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Evaluation Study

Non-crosslinked hyaluronic acid mesotherapy and hydro-exfoliation plus infrared technology: a combination protocol to improve skin quality

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DISCLOSURE: ALL AUTHORS REPORT NO CONFLICTS OF INTEREST RELEVANT TO THIS ARTICLE.

ABSTRACT

Smooth, healthy-looking skin is a desired aesthetic goal for all age groups. This study evaluated a new protocol combining non-crosslinked hyaluronic acid (HA) with hydro-exfoliation and infrared technology for improving skin quality parameters. This retrospective, single-center medical data analysis included subjects aged 18 to 65 in good general health, with signs of skin atrophy or aging in the face or neck area. On Day 0, subjects underwent mesotherapy with injections of non-crosslinked HA (18 mg/mL) with 0.01% calcium hydroxyapatite, glycine, and l-proline to a depth of 0.5 to 4 mm. On Day 7, this was followed by treatment with a combined hydro-exfoliation and infrared device. Visual improvements in skin quality parameters (wrinkles, pores, brown spots, texture, and oiliness) were assessed by a blinded evaluator using photographs taken prior to treatment and 2 weeks after the final treatment with a facial analysis imaging system. The medical data analysis included 22 subjects with a mean age of 45 years (range 28 to 65 years). Comparison of post-treatment with baseline images showed improvements in wrinkles of 13%-23%, pores of 16%-30%, skin texture of 15%-28%, and oiliness of 10%-33%; brown spots improved by 0.1%-0.7%. All treatments were well tolerated. In conclusion, the combination of non-crosslinked HA mesotherapy, hydro-exfoliation, and infrared technology led to visible improvements in several skin quality parameters across a wide age range. While the study demonstrated cosmetic benefits, further research is needed to assess the safety profile of these treatments in more detail, as the current methodology was not designed to specifically evaluate device safety.

INTRODUCTION

Skin quality is a crucial indicator of overall health and attractiveness, influencing how people perceive both themselves and others. While the current literature tends to focus more on age-related changes in skin quality rather than on skin quality, there is a growing demand across all age groups for products and treatments that improve skin tone, surface evenness, firmness, and overall glow (1, 2). These desires are universal, spanning different ethnicities and gender groups, with both men and women seeking treatments to maintain or enhance their skin's appearance (1).

State of the Art on Skin Quality Treatments

The skin's ability to regenerate and maintain its quality is intricately linked to the process of skin cell turnover, which declines with age. In younger adults, the turnover process takes approximately 20 days, while in individuals over 50 years of age, it can extend to over 30 days (3). This slower turnover is compounded by external factors, including diet, lifestyle choices, and environmental exposure. Habits such as smoking, alcohol consumption, poor nutrition, and lack of sleep further impede the skin renewal process, leading to a decline in visible skin quality. Additionally, the natural production of collagen—the protein responsible for skin's firmness and elasticity—decreases by 1.0% to 1.5% per year after age 25, contributing to the formation of fine lines and wrinkles (4). Traditional topical treatments often target only the surface of the skin. However, since multiple tissue layers contribute to visible skin quality, surface-level treatments may not produce the desired long-term results. For optimal outcomes, a holistic approach that addresses the deeper layers of skin is required. This has led to the development of multilayer treatment strategies that target both the epidermis and dermis (1, 3).

Several aesthetic procedures are known to promote cell renewal at both the epidermal and dermal levels.

These include techniques such as ultrasound therapy, fractional lasers, deep chemical peeling, mesotherapy, and microneedling (1). Among these, mesotherapy is particularly well-regarded for its ability to deliver active agents, including hyaluronic acid (HA), directly into the skin. This allows for deep hydration, nourishment, and stimulation of skin repair processes. Mesotherapy is often combined with exfoliating agents or skin turnover enhancers, which further support skin renewal and rejuvenation.

Hydro-exfoliation, also known as water peeling, is a gentler, mechanical exfoliation method. Hydro-exfoliation uses microscopic droplets to achieve precise exfoliation, deep cleansing, and hydration simultaneously. Unlike more abrasive techniques, it provides a milder, less invasive approach to exfoliation while still delivering visible improvements in skin quality.

