

Ultra-Rapid Relief of Skin Pruritus by a 10% High-Concentration 35 kDa Hyaluronic Acid Fragment Gel: A Case Series

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Abstract

High concentrations of hyaluronic acid (HA) have been associated with reduced itch responses in certain biological systems, suggesting a potential role for HA fragments in pruritus modulation. This case series evaluated the preliminary efficacy and safety of a 10% high-concentration 35 kDa HA fragment gel (HA35 gel) for the management of human skin pruritus. Methods: This case series included five patients with moderate-to-severe pruritus of diverse etiologies, including eczema, neurodermatitis, insect bites, urticaria, and post-operative wound-associated pruritus. HA35 gel was applied topically to affected areas. Pruritus intensity was assessed using a Numerical Rating Scale (NRS) at baseline and selected post-application time points, including an early patient-reported onset assessment at approximately 10 seconds and extended follow-up intervals of up to 24 hours, depending on individual symptom evolution. Results: Across all cases, topical application of HA35 gel was associated with a rapid reduction in pruritus intensity, with marked relief reported within seconds after application. In most patients, symptom control persisted for several hours, with sustained relief observed for approximately 8 - 12 hours. No local irritation, allergic reactions, or other adverse skin events were reported during the observation period. Conclusion: In this small case series, topical application of a 10% high-concentration HA35 gel was associated with rapid and sustained alleviation of pruritus across different etiologies, accompanied by improvement in inflammatory skin signs. These findings should be interpreted as hypothesis-generating and suggest that HA35 gel may represent a potential fast-acting, non-steroidal topical option for pruritus management, warranting further controlled investigation.

Keywords

Skin Pruritus, Hyaluronic Acid Fragment, HA35, Rapid Itch Relief, Case Series

1. Introduction

The naked mole rat (NMR) is an exceptionally long-lived mammal characterized by an unusually high concentration of HA in its tissues, reaching approximately 6% [1]-[5]. This remarkable abundance of HA has been associated with several distinctive physiological traits of the species, including extreme longevity, exceptionally low tumor incidence, and marked resistance to inflammation and pain [1]-[5]. Notably, NMRs rarely exhibit “itching” behavior. Experimental studies have shown that histamine, a potent pruritogenic agent in humans, induces pronounced itching responses in human skin but has little to no effect on naked mole rat skin [6]. These findings suggest that the elevated HA concentration in naked mole rat tissues may play a role in suppressing or blocking pruritic signaling pathways, conferring an inherent anti-pruritic property.

Inspired by this physiological phenomenon, our previous research led to the development of a 10% high-concentration HA35 gel. Experimental results demonstrated that topical application of this formulation to human skin produced rapid and pronounced relief of itching (International Patent Application No. PCT/2025/01344377) and redness [1] [7]-[9]. Further mechanistic investigations revealed that the analgesic, anti-pruritic, and anti-inflammatory effects of high-concentration HA fragments may be mediated through modulation of TRPV1/A1 calcium ion channels and the lymphatic receptor LYVE-1 [10]-[17]. These findings indicate that high-concentration HA fragments possess multi-target neuro-regulatory and anti-inflammatory bioactivity.

Pruritus is an unpleasant sensation that evokes the urge to scratch and is a major symptom of numerous inflammatory skin disorders [18]. Chronic pruritus significantly impairs patients’ quality of life and often fails to respond adequately to conventional therapies such as antihistamines or corticosteroids. While HA has been widely studied for its anti-inflammatory and tissue-protective properties [1]-[6], research specifically focusing on the antipruritic effects of low-molecular-weight HA fragments remains limited, with most existing work centered on high-molecular-weight HA or general skin barrier modulation. Therefore, a topical HA fragment therapy inspired by the physiology of the naked mole rat offers a promising, non-steroidal, and biocompatible approach for pruritus management.

This study presents a case series designed to preliminarily evaluate the anti-pruritic efficacy and safety of the 10% high-concentration HA35 gel in patients with moderate to severe skin pruritus. Five patients with clinically significant itching were enrolled and followed after topical application to assess the clinical potential of high-concentration HA fragments and explore their possible mechanistic relationship to the naked mole rat’s unique physiological traits.

2. Case Reports

2.1. Patient Information and Baseline Clinical Characteristics

Patients were identified and treated between March 2025 and October 2025 in the outpatient Pain Medicine Department of The Affiliated Hospital of Qingdao University, Qingdao, China. This study was conducted as a descriptive case series in routine clinical practice. Patients presenting with clinically significant pruritus who were willing to try a non-steroidal topical intervention were included as a convenience sample. Clinical diagnoses were established by experienced physicians based on characteristic medical history and physical examination findings. All cases were physician-diagnosed, and no self-diagnosed cases were included. Given the exploratory nature of this case series, patient recruitment was not consecutive, and standardized diagnostic scoring systems or formal screening logs were not applied.

