EFFECTS OF COMBINATION TREATMENT OF LONG-PULSED ND: YAG 1064NM LASER WITH 15% GLYCOLIC ACID FOR FACIAL REJUVENATION

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ABSTRACT

This prospective interventional study investigated the effectiveness of combining long-pulsed Nd: YAG 1064nm laser with 15% glycolic acid for facial rejuvenation in 15 participants, Southeast Asian ethnicity, aged 35-50 years with Fitzpatrick skin types III-V. Each subject underwent 3 treatment sessions at four-week intervals, with outcomes assessed using the Physician Global Aesthetic Improvement Scale (GAIS) at weeks 4, 8, and 12, along with wrinkle severity, skin viscoelasticity, and trans-epidermal water loss (TEWL) from baseline to follow-up. Patient satisfaction was recorded at week 12, and adverse events were monitored throughout. Results demonstrated progressive improvements in GAIS, significant reductions in wrinkles, increased skin viscoelasticity, and decreased TEWL, reflecting enhanced dermal structure and barrier function. All participants expressed high to complete satisfaction, and no serious side effects such as scarring, hyperpigmentation, or prolonged erythema were reported. These findings indicate that the combined therapy is a safe, well-tolerated, and effective approach to facial rejuvenation, offering synergistic benefits by targeting both dermal remodeling and epidermal renewal pathways, and highlighting its potential as a valuable minimally invasive treatment option.

Keywords: Skin Aging, Facial Rejuvenation, Nd: YAG Laser, Non-ablative Laser, Glycolic Acid

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INTRODUCTION

Human skin serves as a decorative and vital organ of emotional expression in addition to being a protective barrier (Kligman & Koblenzer, 1997). Moreover, a youthful appearance boosts self-esteem and social interactions, reflecting both health and personality. Common signs of facial aging include wrinkles, frown lines, nasolabial folds, eyelid laxity, under-eye hollowness, and a receding hairline (Gupta & Gilchrest, 2005).

In response to these visible changes, facial skin rejuvenation has become increasingly popular over the past decades, with the goal of restoring youthful dermal structure and epidermal function. To achieve these outcomes, a range of treatments are employed, including chemical peels, fillers, laser therapies, botulinum toxin, and surgical lifts. Among these approaches, laser ablation has gained particular attention due to its effectiveness and relatively shorter recovery time, and it can be classified as either ablative or non-ablative (Hong et al., 2015). However, non-ablative lasers are often preferred, even though their results are comparatively slower and less dramatic (Kim & Geronemus, 2004).

Specifically, the long-pulsed Nd: YAG 1064nm laser (LPND), a non-ablative laser, penetrates deeply into the dermis to stimulate collagen and elastin regeneration while preserving the epidermis. By selectively targeting dermal chromophores such as melanin, oxyhemoglobin, and water, with lower epidermal absorption than visible-light lasers, it effectively minimizes risks like blistering and eschar formation. As a result, this controlled photothermal effect improves skin laxity, elasticity, and fine lines, making the treatment both effective and safe for patients with darker skin tones (Hong et al., 2015).

In addition to laser therapies, chemical peels are extensively utilized to treat melasma, acne, scars, and age-related skin changes. Their mechanism involves keratolysis and stimulation of cellular activity within both the epidermis and dermis, enhancing keratinocyte differentiation and neocollagenesis. Among these, alpha-hydroxy acid (AHA) peels, particularly glycolic acid (GA), are widely favored due to their safety, minimal downtime, and rapid efficacy. GA's small molecular size and hydrophilic nature allow for effective dermal penetration. Furthermore, topical 15% GA specifically induces pronounced stratum corneum desquamation, increases epidermal keratinocyte proliferation, and moderately enhances dermal collagen, with treatment protocols adjustable through concentration, pH, and exposure time (Rouvrais et al., 2018).

Building on the complementary mechanisms of both treatments, the present study is designed to investigate the effects of combining the long-pulsed Nd: YAG 1064nm laser with 15% glycolic acid for facial rejuvenation.

