Original Contribution

Clinical tolerance and efficacy of capryloyl salicylic acid peel compared to a glycolic acid peel in subjects with fine lines/wrinkles and hyperpigmented skin

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Summary

Background Several chemical agents are currently used to perform superficial peels of the face to reduce facial hyperpigmentation and fine lines/wrinkles. Some of the most commonly used agents are alpha hydroxyl acids, such as glycolic acid (GA), or beta hydroxy acid, such as salicylic acid.

Aim This study aims to compare the efficacy of GA to that of a novel derivative of salicylic acid, capryloyl salicylic acid (LHA).

Subjects/Methods In a split-face study, 50 female volunteers between the ages of 35 and 60 years with mild to moderate facial hyperpigmentation and fine lines/wrinkles were randomized and LHA or GA peel was applied to one side of the face. Increasing peel concentrations were applied (5–10% LHA or 20–50% GA) based on the tolerance level of the subjects and clinical observations of an expert dermatologist for 12 weeks at biweekly intervals.

Results Of the 44 volunteers who completed the study, at 12 weeks 41% of LHA-treated and 30% of GA-treated subjects demonstrated significant reduction of fine lines/wrinkles compared to baseline. Forty-six percent of LHA-treated subjects and 34% of GA-treated subjects showed significant reduction of hyperpigmentation compared to baseline. LHA treatment was better than GA peels, although there were no statistically significant differences between the two groups.

Conclusions Five percent to 10% of LHA peel is generally safe and as effective as 20–50% GA peel in reducing facial hyperpigmentation and fine lines/wrinkles.

Keywords: glycolic, capryloyl salicylic, LHA, lines and wrinkles, pigmentation

Introduction

Chemical peeling is the application of one or more exfoliating agents to improve skin rejuvenation and to reduce age-related changes, including hyperpigmentation and fine lines/wrinkles. Several chemical agents are currently used to perform superficial chemical peels of the face, including trichloracetic acid, alpha hydroxy acids, and Jessner's solution (14% lactic acid, 14% resorcinol, and 14% salicylic acid). Alpha hydroxy acids, in particular, glycolic acid (GA), are commonly used chemical peel agents. GA peels in concentration ranging from 20% to 50% have been shown to be effective in reducing facial hyperpigmentation and fine lines/wrinkles. Even higher concentration of GA solutions (70%) has also been used as superficial chemical peeling agents.[1–4]

Kligman *et al.* have developed salicylic acid, a beta hydroxy acid (30% in a hydro-ethanolic vehicle), as

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an alternative peel to GA. The benefits of salicylic acid peels are claimed to be resurfacing moderately photodamaged facial skin, fading of pigment spots, decreased surface roughness, and reduction of fine lines.[5] Derivatives of salicylic acid, especially long-chain fatty acyl conjugates of salicylic acid, have been claimed to be more effective at lower concentrations for skin peeling use.[6] A lipophilized derivative of salicylic acid, 2-hydroxyl-5-octanoyl benzoic acid, or capryloyl salicylic acid (LHA), has been shown to be an effective exfoliating agent due to its reduced penetration in the skin.[7]

In this study, we compared the effects of GA with LHA on skin rejuvenation and reduction of hyperpigmentation and fine lines/wrinkles. We compared the safety and efficacy of 5–10% LHA to 20–50% GA in reducing facial hyperpigmentation and fine lines/wrinkles in a clinical trial of 12 weeks' duration with 50 female subjects.

Methods

Subjects

Fifty female volunteers between the ages of 35 and 60 years with mild to moderate facial hyperpigmentation and fine lines/wrinkles were enrolled in a 12-week study. The study was conducted as a single-blinded, biweekly product application of either of two peels on one side of the face. Qualified subjects were randomized to the right or left side of the face for the LHA product, and the opposite side of the face was treated with the GA product. Subjects were given cleanser, toner, and moisturizer regimen, including a sunscreen for 2 weeks before starting the study and throughout the study for home use.

Baseline visit (week 1)

At the baseline visit (week 1), the dermatologist conducted a pre-peel irritation assessment using a 4-point scale (Table 1) and a dermatologic evaluation using a 6-point scale (Table 2). The subject's face was cleansed with the cleanser and followed by toner application and then applied one coat of 5% LHA peel on one side of the face according to the randomization scheme and one coat of the 20% GA peel on the opposite side of the face. The LHA peel solution remained on one side of the face without rinsing; the GA peel solution remained on the other side of the face until color change, but no longer than 2 min. After color change or 2 min, whichever came first, neutralizer solution was applied until the subject felt no tingling or burning sensations. The neutralized area was then rinsed with water-soaked gauze. A moisturizer was applied to the whole face. Thirty- to 60-min post-peel application, the subject's face was reevaluated for irritation by the dermatologist, and a subjective evaluation for fine line/wrinkles and for pigmentation was made.