Infrared (IR) irradiation is another technique known to improve skin texture by stimulating dermal fibroblasts to increase collagen production (5). Research has demonstrated that IR irradiation, a non-ablative method, can trigger dermal remodeling, encouraging the production of collagen types I and III and elastin. This leads to improved skin texture, elasticity, and firmness without damaging the epidermis (6). IR therapy is a well-tolerated option in non-invasive aesthetic treatments and is commonly used in combination with other procedures to achieve comprehensive skin rejuvenation.

Current Trends in Aesthetic Medicine

In aesthetic medicine, combining multiple technologies is becoming increasingly popular to address a range of underlying causes of skin imperfections. By using different modalities, clinicians can simultaneously target several aspects of skin aging or damage, providing more effective and long-lasting results (7–9). This approach has shown to be particularly useful in cases where patients present with a combination of wrinkles, uneven skin texture, and loss of firmness. Recent advancements have allowed for the integration of mesotherapy, hydro-exfoliation, and infrared irradiation into a single, cohesive treatment plan that tackles both superficial and deeper skin layers.

This retrospective study evaluates the combined effects of two complementary treatment protocols aimed at improving skin quality: (i) mesotherapy with a non-crosslinked hyaluronic acid (HA) supplemented with calcium hydroxyapatite and essential amino acids, followed by (ii) hydro-exfoliation and infrared thermo-lifting using a single device.

In this study, the null hypothesis (H0) is that the combination of non-crosslinked HA mesotherapy and infrared treatment does not significantly improve skin quality parameters such as wrinkles, pores, skin texture, and overall skin appearance compared to baseline. The alternative hypothesis (H1) is that this combined treatment does lead to significant improvements in these skin quality parameters. To test these hypotheses, we will assess skin quality improvements 14 days after the final procedure, using a combination of visual and instrumental analysis. This study aims to determine whether these two complementary treatments can provide measurable enhancements in skin quality and whether they are a viable option for patients seeking non-invasive aesthetic improvements.

MATERIALS AND METHODS

Participant Selection

This retrospective, single-center analysis of medical records included subjects aged 18 to 65 years, in good general health, who were diagnosed with skin atrophy or laxity in the treatment area by the investigator, and who underwent treatment between January 2024 and July 2024.

Treatment Protocol

All patients included in this analysis attended two visits, spaced 1 week apart. Treatment areas varied per patient, including the face, neck, and décolleté. On Day 0, mesotherapy was performed with injections of non-crosslinked hyaluronic acid (HA) (18 mg/mL) combined with 0.01% calcium hydroxyapatite, glycine, and l-proline (Neauvia Hydro Deluxe, Matex Lab, Switzerland). Multiple intradermal or subcutaneous injections (0.5 to 4 mm depth) of small HA volumes were administered using a 30G needle and a pre-filled 2.5 ml syringe. Local topical anesthesia was available, though not all patients required it.

On Day 7, patients underwent a hydro-exfoliation and infrared treatment of the entire face (Berger&Kraft Medical Sp. z o.o., Poland). Hydro-exfoliation involves using accelerated microscopic droplets for deep cleansing and hydration. The infrared component used a lamp with an inverted filter, emitting radiation in the 700–1800 nm range. The power was constant, and energy density per pulse (J/cm²) was operator-set, with the device adjusting pulse duration according to energy density. The treatment involved 2-3 passes, with energy settings of 35–45 J/cm², heating the deep dermal layers up to 65°C based on patient sensitivity and comfort. Continuous cooling provided surface protection throughout the procedure. The procedure was painless, required no prior preparation, and did not necessitate local anesthesia.

Evaluation of Skin Quality

A blinded evaluator (dermatologist) assessed visual skin quality improvements using photographs (frontal full-face, left and right side views) taken before treatment and 2 weeks after the final session. Images were captured with a facial analysis camera (3D LifeViz by QuantifiCare, France), which provided quantitative data on skin features such as wrinkles, pores, brown spots, texture, and oiliness. This objective analysis enabled a quantitative comparison of skin parameters before and after treatment.