LITERATURE REVIEWS

Skin Anatomy and Skin Aging

The skin, the body's largest organ, covers its entire external surface and is composed of three main layers: the epidermis, dermis, and hypodermis. Each layer possesses distinct anatomical features and fulfills specific physiological functions. Beyond serving as the body's first line of defense against pathogens, ultraviolet (UV) radiation, and harmful chemicals, the skin also provides mechanical protection, helps regulate body temperature, and controls water loss to the environment (Yousef & Sharma, 2017). Aging is an unavoidable process marked by complex changes that gradually reduce youthful characteristics. Common facial aging signs include hairline recession, forehead wrinkles, eyelid drooping, under-eye hollows, deepened nasolabial folds, facial lines, and jawline sagging (Panda & Chowdhary, 2021).

Long-pulsed Nd: YAG 1064nm Laser for Facial Rejuvenation

The Nd: YAG laser, first demonstrated in 1964, employs a neodymium-doped yttrium aluminum garnet crystal to generate near-infrared laser light. The crystal is energized by a high-intensity lamp, either a flashtube or diode—within a resonant cavity that amplifies the laser output, requiring optimal ion population inversion before activation. Nd: YAG lasers can emit multiple wavelengths, including 1064, 940, 1120, 1320, and 1440 nm, all within the near-infrared spectrum. They typically operate in pulsed modes, often using Q-switching, but can also function in continuous-wave mode, providing versatility for a range of therapeutic and aesthetic applications. (Geusic et al., 1964). The Nd: YAG laser with a wavelength of 1064nm penetrates the dermis to a depth of its peak at more than 4mm. The laser has major skin chromophores comprising melanin, oxyhemoglobin, and water, in comparison with visible-spectrum lasers, its absorbance of melanin and oxyhemoglobin is less (Meesters et al., 2014). Owing to its low melanin absorption, the 1064 nm Nd: YAG laser deposits minimal energy within the epidermis, decreasing the incidence of side effects like blistering or eschar. This enables deeper tissue penetration and safe application in darker skin tones (Taylor & Prokopenko, 2006). Via energy deposition within the deep dermis, the laser induces thermal injury, which in turn triggers the production and remodeling of collagen and elastin, whilst sparing the epidermis. This sequence of events contributes to enhanced skin laxity and elasticity, reduction of wrinkles, and improvement in overall skin tone, culminating in facial rejuvenation (Hong et al., 2015). The heating process primarily affects the dermis through non-selective heating of the dermis which initiates a cascade of regenerative processes, primarily involving collagen remodeling. This process is characterized by fibroblast proliferation and increased collagen synthesis, with remodeling activity beginning to rise approximately three weeks after laser exposure, continuing for up to five weeks, and reaching its peak around the fourth week. In addition to stimulating collagen production, dermal heating also promotes elastin regeneration, contributing to long-term stimulation of elastin fibers and overall improvement in skin structure and quality (Tanaka & Matsuo, 2011). Histological studies by Dayan et al. showed that long-pulsed Nd: YAG 1064 nm laser resurfacing induces dermal rejuvenation, marked by increased epidermal keratinocytes, collagen, elastin, and glycosaminoglycans, alongside displacement of degenerated elastic connective tissue, collectively enhancing skin remodeling (Dayan et al., 2003). Studies reported that the long-pulsed Nd: YAG 1064nm laser effectively improves skin laxity and reduces wrinkles, supporting its application in skin-tightening procedures (Key, 2007; Taylor & Prokopenko, 2006). In this study, we employed Hyperion® Laser, manufactured by LASEROPTEK, Korea.

