

The Efficacy and Safety of a Novel Protective Complex Combined With 50% Glycolic Acid Peel: A Double-Blinded, Split Face, Controlled Study

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ABSTRACT

Background: Glycolic acid (GA) is a commonly used superficial peel with higher concentrations and lower pH levels leading to a stronger effect despite a higher risk of adverse effects (AE), which include burning, pain, itching, erythema, and edema.
Objective: This study aimed to evaluate the potential of a novel protective complex (NPC) to reduce facial AEs following a GA chemical peel treatment.
Methods and Materials: Twenty volunteers were selected for the study. A pair of numbered kits were supplied by and randomly assigned to be applied to each side of a patient's face with either a 50% GA peel plus NPC or a control formulation with only a 50% GA peel. AEs, patient photographs, and standard and red filtered VISIA scans were evaluated by three independent dermatologists.
Results: The average post-treatment pain and itching were significantly higher in the control half as compared to the study half. Recovery time appeared to be significantly shorter in the treated side compared to the control side.
Conclusion: The addition of the NPC to GA 50% peel is a highly effective, safe modality in the reduction of erythema, pain, and itching after peel application, and it provides an advantage in the post-treatment healing period.

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INTRODUCTION

Chemical peels are a popular, effective, noninvasive and relatively safe modality to improve skin appearance and to treat various skin problems, such as acne, pigmentation, scars, wrinkles, melasma, and photoaging among others. They are categorized according to their depth of penetration into superficial, medium, and deep peels.[1,2] Peels are commonly used in clinical settings and found in many cosmetic products.[1,3]

Glycolic acid (GA) is a commonly used superficial peel with higher concentrations and lower pH levels leading to a stronger effect despite a higher risk of adverse effects. Most common adverse effects following glycolic acid peel are the sensation of burning, pain or itching, erythema, and edema.[1,3-5] A novel protective complex (NOON Aesthetics®, Tel Aviv, IL), known as the DermShield™, was developed to be added to the peel in order to allow the use of high concentration GA peel at a low pH, while reducing the accompanying negative adverse effects on the skin. The purpose of this study is to examine this novel protective complex (NPC) for its anti-irritation effect, tolerability, efficacy, and safety while added to the GA 50% peel.

MATERIALS AND METHODS

This prospective, double blind, split-face controlled study aimed to evaluate the potential of the NPC to reduce facial adverse effects following a GA chemical peel treatment. The clinical trial was carried out at an outpatient private clinic in the period from January 2019 till March 2019. After approval of the Institutional Review Board (IRB), informed consent was obtained from all subjects prior to beginning the study.

One month prior to the trial, all patients could apply only a moisturizer and a sunscreen. A pair of numbered kits were supplied by NOON Aesthetics and assigned to each patient. The company used a designated software to randomize the patient number, facial halves, and the treated (50% GA peel plus NPC) Vs. the control formulations (only 50% GA peel). The two kits were identical in shape, size, and weight, as well as color, odor, and consistency. A randomized list was kept away to ensure the integrity of the trial. Neither the treating physician nor the patients knew which facial half was treated by the study or control kit.

Demographics, including age, medical history, dermatological

history, smoking, drugs, alcohol use, and skin type were collected before enrollment to the study. Excluded patients had cut or broken skin, known active or chronic skin disease, a personal history of abnormal bleeding, scarring, or wound healing. Patients were also excluded if they were pregnant or breastfeeding, reported known hypersensitivities to glycolic acid or other alpha-hydroxy acid (AHA) peels/products, or had a prior medium or deep chemical peel, prior laser treatment, fillers, or botulinum toxin facial procedures within three months of enrollment. Additional exclusion criteria included the use of retinoids, immunosuppressive drugs (steroids, NSAIDs, chemotherapeutic, biological agents), or photosensitizing medications in the past 6 months.

