Clinical, Cosmetic and Investigational Dermatology

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

A Prospective, Multicenter, Randomized, Assessor-Blinded Study Assessing the Efficacy and Safety of Injectable Non-Cross-Linked Hyaluronic Acid for Improving Facial Skin Rejuvenation

Haiyan Cheng[1], Meng Jiang[1], Shan Zhong[1], Xinhai Liu[2], Dongsheng Cao[3], Qiuyuan Feng[4], Yongzhong Li[5], Wei Xu[1]

[1]Department of Dermatology, Beijing Friendship Hospital, Capital Medical University, Beijing, People's Republic of China; [2]Department of Plastic Surgery, Beijing Luhe Hospital, Capital Medical University, Beijing, People's Republic of China; [3]Department of Plastic and Wound Repair Surgery, The Second Affiliated Hospital of Anhui Medical University, Hefei, People's Republic of China; [4]Department of Medical Aesthetics, Yixing People's Hospital, Yixing, People's Republic of China; [5]Department of Plastic Surgery, Wuxi No. 2 People's Hospital, Wuxi, People's Republic of China

Correspondence: Wei Xu, Department of Dermatology, Beijing Friendship Hospital, Capital Medical University, Beijing, People's Republic of China, Tel +86-137-0129-6490, Email 2403649155@qq.com

Objective: To evaluate the efficacy and safety of an injectable non-cross-linked hyaluronic acid (NCHA) solution in improving facial skin appearance.

Methods: This prospective, multicenter, randomized, no-treatment–controlled, assessor-blinded, superiority clinical trial was conducted from December 2023 to July 2024 with 448 adults (224 per arm). The treatment group received full-face intradermal injections of NCHA (4 mL/session) at baseline, day 28, and day 56; the control group followed routine skincare and underwent the same injection protocol after day 84. The treatment group underwent skin hydration measurement, elasticity measurement (two objective assessments), global aesthetic improvement scale, skin roughness score, and fine line score (three subjective assessments) at baseline; day 28 and 56; and 7/14/28 days after the last injection (day 63/70/84). The control group completed the same assessments at baseline, 28, 56, 63, 70, and 84 days after randomization.

Results: In the treatment group, 212 subjects (94.64%) completed the study, compared to 209 (93.3%) in the control group. Hydration increased steadily in the treatment group, exceeding that of the control at all post-treatment time points ($P<0.001$). Elasticity improvements at 7/14/28 days after the final injection were significantly greater than those in the control group ($P<0.05$). GAIS, ASRS, and AFLS all favored the treatment arm. Serious adverse events were not observed.

Conclusion: Full-face intradermal NCHA improved skin hydration, elasticity, texture, and fine lines with a favorable safety profile.

Chinese Clinical Trial Registry: ChiCTR2300078169.

Keywords: non-cross-linked hyaluronic acid, facial skin rejuvenation, efficacy, safety

Introduction

Skin aging is a complex biological process driven by intrinsic senescence and extrinsic stimuli, with typical facial manifestations including reduced hydration, degradation of elastic and collagen fibers, rough epidermal texture, and fine line formation. These changes impair both facial aesthetic appearance and skin physiological health by disrupting the skin barrier function. With the advancement of minimally invasive aesthetic medicine, skin biorevitalization-centered non-surgical therapies have become the mainstream option for facial rejuvenation. Among these, intradermal injection of non-cross-linked hyaluronic acid (NCHA) stands as a classic skin biorevitalization therapy. It has been widely applied in clinical practice due to its high biocompatibility, immediate hydrating and moisturizing effects, and potential biostimulatory action on dermal regeneration. Moreover, it can be administered alone or as part of combination therapy to achieve

https://doi.org/10.2147/CCID.S590699
Received: 21 December 2025
Accepted: 23 March 2026
Published: 7 April 2026

anti-aging efficacy.[1–3] In 2022, injectable HA solutions were classified as Class III medical devices in China, further standardizing their clinical application in intradermal bio-revitalization.

Several global clinical studies have verified NCHA's efficacy in enhancing facial skin hydration, elasticity and texture,[4,5] yet critical limitations persist in existing research: most studies are single-center with small sample sizes, lacking robust multicenter evidence for diverse populations, and therapeutic protocols and evaluation systems remain unstandardized, leading to poor comparability of results due to variable dosages and treatment intervals. Despite NCHA's well-documented benefits, clinical practice urgently requires targeted, standardized protocols and large-sample data for the Chinese population to support evidence-based decision-making.

Herein, we conducted a multicenter, randomized, no-treatment-controlled, assessor-blinded superiority trial enrolling 448 Chinese subjects with facial aging signs. Full-face intradermal NCHA injections were administered via a standardized electronic device once every four weeks for three sessions. We systematically investigated the protocol's efficacy and safety, and analyzed dynamic changes in therapeutic effects. This study aims to provide high-quality, large-sample multicenter evidence for NCHA-based facial rejuvenation in Chinese populations, and further enrich the clinical application system of minimally invasive aesthetic medicine in skin bio-revitalization.