Glycolic Acid for Facial Rejuvenation

Chemical peels are widely used by dermatologists to treat conditions such as melasma, acne, scars, and aging by exfoliating the skin and stimulating cellular activity in both the epidermis and dermis, thereby promoting keratinocyte differentiation and collagen production. Alpha-hydroxy acids (AHAs), a common group of peeling agents, are organic compounds with a carboxylic group and a hydroxyl group on the adjacent carbon. They occur naturally in fruits and other botanical sources and can also be synthesized for clinical use (Babilas et al., 2012). Glycolic acid (GA), an alpha-hydroxy acid (AHA), is widely used in dermatology for its safety, minimal downtime, and rapid clinical effects. Its small molecular size and hydrophilic nature allow it to penetrate the skin effectively, enhancing efficacy. GA peels are highly adaptable, with concentration, pH, and application time adjustable to meet specific therapeutic goals and individual patient skin characteristics (Rouvrais et al., 2018). According to the FDA, the recommended safe concentration range of glycolic acid for use as a skin peeling agent is between 3% and 67% (Roth GmbH, n.d.). Studies have shown that glycolic acid can be used effectively as both a superficial and medium-depth peel for treating photoaged skin. These peels induce histological changes in the epidermis, restoring a more organized structure. Post-treatment, columnar keratinocytes regain normal polarity, and melanocytes along with melanin granules become more uniformly distributed, enhancing overall epidermal morphology (Kubiak et al., 2020). Narda et al. reported that 15% glycolic acid effectively promotes desquamation, increases keratinocyte proliferation, and enhances collagen production without causing inflammation. At pH 4, this concentration provides an optimal balance of exfoliation and collagen stimulation while remaining well tolerated and minimally irritating (Narda et al., 2021). In this study, we utilized 15% glycolic acid. It is colorless, clear to light yellow liquid, which is manufactured by Skin Intimate Company. The formulation was adjusted to pH 4 with aminomethyl propanol.

Combination of Long-pulsed Nd: YAG Laser and Glycolic Acid for Facial Rejuvenation

The combination of long-pulsed Nd: YAG 1064nm laser and glycolic acid (GA) provides a synergistic approach to facial rejuvenation by targeting both dermal and epidermal layers. Combined, these modalities provide comprehensive rejuvenation: the long-pulsed Nd: YAG 1064 nm laser remodels the deep dermis to enhance structural integrity (Dayan et al., 2003; Hong et al., 2015; Tanaka & Matsuo, 2011), while GA, specifically, 15% GA at pH 4, optimizes epidermal renewal, texture, and pigmentation while maintaining good tolerability (Narda et al., 2021). This dual approach maximizes efficacy, minimizes downtime, and reduces risks, offering a safe, non-ablative strategy suitable for multiple skin phototypes.

RESEARCH METHODOLOGY

Fifteen healthy adults aged 35-50 years with Fitzpatrick skin types III-V will be recruited at Mae Fah Luang University Hospital, Bangkok. Participants will be fully briefed on the study's objectives, procedures, potential risks, and benefits, and written informed consent will be obtained prior to enrollment. Baseline assessments will include medical history, standardized facial photography using the VISIA® Complexion Analysis System, and objective skin evaluations with VISIA® for wrinkle scoring, the Cutometer® MPA 580 for elasticity, and the Tewameter® TM 300 for trans-epidermal water loss (TEWL), conducted under controlled room temperature (20-22 °C) and humidity (40-60%) after face washing and natural drying for 15 minutes. Topical anesthetic (EMLA cream) will be applied for 30 minutes and then removed, after which protective petroleum jelly will be placed around sensitive areas, and 1 cc of 15% glycolic acid will be applied evenly to the face for two minutes before rinsing. The Hyperion® Nd: YAG laser will then be administered at 1064 nm, 5 mm spot size, 0.3 ms pulse duration, 15 J/cm² fluence, and 10 Hz frequency, performing three passes over the cheeks, forehead, chin, and T-zone, with the handpiece maintained approximately 2 cm from the skin and moved horizontally and vertically for uniform coverage. KOOLIO air-cooling at -30 °C will be applied throughout the procedure to minimize discomfort and thermal injury. Post-treatment care includes daily sunscreen application (SPF $\geq$ 30) and avoidance of skincare products containing retinol, AHA, BHA, PHA, or TCA to prevent interference with assessments. Follow-up evaluations are scheduled at weeks 4, 8, and 12, including repeat VISIA® imaging, Cutometer® and Tewameter® measurements, and recording of the Physician Global Aesthetic Improvement Scale (GAIS) at each visit, with patient satisfaction assessed at week 12 using a standardized questionnaire scored from 0 (not satisfied) to 4 (complete satisfaction). Effectiveness will be evaluated by comparing mean changes in GAIS at weeks 4, 8, and 12, as well as wrinkle score, skin elasticity, and TEWL from baseline to weeks 4, 8, and 12, while safety will be monitored by documenting adverse events, including pain, erythema, swelling, or pigmentary changes, at each visit.

