Glycolic Acid Peels Versus Salicylic–Mandelic Acid Peels in Active Acne Vulgaris and Post-Acne Scarring and Hyperpigmentation: A Comparative Study

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BACKGROUND Many clinicians have used glycolic acid (GA) peels for facial acne, scarring, and hyperpigmentation, mainly in lighter skin types. Salicylic–mandelic acid combination peels (SMPs) are a newer modality, and there have been no well-controlled studies comparing them with other conventional agents.

OBJECTIVE To compare the therapeutic efficacy and tolerability of 35% GA peels and 20% salicylic–10% mandelic acid peels in active acne and post-acne scarring and hyperpigmentation.

METHODS AND MATERIALS Forty-four patients with facial acne and post-acne scarring and hyperpigmentation were divided into two groups, with one receiving GA peels and the other SMPs at fortnightly intervals for six sessions. The treating physician performed objective evaluation of treatment outcomes. The patients, the treating physician, and an independent observer made subjective assessments. Side effects of both agents were also noted.

RESULTS Both the agents were effective, but SMPs had a higher efficacy for most active acne lesions ($p < .001$) and hyperpigmentation ($p < .001$). Side effects were also lesser with SMPs.

CONCLUSION Both the agents were effective and safe in Indian patients, with SMPs being better for active acne and post-acne hyperpigmentation.

Timpac Engineers, New Delhi, India, provided the NeoStrata salicylic-mandelic peel.

Acne vulgaris is the most prevalent skin disease and the single most common reason for visits to dermatologists.[1,2] Acne resolves completely without major sequelae in most patients, but in a few, it may leave behind disfiguring scarring or hyperpigmentation. The risk of these sequelae is higher in patients with dark skins living in areas with high sun exposure, including Asians. Thus an early, aggressive, and multipronged approach is all the more essential in Asian skins. Chemical peeling has been used for acne for many years. In addition to its epidermal resurfacing properties, it leads to remodeling of collagen and elastin fibers and deposition of glycosaminoglycans, thereby decreasing scars, too. Because of the resurfacing of the epidermis, the melanin content is decreased, and it is more evenly distributed, improving hyperpigmentation.

Alpha hydroxy acids (AHAs) and beta hydroxy acids (BHAs) are the most commonly used agents. Glycolic acid (GA) peel, an AHA, has been widely used for pigmentary dyschromias and acne,[3–8] but few studies have evaluated GA peels in dark skins, including Asian patients.[9] Salicylic–mandelic acid peel (SMP) is a newer combination peel that combines the properties of a BHA and an AHA. Salicylic acid is lipophilic and thus penetrates active acne lesions quickly.[10,11] Mandelic acid is one of the largest AHAs and penetrates the epidermis more slowly and uniformly, making it an ideal peeling agent for the sensitive skins of patients with severe acne and pigmentation.[12] Owing to its large structure, its penetration as a chemical peeling agent has not been easily evaluated or used. The combination of these two agents should thus be effective for the treatment

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of acne and its sequelae, but there are no published studies using these SMPs for acne. Therefore, the present study, which aimed at determining the efficacy and side effects of GA peels and SMPs for the treatment of acne and post-acne scarring and hyperpigmentation, was undertaken.

Materials and Methods

Forty-four Indian patients with Fitzpatrick skin types IV to VI with acne vulgaris and post-acne scarring and hyperpigmentation not responding to conventional treatment for 3 or more months were included in the study. Patients with a history of hypertrophic scarring, keloids, active or recurrent herpes, oral isotretinoin therapy within the previous 6 months, or hypersensitivity to aspirin were excluded from the study.

Evaluation of Active Acne

Evaluation of active acne was done using a method devised by Michaelsson and colleagues (Table 1).[13]

By multiplying number of each type by its severity index and adding each sum, a total acne score was obtained. Assessment of acne lesions was done at baseline (0 weeks) and at each visit (2, 4, 6, 8, 10, 12, and 24 weeks).

TABLE 1. Evaluation of Active Acne*

Lesion	*Severity Index*	*Definition*
Comedone	0.5	Horny follicular plug and pinhead-sized follicular papules
Papule	1.0	Infiltrated papules 2–8 mm
Pustule	2.0	Pustules >2 mm with surrounding inflammation
Infiltrate	3.0	Nodules and infiltrates >8 mm and coalescent papules where individual papules cannot be distinguished
Cyst	4.0	Lesions where infiltrate has broken down to form discharging cyst

*Michaelsson and colleagues.[13]

Evaluation of Post-Acne Scars and Hyperpigmentation

The post-acne scars were classified as icepick, boxcar, and rolling according to the classification described by Jacob and colleagues, and the total number of each type was calculated.[14]

The extent of post-acne hyperpigmentation was assessed by calculating the approximate surface area involved. The right and left cheeks and the forehead were taken to constitute 30% each, and the chin accounted for 10%. Assessment of post-acne scars and hyperpigmentation was also done at baseline (0 weeks) and at each visit (2, 4, 6, 8, 10, 12, and 24 weeks).

