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Cosmetic

A Deceptively Simple Solution for Refractory Melasma: Glycolic Acid Peels and Hydroquinone at Home

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Summary: Although various treatment methods for melasma have developed, substantial improvement of the condition is sometimes difficult. We have experientially found that some of refractory melasma caused by daily friction can easily be treated by using a combination of a peeling agent (20% glycolic acid) and a depigmenting agent (5% hydroquinone) twice daily at home. And here, by performing skin biopsies, we revealed the pathological mechanism: hyperkeratosis caused by repeated physical stimulus, which prevents infiltration of topical therapeutic agents, was dramatically reduced by chemical peeling, resulting that the melanin pigments were effectively cleared by topical hydroquinone. *(Plast Reconstr Surg Glob Open 2017;5:e1335; doi: 10.1097/GOX.0000000000001335; Published online 19 May 2017.)*

Melasma is known as acquired symmetrical epidermal melanosis, which is generally evident on the malar prominence and upper cheek.[1] Despite development of treatment modalities for melasma such as lasers, tretinoin, hydroquinone, and chemical peels, these often end with limited improvement, a prolonged therapeutic period, or even worsening of the disease, especially in patients with naturally darker skin.[2] Through experience of treating hundreds of melasma patients, we know that melasma related with alteration of female sex hormone profiles (original melasma) is not actually so common, and most patients develop melasma due to daily friction, such as removing cosmetics, scrubbing the face, or facial massages (frictional melasma).[1] Also, we have found that some cases of frictional melasma, which are resistant to various treatments, are actually easy to treat by a simple treatment using glycolic acid peels and topical hydroquinone at home; although this is not a new method of treatment, there are some tips for treatment protocol and patient selection. Here, we present the cases with pathological findings to show the underlying treatment mechanism.

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METHODS AND RESULTS

Twenty-two consecutive patients, aged from 41 to 57 years, received melasma treatment using 0.4% tretinoin and 5% hydroquinone twice a day for 2 months.[2] Two investigators (certified plastic surgeons), who did not perform treatment, evaluated the face of each patient using the Investigator's Overall Hyperpigmentation scale (0, none; 1–3, mild; 4–6, moderate; 7–9, severe). Among the 22 patients, 7 patients (31.8%) were judged as poorly improved (still having a hyperpigmentation score of "moderate" or "severe"); they were clinically diagnosed with frictional melasma caused by excessive daily friction and did not present good treatment response by tretinoin such as erythema and scaling. Then, all 7 patients who were unsuccessfully treated, and 7 randomly selected patients who were successfully treated, were examined by means of 1.5-mm punch biopsy after approval from institutional review board and informed consent from the subjects. Interestingly, histological findings revealed not only remaining epidermal melanosis but also marked hyperkeratosis in the unsuccessfully treated patients; the average and SD of the keratin layer thickness were as follows: the patients successfully treated by the first treatment (17.5±3.8 μm) and the patients unsuccessfully treated by the first treatment (31.4±6.2 μm; Table 1). We provided a modified treatment for the 7 unsuccessfully treated patients by

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Table 1. Treatment Results in Normal and Refractory Melasma (n = 7 in Each Group)

	Keratin Layer Thickness (μm)		Hyperpigmentation Score (Range)			
Melasma Subtype	2 Months	4 Months	Pre	2 Months	4 Months	10 Months
Normal	17.5±3.8	—	6.29 (5–7)	1.29 (0–3)	1.43 (0–3)	1.57 (1–2)
Refractory	31.4±6.2	24.6±5.1	6.57 (5–8)	6.14 (4–8)	1.71 (1–2)	1.86 (1–2)

Two months, just after tretinoin–hydroquinone therapy; 4 months, just after glycolic acid-hydroquinone therapy; 10 months, 6 months after the completion of therapy.