RESEARCH RESULTS

Demographic Data

15 healthy participants (10 females, 5 males; mean age = 38.19 ± 4.09 years) were enrolled. All participants were of Southeast Asian ethnicity. According to Fitzpatrick skin classification, 9 participants had type III skin, 4 had type IV, and 2 had type V. None had a history of active skin disease such as melasma, active acne, psoriasis, keloid formation, or known allergies. All participants also reported no history of systemic diseases, hormonal disorders, or prior aesthetic procedures that could influence skin rejuvenation outcomes.

Clinical Evaluation

Statistical analyses were performed using SPSS software (IBM, version 2.1.0) under renewal quote number 26,500,879 from Mae Fah Luang University, Chiang Rai, Thailand. Repeated-measures ANOVA was applied to evaluate changes over time, followed by Bonferroni post-hoc tests for multiple comparisons. Statistical significance was defined as $p < 0.05$, and 95% confidence intervals (CIs) were reported for key outcome measures to indicate the precision of the estimates.

The Physician Global Aesthetic Improvement Scale (GAIS) demonstrated progressive improvement from week 4 (3.4 ± 0.51) to week 8 (4.3 ± 0.46) and week 12 (4.8 ± 0.41), with significant differences across time points ($p < 0.001$, $\eta^2 = 0.832$). Post-hoc analysis confirmed incremental improvement at each follow-up (all $p < 0.05$). The mean increase from week 4 to week 12 was 1.4 (95% CI [1.08-1.72], $p < 0.001$).

Table 1 Physician GAIS Scores: Statistical Evaluation at 4th, 8th, and 12th Week

Follow-up	Mean ± SD
4th week	3.4 ± 0.51
8th week	4.3 ± 0.46
12th week	4.8 ± 0.41
P-value	**<0.001**
Partial η²	**0.832**

Table 2 Multiple Post-Hoc Analysis of GAIS Outcomes

Pairwise	Mean difference	P-value
4th week-8th week	-0.87	<0.001
4th week-12th week	-1.4	<0.001
8th week-12th week	-0.53	0.002

Wrinkle scores decreased significantly from baseline (57.51 ± 14.01) to week 4 (44.80 ± 14.81), week 8 (32.23 ± 8.60), and week 12 (22.48 ± 7.74) ($p < 0.001$, $\eta^2 = 0.830$). Pairwise comparisons indicated a mean reduction of 35.03 points from baseline to week 12 (95% CI [25.94-44.12], $p < 0.001$).

Table 3 Wrinkle Scores: Statistical Evaluation at Baseline, 4th, 8th, and 12th Week

Follow-up	Mean ± SD
Baseline	57.51 ± 14.01
4th week	44.80 ± 14.81
8th week	32.23 ± 8.60
12th week	22.48 ± 7.74
P-value	**<0.001**
Partial η²	**0.830**

Table 4 Multiple Post-Hoc Analysis of Wrinkle Score Outcomes

Pairwise	Mean difference	P-value
Baseline-4th week	12.71	0.027
Baseline-8th week	25.28	<0.001
Baseline-12th week	35.03	<0.001
4th week-8th week	12.56	0.010
4th week-12th week	22.32	<0.001
8th week-12th week	9.754	0.004

Skin elasticity, assessed by Cutometer, showed significant improvement from baseline (54.10 ± 10.96) to week 4 (66.76 ± 8.83), week 8 (80.80 ± 8.35), and week 12 (88.58 ± 7.43) ($p < 0.001$, $\eta^2 = 0.826$). The overall increase of 30.35 points from baseline to week 12 was statistically significant (95% CI [21.45-39.25], $p < 0.001$).

