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Case Series

Exploratory clinical observations of high-dose oral 70 k da hyaluronan fragments in subcutaneous fat reduction, inflammatory erythema, and facial vitality: A case series

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Abstract

Background: The naked mole-rat exhibits unusually high tissue concentrations of hyaluronic acid and minimal subcutaneous adipose tissue, which has stimulated interest in the potential biological roles of HA in tissue homeostasis. This exploratory case series aimed to document clinical observations following high-dose oral administration of 70 kDa HA fragments with respect to perceived changes in subcutaneous fullness, facial erythema, and facial vitality.

Materials and Methods: Eleven Asian participants received oral 70 kDa HA fragments (5 g/day) for 40 consecutive days. Changes in perceived subcutaneous fullness, facial erythema, and facial vitality were evaluated using a modified 0–10 Visual Analog Scale (VAS). Safety and gastrointestinal tolerance were monitored throughout the intervention period.

Results: After 40 days of administration, participants reported varying degrees of perceived reduction in facial and/or body subcutaneous fullness, along with improvements in facial erythema and vitality. Some participants noted visible changes as early as day 7. No adverse events were reported during the intervention period. Incidental improvements in gastrointestinal comfort and dry eye symptoms were also reported by a subset of participants.

Conclusions: High-dose oral 70 kDa HA fragments were well tolerated in this exploratory case series and were associated with self-reported improvements in subcutaneous fullness appearance, facial erythema, and facial vitality. These preliminary observations warrant further investigation in larger controlled studies incorporating objective measurements.

Keywords: Hyaluronan fragments, Oral administration, Subcutaneous fat reduction, Anti-inflammation, Facial contour improvement.

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1. Introduction

Hyaluronic acid (HA) is a naturally occurring glycosaminoglycan widely distributed in connective tissues, where it contributes to extracellular matrix organization, tissue hydration, and structural integrity. Beyond its established roles in skin hydration and joint lubrication, HA has also been implicated in inflammatory regulation and tissue remodeling processes in various tissues.[1-3]

The naked mole-rat (NMR), a long-lived rodent species characterized by unusually high tissue concentrations of high–molecular–weight HA, has attracted scientific interest due to its resistance to cancer and age-related pathologies.[3,4] Studies have suggested that the unique HA metabolism in this species may contribute to its distinctive biological characteristics.[4-6] These findings have stimulated broader interest in the potential systemic biological roles of HA and its molecular weight–dependent properties.

In recent years, attention has increasingly focused on low–molecular–weight HA fragments. Experimental studies have suggested that specific enzymatically derived HA fragments may influence adipocyte differentiation and lipid metabolism in vitro and in animal models.[7,8] Additional work has indicated that orally administered low–molecular–weight

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HA fragments are rapidly absorbed via the intestinal lymphatic system, confirming systemic bioavailability following oral administration.[9] Although oral HA supplementation has been investigated primarily in the context of joint health and skin hydration, clinical studies generally report favorable safety and tolerability profiles.[10,10] However, clinical evidence evaluating the potential effects of orally administered HA fragments on subcutaneous fat distribution or inflammatory facial skin parameters remains limited. Therefore, the present study was designed as an exploratory clinical case series to document observational findings following high-dose oral administration of 70 kDa HA fragments in individuals seeking non-invasive aesthetic improvement (**Figure 1**). The primary objective was to describe changes in perceived subcutaneous fullness and inflammatory facial erythema during a 40-day intervention period, as well as to assess tolerability.

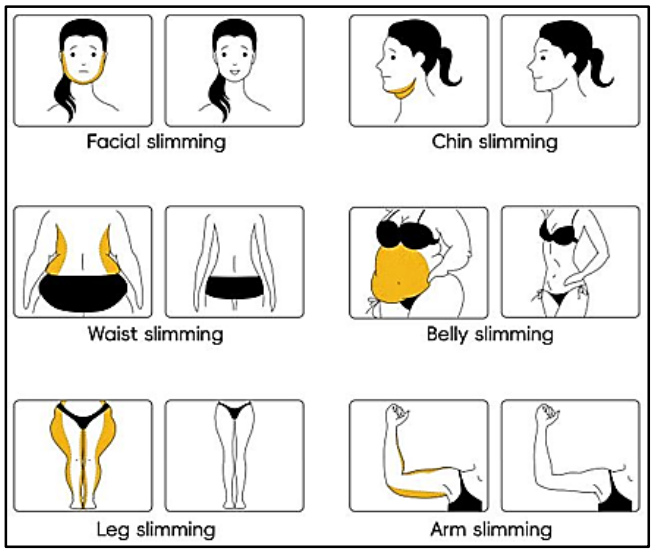

Figure 1: Schematic illustration of the pattern of body fat elimination after injection

2. Case presentation

2.1. Patient information

This case series included 11 Asian participants (7 females and 4 males) who presented to the Department of Aesthetic Medicine at Changchun Jiahe Plastic Surgery Hospital, China. All participants sought non-invasive improvement of facial contour and skin condition, primarily due to concerns related to subcutaneous fat accumulation or facial laxity, most commonly manifested as facial fullness and double chin.

