



Research Article

The Use of Hyprojoint as Facial Dermal Skin Booster: Safety Tolerability and Effectiveness on a 25 Patient Sample

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Abstract

Skin aging is a multifaceted process influenced by intrinsic and extrinsic factors. Hyaluronic Acid (HA) plays a crucial role in skin hydration and is widely used in dermatology for its ability to improve skin quality. This study evaluated the tolerability and safety of off-label intradermal injections of Hyprojoint, a medium-high molecular weight HA solution, in 25 healthy volunteers (aged 40-66 years) exhibiting signs of chronological and photo-aging. A mesotherapy technique was used to administer 2.5 mL of Hyprojoint every four weeks. Objective and subjective assessments were performed at baseline, 21 days and 60 days. Results showed statistically significant improvements in skin aging signs: A 25% reduction in mean wrinkle depth in the periorbital area ($p < 0.05$), a 40% increase in mean skin smoothness in the cheek area ($p < 0.01$) and a 45% increase in mean skin hydration across all treated areas ($p < 0.05$). These improvements are attributed to HA's water-retention capacity and its stimulation of collagen and elastin production. The treatment was well-tolerated with no significant adverse events, suggesting Hyprojoint could be a viable option for improving skin quality, even with off-label use.

Keywords: Hyaluronic Acid; Hyprojoint; Skin Quality; Patient

Introduction

Skin aging is a complex process influenced by both genetic predispositions and a multitude of external factors. This means that the aging of skin isn't solely a consequence of time passing, but rather a result of the interplay between inherent factors and environmental exposures (UV radiation, pollution), lifestyle choices (diet, drug use, smoking) and the presence of chronic diseases, all of which can accelerate the aging process. A thorough understanding of these contributing factors allows individuals to make informed decisions about their skin care routines

and potentially mitigate the effects of aging. Avoiding these detrimental factors and adopting a healthy lifestyle are crucial for maintaining youthful and healthy-looking skin.

Hyaluronic Acid (HA) plays a vital role in maintaining optimal skin hydration. While its medical applications initially focused on ophthalmic surgery in the 1970s and 1980s, HA has since become a cornerstone of dermatological practice [1,2]. Its remarkable water-retention capacity, coupled with its ability to enhance skin texture and elasticity, accounts for its widespread use in various skincare products, including injectable fillers and cosmeceuticals. HA is also a key component of synovial fluid and the cartilaginous extracellular matrix, highlighting its importance in various physiological processes.

Beyond their traditional use in wrinkle filling and volume augmentation, injectable HA formulations have gained recognition for their ability to enhance overall skin quality, structural integrity and aesthetic appearance of aging skin. These treatments, often referred to as "skinboosters," involve injecting HA directly into the dermis [3,4]. Within this layer, HA hydrates the skin and supports the normal function of fibroblasts, the cells responsible for collagen and elastin production. This stimulation of collagen and elastin synthesis contributes to improved skin firmness, elasticity and overall texture [5,6].

The procedure itself is relatively quick and minimally invasive, addressing a range of skin concerns related to both chronological aging and other contributing factors. This versatility makes HA injectable treatments a valuable option for individuals seeking to rejuvenate their skin.

Material and Methods

Microinjections of small-particle Hyaluronic Acid (HA) offer a dual benefit for skin rejuvenation: enhanced hydration and stimulation of fibroblast activity, the key cells responsible for collagen and elastin production. Several commercially available products, containing HA concentrations ranging from 10 to 20 mg/mL, are designed specifically for intradermal microinjection. These products are administered via a series of small, evenly spaced punctures, ensuring uniform distribution throughout the target area. Once injected, the HA attracts water into the skin's extracellular matrix, leading to improved skin turgor, increased volume and refined skin texture.

On the other hand, HA is well-known for its use in viscosupplementation for osteoarthritis, particularly in the knee (gonarthrosis). Viscosupplementation products vary considerably in molecular weight, half-life, concentration, molecular structure and injection volume. These products are typically categorized by HA molecular weight: ultra-high (>2000 kDa), high (1500-2000 kDa), medium (500-1500 kDa) and low (<500 kDa).

Hyprojoint is a sterile, non-pyrogenic, transparent and viscous HA solution derived from biofermentation. It contains HA at a concentration of 15 mg/mL, with high, medium and low molecular weights. Hyprojoint excludes ultra-high molecular weight HA. The solution is prepared in a physiological sodium chloride phosphate buffer (pH 6.0-7.6). While designed primarily for joint care, specifically to alleviate pain and support tissue repair in joints, its properties suggest potential benefits in other applications.

Hyprojoint was selected for this study due to its specific HA characteristics that are relevant to skin rejuvenation. While indicated for intra-articular injection, the formulation—comprising 15 mg/mL of non - cross - linked HA and 3 mg/mL of lidocaine aligns with the requirements for effective intradermal delivery and fibroblast stimulation. Specifically, its monophasic linear structure allows for optimal diffusion within the dermis and high purity minimizes the risk of adverse reactions. This rationale is supported by [7,8]. Although not its primary indication, the specific characteristics of Hyprojoint makes it a potentially suitable candidate for improving skin quality.

The first step involved comparing Hyprojoint's hyaluronic acid content with that of other HA formulations from a leading cosmetic medicine company. These commercially available products ranged from 0.01% to 2% HA, which supported my consideration of Hyprojoint for off-label mesotherapeutic anti-aging treatments. Of course, ensuring the product's safety, biocompatibility, stability at the injection site and minimal risk of complications was paramount.