Table 5 Cutometer Scores: Statistical Evaluation at Baseline, 4th, 8th, and 12th Week

Follow-up	Mean ± SD
Baseline	54.10 ± 10.96
4th week	66.76 ± 8.83
8th week	80.80 ± 8.35
12th week	88.58 ± 7.43
P-value	**<0.001**
Partial η^2	**0.826**

Table 6 Multiple Post-Hoc Analysis of Cutometer Score Outcomes

Pairwise	Mean difference	P-value
Baseline-4th week	-12.66	0.002
Baseline-8th week	-26.70	<0.001
Baseline-12th week	-30.35	<0.001
4th week-8th week	-14.04	<0.001
4th week-12th week	-17.69	<0.001
8th week-12th week	-7.78	0.015

Trans-epidermal water loss (TEWL), measured by Tewameter, progressively decreased from 19.23 ± 4.01 at baseline to 15.89 ± 2.79 at week 4, 13.85 ± 1.95 at week 8, and 10.34 ± 2.02 at week 12 ($p < 0.001$, $\eta^2 = 0.838$). The mean reduction of 8.89 points corresponded to a 95% CI of [6.32-11.46], confirming a significant enhancement in skin barrier function ($p < 0.001$).

Table 7 Tewameter Scores: Statistical Evaluation at Baseline, 4th, 8th, and 12th Week

Follow-up	Mean ± SD
Baseline	19.23 ± 4.01
4th week	15.89 ± 2.79
8th week	13.85 ± 1.95
12th week	10.34 ± 2.02
P-value	**<0.001**
Partial η^2	**0.838**

Table 8 Multiple Post-Hoc Analysis of Tewameter Score Outcomes

Pairwise	Mean difference	P-value
Baseline-4th week	3.34	0.016
Baseline-8th week	5.37	<0.001
Baseline-12th week	8.89	<0.001
4th week-8th week	2.03	0.033
4th week-12th week	5.55	<0.001
8th week-12th week	3.51	<0.001

At the final assessment, 10 participants reported complete satisfaction and 5 reported high satisfaction (Table 9).

Table 9 Frequency of Participant's Satisfaction Score

Participant's Satisfaction Score	n=15
Not satisfied (0)	-
Slightly satisfied (1)	-
Moderately satisfied (2)	-
Highly satisfied (3)	5
Complete satisfaction (4)	10

Throughout the treatment period, the combined application of long-pulsed Nd: YAG 1064 nm laser and 15% glycolic acid was well tolerated, with no observed or reported adverse effects such as erythema, edema, blister formation, post-inflammatory hyperpigmentation, infection, or scarring, indicating a favorable safety profile.