Participants ranged in age from 28 to 69 years. Facial fat accumulation was attributed to multiple factors, including postpartum hormonal changes, natural aging, collagen loss, and sedentary lifestyle. The mean participant height was 168.4 ± 7.2 cm, and the mean baseline body weight was 72.3 ± 9.8 kg. Except for Case 11, none of the participants had a history of chronic systemic disease. Case 11 had a 20-year history of hypertension and a 15-year history of type 2 diabetes mellitus, both managed with stable oral medications.

Cases 1 and 11 reported persistent dry eye symptoms, while Cases 10 and 11 presented with chronic bowel dysfunction characterized by approximately four bowel movements per day. Given the potential association between these symptoms and the mucosal regulatory effects of HA, they were included as secondary observational endpoints. All participants refrained from fat-reduction procedures, cosmetic injections, or facial rejuvenation treatments for at least two weeks prior to study initiation.

2.2. Treatment protocol

All participants received oral administration of 5 g of food-grade low–molecular-weight hyaluronan fragments (average molecular weight approximately 70 kDa; manufacturing specification range: 60–80 kDa; Product Code: Q/0285HND042) once daily in the morning on an empty stomach for 40 consecutive days. The preparation was provided by Qingdao Hynaut Laboratory, consisting of purified sodium hyaluronate fragments with no additional pharmacologically active excipients. The 5 g/day dose was selected based on preclinical safety data and previously reported human tolerability studies of oral hyaluronan fragments.[12-14] No formal dose-ranging study was conducted for this exploratory case series.

Participants were strictly instructed to maintain their habitual diet and physical activity throughout the study period to eliminate confounding factors from lifestyle modifications. Compliance with daily administration was monitored via a dual verification method: daily electronic self-reporting logs by participants (recording administration time and any deviations) and in-person follow-up verification (on day 7, 14, 28, and 40) by attending physicians, who reviewed the logs and confirmed the remaining quantity of the study product. No compensatory doses were allowed for any missed administration.

2.3. Evaluation methods

Participants independently assessed clinical outcomes using a modified 0–10 Visual Analog Scale (VAS)[14,15] at baseline and after the 40-day treatment period. The VAS is widely used in clinical and aesthetic research to capture subjective patient-reported outcomes related to facial contour, skin appearance, and inflammatory symptoms.[14,15] Four domains were evaluated: subcutaneous fat reduction, inflammatory erythema/skin tone improvement, facial vitality enhancement, and gastrointestinal tolerance.

For fat reduction assessment, six anatomical regions were evaluated: cheek fullness, double chin prominence, upper eyelid thickness, posterior upper arm fullness, thigh subcutaneous fullness, and abdominal subcutaneous fat thickness assessed by a manual pinch test. Scores ranged from 0 (no perceptible reduction) to 10 (ideal aesthetic

outcome). Body weight was measured at baseline and after treatment using a calibrated digital scale. Erythema/skin tone and facial vitality scores ranged from 0 (no improvement) to 10 (complete resolution or ideal state). Gastrointestinal tolerance was scored from 0 (no discomfort) to 10 (severe intolerable discomfort) based on subjective discomfort and bowel frequency. Standardized scoring criteria were provided to participants to reduce subjective variability.

Additional observations, including dry eye symptoms and appetite changes, were recorded daily and reviewed by attending physicians during follow-up assessments.

2.4. Statistical analysis and result interpretation

Descriptive statistics were used to summarize study outcomes. Continuous variables are presented as mean ± standard deviation (SD).

Given the exploratory nature and small sample size of this case series, no inferential statistical analyses were performed. Clinical outcomes were interpreted descriptively based on changes in participant-reported Visual Analog Scale (VAS) scores and observed clinical trends over the 40-day intervention period. For exploratory reference, a VAS score ≥4 (0–10 scale) was considered to represent a perceptible clinical improvement. Qualitative observations, including changes in facial contour, erythema, gastrointestinal symptoms, and dry eye symptoms, were documented during follow-up visits and interpreted descriptively in relation to the treatment period. All interpretations were limited to observational associations between oral 70 kDa HA fragment administration and reported outcomes, without causal inference.

