, revealed that almost three fourths of the patients noted improvement on the side that was peeled. This subjective patient bias emphasizes the importance of masking and controls in the performance of clinical trials. It may also explain why glycolic acid peels are so popular among patients. Perhaps the smoothening and softening of the skin produced by these peels is responsible for their high acceptance rather than their ability to reduce hyperpigmentation.

Standardized photographs were taken of all patients with 35-mm color, polarized color, and UV photographs at baseline and at the end of the study (stereotactic camera; Canfield Scientific Inc, Fairfield, NJ). Ultraviolet reflectance photography is especially useful for detecting changes in pigmentation over time, as epidermal melanin detection using UV photography is 10 times more sensitive than with visible light.\(^10\)\(^,\)\(^11\)

The use of polarized filters with color photography was an excellent method of enhancing pigmentation in
photographs of patients, as shown in Figure 3 and Figure 4. Ultraviolet reflectance photography is also a valuable tool to accentuate pigmentation; however, patients must wash and degrease the face before photography to prevent reflection from the skin surface, which obscures the assessment of pigmentation. The mexameter served as a reproducible, easy-to-use tool for the objective measurement of pigmentation.

The effect of glycolic acid peels on skin is determined by the concentration of the acid, pH, product formulation, duration of time the acid remains on the skin, skin thickness, and sensitivity.12 The glycolic acid used in this study was a nonbuffered, nonneutralized glycolic acid ester with a pH of 1.5 (20%) and 1.1 (30%) in individually packaged moistened pads. Although higher concentrations of glycolic acid could have been used, glycolic acid peels greater than 30% often lead to irritation and may cause paradoxical hyperpigmentation in brown-skinned patients. An adequate peel was obtained in our patients using 20% and 30% glycolic acid based on the

Table 2. Physician and Patient Global Evaluation of Which Side Had Improved, and to What Degree, Compared With the Opposite Side*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Physicians, No. (N = 18)</th>
<th>Patients, No. (N = 18)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Peeled Side</td>
<td>Nonpeeled Side</td>
</tr>
<tr>
<td>Slight improvement, barely noticeable</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Moderate improvement, noticeable</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Obvious improvement</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Very marked improvement</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Subtotal</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>No difference between the 2 sides and no improvement</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Total</td>
<td>17†</td>
<td>NA</td>
</tr>
</tbody>
</table>

*NA indicates not applicable.
†Physician global evaluation was not performed on 1 patient.
‡Patient global evaluation was not performed by 2 patients.

Figure 3. Standard photography using polarized filters at baseline (A) and at the end of the study (B) on the nonpeeled side of a patient with Fitzpatrick skin type IV.
observation that most felt some tingling during the peel or developed mild erythema. Indeed, only 3 patients were able to tolerate a peel duration of 5 minutes. Four patients developed significant erythema with the 20% and 30% peels, without epidermolysis or erosions, indicating that higher-strength peels might have resulted in greater morbidity.

Because improvement was noted on both sides of the face after 8 weeks, we conclude that 4% topical HQ with a daily sunscreen is effective in the treatment of melasma. The application of 4 glycolic acid peels of 20% to 30% in 8 weeks did not enhance the hypopigmenting effect of HQ alone. Further studies using patients of different racial backgrounds, more peels over a longer period, different peeling agents, or combined with recently developed treatments such as microdermabrasion might be considered in the future to find better ways of treating melasma.

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