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(CASE REPORT)

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Rapid Relief of Nasopharyngeal and Posterior Pharyngeal Inflammatory Symptoms After Nasopharyngeal Administration of High-Concentration 35 kDa Hyaluronan: A Case Series

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Abstract

Background: Chronic rhinitis and chronic pharyngitis are common upper airway inflammatory conditions that significantly impair quality of life. Effective non-pharmacological interventions for rapid symptom relief remain limited. Objective: To evaluate the symptom-relieving effects of nasopharyngeal administration of high-concentration 35 kDa hyaluronic acid fragments (HA35) in individuals with chronic nasopharyngeal and posterior pharyngeal inflammatory discomfort, and to assess changes in subjective mental clarity. Methods: This case series included seven volunteers with concomitant chronic rhinitis and chronic pharyngitis. Participants received a 13.6% high-concentration HA35 nasopharyngeal care gel twice daily for 10 consecutive days. A standardized 0–10 numerical rating scale (NRS) was used to assess nasopharyngeal discomfort, posterior pharyngeal discomfort, nasal airflow, overall inflammatory symptom severity, and subjective mental clarity at predefined time points. Results: Within 30 minutes of the first administration, nasopharyngeal discomfort, posterior pharyngeal discomfort, sneezing, cough, and nasal obstruction scores decreased markedly in all participants. After 10 days of continuous treatment, symptoms of chronic rhinitis and pharyngitis were substantially alleviated, with most scores reduced to mild levels or near resolution. All participants reported a notable improvement in subjective mental clarity within 1–3 hours following the first morning administration. Three participants experienced transient difficulty initiating sleep when the product was administered shortly before bedtime. Conclusion: In this case series, nasopharyngeal administration of high-concentration HA35 was associated with rapid relief of upper airway inflammatory discomfort and improved subjective mental clarity.

Keywords: Hyaluronic acid fragments; Chronic rhinitis; Chronic pharyngitis; Nasopharyngeal administration; Case series

1. Introduction

Chronic rhinitis and chronic pharyngitis are common disorders encountered in otolaryngology and are characterized by persistent hyperemia, edema, and accumulation of inflammatory mediators within the nasal and pharyngeal mucosa. Patients frequently present with nasal obstruction, sneezing, throat clearing, coughing, and sensations of head heaviness or mental fog. Although antihistamines, topical corticosteroids, and decongestants are widely used in clinical practice, their delayed onset of action, variable efficacy, and potential adverse effects with long-term use remain significant clinical challenges [1].

The nasopharyngeal and posterior pharyngeal mucosa are richly supplied with lymphatic networks (Figure 1) and immunologically active cells, serving as key anatomical structures for local immune defense and inflammatory clearance in the upper airway. Previous studies have suggested that, under chronic inflammatory conditions, impaired mucosal

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lymphatic drainage leads to prolonged retention of inflammatory mediators and interstitial fluid, contributing to the persistence of symptoms [2]. Therefore, strategies aimed at enhancing lymphatic drainage and promoting resolution of inflammation represent an important therapeutic direction for chronic mucosal inflammatory diseases.

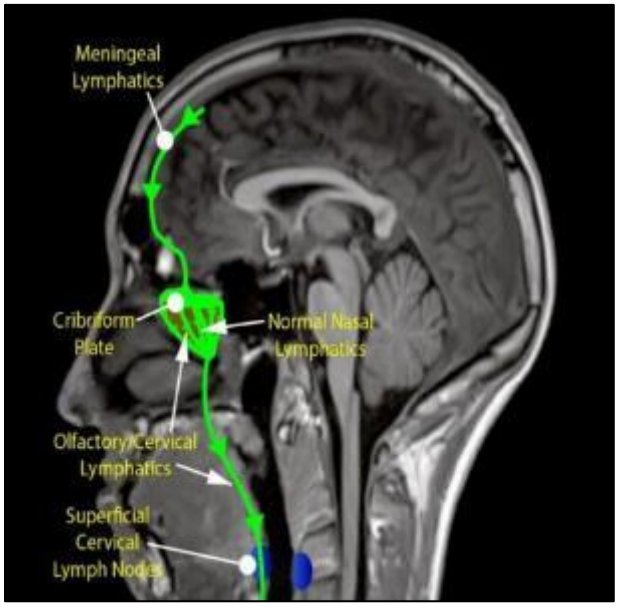

Figure 1 Schematic illustration of the cerebral lymphatic network

Accumulating evidence indicates that low-molecular-weight HA35 can facilitate lymphatic circulation and promote clearance of inflammatory mediators [3,4]. In parallel, the naked mole-rat—whose skin and mucosal tissues contain unusually high concentrations of hyaluronic acid (HA)—rarely develops common mucosal inflammatory diseases such as chronic rhinitis and pharyngitis [5,6]. This observation supports the hypothesis that high-concentration HA may play a critical role in maintaining mucosal homeostasis and suppressing chronic inflammation.