In total, five patients with moderate to severe skin pruritus of different etiologies were included. Case 1 was a 66-year-old man with a 10-year history of recurrent bilateral inguinal eczema accompanied by chronic pruritus. The itching was intermittent but recurrent, often exacerbated by emotional stress or sweating. Repeated scratching provided only transient relief and frequently resulted in localized skin thickening and mildly raised swelling. At baseline, the patient reported moderate to severe itching that interfered with comfort during daily activities. Case 2 was a 52-year-old man with a one-month history of newly developed neurodermatitis on the posterior neck. The affected area was characterized by rough skin texture and persistent itching without obvious swelling or erythema. Symptoms were aggravated by prolonged sitting and neck movement, and baseline pruritus severity was rated as moderate. Case 3 was a 42-year-old woman with acute but severe pruritus following insect bites. Scratching rapidly induced visible and palpable raised lesions at the affected sites, and itching intensity was described as severe at baseline, with difficulty refraining from scratching. Case 4 was a 30-year-old man with urticaria affecting the upper and mid-back. The lesions appeared as red or pale wheal-like plaques of varying sizes with well-demarcated borders and occasional coalescence into larger patches. Due to the anatomical location, effective self-scratching was difficult, and the patient reported persistent itching at baseline despite avoidance of known triggers. Case 5 was a 55-year-old man who developed postoperative pruritus two days after hair transplantation surgery. Multiple small erythematous swellings were present on the scalp, accompanied by continuous itching that disrupted rest and led to frequent attempts at scratching. All patients presented with persistent itching that significantly affected daily comfort and quality of life and reported insufficient or unsatisfactory symptom control with conventional self-care measures prior to enrollment. None of the patients had received topical corticosteroids, antihistamines, systemic antipruritic agents, or other investigational treatments within two weeks before participation. All participants were fully capable of understanding and independently completing standardized symptom assessments using the NRS.

2.2. Intervention and Assessment

Following baseline assessment, the HA35 gel (Q/0285HND045) was applied topically to the affected areas. The gel was evenly spread to form a thin, continuous layer sufficient to cover the pruritic lesions without visible excess accumulation.

Pruritus intensity was evaluated using a NRS at baseline (within 5 minutes prior to application) and at selected post-application time points, including approximately 10 seconds, 45 minutes, 8 hours, 12 hours, and 24 hours after application [19] [20]. Given the heterogeneity of pruritus etiologies and symptom duration among patients, follow-up assessments were adapted to individual clinical courses rather than performed at identical fixed time points for all cases.

Prior to treatment, patients were instructed that NRS scoring should reflect the subjective sensation of itch itself, rather than other cutaneous sensations such as cooling, moisturizing, pressure, or gel contact. The approximately 10-second time point was included to capture early patient-reported perception of itch relief. Patients were asked to indicate whether the pruritic sensation or urge to scratch persisted, independent of awareness of gel presence on the skin. A score of 0 (“no itching”) was recorded only when patients subjectively perceived complete cessation of itch. All participants were cognitively able to understand and complete the NRS assessments. The NRS ranged from 0 (“no itching”) to 10 (“worst imaginable itching”). The primary outcome measure was the change in NRS scores over time, used to describe both early and sustained antipruritic responses following HA35 gel application. No placebo control or sensory-matched comparator was included; therefore, early assessments were intended to reflect patient-reported onset of symptom relief rather than to establish pharmacodynamic causality.

2.3. Results

All five patients completed the observation period and were included in the analysis. Following topical application of the 10% high-concentration HA35 gel, all patients reported a rapid reduction in pruritus intensity across different etiologies. At the approximately 10-second assessment, patients reported complete cessation of perceived itch, with NRS scores decreasing from moderate-to-severe baseline levels (NRS 6 - 8) to 0 (Tables 1-3).

The antipruritic effect was sustained for several hours in most cases. In patients with inflammatory or neurogenic pruritus, including eczema, neurodermatitis,

Table 1. NRS scores (0 - 10) of Cases 1 - 3 treated with 10% HA35 gel at different time points.

Case	Cause of pruritus	Within 5 min before application	10 s after application	8 h after application	12 h after application
1	Eczema	7	0	0	2
2	Newly developed neurodermatitis	6	0	0	0
3	Insect bite	8	0	0	—

Note: Individualized follow-up time points; 24-hour assessment not required for Case 3 (“—”).

Table 2. NRS scores (0 - 10) of Case 4 treated with 10% HA35 gel at different time points.

Case	Cause of pruritus	Within 5 min before application	10 s after application	45 min after application	8 h after application	12 h after application
4	Urticaria	7	0	0	0	0

Note: Individualized follow-up time points; additional 45-minute assessment for Case 4.

Table 3. NRS scores (0 - 10) of Case 5 treated with 10% HA35 gel at different time points.

Case	Cause of pruritus	Within 5 min before application	10 s after application	8 h after application	24 h after application
5	Fresh postoperative scalp wound	7	0	0	2

Note: Individualized follow-up time points; 24-hour assessment included for Case 5.

insect bite-related pruritus, and urticaria, symptom relief persisted for at least 8 hours. In several cases, including neurodermatitis, insect bite-related pruritus, and urticaria, complete relief was reported for up to 12 hours. Mild recurrence of pruritus was observed in a subset of patients at later time points (12 - 24 hours), most notably in the case of eczema; however, symptom severity remained substantially lower than baseline levels.