Materials and Methods

Study Design and Participants

This prospective, multicenter, randomized, non-treatment-controlled, assessor-blinded superiority trial was conducted from December 2023 to July 2024 at five centers in China. A total of 448 adults were randomized 1:1 to treatment or control groups. The treatment group included 11 men and 211 women aged 21–64 years (mean 35.36). The control group included 14 men and 210 women aged 20–64 years (mean 35.44).

Inclusion and Exclusion Criteria

Eligible participants were aged 18–65 years (Fitzpatrick skin types II–IV) and presented with at least one of the following skin concerns: dullness, xerosis, mildly reduced elasticity or fine lines.

Exclusion criteria included allergy/hypersensitivity to HA components or topical anesthetics; granulomatous disease or keloid tendency; active/progressive dermatoses at treatment sites; facial tattoos/scars/deformities/non-healed wounds/masses; coagulation abnormalities or thrombolytic/anticoagulant/antiplatelet use within 2 weeks; permanent/semi-permanent fillers, autologous fat, or surgical lifting within 1 year; energy-based treatments or botulinum toxin on the face within 6 months; pregnancy/lactation; anticipated high UV exposure or photosensitizers; unrealistic expectations; or investigator-assessed unsuitability. Written informed consent was obtained from all patients. Ethics approval: Beijing Friendship Hospital (No. 2023-P1-Device-022-02).

Interventions

The faces were cleansed, and 5% lidocaine cream (~30 g) was applied for ~40 min and then removed. After antisepsis, a mechanical injector (Skin 2 Skin Med; Xiangtan Weiying Medical Device Co., Ltd., China) delivered NCHA solution (2.0 mL/vial; Hainan Xiruida Biotechnology Co., Ltd., China) intradermally across the full face (4 mL/session), excluding the upper eyelid skin. The injection depth was standardized: 1.0 mm for the forehead and lower eyelid areas, and 1.2 mm for all other facial regions, including the perioral area. Post-procedural care included cooling masks for 15–20 min, a 1-week course of hydrating masks, gentle skincare, and strict photoprotection for 1 month. The treatment group sessions occurred at baseline, day 28, and day 56, whereas the control group maintained routine skincare.

Outcome Measures and Assessments

Objective outcomes: Skin hydration using Corneometer CM 825 and elasticity using Cutometer MPA 580 (Courage & Khazaka, Cologne, Germany) at the mid-forehead, bilateral zygomatic eminences, and mid-chin (triplicates per site; averaged). The treatment group underwent these assessments at baseline; days 28 and 56; and 7/14/28 days after the last

injection (days 63/70/84). The control group completed the same assessments at baseline and 28, 56, 63, 70, and 84 days after randomization.

Subjective outcomes: GAIS (Global Aesthetic Improvement Scale, 1=Very significant improvement, 2= Significant improvement, 3=Moderate improvement, 4=no change, 5=worse than before); ASRS (Allergan Skin Roughness Scale, 0=None – Smooth skin texture without visible roughness, 1=Mild – Slightly rough texture with minimal unevenness, 2=Moderate – Moderately rough texture with visible unevenness, possible early elastosis, 3=Poor – Markedly rough texture with intersecting fine lines, some elastosis, 4=Severe – Very rough texture with deep intersecting wrinkles and significant elastosis); AFLS (Allergan Fine Wrinkle Scale, 0=None – No fine wrinkles, 1=Mild – 1–2 shallow fine lines, 2=Moderate – 3–5 shallow fine lines, 3=Poor – More than 5 superficial lines without crisscrossing, 4=Severe – Diffuse superficial wrinkles with intersecting patterns). Two blinded assessors independently rated the photographs and discordance was adjudicated by a senior reviewer. Participants self-rated the GAIS at each time point. The treatment group underwent these assessments on days 28 and 56; and 7/14/28 days after the last injection (days 63/70/84). The control group completed the same assessments 28, 56, 63, 70, and 84 days after randomization.

Safety Monitoring

Local/systemic adverse events, laboratory tests (CBC, urinalysis, and hepatic/renal panels), and ECGs were recorded throughout the trial.

Statistical Analysis

Analyses were conducted using SAS 9.4, and PASS 2021. Continuous variables were compared using *t*-tests or Wilcoxon rank-sum tests, as appropriate; categorical data were compared using χ^2 or exact tests; and ordinal data were compared using Wilcoxon rank-sum or Cochran–Mantel–Haenszel tests. Statistical significance was set at $P<0.05$.

Results

Participant Disposition

Of the 448 randomized participants (224 per group), 212/224 (94.6%) in the treatment group and 209/224 (93.3%) in the control group completed all sessions and follow-ups.

