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ORIGINAL RESEARCH

Efficacy of Polynucleotide for the Recovery of Depressed Lesions Following Steroid-Based Lipolysis Injections

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Background: Steroid-containing lipolysis injections may rarely induce facial lipoatrophy, resulting in persistent contour deformities and psychological distress. In compromised tissues, conventional fillers may pose safety concerns, prompting interest in treatment approaches that support local tissue recovery.

Objective: To evaluate the clinical efficacy and safety of polynucleotide (PN) injection for facial lipoatrophy caused by steroid-containing lipolysis injections.

Methods: This retrospective clinical study included six patients who developed facial lipoatrophy following steroid-containing lipolysis injectionsand were treated with PN (Rejuran®, 20 mg/mL). PN was administered using a combination of intradermal microinjections and superficial subcutaneous bolus injections at 2–4-week intervals. Clinical outcomes were assessed using the Physician's Global Assessment (PGA; 1–5 scale) based on standardized photographic comparisons, along with patient-reported satisfaction.

Results: All patients demonstrated meaningful improvement in facial contour following PN treatment. Three patients achieved near-complete resolution (PGA 5), while the remaining three showed substantial improvement (PGA 4). Improvement progressed gradually with repeated sessions. No treatment-related adverse events were observed.

Conclusion: PN injection appears to be a safe and effective tissue-supportive option for managing facial lipoatrophy following steroid-containing lipolysis injections. Larger prospective studies are warranted to establish standardized treatment protocols.

Keywords: polynucleotide, facial lipoatrophy, steroid-induced atrophy, tissue recovery, injectable treatment, aesthetic complications

Introduction

Facial lipoatrophy is an uncommon but clinically significant complication that may occur following steroid-containing lipolysis injections. Although spontaneous recovery of injection-induced facial lipoatrophy has been reported, the clinical course is often slow and unpredictable Corticosteroid-induced subcutaneous fat atrophy typically becomes apparent within 1–3 months after injection and may gradually improve without intervention over time. Previous reports indicate that clinically meaningful spontaneous recovery commonly requires 6–12 months of observation, while complete or near-complete resolution may take up to 1–2 years in some cases.[1] Importantly, persistent focal depressions beyond this period have also been described, frequently prompting patients to seek procedural correction.

In this context, the management of iatrogenic facial lipoatrophy remains challenging, as focal depressions can lead to prolonged aesthetic dissatisfaction and psychological distress, particularly when visible facial subunits are involved. These clinical limitations highlight the need for treatment strategies that can alleviate patient discomfort more rapidly than natural recovery alone, while promoting biologic tissue restoration rather than relying solely on immediate mechanical volume replacement.

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Polynucleotides (PN) are DNA fragments derived primarily from salmon germ cells, purified to a high degree, with minimal residual cellular components. PN have been increasingly utilized in aesthetic medicine for their active modulation of the dermal microenvironment. Experimental studies have demonstrated that PN enhances fibroblast migration and proliferation, promotes collagen type I and III synthesis, and supports extracellular matrix remodeling without cytotoxic effects.[2] Mechanistic investigations further reveal that PN regulates macrophage-fibroblast interactions by activating the adenosine A2A receptor pathway, leading to reduced oxidative stress, M2 macrophage polarization, and subsequent enhancement of collagen synthesis in senescent skin models.[3]

Clinically, intradermal PN injection has been associated with measurable improvements in skin quality parameters. A pilot study demonstrated that PN significantly increased dermal water retention and reduced transepidermal water loss following PN injection,[4] while other studies have reported the use of PN injection in scar remodeling,[5] skin rejuvenation,[6] and periocular rejuvenation[7] because of its beneficial effects on skin texture, elasticity, and overall rejuvenation outcomes. More recently, proof-of-concept reports have suggested that PN injections may also be effective in the treatment of iatrogenic facial fat atrophy; however, available evidence remains limited to small case reports.[8]

The present study aims to evaluate the clinical efficacy and safety of PN injections in patients with facial lipoatrophy following steroid-containing lipolysis injections. By presenting a retrospective case series with standardized outcome assessment, this study seeks to expand current evidence and further clarify the potential role of PN-mediated local contour recovery in aesthetic practice.

Materials and Methods

Study Design and Patients

This retrospective clinical study reviewed patients who presented with facial lipoatrophy following steroid or lipolysis injections and subsequently underwent PN treatment at a single aesthetic clinic.

Between April 2025 and July 2025, nine patients were evaluated for post-injection facial lipoatrophy. Six patients who received PN treatment and had adequate photographic documentation for comparison were included in the final analysis. All included patients developed facial lipoatrophy after steroid-containing lipolysis injections. Written informed consent for the use of clinical data and images was obtained from all participants prior to inclusion.
Inclusion criteria were:

(1) Clinically evident focal facial depression(s) identified 2–4 weeks after steroid-containing lipolysis injection
(2) Persistence of the lesion without early spontaneous improvement and clinical judgment that prompt recovery was unlikely
(3) Completion of at least one PN treatment session with follow-up evaluation.