In addition to itch relief, patients reported gradual improvement in visible inflammatory signs, including erythema, wheals, and scratch-induced swelling. According to patient-reported observations, these changes generally became apparent within approximately 45 - 60 minutes after application and were most evident in cases involving urticaria and insect bite-related reactions.

No local irritation, allergic responses, or other adverse skin reactions were reported in any patient during the observation period.

3. Discussion

This case series describes the clinical effects of a 10% high-concentration HA35 gel in patients with skin pruritus of diverse etiologies. Across all cases, topical application was associated with a rapid patient-reported reduction in itch sensation within seconds and sustained antipruritic effects lasting several hours, with minimal recurrence at later time points. These observations suggest that high-concentration HA35 gel may provide both immediate and durable relief of pruritus arising from inflammatory and post-traumatic conditions.

In addition to itch suppression, several patients reported gradual improvement in visible inflammatory signs, including erythema, wheals, and scratch-induced swelling. This observation is consistent with previously reported anti-inflammatory properties of HA35 in experimental and clinical settings [7] [11] [12]. Notably, the onset of itch relief observed in this study occurred within seconds, which is substantially faster than that typically reported for conventional topical therapies. Although an immediate sensory effect from the gel vehicle may contribute to the perception of itch relief at the 10-second time point, patients were in-

structured to distinguish itch sensation from cooling or moisturizing effects, and this early assessment was intended to capture patient-reported onset rather than to establish sustained pharmacologic efficacy.

One possible hypothesis is that rapid neurocutaneous signaling mechanisms at the skin surface may contribute to the observed early itch suppression. Previous studies have demonstrated that hyaluronan fragments can modulate transient receptor potential channels, particularly TRPV1 and TRPA1, which play critical roles in itch and pain transmission [5] [10] [15]-[17]. In the context of the present case series, these prior findings provide a plausible mechanistic framework rather than direct evidence. Modulation of these channels at peripheral sensory nerve endings could hypothetically suppress pruritic signaling before central processing occurs. In parallel, interactions between HA fragments and the lymphatic endothelial receptor LYVE-1 have been proposed to facilitate lymphatic drainage and clearance of inflammatory mediators, which may contribute to sustained symptom relief and resolution of local swelling [11]-[14]. Although these mechanisms were not directly investigated in the present study, they remain biologically plausible hypotheses consistent with both the rapid onset and prolonged effects observed.

An additional conceptual perspective is provided by studies of the naked mole rat, a long-lived mammalian species characterized by exceptionally high concentrations of hyaluronic acid in its skin and connective tissues. Naked mole rats exhibit remarkable resistance to chronic inflammation and itch-related behaviors [1]-[4] [6]. Notably, histamine-induced itch is largely absent in this species, suggesting a potential association between HA-rich tissue environments and suppressed pruritic signaling [6]. While speculative, the rapid antipruritic effects observed with high-concentration HA35 gel in humans may partially resemble aspects of this naturally HA-enriched skin microenvironment. This comparison is intended as a biological analogy rather than a mechanistic inference and does not constitute direct evidence of shared pathways.

Several limitations of this case series should be acknowledged. The sample size was small, and the study lacked a control group, limiting the ability to establish causal relationships. In addition, symptom severity and pruritus intensity were primarily evaluated using a Numerical Rating Scale. Although this scale is not itch-specific, it has been widely used for the subjective quantification of symptom intensity across different sensory modalities, including pain and pruritus, particularly in exploratory and case-based clinical studies. Moreover, objective dermatologic assessments such as standardized erythema or wheal scoring systems and serial clinical photographs were not systematically collected, which limits the ability to quantify changes in visible skin manifestations. Therefore, the findings of this study should be interpreted as hypothesis-generating observations. Further studies with larger cohorts, appropriate control groups, and objective outcome measures are warranted to validate the therapeutic effects observed and to clarify the underlying biological mechanisms.

4. Conclusion

The 10% high-concentration HA35 gel was associated with rapid and sustained relief of skin pruritus of different etiologies, with patient-reported itch resolution occurring within seconds of topical application and effects lasting for several hours. Associated erythema and swelling were also reduced, and no local adverse reactions were observed. These findings suggest that high-concentration HA35 gel may serve as a fast-acting, non-steroidal topical option for the management of pruritus and inflammation.

Conflicts of Interest

Xiaoxiao Jia, Jessica H Hui, and Mizhou Hui are employees of Hynaut Laboratories, the developer of the HA35 gel evaluated in this study. This product is covered by the international patent application PCT/2025/01344377, with Mizhou Hui listed as an inventor. Fenghe Xu and Vera Gorbunova declare no conflicts of interest. The funders had no role in the study design, data analysis, manuscript writing, or publication decision.

Ethics Statement

This case series involved retrospective reporting of routine clinical care. Written informed consent for treatment and publication was obtained from all patients. Formal institutional review board approval was not required according to local regulations for case series reporting.

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