Skin Hydration

Baseline hydration was slightly lower in the treatment group; thereafter, hydration increased steadily and exceeded that of the control at all post-treatment time points (all $P<0.001$). Figure 1

Skin Elasticity

Baseline elasticity did not differ. Improvements from baseline on days 63, 70, and 84 were significantly greater in the treatment group than in the control group (all $P<0.05$). Figure 2

GAIS

Under both blinded assessors assessment and subject self-assessment, the treatment group demonstrated higher improvement satisfaction than the control group at all corresponding time points.

The blinded assessors' GAIS ratings in the treatment arm shifted toward improvement across visits. At 28 days after the first injection (day 28), the ratings were as follows: 2 (much improved), 4.25%; 3 (improved), 56.13%; and 4 (no change), 39.62%. By 28 days after the last injection (day 84), the ratings were 2 (much improved), 23.58%; 3 (improved), 66.51%; and 4 (no change), 9.91%. In the control group, the distributions at the matched time points were largely stable, with ≥90% rated as unchanged. Figure 3

Participant self-ratings parallel to assessor assessments. On day 28:1 (very much improved), 8.49%; 2 (much improved), 22.17%; 3 (improved), 65.57%; 4 (no change), 3.30%; and 5 (worse), 0.47%. On day 84: 1 (very much improved), 17.45%; 2 (much improved), 43.87%; 3 (improved), 37.26%; 4 (no change), 0.94%; and 5 (worse), 0.47%. Figures 4–6

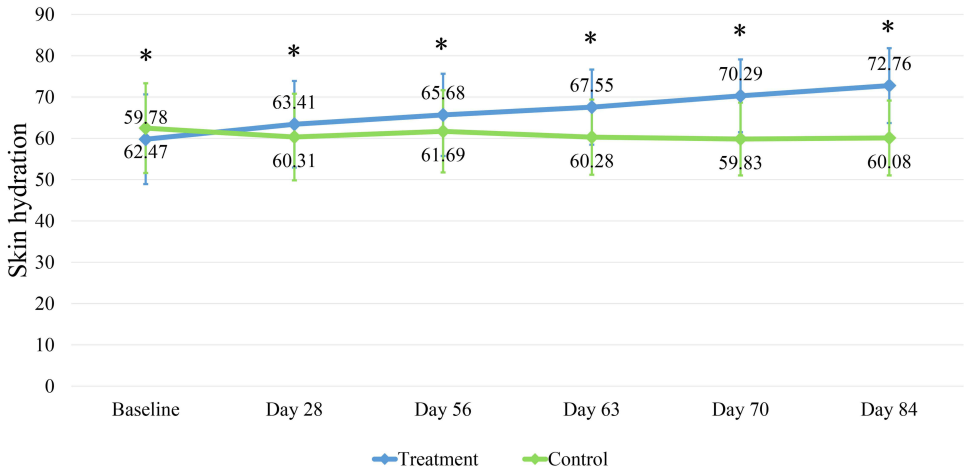

Figure 1 Skin hydration levels in the treatment group (n=212) vs. control group (n=209) across time points. An asterisk (*) indicates a statistically significant difference between the two groups, with $P < 0.05$.

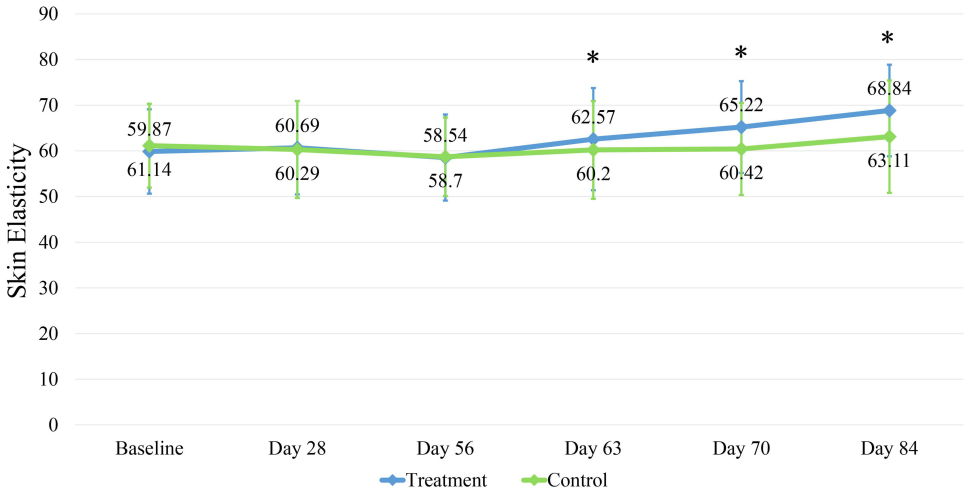

Figure 2 Skin elasticity levels in the treatment group (n=212) vs. control group (n=209) across time points. An asterisk (*) indicates a statistically significant difference between the two groups, with $P < 0.05$.