Table 1 Skin irritation assessment.

Parameters	Grading scale
Erythema; dryness/scaling; edema	0 = None, 1 = Mild, 2 = Moderate, 3 = Severe

Table 2 Dermatologic evaluation.

Parameters	Grading scale
Fine lines/wrinkles	0 = None; 1 = slight fine lines, barely visible; 2 = slight but definite fine lines, visible; 3 = obvious lines, shallow indentations visible; 4 = Coarse deep wrinkles; 5 = Very deep furrows
Hyperpigmentation	0 = None; 1 = slight, a few small patches; 2 = mild, few small dark patches; 3 = moderate, few darker patches and/or several hyperpigmented areas; 4 = Severe, numerous dark patches of hyperpigmented skin; 5 = Very severe: large patches, or numerous patches extending over a large area of the skin, showing dark coloration

Biweekly visits

If the subject tolerated the first 5% LHA and 20% GA peel applied at baseline (week 1) with a dermatologic and subjective score of 2 or less, the second peel at week 3 was carried out at a higher concentration of LHA (10%) or GA (30%). The highest level of peeling agent used in this study was 10% for LHA and 50% for GA (on week 5) subject to tolerance threshold. If the dermatologist determined that a subject would be unable to tolerate the levels of LHA or GA used in the previous week, the subsequent biweekly peels were continued with the next lower levels of LHA or GA. Subjects were instructed to come back at weeks 3, 5, 7, 9, and 11 to have each peel regimen repeated. At week 12, subjects returned for the final evaluation by the dermatologist. At all time points, the subject's face was reevaluated for irritation by the dermatologist, and subjective evaluation for fine line/wrinkles and for pigmentation was done 30 to 60 min post-peel application.

Statistical analysis of data

The changes from baseline for the 50 subjects for fine lines/wrinkles and hyperpigmentation were calculated in a scale of +2, +1, 0, –1, or –2 (+ indicating improvement; 0 indicating no change from baseline; – indicating change for the worse). These numbers were analyzed using the Wilcoxon signed rank test. Changes from baseline pre-peel were compared to baseline pre-peel values. Statistical analysis was done using the SMYDERM, SAS program.

Results

Of the 50 subjects enrolled in the study, 44 completed the study (88%). Compliance was generally good, and there was low incidence of adverse events. One subject experienced moderate stinging for 1–2 h and moderate scaling lasting 2–3 days on the LHA peel side and moderate localized rash 1–2 h post-peel on the GA peel – treated side of her face. Three subjects who experienced erythema with stinging and burning on the LHA-treated side were discontinued from the study. These adverse events resolved within 1 week of onset. In summary, this study demonstrate that 5–10% LHA peel is tolerated well and as safe as 20–50% GA peel.

At the end of the 12 weeks, 41% of the subjects showed statistically significant improvements in fine lines/wrinkles on the side of the face treated with LHA peel and 30% on the glycolic-treated site (Fig. 1). Reductions in fine lines/wrinkles were evident from week 9 for both treatments ($P = 0.003$ for LHA and $P = 0.008$ for GA). At all time points beyond week 9, LHA peel showed greater improvement than GA, although the difference between the two treatments was not statistically significant at any time point.

Likewise, significant improvement in pigmentation was seen in 46% on LHA-treated side and 34% on the GA-treated side (Fig. 2) at the end of 12-week treatment. Statistically significant improvements in pigmentation from baseline (skin brightening effect) was evident from week 7 for LHA peel ($P = 0.031$) and week 11 for glycolic peel ($P = 0.002$). These improvements continued until the end of the study at week 12 ($P < 0.001$ for both groups). There were no significant differences between the two peel products.

There were no significant changes in erythema for either LHA or GA from baseline values when compared with pre-peel to pre-peel and post-peel to post-peel at different weeks. Overall, there were no statistically significant differences between the two products. The dryness/scaling showed significant reductions for LHA peel from pre-peel baseline values at week 3 ($P = 0.013$), week 5 ($P = 0.031$), and week 11 ($P < 0.001$). There was no statistically significant improvement for GA peel except for week 9 ($P = 0.004$). In general, LHA appeared to reduce dryness/scaling parameter better than GA peel.