Post-Procedure Recommendations

Subjects were advised not to apply pressure or use cosmetic products on treated areas within 24 hours after treatment. They were also advised to avoid direct sunlight and UVA-B exposure (e.g., tanning beds) for 2 weeks following treatment.

This study was conducted as a retrospective analysis of medical records. In accordance with routine clinical practice, all participants provided written informed consent prior to the first treatment and consent for the use of photographic images for analysis.

RESULTS

The study recruited 22 subjects (21 women and 1 man) with a mean age of 45 years (range 28 to 65 years); the majority had Fitzpatrick skin types II-III. All subjects underwent all treatments and completed the 2 sessions. Comparison of post-treatment with baseline images showed enhanced skin tone and quality. Observed changes in the face area included improvements in wrinkles (13%-23%), pores (16%-30%), skin texture (15%-28%), and oiliness (10%-33%) (Fig. 1). The smallest improvement was observed in brown spots, with changes of only 0.1%-0.7%. Fig. 2 shows baseline and 2-week results across QuantifiCare measurements. Other than slight redness that disappeared within hours, no adverse events were reported. Patients reported a ‘glow effect’ on the treatment day. Patients indicated that the neck, décolleté, and periocular area were the most impacted in the weeks and months post-treatment. Reported improvements included thicker skin sensation, reduced elastosis, and a more radiant glow. Patients with sensitive, reactive skin and even eczema noted correction of these conditions following the treatment protocol.

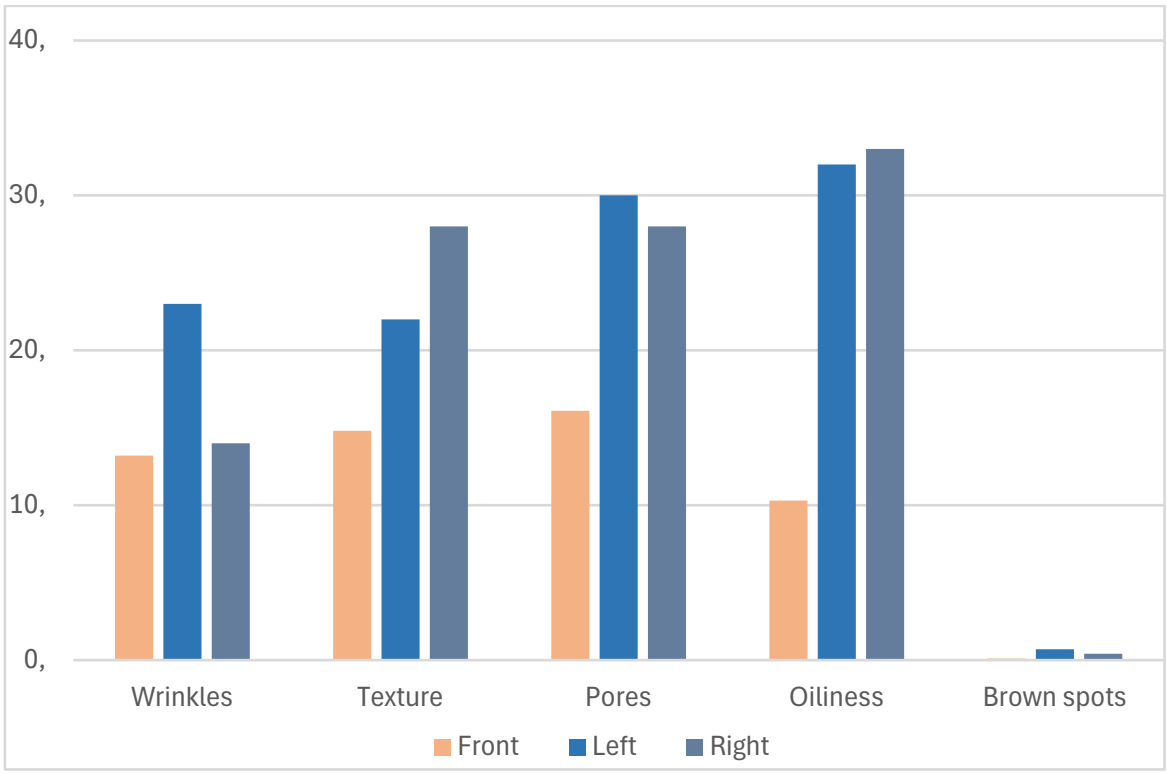
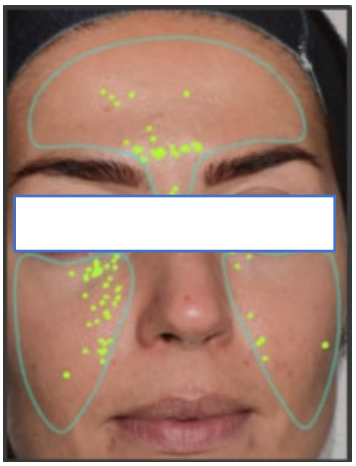
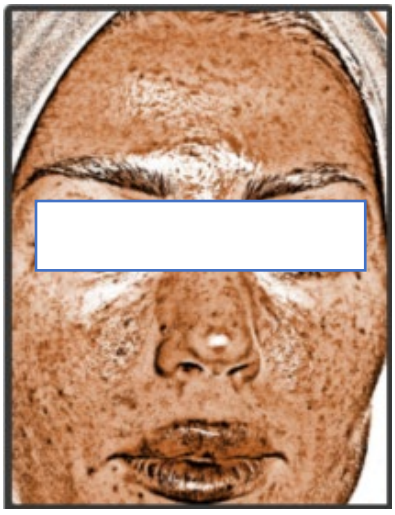