ASRS and AFLS

There were no statistically significant differences in skin roughness or fine lines between the treatment and control groups at baseline. After treatment, The ASRS and AFLS distributions shifted toward lower severity grades in the treatment arm across the time points, with minimal changes in the controls. By day 84, the ASRS grades 0–2 comprised approximately 87% of the treatment group. Figures 7–8

Safety

Serious adverse events were not observed. Local reactions (eg, erythema, wheals, and pain) were transient and resolved within days. One male participant developed post-procedural facial hyperpigmentation, and laboratory and ECG findings were unremarkable throughout the trial.

Discussion

This study evaluated the efficacy and safety of a NCHA injection solution in improving facial skin appearance. The results demonstrated that, after three injections, the treatment group showed significantly better outcomes than the control

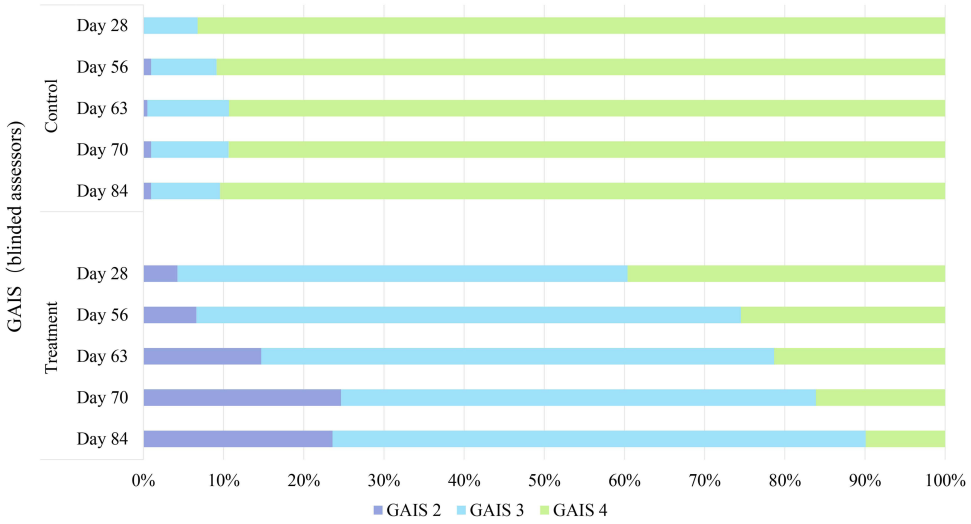

Figure 3 Distribution of Global Aesthetic Improvement Scale (GAIS) scores rated by blinded assessors in the treatment and control groups at different time points.
Notes: No participants scored 0 or 5 in either group. Missing values: treatment group, n=1 at days 7 and 14 after the last injection; control group, n=2 (day 28), n=1 (day 56), n=3 (day 63), n=2 (day 70) after randomization.

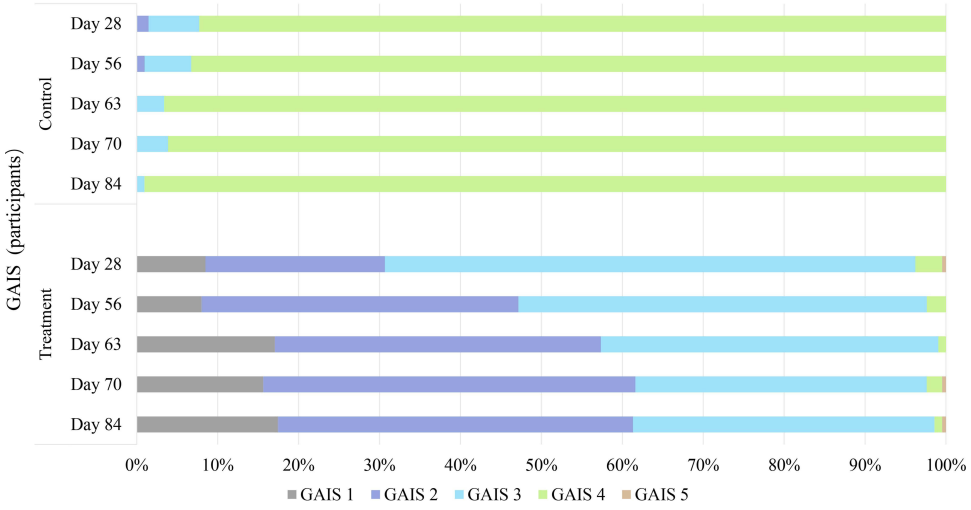

Figure 4 Distribution of participant self-rated Global Aesthetic Improvement Scale (GAIS) scores in the treatment and control groups at different time points.
Notes: Missing values: treatment group, n=1 at days 7 and 14 after the last injection; control group, n=2 (day 28), n=1 (day 56), n=3 (day 63), n=2 (day 70) after randomization.

group in terms of skin hydration, elasticity, overall aesthetic improvement, skin roughness, and fine wrinkle scores, with a favorable safety profile.