Exclusion criteria included:

(1) Concurrent or prior volumizing treatments (eg, dermal fillers or fat grafting) in the affected area during follow-up
(2) Active infection or inflammatory skin disease at the treatment site
(3) Insufficient photographic documentation.

Treatment Protocol

PN (Rejuran®, 20 mg/mL) was administered using a combination of intradermal microinjection and superficial subcutaneous bolus techniques, tailored to lesion depth and extent. The 20 mg/mL concentration was selected because it corresponds to the commercially available formulation of Rejuran used in routine clinical practice. Rejuran is widely used for tissue repair and skin quality support in aesthetic practice. As this study was retrospective and descriptive in nature, no comparison among different PN concentrations was performed.

For intradermal treatment, approximately 0.01–0.1 mL of PN was injected per point using a serial puncture technique. Additional small bolus injections were placed in the superficial subcutaneous layer to address deeper volume deficits.

Total injection volumes per session ranged from 0.6 to 1.0 mL. Treatment sessions were performed at intervals of 2–4 weeks, with the total number of sessions determined by clinical response. PN treatment was initiated when a clinically definite focal depression had become apparent and was judged unlikely to resolve promptly, particularly in cosmetically sensitive facial areas associated with substantial patient distress. Rather than representing transient early swelling changes, these lesions had already formed clear contour deformities, and early tissue-supportive treatment was therefore selected instead of prolonged observation alone. The number of sessions and treatment intervals were individualized according to lesion depth, extent, anatomic location, and clinical response, reflecting real-world practice rather than a fixed protocol.

Outcome Assessment

Clinical outcomes were assessed using the Physician's Global Assessment (PGA), a 5-point scale ranging from 1 (no improvement) to 5 (near-complete resolution). PGA scores were determined by experienced physicians based on standardized pre- and post-treatment photographs obtained under consistent lighting conditions, facial positioning, and neutral expression. PGA was used as a pragmatic investigator-assessed clinical scale for serial photographic comparison in this retrospective case series. Although not a disease-specific validated instrument for injection-induced facial lipoatrophy, it was employed to provide consistent global assessment across patients.Patient-reported satisfaction was recorded as supportive outcome data during follow-up visits.

Safety Evaluation

Patients were monitored for treatment-related adverse events, including pain, prolonged erythema, nodules, infection, vascular compromise, or delayed inflammatory reactions. All adverse events were documented throughout treatment and follow-up.

Results

Patient Characteristics

Six female patients were included, with ages ranging from 19 to 42 years. Lipoatrophic lesions were located in various facial subunits, including the cheeks, midface, lower face, and submental region. The number of depressed lesions per patient ranged from 1 to 3 (Table 1). All patients had undergone steroid-containing lipolysis injections prior to the development of facial lipoatrophy.All patients completed PN treatment and follow-up with standardized photographic documentation.

Table 1 Clinical Characteristics and Outcomes of Six Patients with Facial Lipoatrophy After Steroid-Containing Lipolysis Injections Treated with Polynucleotide Injections

Case	Year of Birth	Location/Lesions	PN sessions	Interval	PGA outcome	Final Assessment After Last Session
1	2004	Left lower face/1	2	4 weeks	5/5	2–4 weeks
2	1997	Left midface/2	2	2 weeks	5/5	2–4 weeks
3	1982	Bilateral cheeks/2	3	3 weeks	5/5	2–4 weeks
4	1994	Submental/3	1	—	4/4	2–4 weeks
5	1992	Cheeks (R2, L1)/3	2	4–5 weeks	4/4	2–4 weeks
6	2001	Cheeks (bilateral)/2	2	2 weeks	4/4	2–4 weeks

Note: All patients developed facial lipoatrophy after steroid-containing lipolysis injections.1.
Abbreviation: PGA, Physician's Global Assessment.

Clinical Outcomes

All patients exhibited visible and clinically meaningful improvement in facial contour following PN treatment. Improvement was gradual and increased with repeated sessions.

Final outcome assessment was performed 2–4 weeks after the last PN treatment session, depending on each patient's follow-up schedule.At final follow-up, 3 patients achieved near-complete resolution (PGA 5), while the remaining 3 demonstrated substantial improvement (PGA 4). A tendency toward a greater number of treatment sessions was observed in patients with deeper or multiple lesions, whereas more superficial depressions responded favorably with fewer sessions (Figure 1).

(Figure 1) Shows Representative Clinical Improvement After PN Treatment.