Procedure

Our institution's research review committee approved the study protocol. The procedure was explained in detail, and written informed consent was obtained from all patients included in the study. Consent was taken from the parent or guardian if the patient was younger than 18. All oral and topical medications being taken for acne were discontinued 4 weeks before peeling.

The patients were divided into two age- and sex-matched groups (A and B). Group A comprised 22 patients who received fortnightly 35% GA peels and Group B comprised 22 patients who received fortnightly 20% salicylic–10% mandelic acid peels. Six peeling sessions were conducted for each group at Weeks 0, 2, 4, 6, 8, and 10. At the first visit, a test peel with 10% GA or SMP was performed on a 1- × 1-cm area in the right retro-auricular area. The patients were reviewed after 1 week, and if they tolerated the peel well, they were taken up for full face peels. Patients were asked to first wash their face with water. They were then asked to lie down in a 45° semi-reclining position with eyes closed. The patients wore a surgical cap to pull back their hair and cover the ears. Degreasing was done by scrubbing with cotton gauze soaked with spirit, followed by one soaked with acetone. Sensitive areas of the

face like the lips and nasolabial folds were protected with a thin layer of petrolatum. GA peel or SMP was then applied over the face using a fan-shaped sable brush in a predetermined clockwise manner starting over the forehead, right cheek, chin, left cheek, nose, upper lip, and lastly the infraorbital areas, taking 30 to 35 seconds to accomplish and using approximately 0.8 to 1.0 mL per session. The peeled areas were observed for the development of erythema for GA peels, which was considered the end point of peeling. The patients were also asked to report when they felt a stinging or burning sensation with GA peels, which was considered the alternative end point in patients in whom erythema could not be discerned (because of dark skin color). With SMP, the patients experienced a stinging sensation that lasted for 3 to 5 minutes. After the cessation of this stinging sensation, most patients developed a uniform white crystalline precipitate, "pseudofrost," in the peeled areas (indicating the deposition of salicylic acid after its hydroethanolic vehicle had volatilized). This was considered the end point of peeling. In patients who did not develop the pseudofrost, the cessation of the stinging sensation was considered the end point. Care was taken not to allow blanching to appear, which was indicative of a deeper peel causing epidermolysis. The duration of each peeling session with GA was serially increased by 1 minute at each visit until a maximum of 5 minutes and varied from 1 to 5 minutes. The total duration of the peeling sessions varied from 3 to 5 minutes with SMP.

As soon as the end point was reached, the peel was neutralized by asking the patients to wash their faces with copious amounts of cool tap water. They were then asked to pat, and not rub, the face dry. The patients were asked to apply a sunscreen with a sun protection factor (SPF) of greater than 15 on their faces before leaving the clinic. They were sent home with instructions to apply a moisturizing cream if the facial skin felt too dry, to avoid or minimize sun exposure, and to apply sunscreen whenever exposed to the sun. They were cautioned not to apply any cream or face wash containing AHAs, salicylic acid, or retinoids.

The patients were followed up 2 weeks after the last peel (Week 12) and again 3 months later (24 weeks).

Assessment

The treating physician made an objective assessment of the changes in active acne lesions, post-acne scarring, and hyperpigmentation at each visit.

The patient, the treating physician, and an independent observer also made a subjective assessment of the response on a 5-point visual analog scale: good ($>60\%$), fair (31–60%), poor ($<30\%$), no change, or worse. These assessments were made at Weeks 4, 8, 12, and 24. Clinical photographs using standardized positioning were taken at baseline and at 4, 8, 12, and 24 weeks. The side effects seen with both agents in the two groups during the peeling period and during follow-up were noted in the proforma.

Statistical Analysis

The data were analyzed using the paired *t*-test for parametric data and the Wilcoxon signed rank test and Mann-Whitney *U* test for nonparametric data. $p<.05$ was taken as significant.

Results

All 44 patients (33 women and 11 men) completed the study. The mean age of the patients was 22 ± 3.0 (range 16.0–27.0). Half of the patients were aged 20 to 24 years. Onset of acne occurred between the ages of 14 and 16 in 59.1% of the patients. The interval between onset of acne and scarring was 2 to 4 years in 52.3% of patients. All of the study subjects had used topical retinoids and antibiotics before entering the study. Oral antibiotics had been prescribed to 72.7% of the patients at some point during the course of their disease, although none had ever taken oral isotretinoin.