Fig. 1. *Percentage improvements in face skin quality measures after treatment with non- crosslinked HA followed by hydro-exfoliation and infrared technology. Results show improvement at 2 weeks after last treatment compared with baseline assessed with the QuantifiCare device.*

Pores



Brown areas



Texture

Fig. 2. *QuantifiCare results at baseline and 2 weeks after the final treatment.*

In a very recent study involving twenty women with an average age of 45, mesotherapy was applied using low molecular weight hyaluronic acid combined with amino acids to rejuvenate facial skin. Histological analysis showed an increase in fibroblast activity, resulting in the production of type III reticular collagen and an increase in blood vessels and epidermal thickness. However, ultrasound data analysis before and after treatment did not show statistically significant differences in skin thickness in the zygomatic area, chin, and mandibular angle (10). In our review of medical records, we did not have the opportunity to conduct such an in-depth study, focusing instead on the aesthetic effect of the treatment using non-crosslinked hyaluronic acid with a low concentration of CaHA in combination with an IR device.

Statistical analysis has not been conducted for the results presented; the data is shown solely in comparison to the baseline to provide a general illustration of the observed aesthetic effects. One of the limitations of this study is the absence of a formal evaluation of patient satisfaction using standardized scales such as the Visual Analogue Scale (VAS) or the Global Aesthetic Improvement Scale (GAIS). The retrospective nature of the data collection did not allow for the inclusion of such measures. While this limitation restricts a more objective assessment of patient satisfaction and operator perspectives, the observed outcomes nonetheless provide valuable insights into the aesthetic effects of the intervention.

We recognize the importance of incorporating both patient and operator satisfaction measures in future research. Prospective studies with appropriate satisfaction scales will enable a more comprehensive evaluation of the results and ensure a better understanding of both subjective and objective outcomes. Including these assessments will allow for a more thorough analysis of the treatment's efficacy from the perspectives of all parties involved.

DISCUSSION

In this study, a treatment protocol combining non-crosslinked HA mesotherapy with hydro-exfoliation and infrared thermo-lifting resulted in clinically significant improvements in skin quality. This included reduced fine lines and wrinkles, a reduction in the number and size of enlarged pores, improved skin texture, and reduced oiliness. The first step in the protocol involved a procedure with a high concentration of non-crosslinked HA, CaHA, and amino acids. Several small aliquots were injected deep dermally, providing a long-lasting nourishing and moisturizing effect. The addition of CaHA, even at a very low concentration of

0.01%, may allow the collagen-stimulating properties of this agent to be utilized, which in turn could reduce skin laxity without a volumizing effect (11-13). Production of extracellular matrix proteins in dermal fibroblasts is affected by the availability of key amino acids (14, 15), particularly glycine and proline, which comprise a major portion of the primary amino acid sequence of collagen (16). Glycine had the strongest effect on collagen production in a comparison of 20 amino acids added to human dermal fibroblasts (16), and exogenous proline has been shown to stimulate type I collagen in human skin fibroblasts (17).