The purpose of mesotherapy is to deliver skin nutrients, such as HA, vitamins, amino acids, and platelet-rich plasma (PRP), to the subepidermal layer via microneedling, thereby achieving hydration, brightening, and anti-aging effects.[6–8] Among these, hyaluronic acid is widely used owing to its unique physiological properties. As a highly biocompatible acidic mucopolysaccharide, HA is a major component of the extracellular matrix, and over half of it is naturally present in skin tissue.[9] Its molecular structure consists of repeating disaccharide units, giving it exceptional water retention capacity, earning it the title of the "natural moisturizing factor." It is now widely employed in facial rejuvenation treatments.[10–12]

This study revealed that although skin hydration in the treatment group was slightly lower than that of the control group at baseline, it significantly exceeded that of the control group at 28 days after the first injection, 28 days after

https://doi.org/10.2147/CCID.S590699

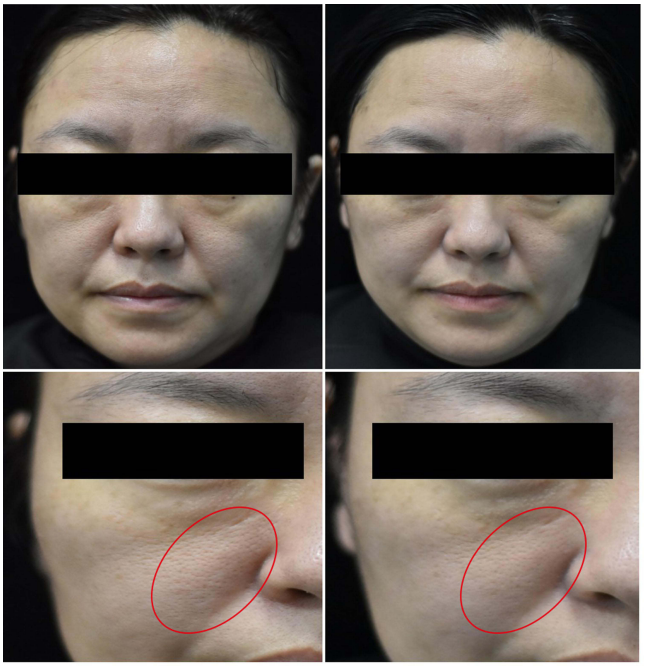

Figure 5 Comparison of treatment group before treatment and 7 days after the final treatment: the skin appears brighter and pores appear smaller. Written informed consent was obtained from the patient for the publication of this clinical image.

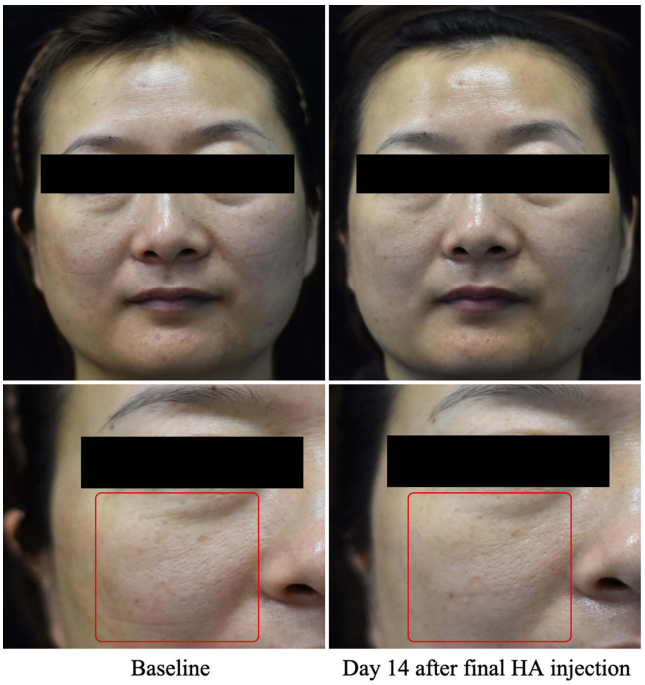

Figure 6 Comparison of treatment group before treatment and 14 days after the final treatment: the skin appears brighter and pores appear smaller, and fine lines around the eyes are reduced. Written informed consent was obtained from the patient for the publication of this clinical image.

the second injection, and 7, 14, and 28 days after the final injection. Furthermore, epidermal hydration exhibited a clear short-term dose-dependent effect, peaking at 28 days after the last treatment, confirming that intradermal NCHA injections can achieve a significant improvement in skin hydration within one month after a single treatment.