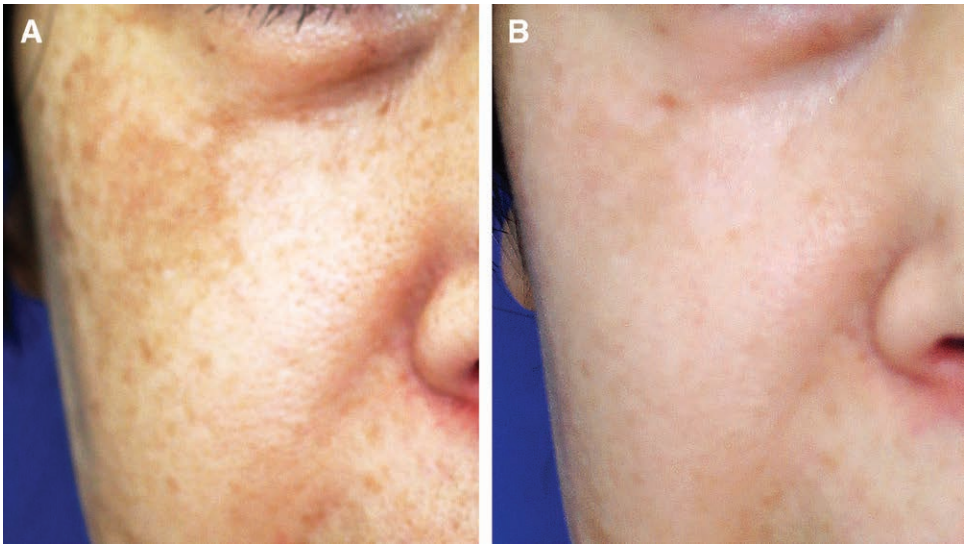

Fig. 1. Macroscopic view of the right cheek of a 53-year-old woman with frictional melasma. A, After 2 months of tretinoin–hydroquinone therapy, skin pigmentation was poorly improved. B, After 2 months of modified treatment using 20% glycolic acid and 5% hydroquinone, the disease condition was dramatically improved.

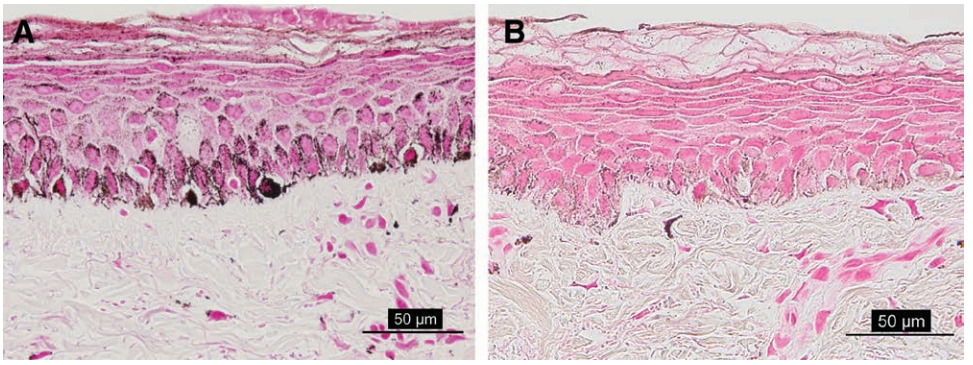

Fig. 2. Photomicrograph of melasma obtained by biopsy from the right cheek skin (Fontana-Masson stain). A, After the first treatment using tretinoin and hydroquinone, remaining epidermal melanosis and hyperkeratosis were observed. B, After the second treatment using glycolic acid and hydroquinone, the thickness of the keratin layer was reduced and the melanin pigments were markedly cleared.

using a peeling agent including 20% glycolic acid (AHA gel; Kiyo, Tokyo, Japan), which can be applied by patients themselves, and 5% hydroquinone twice a day. Two months later, all 7 patients showed excellent clearance of hyperpigmentation and reduced thickness of the keratin layer (24.6±5.1 μm), which were confirmed by a second skin biopsy. Six months after the completion of therapy, there was recurrence of melasma in any of the patients (Table 1). Macroscopic face view and histology of a representative case are shown in Figures 1 and 2.

DISCUSSION

Although various kinds of topical treatments for melasma are widely practiced,[2] melasma still continues to be a difficult problem, and a deeper understanding of the pathogenesis in refractory melasma is needed.[2] As described above,

some patients with melasma did not respond well to topical tretinoin, possibly because hyperkeratosis inhibited infiltration of topical agents and induction of sufficient therapeutic reaction. Although Lee et al.[3] reported that the stratum corneum itself was not significantly different in melasma skin, our results suggested that hyperkeratosis is one of the typical characteristics, at least in long-standing, friction-triggered, and treatment-resistant refractory melasma.

For such patients, the combination use of a peeling agent (which itself has weaker therapeutic effect than tretinoin) achieves therapeutic success as an induction (maximizer) for other topical depigmenting agents (hydroquinone in our study), by removing excess keratin layers. The selection of concentration and frequency of chemical peeling is quite important; in our experience, most patients with melasma refractory to tretinoin–hydroquinone therapy did not respond well to 15% glycolic acid and hydroquinone but were successfully treated by following 20% glycolic acid and hydroquinone therapy (n > 10, data unpublished). While on the other hand, 20–30% glycolic acid every 2 weeks did not enhance treatment efficacy of topical hydroquinone in the report of Hurley et al.[4] We believe that the combination use of "20%" glycolic acid with 5% hydroquinone, both "twice daily at home," is one of the most effective and minimally invasive solutions for treating refractory frictional melasma. However, given the limited number of cases in this study, further studies are required to validate effectiveness, repeatability, and optimality of the treatment protocol.

There is 1 more reason that may make melasma a difficult condition to treat: persistent and repeated inflammation may lead not only to epidermal melanosis but also to melanin incontinence, resulting in melanin deposits on the upper dermis (dermal melasma), which was not observed in histological results of our cases. In such situations, physical modalities, such as lasers combined with chemical peels and topical depigmenting agents, may be very effective for a skin lesion with both epidermal and dermal pigmentation.

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