The second step in the protocol used a device with a two-fold non-invasive mechanism of action: (i) hydro-exfoliation and (ii) infrared thermo-lifting. Hydro-exfoliation is a gentle method of deep cleansing and exfoliating the skin, including congested and enlarged pores. It improves the skin's overall texture and provides deep hydration. The thermal energy delivered by the infrared technology contracts the collagen fibrils to their original length, resulting in immediate skin tightening and lifting to reduce the appearance of wrinkles. The mechanical strength of the collagen fibrils is dependent on covalent cross-links between individual fibrils (18). When collagen is denatured by heat, the intra-molecular hydrogen bonds rupture, and the collagen helices unwind. Tissue tension in human skin increases even though the fibers become shorter because the heat-stable cross-links between the molecules are maintained (19). At the same time, thermal denaturation of collagen and elastin fibers stimulates the fibroblasts and triggers neocollagenesis and elastogenesis. This process occurs gradually, so the final treatment result will be achieved 3 to 6 months after the procedure has taken place. There is no damage to the epidermis, which is protected by contact cooling, and the procedure is painless for the patient, although they may feel sensations of heat and cold. Previous studies with infrared have shown gradual improvements in skin texture and roughness, wrinkles, and color tone and increased fibroblast production of collagen and elastin in histopathology samples from treated skin (5, 8, 20, 21).

In addition to improving wrinkles and skin texture, the combined protocol effectively reduced pore size and density. Enlarged pores are a common cosmetic concern but can be challenging to treat. They are thought to be caused by a combination of factors, including seborrhoea, loss of skin elasticity and tension, and hair follicle size (22). Pore size was improved by up to 30% after the treatments, and oiliness (excess sebum production) by up to 33%, further confirming the benefits of combining different treatment modalities. Similar to other studies (5), hyperpigmented skin lesions showed only minimal improvement with infrared therapy. Treatment of patients with severe hyperpigmentation requires a more personalized approach with a wavelength that reaches the tissue depth at which melanin is located.

This study combined three different treatment modalities in two sessions to enhance skin quality: mesotherapy with a non-crosslinked HA, hydro-exfoliation, and infrared red thermo-lifting. Use of multiple technologies allows the underlying causes of reduced skin quality to be addressed simultaneously whether they are a result of poor skin care, stressful lifestyles, environmental factors or age-related. The study was limited by its relatively small sample size. In addition, the duration of follow-up was not long enough to evaluate the long-term effect of the combined treatments. Further studies, with a larger sample size and a long duration of follow-up in subjects with a range of skin types are now warranted to confirm the synergistic effect and safety of treatment with this novel combination.

While this study provides valuable insights into the combined effects of the proposed treatments, several limitations should be acknowledged. One significant limitation is the absence of a control group, which restricts the ability to draw definitive conclusions about the efficacy of the interventions. A control group would have allowed for a more robust comparison and strengthened the validity of the findings.

Additionally, the current study design does not facilitate the individual evaluation of the proposed treatments. Assessing each treatment in isolation would yield a deeper understanding of their specific contributions to the observed outcomes. Unfortunately, due to the integrated nature of the treatment protocols applied in this study,

such an analysis is not feasible. Future research could benefit from a design that includes a control group and allows for the independent evaluation of each treatment modality, ultimately enhancing the robustness and applicability of the findings.

CONCLUSION

The combination of non-crosslinked HA combined with low concentration of CaHA with hydro-exfoliation and infrared energy led to clinically significant improvements in skin quality including reduced lines and wrinkles, pore size and number, oiliness and improved skin texture. These changes were observed over a range of skin types and age groups. All treatments were well tolerated and can be safely combined to provide enhanced outcomes in face rejuvenation.

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