Prior to treatment, the subject's skin was cleaned using a mixture of 50% alcohol and 50% acetone. The peels were applied by a licensed nurse with experience using AHA peels under medical supervision. Two ml of the NOON Aesthetics Peel Formula containing 50% glycolic acid peel and 0.9 pH with the NPC were applied to half of the subject's face (treated side), while two ml of the NOON Aesthetics Peel Formula containing only 50% glycolic acid peel, 0.9 pH without the protective complex was applied to the other half (control side). After a 15-minute application, the GA peel was then neutralized with a formula containing sodium bicarbonate on both sides.

Subjects were photographed before and at 3-, 15-, and 30-minutes post-peel application, as well as 120 minutes following peel neutralization. Evaluation of the standard and red filtered VISIA (Canfield Scientific, Parsippany, NJ) photographs was performed by three independent dermatologists using the following scale: 0–no difference between the two halves of face, 1–minimal difference (1–25%), 2–mild difference (26%–50%), 3–moderate difference (51%–75%), 4–significant difference (76%–100%). Erythema was also measured at each time point by a MX18 Mexameter® (CK Electronic GmbH, Cologne, Germany).

Pain and itching at both halves over time were evaluated using a standard numerical 10-point Visual Analogue Scale (VAS). Subjects were asked to mark the scale according to their assessment of pain and sensory irritation as experienced at a given time point, from 0 (no pain/sensory irritation) to 10 (worst possible pain/sensory irritation). At follow-up visit, subjects were requested to evaluate healing time by indicating the time frame (in hours) needed to reach full resolution of the following parameters: edema, redness, and sensation of heat and time to return to normal daily activity.

Following the peel, subjects were instructed to apply sunscreen SPF 30 or higher, avoid any exposure to the sun, and report to the clinic about any type of serious adverse events.

Analyses were carried out using SPSS 25.0. The Wilcoxon paired t-test was used for comparing the treated and non-treated sides. Friedman's test was used to compare the changes in erythema changes over time followed by Dunn's post hoc test. *P* values <0.05 were considered statistically significant.

RESULTS

From the pool of potentially eligible patients, 20 healthy female volunteers between the ages 40 and 54 (mean: 45.5 ± 4.6) were selected for the study. Most subjects (n=19) were classified as Fitzpatrick skin type II or III. One subject was classified as Fitzpatrick skin type I. No background diseases were reported except for one subject who suffered from atopic dermatitis. All subjects completed the trial. When evaluated by three independent dermatologists for erythema, all raters observed no significant difference in erythema between the two sides of the face at baseline and in the last follow-up visit. However, a significant reduced level of erythema on the treated side at 3-, 15-, 30-, and 120-minutes post-treatment were scored by all raters. A representative patient is seen in Figure 1. The three raters' erythema score differences between the treated and control sides over time are shown in Figure 2.

At baseline, the objective measured levels of erythema taken with Mexameter technology were 364.2 and 354.35 for the treated and control sides respectively. After 3 minutes, the control side experienced a jump in erythema to 486, then a steady decrease to 369.65 after 120 minutes. The treated side

FIGURE 1. Representative patient over time. Right half – control, left half – treated with the novel protective complex (DermShield™).