3. Result

3.1. General observations

All 11 participants completed the full 40-day oral intervention with a 100% compliance rate confirmed by dual monitoring methods. Following daily administration of 5 g of 70 kDa HA fragments, all participants reported varying degrees of facial and body subcutaneous fat reduction accompanied by subjective improvement in overall appearance. No participant discontinued treatment or withdrew, indicating excellent compliance and tolerability.

3.2. Reduction of facial and body fat

After 40 days of treatment, most participants reported improved facial contour and visibly reduced double chin. Nine participants achieved scores ≥7 for both cheek fullness and double chin reduction. Participant 2 rated both parameters as 10, indicating achievement of their ideal aesthetic outcome (**Figure 2**). Mean reduction scores were 7.2 for cheek fullness, 7.5 for double chin, 7.2 for upper eyelid thickness, 5.8 for upper arm thickness, 5.8 for thigh thickness, and 6.4 for abdominal thickness, demonstrating consistent fat reduction across multiple anatomical regions (**Table 1**).

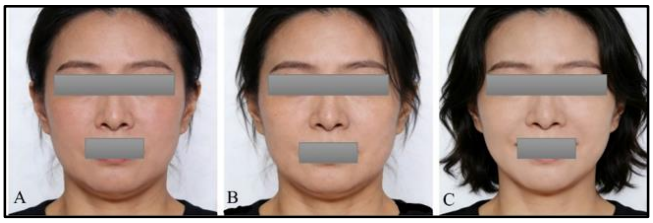

Figure 2: Post-treatment comparison images provided by Participant 2. **A:** Before treatment; **B:** After 7 days of treatment; **C:** After 40 days of treatment.

Table 1: Subcutaneous fat reduction scores after 40 days of oral treatment (0–10 scale)

Parameter	1	2	3	4	5	6	7	8	9	10	11	Mean ± SD
Reduction in cheek fullness	8	10	8	7	7	7	7	8	7	4	6	7.2 ± 1.4
Reduction in double chin	9	10	8	7	7	8	7	9	8	4	6	7.5 ± 2.4
Reduction in eyelid thickness	8	9	8	7	7	7	7	7	8	4	7	7.2 ± 1.2
Reduction in upper arm thickness	7	8	7	6	6	5	5	6	6	3	5	5.8 ± 1.2
Reduction in thigh thickness	7	8	7	6	5	5	5	6	7	3	5	5.8 ± 1.3
Reduction in abdominal thickness	8	9	7	7	6	6	5	7	7	3	6	6.4 ± 1.4

All participants experienced body weight reduction, with a mean decrease of 4.2 kg (range: 2–8 kg) (**Table 2**). Notably, weight loss occurred without dietary restriction or exercise intervention, suggesting a potential direct regulatory effect of oral 70 kDa HA on lipid metabolism.

Table 2: Changes in body weight after 40 days of treatment (kg)

Parameter	1	2	3	4	5	6	7	8	9	10	11	Mean ± SD
Body weight reduction (kg)	3	6	8	4	2	4	5	5	3	2	4	4.2 ± 1.7

Table 3: Scores for reduction in facial erythema and improvement in facial vitality after 7 days

Parameter	1	2	3	4	5	6	7	8	9	10	11	Mean ± SD
Reduction in inflammatory erythema	5	7	7	5	5	5	5	5	6	5	6	5.5 ± 0.8
Improvement in facial vitality and expressiveness	5	7	6	6	6	6	6	6	6	5	6	5.5 ± 0.8

3.3. Improvement in skin condition and facial vitality

Most participants reported noticeable improvements in facial complexion and vitality as early as day 7 (**Figure 2**). The mean score for reduction in inflammatory erythema was 5.5 ± 0.8, indicating mild-to-moderate improvement. Facial vitality scores were similarly elevated (5.5 ± 0.8), with participants describing brighter skin tone, reduced flushing, and enhanced expressiveness (**Table 3**).