Safety Outcomes

PN treatment was well tolerated in all patients. No treatment-related adverse events, including prolonged erythema, nodules, infection, vascular compromise, or delayed inflammatory reactions, were observed. Mild, transient discomfort at injection sites resolved spontaneously without intervention.

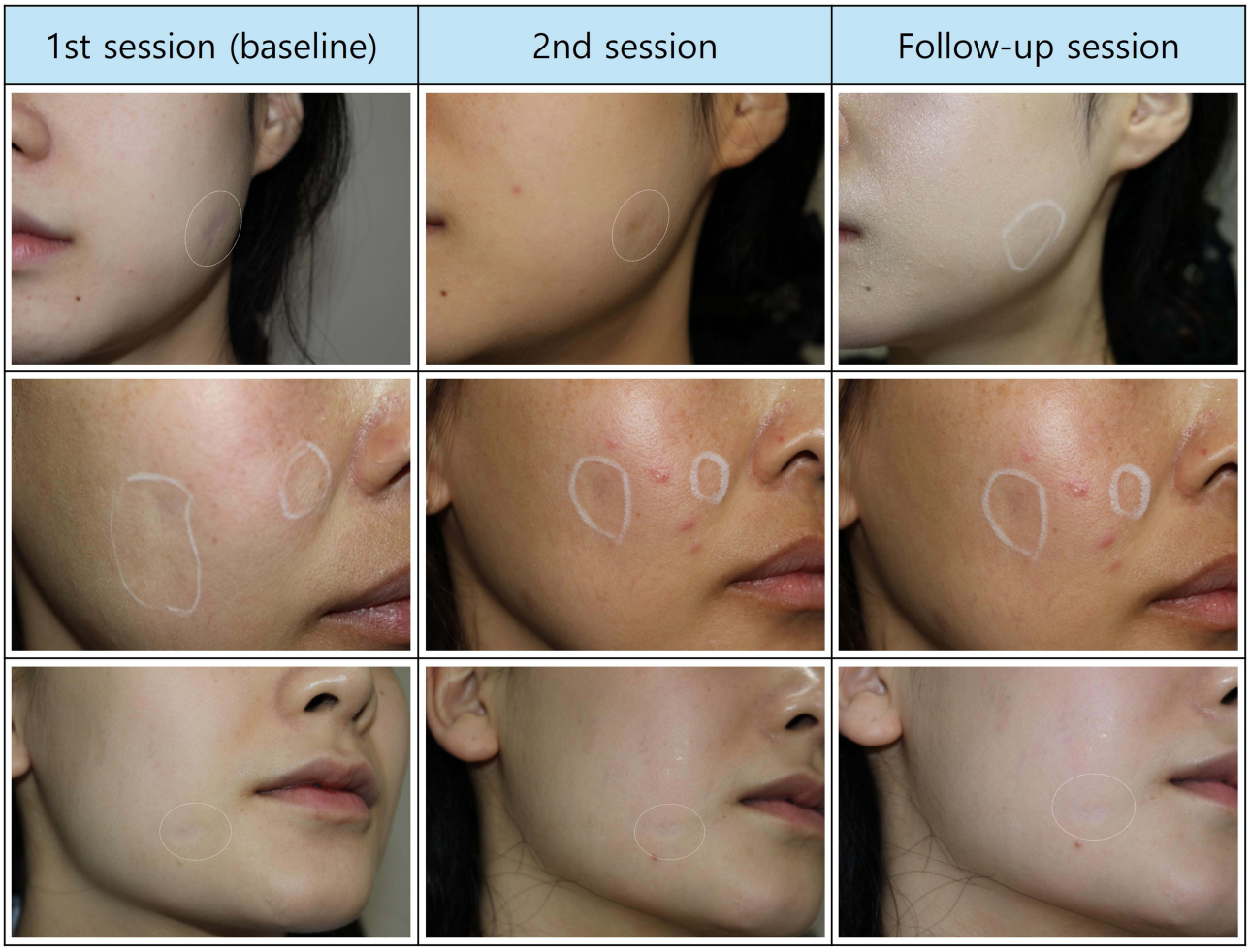

Figure 1 Representative clinical photographs demonstrating improvement of steroid-induced facial lipoatrophy following polynucleotide injection. Standardized clinical photographs obtained at baseline (prior to the first PN injection), after the second treatment session, and at follow-up after the final session. Progressive restoration of soft-tissue volume and improvement of contour depression are observed at the previously atrophic sites (outlined). No treatment-related adverse effects were noted during the follow-up period.

Discussion

This retrospective clinical study suggests that PN injection may represent a safe tissue-supportive option for facial lipoatrophy following steroid-containing lipolysis injections.

Consistent improvement in facial contour was observed across all patients, with outcomes ranging from substantial improvement to near-complete resolution. Importantly, improvement occurred gradually over successive treatment sessions, a pattern more compatible with progressive changes in tissue quality than with immediate volumizing effects.