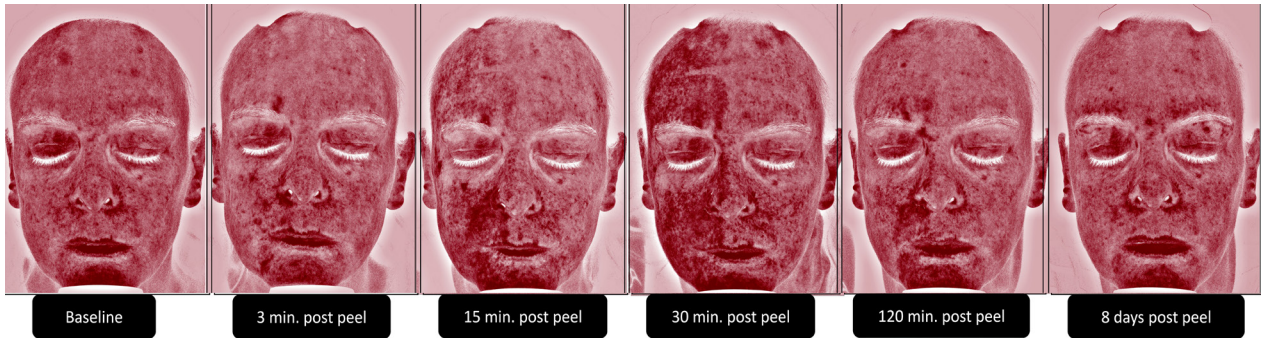

FIGURE 2. Erythema score by raters over time. Insignificant differences between treated and control sides were evaluated by the raters at baseline and follow-up observations. Significant differences between study and treated sides were scored by all raters at 15 minutes, 30 minutes, and 2 hours post-peel (*P*<0.001).

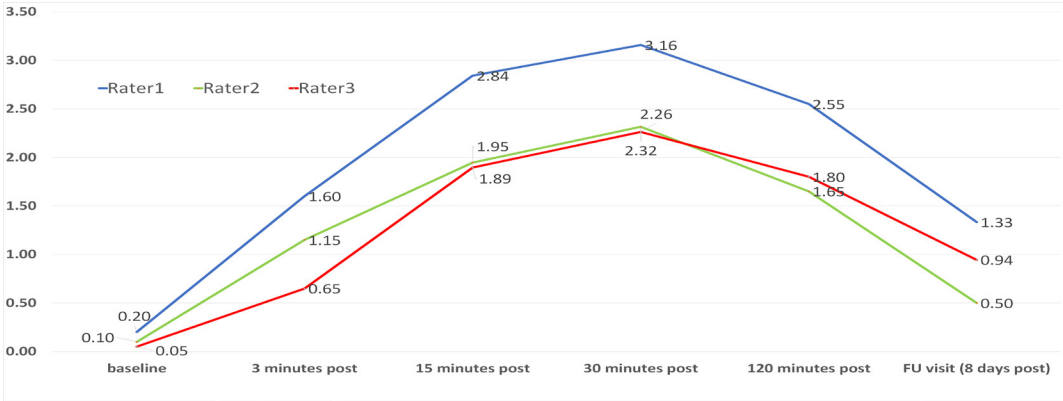

TABLE 1.

Time of Resolution (in hours) of Treated Versus Control Side								
	Edema		Redness		Post Treatment Recovery Time		Hispanic/Latino[a]	
	Treated	Control	Treated	Control	Treated	Control	Treated	Control
Mean (sd)	8.4 (16.1)	47.4 (60.1)	24.0 (29.9)	57.1 (42.7)	9.7 (16.3)	42.1 (61.3)	4.1 (8.7)	27.2 (32.4)
P value	0.006		0.016		0.030		0.012	

experienced a jump in erythema to 381.0 after 3 minutes. Then a decrease in erythema to sub-baseline levels was observed with Mexameter at 351.65 after 120 minutes. At 30 minutes, mean erythema score was significantly higher on the control side in comparison to the treated side (453.6 ± 55.2 vs 359.8 ± 58.1, *P*-value =0.008)

The average pain and itching, at 3-, 15-, 30-, and 120-minutes post treatment were significantly higher in the control half as compared to the study half. On the treated side, itching and pain were rated using the VAS as 1.15 and 2.0, respectively, at 3 minutes after application, steadily decreasing to 0.15 and 0.10 after 120 minutes. The control side was subject to itching and pain rated as 5.05 and 6.50, respectively, 3 minutes after application, and remained at 0.45 and 1.35, respectively, after 120 minutes.

Post treatment recovery time (till full resolution of facial redness, edema, heat sensation) as well as time to return to normal daily activity appeared to be significantly shorter in the treated side compared to the control side (Table 1). More reported AE with mild to moderate severities were reported in the control halves, which included acne, sensation of burning, erythema, rash, itching, and dryness for an average of 3.89 days (range, 2 to 8 days).