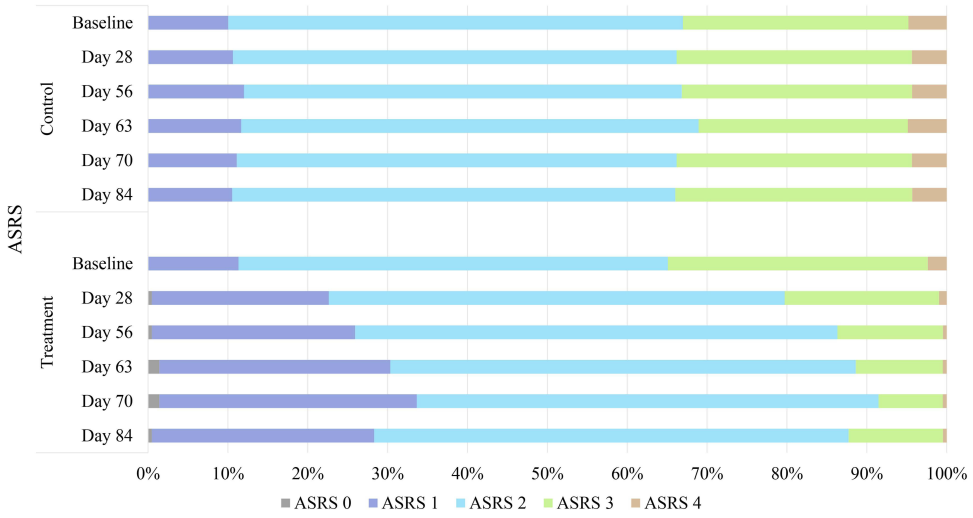

Figure 7 Distribution of Allergan Skin Roughness Scale (ASRS) scores in the treatment and control groups at different time points.
Notes: Missing values: treatment group, n=1 at days 7 and 14 after the last injection; control group, n=2 (day 28), n=1 (day 56), n=3 (day 63), n=2 (day 70) after randomization.

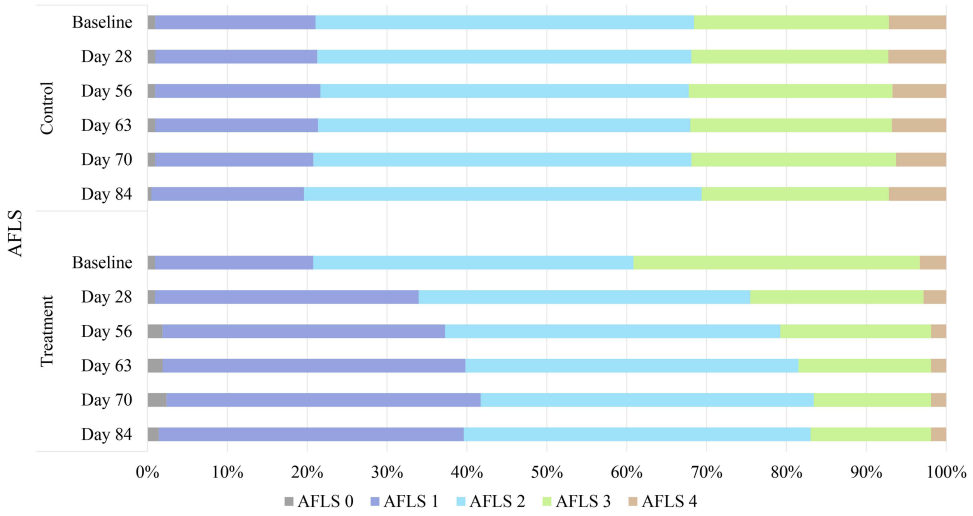

Figure 8 Distribution of Allergan Fine Wrinkle Scale (AFLS) scores in the treatment and control groups at different time points.
Notes: Missing values: treatment group, n=1 at days 7 and 14 after the last injection; control group, n=2 (day 28), n=1 (day 56), n=3 (day 63), n=2 (day 70) after randomization.

At the final follow-up, the treatment group showed an 8.98±13.24 increase in elasticity compared to the baseline, demonstrating statistically significant differences compared to the control group (P<0.001). However, no significant elasticity changes were observed 28 days after the first injection, suggesting that the biostimulatory effects of HA may require time and cumulative treatment. Enhanced synthesis of elastin and collagen is considered to be a key mechanism by which HA promotes skin rejuvenation. Animal studies have shown that HA activates the TGF-β/Smad signaling pathway, thereby stimulating fibroblast proliferation.[13] In vitro experiments further confirmed that HA promoted the differentiation of fibroblasts and keratinocytes, consistent with the delayed elasticity improvement observed in this study.[14] Additionally, the microneedling procedure serves as a mechanical stimulus that synergistically enhances collagen and elastin production.[15]

According to the GAIS results, the final follow-up at 28 days after the last injection revealed that 90.09% of subjects in the treatment group achieved "moderate improvement" or higher ratings, significantly surpassing 9.57% in the control group. This outcome closely aligns with improvements in objective metrics (hydration and elasticity), validating the clinical

https://doi.org/10.2147/CCID.S590699

significance of this therapy. Meanwhile, the self-reported "very significant improvement" rate increased from 8.49% after the first injection to 17.45% at the final follow-up, suggesting enhanced subjective satisfaction with cumulative treatments, potentially linked to psychological adaptation and efficacy. During detailed patient interviews, most patients reported noticeable improvements in skin hydration, roughness, radiance, and periorbital fine lines within one week post-treatment.