Objective evaluation of treatment outcomes done by the treating physician revealed the following.

Comedones: Both agents produced a significant reduction in comedones, although SMPs brought about a significant change earlier (at 4 weeks). The difference between the two agents was statistically significant from 8 weeks onwards ($p = .01$). The change in comedones (Week 0 to Week 24) with GA peel was 20.9% and with SPM was 45.7%, which was statistically significantly different ($p < .001$).

Papules: Although both of the agents led to significant improvement at the end of the study, the effect of SMPs was apparent much earlier. However, the papules were seen to increase after peeling with SMPs was discontinued, and the difference between the effects of the two agents decreased from 12 weeks ($p < .001$) to 24 weeks ($p = .02$) (Figure 1). The change in papules (Week 0 to Week 24) was 27.3% with the GA peel and 47.7% with the SMP ($p = .02$).

Pustules: Both the agents led to highly significant improvement throughout the study, although the pustules were seen to increase after peeling with SMPs was discontinued at 12 weeks, and the difference between the effects of the two agents decreased from 12 weeks ($p = .002$) to 24 weeks ($p = .04$). The change in pustules (Week 0 to Week 24) was 34.7% with GA peels and 58.4% with SPMs ($p = .02$).

Nodules and cysts: No significant improvement in nodules and cysts was noticed with either agent.

Total Acne Score: Although both of the agents led to highly significant ($p < .001$) improvement in the total acne score, SPMs were seen to be more effective (Figure 2), with a significant difference from 12 weeks onward. The change in total acne score (Week 0 to Week 24) was 27.3% with GA peel and 52.3% with SPM ($P < .001$).

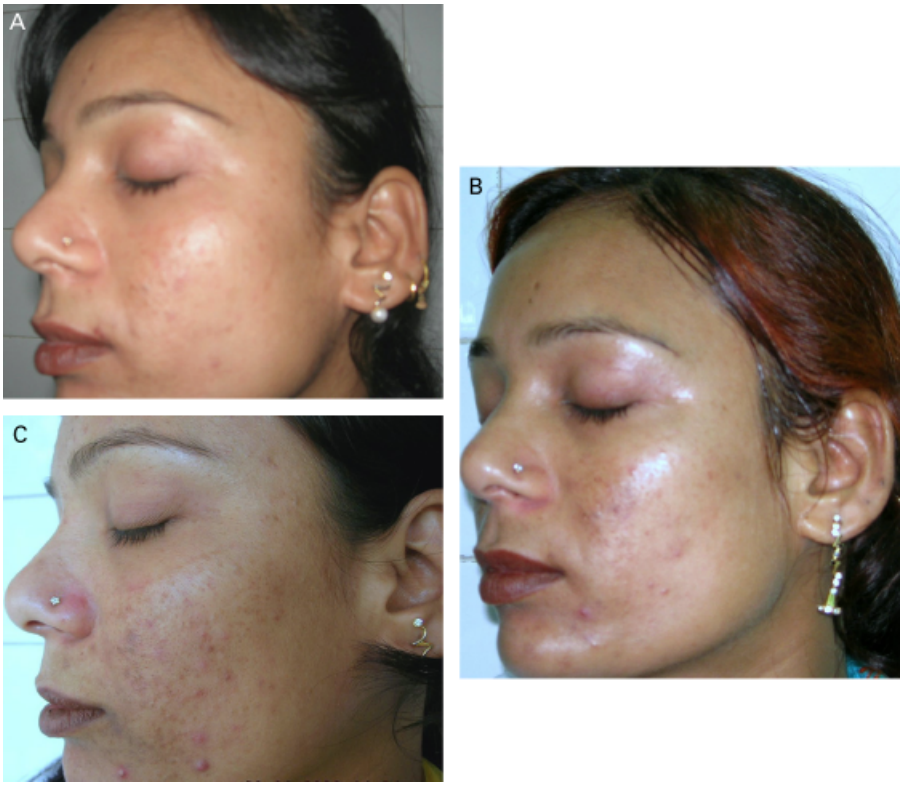

Figure 1. (A–C) Results with salicylic–mandelic acid peeling. (A) Baseline photographs showing multiple active acne lesions with post-acne hyperpigmentation. (B) Photographs at 12 weeks depicting noticeable reduction in active acne lesions and hyperpigmentation. (C) Photographs at 24 weeks showing significant decrease in acne lesions and post-acne hyperpigmentation, with overall improvement in skin texture.