DISCUSSION & CONCLUSION

This study assessed the effectiveness of combining long-pulsed Nd: YAG 1064nm laser with 15% glycolic acid for facial rejuvenation in 15 participants (aged 35-50 years, Fitzpatrick skin types III-V). Participants received three sessions at four-week intervals, with outcomes evaluated using GAIS, wrinkle score, skin elasticity, trans-epidermal water loss, satisfaction, and adverse events. GAIS scores demonstrated significant and progressive improvement across all follow-up visits, indicating a steady improvement in overall facial appearance. Wrinkle scores significantly decreased, reflecting improved surface smoothness, while skin elasticity increased, suggesting enhanced dermal firmness due to neocollagenesis. The reduction in TEWL indicated improved epidermal barrier function and hydration. These results align with the established mechanisms of glycolic acid in stimulating epidermal renewal and collagen production (Narda et al., 2021) and those of long-pulsed Nd: YAG laser in dermal collagen remodeling (Hong et al., 2015). Importantly, this study's findings are consistent with previous evidence supporting the individual efficacy of each treatment modality. Studies have demonstrated that long-pulsed Nd: YAG laser significantly improves skin laxity, elasticity, and fine lines (Dayan et al., 2003; Key, 2007; Taylor & Prokopenko, 2006), while glycolic acid peels promote epidermal turnover, smoothen texture, and enhance collagen synthesis (Kubiak et al., 2020; Narda et al., 2021). However, the present findings go further by confirming that combining these two non-ablative modalities produces synergistic benefits, improving both dermal and epidermal parameters while maintaining an excellent safety profile. Furthermore, the synergistic effect observed in this study is in line with other combination approaches in aesthetic dermatology. For instance, study by (Shin et al., 2012) found that combining platelet-rich plasma (PRP) with non-ablative fractional laser therapy enhances skin rejuvenation more effectively than laser alone. In 22 Korean women, the combination treatment improved skin elasticity, reduced redness, and increased collagen and fibroblast activity without added side effects. Histological analysis showed greater dermal thickness and a longer dermo-epidermal junction, indicating that PRP boosts laser-induced regeneration through growth factor-mediated collagen synthesis. Similarly, (Park et al., 2011) conducted a randomized, split-face, observer-blinded trial evaluating 1064nm Q-switched Nd: YAG laser with 30% glycolic acid peels versus laser alone in adults with Fitzpatrick skin types III-V. The combination treatment side showed greater reductions in Mexameter scores and modified MASI scores compared to laser monotherapy. Participants' satisfaction was higher for the combination side (75% good/excellent) versus laser alone (38%), with only mild, transient side effects such as erythema, slight burning, and mild facial edema, all resolving within 3 hours. Superficial peeling was observed and managed with emollients, without permanent scarring or hypopigmentation. Than et al. evaluated the combination of fractional picosecond laser (1064nm) and 20% glycolic acid peeling for facial rejuvenation in 12 participants. After three sessions, results showed significant wrinkle reduction (up to 95%), improved elasticity (+88%), and reduced water loss (−84%), with no serious side effects. The combination proved safe and effective treatment for improving skin texture and firmness (Than et al., 2024).

In this context, the current study contributes new insight by demonstrating that the combination of long-pulsed Nd: YAG 1064nm laser and 15% glycolic acid—a gentler, non-ablative pairing—achieves comparable rejuvenation outcomes while maintaining minimal downtime and excellent tolerability. Unlike stronger or ablative, this regimen offers a safe and effective alternative for medium to dark skin phototypes, minimizing risks such as post-inflammatory hyperpigmentation.

All participants in this study reported high to complete satisfaction, and no adverse events (erythema, hyperpigmentation, or scarring) were observed, further underscoring the combination's favorable safety profile.

The combination treatment of long-pulsed Nd: YAG 1064nm laser and 15% glycolic acid is a safe, well-tolerated, and effective modality for facial rejuvenation in Fitzpatrick skin types III-V. The therapy significantly improved GAIS scores, reduced wrinkles, enhanced skin elasticity, and strengthened the skin barrier, yielding high participant satisfaction without complications. Compared with previously studied monotherapies and combination treatments, this protocol provides a balanced, minimally invasive approach that delivers synergistic benefits across both dermal and epidermal layers.

The implications of this research suggest that integrating mild chemical exfoliation with non-ablative laser stimulation may optimize rejuvenation outcomes while reducing the risk of complications common with more aggressive procedures.

Future research should focus on optimizing treatment parameters such as laser fluence, pulse duration, and glycolic acid concentration to refine efficacy and safety profiles across diverse skin phototypes. Moreover, studies with larger sample sizes, longer follow-up durations, histological verification, and randomized controlled designs are recommended to assess long-term collagen remodeling, durability of results, and comparative effectiveness versus other combination modalities. Such investigations will help establish evidence-based protocols for individualized, safe, and effective facial rejuvenation strategies.

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