Improvements in skin roughness and fine line scores further support the clinical value of non–cross-linked HA intradermal injection therapy. Comparative data analysis revealed a statistically significant increase in the proportion of subjects showing facial skin improvement with cumulative treatment sessions compared with baseline. These findings are consistent with previous studies documenting HA's efficacy in photoaged skin rejuvenation, which is attributed to its dual mechanisms.[16,17] 1, Micro-filling effects: Immediate correction of superficial wrinkles and volume loss; 2, Collagen stimulation: long-term dermal remodeling via fibroblast activation and extracellular matrix synthesis.

Regarding safety, only one case of injection site hyperpigmentation was reported in the treatment group and no other serious adverse events were observed. Upon detailed inquiry, this male participant was admitted to not using any sun protection measures posttreatment. After receiving education on daily sun protection and topical whitening products, pigmentation resolved within approximately three months.

Through this clinical trial, we obtained valuable practical experience. Despite 40 minutes of topical anesthesia application prior to treatment, patients may experience varying degrees of tolerable pain in the periocular, perinasal, perioral and facial contour areas. This is likely associated with individual pain tolerance, anesthetic sensitivity, and thickness/evenness of topical anesthetic application. For thin skin areas (eg, eyelids) and low-fat regions (eg, forehead), we recommend shortening the needle insertion depth to achieve higher treatment compliance. If the subject is particularly sensitive to pain, the needle protrusion length should be adjusted to the shortest setting, which reduces nerve stimulation but requires precise skin contact to prevent leakage. Postinjection, minimal bleeding, or slightly delayed punctate bleeding is ideal. A longer needle protrusion (>1.5 mm) may increase pain sensitivity, accompanied by visible wheal formation and rapid, nonactive bleeding at the puncture site. The wheal generally resolves spontaneously within 12–48 h, whereas minor puncture bleeding subsides after cold compression. No significant difference in final therapeutic efficacy was observed in subjects with either shallow or deep injection layers. Therefore, selecting a needle length that the patient can tolerate is recommended. While the treatment in this study was minimally invasive, patients should strictly avoid postoperative sun exposure to minimize the risk of pigmentation in the treated area.

In summary, this study demonstrated the safety and efficacy of NCHA injections for facial rejuvenation, thus providing a novel therapeutic option in the minimally invasive aesthetic field. Future research should extend follow-up durations and increase treatment frequency to evaluate the long-term maintenance effects and cumulative benefits of repeated treatment. Additionally, exploring combination therapies could further address the diverse needs of patients seeking aesthetic enhancements.

Conclusion

This study demonstrated that full-face intradermal injections of NCHA significantly enhanced short-term facial skin hydration, elasticity, and overall appearance, with an excellent safety profile. Meanwhile, 90.09% of treated subjects achieved "moderate improvement" or better on GAIS by day 84 compared with 9.57% in controls, and no serious adverse events were reported, making the three-session regimen (baseline, days 28 and 56) a valuable minimally invasive option for facial rejuvenation through HA microfilling and long-term collagen stimulation.

Data Sharing Statement

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request, subject to ethical and legal constraints.

Ethics Approval and Informed Consent

This study was approved by the Ethics Committee of Beijing Friendship Hospital (No. 2023-P1-Device-022-02). Our study complies with the Declaration of Helsinki. Written informed consent was obtained from all participants. Trial registration: ChiCTR2300078169.

Consent for Publication

We've reached a consent that all the data and images could be published. We confirm that all patients whose clinical images are presented in this manuscript have provided written informed consent for the publication of their identifiable facial photographs. All study data and associated images have been approved by the participants for open publication in this journal.

Acknowledgment

We express our gratitude to Yan Li/Jian Zhao for screening the subjects, Xin Yu/Man Li for conducting this study, and Leyi Wang/Xueqing Zhu for their ratings.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

There is no funding to report.

Disclosure

The authors declare no competing interests in this work.