Our group's previous investigations have further demonstrated that topical application of high-concentration HA35 can relieve skin pruritus within seconds and superficial pain within approximately one minute (International Patent Application No. PCT/2025/01344377) [7]. However, conventional pharmacokinetic models are insufficient to explain how HA35 could penetrate subcutaneous structures within such short time frames, suggesting that its biological effects may not rely on classic molecular diffusion mechanisms but may instead involve sensory–immune interactions or lymphatic system modulation[3,4]. Based on this background, the present study administered high-concentration HA35 via the nasopharyngeal route to observe its clinical effects on chronic nasopharyngeal and posterior pharyngeal inflammatory discomfort, and to explore whether this intervention might influence subjective mental clarity potentially associated with nasopharyngeal lymphatic and cerebrospinal fluid drainage pathways.

2. Case reports

2.1. Participant Information

This case series included seven Asian volunteers (four females and three males) who had long-standing chronic rhinitis accompanied by chronic pharyngitis. All participants experienced recurrent nasopharyngeal discomfort in daily life, including nasal obstruction, sneezing, foreign body sensation in the posterior pharynx, or irritative cough, and voluntarily agreed to receive a non-pharmacological nasopharyngeal local care intervention.

The age of the participants ranged from 28 to 70 years. Participant 1 was a 28-year-old male with a normal body mass index (BMI) who performed prolonged sedentary desk work and reported frequent morning nasal congestion and throat-clearing cough. He had no confirmed history of allergic rhinitis. Participant 2 was a 42-year-old female with a normal BMI who reported long-term recurrent nasal itching, paroxysmal sneezing, and a sticky sensation in the posterior pharynx, accompanied by mild head heaviness. Participant 3 was a 56-year-old female with prominent chronic nasal obstruction and a persistent foreign body sensation in the posterior pharynx, with symptoms worsening in the morning. She had no prior history of upper airway surgery. Participant 4 was a 70-year-old female with a multi-year

history of age-related chronic rhinitis, characterized by poor nasal airflow and recurrent irritative cough originating from the posterior pharynx. Participant 5 was a 65-year-old male with a history of long-term smoking; he had quit smoking prior to enrollment but continued to experience stable symptoms of chronic rhinitis and pharyngitis. Participant 6 was a 68-year-old male who reported frequent nasal obstruction and throat clearing, along with marked posterior pharyngeal discomfort. He did not use intranasal corticosteroids regularly. Participant 7 was a 63-year-old female who experienced pronounced morning nasal congestion and dryness with itching in the posterior pharynx, with symptoms persisting for more than one year.

All participants possessed full decision-making capacity, were able to proficiently use the standardized 0–10 NRS [8–11], and independently completed symptom self-assessments and records. None of the participants had used antihistamines, intranasal corticosteroids, decongestants, or other local nasopharyngeal therapeutic preparations, nor had they undergone related physical therapies within two weeks prior to enrollment.

2.2. Intervention

All participants received the same intervention protocol. The intervention material consisted of a 13.6% high-concentration HA35 nasopharyngeal care gel (Product Standard No.: Q/0285HND 048).

During each treatment session, one unit of gel was administered into each nostril. The gel was slowly advanced through the nasal cavity to reach the nasopharyngeal and posterior pharyngeal regions (Figure 2), allowing adequate coverage of the nasopharyngeal and posterior pharyngeal mucosal surfaces.

The administration regimen consisted of twice-daily application (morning and evening), with two units per session (one per nostril), totaling four units per day, for 10 consecutive days. Throughout the treatment period, participants were instructed to maintain their usual lifestyle and refrain from using any additional nasopharyngeal care or therapeutic products.

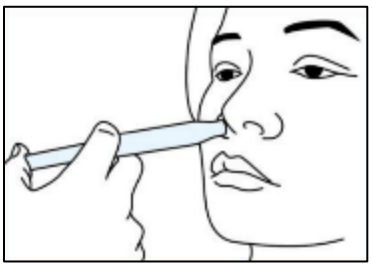

Figure 2 Schematic illustration of the HA35 administration procedure

2.3. Outcome Assessment

A standardized 0–10 NRS [8–11] was used to quantitatively assess symptom changes at baseline, 30 minutes after the first administration, and after completion of the 10-day treatment period. The assessment domains included the following:

Nasopharyngeal discomfort and associated sneezing: A score of 0 indicated no nasopharyngeal discomfort or sneezing, whereas a score of 10 represented the most severe imaginable nasopharyngeal discomfort with frequent sneezing. Posterior pharyngeal discomfort and associated cough: A score of 0 indicated no posterior pharyngeal discomfort or cough, whereas a score of 10 represented the most severe imaginable posterior pharyngeal irritation and cough. Nasal airflow: A score of 0 represented normal nasal airflow without a sensation of obstruction, whereas a score of 10 indicated the most severe imaginable nasal obstruction. Overall severity of rhinitis and pharyngitis symptoms (assessed after continuous treatment): A score of 0 indicated absence of rhinitis or pharyngitis symptoms, whereas a score of 10 represented the most severe imaginable symptom state. Subjective mental clarity: A score of 0 represented normal mental clarity, whereas a score of 10 represented the poorest imaginable level of mental clarity. This parameter was recorded at 1, 2, and 3 hours following the first morning administration.