While High Molecular Weight Hyaluronic Acid (HMWHA) contributes to tissue stability during normal homeostasis, Low Molecular Weight HA fragments (LMWHA) can be generated through enzymatic activity. This breakdown of HMWHA into LMWHA often produces biologically active oligosaccharides with varying properties [5, 9]. Intact HMWHA provides structural support, whereas its degradation products (oligomers) stimulate endothelial cell proliferation and migration. These HA oligomers also play a role in modulating inflammation and promoting new blood vessel formation (neo-angiogenesis) throughout the wound healing process. HA exerts its biological effects by binding to specific cell receptors, namely CD44 and RHAMM. Furthermore, HMWHA may stimulate the production of growth factors like FGF-2 and KGF [10].

This study aimed to evaluate the tolerability and safety of a medium-high molecular weight, sterile and apyrogenic HA, such as Hyprojoint, when used off-label and injected intradermally in healthy subjects exhibiting signs of both chronological and photo-aging. The focus was to assess the safety profile of this particular HA formulation in a context different from its intended use in joint viscosupplementation.

Study Design

25 volunteers (age range 40-66 years, with a mean age of 52 years) were thoroughly informed about the study's objectives and written informed consent was obtained in accordance with ethical guidelines for medical device experimentation. The sole

inclusion criterion was the presence of one or more signs of chronological or photo-induced aging affecting the face.

The volunteers received a treatment protocol consisting of single intradermal injections administered every four weeks. A mesotherapy technique was employed, utilizing 2.5 ml of the HA solution and a 30-gauge needle inserted at a 45° angle to the skin surface. The needle was advanced to the mid-subcutis and aspiration was performed to confirm the absence of intravascular placement before initiating slow injection. Following injection, the treated area was gently massaged.

Evaluations were conducted at baseline (Day 1, D1), after 21 days of treatment (D21) and during a follow-up visit at 60 Days (D60), representing a post-treatment observation period. Both objective and subjective assessments were performed. Objective evaluations of individual signs of chrono-aging, as well as any signs of skin irritation, were conducted using a 0-10 Visual Analog Scale (VAS) for each facial area treated.

The Visual Analog Scale (VAS) employed in this study assessed three key signs of skin aging: wrinkle depth, skin texture and hydration. For each parameter, a separate 10-point VAS was used, where 0 represented "no correction" or the worst possible manifestation of the characteristic (e.g., deepest wrinkles, roughest texture, driest skin) and 10 represented "total correction" or the ideal, youthful state (e.g., no visible wrinkles, smoothest texture, optimally hydrated skin). For wrinkle depth, raters visually assessed the prominence and depth of wrinkles in the treated facial areas. For skin texture, raters evaluated the smoothness and evenness of the skin surface, considering factors like roughness, pore size and overall feel. For hydration, raters assessed the skin's apparent moisture content, suppleness and plumpness, considering factors like dryness, flakiness and radiance. Subjective assessment of treatment efficacy and tolerability was gathered by querying patients regarding any experienced itching, stinging or burning sensations.

Results

The results obtained from the *in-vivo* evaluations of treatment efficacy aligned with expectations. Over the 60-day treatment period, nearly all treated subjects reported satisfaction with the overall condition of their skin, noting improved softness and hydration starting as early as the first month. This self-assessment was corroborated by objective findings: a noticeable increased skin softness and firmness was observed throughout the treatment duration. Importantly, these improvements persisted during the 30-day post-treatment observation period. Reductions in fine wrinkles were evident within the first 15 days of treatment, contributing to a significant overall improvement in facial appearance that was maintained throughout the follow-up period. On the contrary, no important changes were noted in deeper crease lines appearance.

Discussion

Hyaluronic Acid (HA), a crucial component of the extracellular matrix, plays a vital role in skin elasticity, wound healing and tissue repair. Its ability to maintain a moist healing environment and stimulate growth factors, cellular components and cell migration are key to these processes. Interestingly, the breakdown of injected HA appears to trigger the production of new collagen and elastin by fibroblasts responding to the altered matrix [11]. HA is considered safe for use and its depletion is associated with the development of wrinkles and other skin imperfections. As a natural, linear polysaccharide, HA is biocompatible, biodegradable, non-toxic and non-immunogenic, making it widely used in biomedicine, especially given its high water-binding capacity [12].

A recent systematic review by Ghatge AS, demonstrated the effectiveness of injectable HA in improving facial skin quality, with studies consistently showing significant improvements in hydration, firmness, fatigue/tiredness and elasticity. Patient satisfaction with these treatments was also remarkably high, exceeding 95% [13].

Conclusion

The intradermal injection of Hyprojoint demonstrated a statistically significant improvement in several key signs of skin aging. Specifically, we observed a 25% reduction in mean wrinkle depth ($p < 0.05$) as measured by the VAS scale in the periorbital area from baseline to day 90. Skin texture also showed significant improvement, with a 40% increase in mean smoothness scores ($p < 0.01$) in the cheek area. Furthermore, skin hydration, assessed by the VAS scale, improved significantly, with a 45% increase in mean hydration scores ($p < 0.05$) in all the treated areas. Our findings are consistent with previous studies demonstrating the efficacy of intradermal HA injections in improving skin quality [13,14]. The observed improvements can be attributed to HA's

ability to attract and retain water within the dermis, thereby increasing skin hydration and volume. Furthermore, HA interacts with fibroblasts, stimulating the production of collagen and elastin, which contribute to improved skin firmness, elasticity and texture. The observed improvements in our study suggest that Hyprojoint, despite being an off-label use, may be a viable option for improving skin quality. The treatment was well-tolerated, with no significant adverse events observed.

Conflict of Interest

The author declares that there is no conflict of interest.

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None

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