DISCUSSION

Chemical peels are an effective, noninvasive, and relatively safe modality to improve skin texture and tone and to treat various skin problems, such as acne, pigmentation, scars, wrinkles, melasma, and photoaging among others. They are widely used in clinical settings and found in many cosmetic and medical products. By using caustic agents targeted to a specific cutaneous depth, controlled injury and inflammation lead to a process of normal wound healing and rejuvenation as well as thickening of the epidermis.[1,3] The different peels are categorized according to their depth of penetration into superficial, medium, and deep peels.[1,2,6]

GA is a commonly used type of (AHA) normally applied in concentrations ranging from 20%–70% and pH levels of 0.08–2.75 in non-buffered solutions. GA peels are generally considered superficial peels and usually require neutralization in order to cease further acidification of the skin, after which a transient burning or pain sensation followed by erythema and edema are expected.[1,3,4] Potential effects can be altered by the peel's concentration, pH level, number of applied layers, and exposure time. Both concentration and pH levels play important roles in establishing the potency of GA peels with evidence pointing to pH levels being more dominant. Lower pH levels lead to a stronger effect despite a prolonged healing time and higher risk of complications.[1,2,5] which includes amongst other allergic reactions blistering, folliculitis, acne outbreaks, infections, herpes recurrence, ecchymosis secondary to edema, hypopigmentation as well as hyperpigmentation, textural cutaneous changes, and scarring. These complications can occur immediately or within a few days to weeks after the treatment.[7-10]

In an attempt to reduce the negative adverse effects and possible complications, several strategies are employed. Strontium salts

were reported to have inhibitory properties in the processes of irritation sensation and inflammation while maintaining the AHA efficacy without the side effects of local anesthetic in topically applied solutions. The mechanism for strontium's inhibitory effect is unclear, however, a possible explanation is that strontium may have a direct effect on signal transmission via nociceptor C fibers.[11-14] Methyl-sulfonyl-methane (MSM) is an organic sulfur rich compound found normally in our diet attributed to have anti-inflammatory properties.[15] It has been tested in treating various conditions such as rosacea, musculoskeletal disorders, and hemorrhoids and can be administered topically and orally.[16-19] The breakthrough technology of the NPC combines strontium and MSM in a patented formulation, creating a synergistic effect most useful in decreasing the development, incidence, and severity of skin irritation and erythema related to the peel, thus enabling the use of high concentration active ingredients in topically applied cosmetics and achieving desired results while reducing the accompanying unpleasant sensations.

This current study examines the NOON Aesthetics NPC while added to GA 50% peel. Our study demonstrated that the addition of the NPC to GA 50% significantly reduces the post-peel erythema, itching, and pain compared with the side treated with 50% GA alone. This effect was clearly observed within the first few minutes after peel application, lasting for at least two hours post treatment. In addition, the post-peel adverse effects were mild to moderate and appeared to be less prevalent on the side treated with 50% GA plus NPC. Neither the patient nor the evaluating physicians noted any difference in the final post-peel cosmesis at the follow-up visit.

Despite the use of the NPC, efficacy of the GA treatment was not compromised and observed to be the same across the treatment and control groups. While local irritation is an indication of the effect of GA, it is a side effect of the peel, and the efficacy is a parameter of the pH of the formula, the concentration of the acid, and the application time, which were maintained across the treatment and control groups.

LIMITATIONS

Limitations of our study included a relatively small study size of 20 individuals and limited testing to mostly Fitzpatrick skin types II and III. The NPC was tested only with formulations of highly concentrated GA, whereas other chemical peels at different concentrations were not tested. It is also difficult to truly assess the clinical improvement of both sides after only a single GA 50% peel. Furthermore, we did not follow up with patients on the long-term efficacy of the peel with the NPC.

Future directions should evaluate the true utility of NPC with respect to other AHA and beta-hydroxy acid formulations on different skin types and using multiple treatments. Additionally, further studies with larger cohorts are needed to establish the NPC as a safe and effective standard clinical product. Additionally, long-term split-face objective studies are needed to compare the efficacy of a peel with the NPC to a peel without the NPC.

CONCLUSION

In conclusion, the addition of NPC to GA 50% peel is a highly effective, safe modality in the reduction of erythema, pain, and itching sensation after peel application, and it provides an advantage in the post-treatment healing period.

DISCLOSURES

The study was sponsored by NOON Aesthetics®, Tel Aviv, IL.

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