References

1. Iranmanesh B, Khalili M, Mohammadi S, Amiri R, Aflatoonian M. Employing hyaluronic acid-based mesotherapy for facial rejuvenation. *J Cosmet Dermatol*. 2022;21(12):6605–6618. doi:10.1111/jocd.15341
2. Roohaninasab M, Jafarzadeh A, Zare S, et al. Evaluation of the efficacy, safety, and satisfaction rates of platelet-rich plasma, non-cross-linked hyaluronic acid, and their combination in patients with acne scars treated with fractional CO_2 laser: a randomized, double-blind, split-face comparative study. *Aesthetic Plast Surg*. 2025. doi:10.1007/s00266-025-05359-w
3. Seo SB, Park H, Jo JY, Ryu HJ. Skin rejuvenation effect of the combined PDLLA and non cross-linked hyaluronic acid: a preliminary study. *J Cosmet Dermatol*. 2024;23(3):794–802. doi:10.1111/jocd.16085
4. Chahine S, Marozzi B, Valle A, Michellini L, Lazzari T. Efficacy and safety of non-cross-linked hyaluronic acid injections for facial skin biorevitalization: a single-center, open-label, single-arm, uncontrolled, post-marketing study. *Cureus*. 2025;17(8):e90005. doi:10.7759/cureus.90005
5. Leguina-Ruzzi A, Navarro A, Zambrano M. Efficacy and effectiveness of high molecular weight non-cross-linked hyaluronic acid plus succinic acid mesotherapy in rosacea as adjunct therapy. *J Cosmet Dermatol*. 2025;24(10):e70484. doi:10.1111/jocd.70484
6. Baspeyras M, Rouvrais C, Liégard L, et al. Clinical and biometrological efficacy of a hyaluronic acid-based mesotherapy product: a randomised controlled study. *Arch Dermatol Res*. 2013;305(8):673–682. doi:10.1007/s00403-013-1360-7
7. Iranmanesh B, Rastaghi F, Hashemi NS, Kaveh R. Comparison of the effectiveness of platelet-rich plasma versus tranexamic acid plus vitamin C mesotherapy in the treatment of periorbital hyperpigmentation: a split-site, randomized clinical trial. *J Cosmet Dermatol*. 2024;23(12):4066–4071. doi:10.1111/jocd.16548
8. Scarano A, Qorri E, Sbarbati A, et al. The efficacy of hyaluronic acid fragments with amino acid in combating facial skin aging: an ultrasound and histological study. *J Ultrasound*. 2024;27(3):689–697. doi:10.1007/s40477-024-00925-5
9. Wu GT, Kam J, Bloom JD. Hyaluronic acid basics and rheology. *Clin Plast Surg*. 2023;50(3):391–398. doi:10.1016/j.cps.2022.12.004
10. Luo Y, Tan J, Zhou Y, et al. From crosslinking strategies to biomedical applications of hyaluronic acid-based hydrogels: a review. *Int J Biol Macromol*. 2023;231:123308. doi:10.1016/j.ijbiomac.2023.123308
11. Liao Z, Hong W, Wang S, et al. Efficacy and safety of sodium hyaluronate gel for facial skin rejuvenation. *Dermatol Surg*. 2026. doi:10.1097/DSS.0000000000005042
12. Iaconisi GN, Lunetti P, Gallo N, et al. Hyaluronic Acid: a Powerful Biomolecule with Wide-Ranging Applications-A Comprehensive Review. *Int J Mol Sci*. 2023;24(12):10296. doi:10.3390/ijms241210296
13. Fan Y, Choi TH, Chung JH, Jeon YK, Kim S. Hyaluronic acid-cross-linked filler stimulates collagen type 1 and elastic fiber synthesis in skin through the TGF-β/Smad signaling pathway in a nude mouse model. *J Plast Reconstr Aesthet Surg*. 2019;72(8):1355–1362. doi:10.1016/j.bjps.2019.03.032
14. Galvez-Martin P, Soto-Fernandez C, Romero-Rueda J, et al. A novel hyaluronic acid matrix ingredient with regenerative, anti-aging and antioxidant capacity. *Int J Mol Sci*. 2023;24(5):4774. doi:10.3390/ijms24054774
15. Tehrani L, Tashjian M, Mayrovitz HN. Physiological mechanisms and therapeutic applications of microneedling: a narrative review. *Cureus*. 2025;17(3):e80510. doi:10.7759/cureus.80510

16. Duteil L, Queille-Roussel C, Issa H, Sukmansaya N, Murray J, Fanian F. The effects of a non-crossed-linked hyaluronic acid gel on the aging signs of the face versus normal saline: a randomized, double-blind, placebo-controlled, split-faced study. *J Clin Aesthet Dermatol*. 2023;16(2):29–36.
17. Behrangi E, Dehghani A, Sheikhzadeh F, Goodarzi A, Roohaninasab M. Evaluation and comparison of the efficacy and safety of cross-linked and non-cross-linked hyaluronic acid in combination with botulinum toxin type A in the treatment of atrophic acne scars: a double-blind randomized clinical trial. *Skin Res Technol*. 2024;30(1):e13541. doi:10.1111/srt.13541