The pattern of delayed yet progressive contour restoration observed in this study is consistent with previously described effects of PN on local tissue quality and ECM organization. Rather than acting as a space-occupying filler, PN has been proposed to support tissue remodeling, potentially involving changes in fibroblast activity, microcirculatory status, ECM reorganization, and the local inflammatory milieu.[2,3] Such mechanisms may help restore a permissive tissue microenvironment that supports local soft-tissue recovery and contour restoration, with possible secondary effects on sustained clinical improvement.

PN has previously shown favorable effects on tissue quality in a variety of dermatologic conditions, including scar remodeling, wound healing, and inflammatory skin disorders.[5,6,9,10] The contour recovery observed in the present study may therefore be interpreted as an extension of PN's broader tissue-supportive role across inflammatory, fibrotic, and atrophic tissue states.

Previous reports describing PN use in iatrogenic facial fat atrophy were limited to isolated proof-of-concept cases.[8] The present series expands these findings by demonstrating reproducible outcomes across multiple patients and facial subunits. The observation that deeper or more extensive lesions required additional sessions further supports the concept of gradual tissue remodeling and microenvironmental adaptation rather than immediate correction.

In the present series, treatment was not initiated merely because of recent injection history, but because a clinically evident contour deformity had already developed and was considered unlikely to resolve promptly. Given the visible facial location of the lesions and the substantial distress experienced by patients, early PN treatment was selected as a pragmatic tissue-supportive approach rather than prolonged observation alone.

All patients reported significant bruising at the time of the original steroid-containing lipolysis injections, suggesting that vascular injury or localized inflammatory insult may contribute to subsequent adipose tissue loss. In such contexts, PN's capacity to modulate extracellular matrix remodeling and support microvascular architecture may be particularly relevant in promoting tissue recovery.[2,3]

From a safety standpoint, PN injections may offer advantages over conventional fillers in compromised tissues. Whereas hyaluronic acid fillers are associated with risks such as vascular occlusion and tissue necrosis,[11] PN-mediated contour improvement appears to occur through gradual biologic remodeling, which may account for the favorable safety profile observed in this study.

In addition to extracellular matrix remodeling, alternative or complementary biological mechanisms may contribute to the observed contour improvement.Restoration of localized fat loss could theoretically involve adipogenic processes, including the differentiation of preadipocytes into mature adipocytes. However, current evidence remains insufficient to support a direct adipogenic effect of PN in clinical settings.

Rather than acting as a primary inducer of adipocyte formation, PN may function as a regenerative scaffold that improves the local tissue microenvironment, thereby indirectly supporting adipose tissue recovery. This interpretation is consistent with the gradual pattern of contour restoration observed in our study.

Notably, polydeoxyribonucleotide has been reported to promote adipogenic differentiation via activation of adenosine A2A receptors, suggesting a possible indirect pathway linking PN to adipose tissue remodeling.[12] Nevertheless, such findings are primarily derived from experimental models, and their clinical relevance remains to be further elucidated.

This study is limited by its retrospective design, small sample size, and lack of objective volumetric measurements or histologic evaluation. Treatment intervals and session numbers were not uniform across patients because management was individualized based on lesion characteristics and clinical response; this heterogeneity limits direct quantitative comparison. Objective volumetric analysis using 3-dimensional imaging or digital contour measurement was not performed, which limits the objectivity of outcome assessment. In addition, PGA is a global clinician-reported scale and not a validated disease-specific

outcome instrument for this condition.Nonetheless, the consistent clinical improvement and absence of adverse events provide meaningful preliminary evidence supporting PN as a reconstructive alternative for facial lipoatrophy following steroid-containing lipolysis injections.

Conclusion

PN injections appear to be a safe reconstructive treatment option for managing facial lipoatrophy following steroid-containing lipolysis injections. The gradual pattern of improvement observed in this study may be more consistent with biologically mediated tissue remodeling than with immediate mechanical filling.These findings support further investigation of PN as a treatment modality in compromised facial tissues through larger, prospective studies.

Ethical Approval and Consent to Participate

This retrospective clinical study was reviewed by the Institutional Bioethics Committee designated by the Ministry of Health and Welfare, Republic of Korea, and was granted exemption from formal ethical review (IRB exemption No. P01-202508-01-055), as it involved analysis of previously collected, de-identified data. Written informed consent for the use of clinical data for research purposes was obtained from all participants. The study was conducted in accordance with the principles of the Declaration of Helsinki.

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Disclosure

Sung Min Park and Dongkeun Kenneth Lee contributed equally to this study. D.K.L. and S.M.O. serve as advisory members of PharmaResearch Products Co., Ltd. The remaining authors declare no conflicts of interest in this work.

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