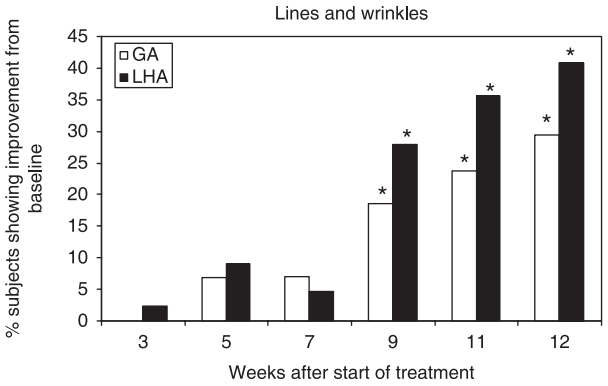

Figure 1 The effects of glycolic acid (GA) or capryloyl salicylic acid (LHA) peel in improving the appearance of lines and wrinkles. Subjects were treated with GA or LHA as described in the Methods section. On the indicated weeks, dermatological evaluation of the face was carried out before the peeling procedure using a scale of 0–5 as described in Table 2. The improvement from baseline (week 0) was calculated for each subject. The percentage of subjects showing improvement from baseline was calculated using the Wilcoxon signed rank test, and statistical analysis was done using the SMYDERM, SAS program. The number of subjects showing improvement from baseline was plotted against the week in the *X* axis. Statistically significant changes ($P < 0.05$) from baseline are indicated by an asterisk (*).

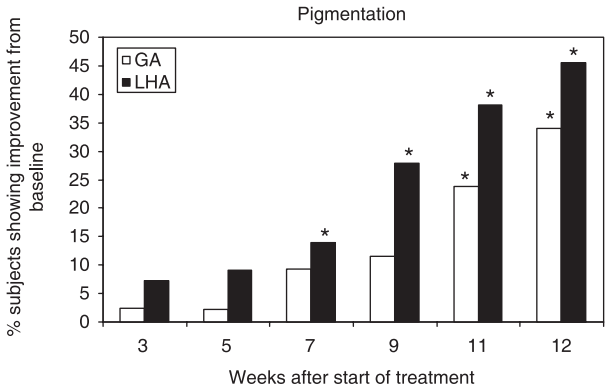

Figure 2 The effects of glycolic acid (GA) or capryloyl salicylic acid (LHA) on reducing hyperpigmentation. The treatment, dermatological evaluation, grading of skin, and calculations are the same as described for Figure 1. Grading scale is indicated in Table 2. Statistically significant improvements in pigmentation ($P < 0.05$) are indicated by an asterisk (*).

Discussion

Early studies using GA peels for photodamaged skin found it to be an ideal adjunct to other cosmetic

procedures.[1] Significant antiaging benefits of 70% GA treatments in skin appearance were demonstrated in another study.[2] Ten percent to 30% topical GA in 2-week intervals for 16 weeks showed that GA is useful especially in superficial scarring and melasma and moderately successful in acne patients with no response in dermal pigmentation.[3] Another study found 50% GA to significantly improve photodamaged skin.[4]

The benefits of topical salicylic acid peels for the treatment of pigment spots, in decreasing surface roughness, and in reducing fine lines have been described by Kligman and Kligman.[5] The safety and efficacy of topical salicylic acid has been well established.[8,9] A derivative of salicylic acid, 2-hydroxy-5-octanoyl benzoic acid or beta-lipohydroxy acid (also referred to as C (8)-lipohydroxy acid or LHA), has also been proposed as an exfoliant and as a treatment for photoaged skin and acne.[6] The lipophilic nature of LHA and its relatively slow penetration in the skin give it an exfoliating effect that is efficient at low concentrations. It appears to have antimicrobial, anti-inflammatory, and anticomedogenic properties, which make it effective against acne.[7]

In this 12-week half-face study, we used the highest concentration of GA or LHA the volunteer could tolerate, and we did not observe any adverse effects. The dose of GA was increased from 20% to a maximum of 50% within 5 weeks if the volunteers tolerated high levels of GA. Likewise, the LHA levels were gradually increased from 5% to 10% over a period of 3 weeks. We found no significant changes in erythema for either LHA or GA peel from baseline values; significant reductions of fine lines/wrinkles from week 9 for both LHA and GA; and significant reduction of hyperpigmentation from week 7 for LHA and from week 11 for GA peels. The effects of LHA were consistently better than those of GA. Forty-one percent of LHA-treated and 30% of GA-treated subjects demonstrated significant reduction of fine lines/wrinkles compared to baseline. Forty-six percent of LHA-treated subjects and 34% of GA-treated subjects showed significant reduction of hyperpigmentation compared to baseline.

In conclusion, this study demonstrates that LHA peels (5–10%) were as safe and as well tolerated as GA peels (20–50%) in this subject population. LHA appears to be slightly better than GA peel in reducing dryness/scaling, in reducing fine lines/wrinkles, and for improving skin pigmentation.

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