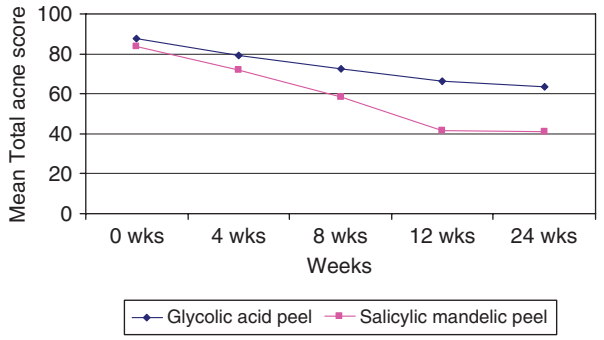

Figure 2. Comparison of effects of glycolic acid peels and salicylic–mandelic acid peels on total acne score.

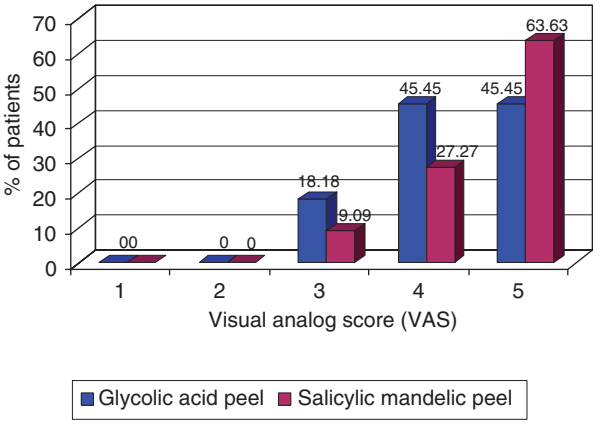

Figure 3. Comparison of visual analog scale with glycolic acid peels and salicylic–mandelic acid peels (patients at 24 weeks).

Icepick scars: The effect of SPMs was apparent earlier (by 4 weeks, $p < .001$) than for GA peels (took 8 weeks), although there was no significant difference between the two agents in their final effect on icepick scars ($p = .10$). Percentage change in icepick scars (Week 0 to Week 24) was 10.4% with GA peels and 13.2% with SPMs ($p = .3$).

Boxcar scars: Both the chemical peels produced highly significant ($p < .001$) improvement by 8 weeks, but there was a statistically significant difference in the mean number of boxcar scars in the two groups at baseline ($p = .02$). No significant difference was seen between the two agents thereafter. The change in boxcar scars from baseline to end of the study was 20.1% with GA peels and 23.3% with SPMs ($p = .02$).

Rolling scars: There was no change in rolling scars with either of the two agents ($p = 1.00$ for both agents).

Post-acne hyperpigmentation: GA peels and SPMs caused highly significant comparable improvement in post-acne hyperpigmentation ($p < .001$), although SPMs obtained a better result at the end of the study ($p = .046$). Percentage change in post-acne hyperpigmentation from baseline to Week 24 was 46.3% with GA peels and 59.8% with SPMs ($p < .001$).

Subjective Assessment

The visual analog scale scores as assessed by the patient, treating physician, and an independent observer all concurred with higher overall assessment for SMPs at the end of the study (Figures 3–5).

Side Effects

A large majority (60.9% for GA peels and 76.1% for SMPs) of patients did not develop any side effect due to peeling; 17.3% patients developed a burning or stinging sensation, and 8.7% of the GA peel group and none of the SPM group had visible desquamation. Dryness was seen more often with SPMs (14.28%). Photosensitivity and initial acne flare (papular and pustular) were seen in one patient each in each group.

Discussion

To the best of our knowledge, there are no published data on SMPs being used for acne. This might be

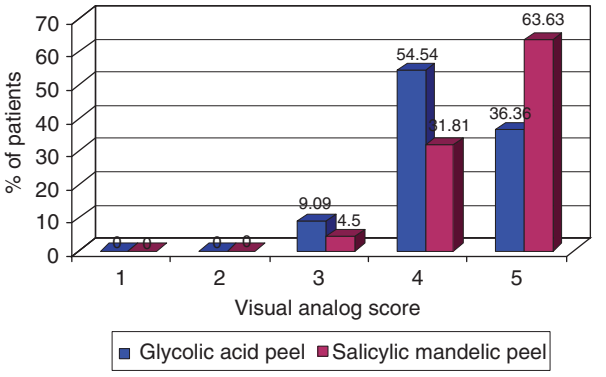

Figure 4. Comparison of visual analog scale with glycolic acid peels and salicylic–mandelic acid peels (treating physician at 24 weeks).