3.4. Gastrointestinal tolerance and additional observations

All participants demonstrated excellent gastrointestinal tolerance to high-dose oral administration, with no reports of gastric pain, bloating, or clinically significant gastrointestinal discomfort during the intervention period. Among participants with pre-existing gastrointestinal symptoms (Cases 10 and 11), rapid symptomatic improvement was observed. Specifically, gastrointestinal comfort scores decreased from a baseline average of 4–5 to 0–1 by day 2 of treatment. In parallel, bowel irregularities associated with gastrointestinal discomfort improved, with defecation frequency normalizing from approximately four times per day to once daily. During long-term follow-up, Case 11 reported a persistent subjective sensation of enhanced satiety or reduced gastric capacity at 6 months post-treatment, suggesting a possible mild appetite-suppressing effect.

In addition, two participants with long-standing refractory dry eye symptoms reported complete symptom resolution after 40 days of treatment, with no recurrence during 4–6 months of follow-up.

4. Discussion

This case series describes the clinical observations associated with 40 days of high-dose oral administration of 70 kDa hyaluronan (HA) fragments in individuals seeking non-invasive aesthetic improvement. Across all 11 participants, varying degrees of subjective reduction in facial and body subcutaneous fullness were reported, accompanied by improvements in inflammatory erythema and perceived facial vitality. No adverse events were observed during the intervention period, indicating good short-term tolerability at the administered dose.[12]

The most consistent observation was the reduction in perceived cheek fullness and double chin prominence (Table 1). Mean scores for these parameters were above 7 on a 0–10 scale, and every participant reported some degree of contour refinement. In addition to localized facial changes, moderate reductions in overall body weight were observed (**Table 2**). Although body composition was not directly measured, the parallel improvement in multiple anatomical regions suggests that the effect was not limited to a single area (**Table 1** and **Table 2**). Whether these changes reflect alterations in adipose tissue distribution, fluid dynamics, or other metabolic factors remains uncertain and warrants further study.

Improvements in facial erythema and vitality were noted in most participants, in some cases within the first week of administration (**Table 3**). HA is widely recognized for its role in extracellular matrix organization, tissue hydration, and inflammatory regulation.[1-4] Preclinical studies have reported that specific low–molecular–weight HA fragments may influence adipocyte biology and inflammatory signaling pathways.[14-16] While the present study did not evaluate molecular or biochemical markers, the clinical observations are consistent with previously described biological properties of HA fragments.[17-19]

An additional observation was the improvement in gastrointestinal comfort in participants with pre-existing bowel irregularities, as well as resolution of dry eye symptoms in two individuals. Oral low-molecular-weight HA fragments are rapidly absorbed via the intestinal lymphatic system and have been reported in experimental models to support mucosal barrier integrity and epithelial homeostasis.[9,20] Although secondary and exploratory in nature, these findings raise the possibility of broader systemic effects that merit further investigation under controlled conditions.

Overall, this series provides preliminary clinical observations suggesting that high-dose oral 70 kDa HA fragments may be associated with changes in perceived subcutaneous fullness and inflammatory skin parameters. The consistency of subjective improvements across participants, together with favorable tolerability, supports the feasibility of further structured clinical evaluation.

This study has several important limitations. First, as an uncontrolled case series without placebo comparison, randomization, or blinding, the findings cannot establish causality. Placebo effects, regression to the mean, natural temporal variation, and lifestyle changes cannot be excluded. Second, primary outcomes were based on patient-reported VAS assessments, which are not validated instruments for adiposity or facial contour quantification. Objective measurements such as imaging-based fat thickness assessment or laboratory biomarkers were not performed. Third, the sample size was small and limited to a single-center cohort of Asian participants, which restricts generalizability. Fourth, result interpretation was limited to descriptive analysis without inferential statistics, consistent with the exploratory study design and pre-defined interpretation approach. Finally, the duration of intervention and follow-up was relatively short, and long-term durability of the observed changes remains unknown. Future studies incorporating controlled designs, objective body composition measurements, and longer follow-up periods are necessary to determine reproducibility, magnitude of effect, and potential mechanisms underlying the clinical observations reported here.

5. Conclusion

In this case series, high-dose oral administration of 70 kDa hyaluronan fragments for 40 days was well tolerated and was associated with patient-reported reductions in facial and body subcutaneous fullness, improvements in inflammatory erythema, and enhanced facial vitality. Although the uncontrolled design limits causal interpretation, the consistency of observations across participants supports further investigation in larger, controlled clinical studies.

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Consent and Ethics Statement: Written informed consent was obtained from the patients for the publication of any potentially identifiable images or data included in this article.

7. Conflict of Interest

Mizhou Hui, Xiaoxiao Jia and Jessica H Hui are employees of Qingdao Hynaut Laboratory, which manufactures the HA35 product evaluated in this study. Ding Mingxing, Ma Wenhai and Vera Gorbunova declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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