In addition, participants' subjective experiences and any potential intervention-related adverse events were documented throughout the study period, including but not limited to nasal irritation, changes in nasal secretions, and alterations in sleep patterns.

2.4. Results

Before treatment, all participants reported moderate nasopharyngeal and posterior pharyngeal discomfort, accompanied by varying degrees of nasal obstruction, sneezing, or chronic cough. In addition, all participants described a general sensation of head heaviness or insufficient mental clarity.

Within 30 minutes after the first administration, nasopharyngeal discomfort and associated sneezing scores decreased markedly from 4.6 ± 1.4 to 0.6 ± 0.4. Posterior pharyngeal discomfort and cough scores decreased from 4.0 ± 0.8 to 0.4 ± 0.6. Nasal airflow scores improved substantially, decreasing from 4.6 ± 1.0 to 0.6 ± 0.4. Several participants experienced mild, transient watery nasal discharge approximately 30 seconds after administration, followed by a clear improvement in nasal airflow.

After 10 consecutive days of treatment, rhinitis symptom scores decreased from 4.2 ± 1.4 to 0.6 ± 0.6, and pharyngitis symptom scores decreased from 5.8 ± 1.8 to 0.8 ± 0.6, indicating sustained relief of chronic inflammatory symptoms.

All participants reported a marked improvement in subjective mental clarity within 1–3 hours after the first morning administration. Mental clarity scores reached the maximum value at 1 hour and remained unchanged thereafter (Table 1). In addition, three participants experienced transient difficulty initiating sleep when the gel was administered approximately one hour before bedtime; these symptoms lasted for approximately 2–4 hours and resolved spontaneously. No other adverse events were observed during the study period.

Table 1 Subjective mental clarity scores at different time points after the first administration (n = 7)

Parameter	Before treatment	1 h after treatment	2 h after treatment	3 h after treatment
Mental clarity	8.0 ± 0.0	10.0 ± 0.0	10.0 ± 0.0	10.0 ± 0.0

3. Discussion

This case series demonstrates that nasopharyngeal administration of high-concentration HA35 can rapidly alleviate nasopharyngeal and posterior pharyngeal inflammatory discomfort and produce sustained improvement in symptoms of chronic rhinitis and pharyngitis with continuous use. Symptom relief occurred shortly after the first administration, suggesting a potential advantage of this intervention in providing rapid onset of action for upper airway mucosal inflammation.

Previous studies have shown that HA35 can preferentially enter and modulate the lymphatic system through binding to the lymphatic endothelial hyaluronan receptor LYVE-1 [3,4,12–15]. Given that the nasopharyngeal mucosa is rich in lymphatic vessels and immunologically active tissues [16–18], local nasopharyngeal administration of high-concentration HA35 may confer enhanced biological responsiveness in this region. Such an effect could facilitate the clearance of inflammatory mediators, interstitial fluid, and metabolic byproducts, thereby alleviating inflammation-related symptoms. This mechanism provides a potential non-pharmacological strategy for managing chronic inflammation of the nasopharynx and posterior pharynx.

In addition, the observed improvement in subjective mental clarity, along with transient sleep-onset difficulty following evening administration in a subset of participants, offers preliminary clinical clues that HA35 may influence central arousal states through modulation of nasopharyngeal lymphatic pathways and their connections to deep lymphatic or cerebrospinal fluid circulation. Although this hypothesis remains speculative, these findings suggest that nasopharyngeal lymphatic modulation may exert effects beyond local mucosal inflammation, potentially impacting central physiological processes.

Several limitations of this study should be acknowledged. The sample size was small, no control group was included, and outcome measures relied primarily on subjective rating scales. As a result, causal relationships cannot be established. The findings should therefore be interpreted as hypothesis-generating. Future studies incorporating larger cohorts, randomized controlled designs, and objective outcome measures—such as imaging assessments or inflammatory and lymphatic biomarkers—are required to further validate the efficacy of nasopharyngeal HA35 administration and to elucidate its underlying mechanisms.

4. Conclusion

In this case series, nasopharyngeal administration of high-concentration HA35 was associated with rapid relief of nasopharyngeal and posterior pharyngeal inflammatory discomfort and with improvements in subjective mental clarity. These preliminary findings warrant further investigation in larger, controlled studies.

Compliance with ethical standards

Acknowledgments

The authors thank all participants for their voluntary involvement in this study.

Disclosure of conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Statement of ethical approval

The study was conducted in accordance with the Declaration of Helsinki. Given the observational nature of this case series and the use of a non-pharmacological care product, formal institutional ethics committee approval was not required.

Statement of informed consent

Written informed consent was obtained from all participants for the use of their data in this case series and for publication.

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