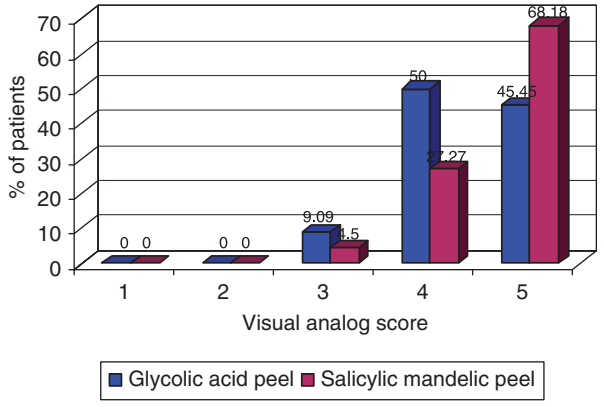

Figure 5. Comparison of visual analog scale with glycolic acid peels and salicylic–mandelic acid peels (independent observer at 24 weeks).

because of the large structure of mandelic acid, which causes slow penetration, thus making it difficult to evaluate it as a peeling agent. However, a few studies have use salicylic acid for treatment of acne. Lee and Kim evaluated the use of 30% salicylic acid in treatment of acne in 35 Asian patients.[15] The salicylic acid was used fortnightly for 12 weeks. They found a significant decrease in mean total facial lesion count, noninflammatory lesions, and mean acne grade reduction at the end of treatment. Grimes used two 20% and three 30% salicylic acid peels at fortnightly intervals in 25 dark-skinned patients with different dermatoses, out of whom nine had acne vulgaris.[16] Moderate (51–75%) to significant (>75%) clearing of acne was seen in 89% of patients. Noninflammatory and inflammatory lesions were seen to clear faster than would ordinarily have occurred with traditional therapy. All patients with oily skin and enlarged pores had significant improvement. The author explained this based on the property of salicylic acid to inhibit microcomedone formation, thus leading to a decrease in follicular openings. Likewise, in the present study, the mean total acne score decreased from 83.9 to 41.1 from baseline to 24 weeks ($p < .001$). Noninflammatory lesions (comedones), papules, and pustules had decreased significantly at the end of treatment. SPMs were well tolerated, and no patient developed post-inflammatory hyperpigmentation/scarring or allergic sensitization.

In this study, SMPs were seen to be significantly better than GA peels in the treatment of noninflammatory lesions (comedones) and papules and pustules. This is because of the unique lipophilic and antiinflammatory properties of salicylic acid, which seems to be the dominant agent in the polyhydroxy acid combination, which seems to be acting on acne. GA, on the other hand, is hydrophilic, which makes it a weaker comedolytic agent. Furthermore, it does not have the antiinflammatory properties of salicylic acid. Although both of the agents led to a subtle decrease in the number of icepick and boxcar scars, the difference between the two did not appear to be clinically significant. Because both of the peeling agents are superficial peels, they serve only to resurface the upper layers of the epidermis. Through an indirect, as-yet-unknown mechanism, both stimulate the dermal fibroblasts to deposit more collagen, elastin, and glycosaminoglycans in the papillary dermis. A more orderly and parallel arrangement of the fibers is also seen with both agents.[17] Thus, a gradual and slight decrease in the number of superficial scars and a decrease in the depth of deeper scars is observed. However, neither of them has a deeper action that could lead to significant improvement in icepick, deep boxcar, and rolling scars.

Both of the agents were effective for post-acne hyperpigmentation, with SPMs showing a greater response (Figure 1). SMPs improve post-acne hyperpigmentation by slightly different mechanisms than GA peels. Salicylic acid is antiinflammatory and thus serves to decrease existing post-acne hyperpigmentation and prevent further inflammation. In addition, Ahn and Kim[18] showed salicylic acid to have a whitening effect on the skin. This effect was seen in the present study too, with patients reporting diffuse lightening of their facial complexion. Mandelic acid has also been shown to be effective in clearing hyperpigmentation in patients who were resistant to other conventional modalities. Although the mean visual analog scale scores were higher for SPM in all three groups, there was no statistically significant difference between SPMs and GA peels.

The findings in our study indicate that GA peels and SMPs are efficacious in acne with post-acne scarring and hyperpigmentation, with SPMs being better for most inflammatory acne lesions and post-acne hyperpigmentation. Therefore the combination of an AHA and a BHA like the SPM may prove to have higher efficacy and better tolerability than the more commonly used AHAs alone in patients with acne and its sequelae.

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