World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(CASE REPORT)

TOPICAL PERIOCULAR APPLICATION OF 10% 35-KDA HYALURONAN GEL FOR PERIOCULAR APPEARANCE AND OCULAR COMFORT: A RETROSPECTIVE CASE SERIES

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World Journal of Advanced Research and Reviews, 2026, 32(01), 1728–1733

Publication history: Received on 15 September 2026; revised on 22 October 2026; accepted on 24 October 2026

Article DOI: https://doi.org/10.30574/wjarr.2026.32.1.2705

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ABSTRACT

High-concentration low-molecular-weight hyaluronan has not been well described for periocular use. We retrospectively reviewed existing records from seven adults who had used a 10% 35-kDa hyaluronan (HA35) gel on the external periocular skin under occlusion for more than 2 hours or overnight once daily for 7 days. The available records contained study-specific 0-10 ratings for ocular discomfort/pain/itch, ocular fatigue, reduced perceived visual brightness, ocular/palpebral conjunctival appearance, lateral canthal wrinkles, upper-eyelid thickness, palpebral fissure enlargement, and periocular tissue softening. Outcomes included participant-reported symptoms and investigator-rated visual or tactile observations. Recorded ocular discomfort/pain/itch and fatigue decreased within 20 minutes of the first application and were rated 0 after seven applications. After 7 days, recorded scores for reduced perceived visual brightness, conjunctival findings, upper-eyelid thickness, and lateral canthal wrinkles decreased, while palpebral fissure enlargement and tissue-softening scores increased. No product-related adverse events were documented in the available records. These retrospective findings suggest potential periocular aesthetic and comfort benefits and warrant controlled studies with objective measurements.

Keywords: Hyaluronan; HA35; Periocular Aesthetics; Eyelid; Ocular Comfort

1 INTRODUCTION

Naked mole-rats are long-lived rodents that produce abundant very-high-molecular-mass hyaluronan. Experimental studies have linked this hyaluronan phenotype to cytoprotection, reduced inflammation, and improved healthspan in cellular and transgenic mouse models.[1,2] These findings concern high- or very-high-molecular-mass hyaluronan and do not establish effects of 35-kDa hyaluronan in humans. A previous human case series reported that topical occlusive application of 10% 35-kDa hyaluronic acid fragment for more than 2 hours or overnight was associated with changes in facial erythema and the appearance of subcutaneous fat (PCT patent application no. PCT/CN2026/097259).[3] On this

basis, the present report retrospectively summarizes existing case records concerning daily topical periocular use of 10% 35-kDa hyaluronic acid fragment for more than 2 hours or overnight for 7 consecutive days and the recorded ocular and periocular observations.

2 RETROSPECTIVE UNCONTROLLED CASE SERIES

2.1 Case identification, consent, and prior product use

Seven adults aged 32–70 years (three men and four women) were identified from existing records generated at the Aesthetic Medicine Department at Hynaut Laboratory between May and July 2026. The records indicated that each individual had reported at least one of the following: ocular dryness, itching, or fatigue; discomfort associated with contact-lens wear; or an interest in improving periocular appearance. No formal exclusion criteria had been applied. All seven individuals reported daily ocular dryness; intermittent ocular itching was also reported. Five were employed and reported prolonged daily computer use, while two were retired. Two were daily contact-lens users. Six had myopia, and one had presbyopia. None had conjunctivitis, cataract, or another reported ocular condition. The records also documented use of eye drops or steam eye masks for eye care and completion of the 7-day observation period by all seven individuals. This report was prepared retrospectively from existing case records; no additional intervention or data collection was undertaken for this report. Written informed consent for publication was obtained from all seven individuals. Case characteristics are summarized in Table 1.

Table 1: Baseline characteristics of the participants (n = 7)

Characteristic	Summary
Age, years	32–70
Men	3 (42.9%)
Women	4 (57.1%)
Daily ocular dryness	7 (100%)
Employed participants reporting prolonged computer use	5 (71.4%)
Retired participants	2 (28.6%)
Daily contact-lens users	2 (28.6%)
Myopia	6 (85.7%)
Presbyopia	1 (14.3%)
Conjunctivitis	0
Cataract	0
Other reported ocular conditions	0

According to the available records, a 10% formulation of 35-kDa sodium hyaluronate gel (product standard no. Q/0285HND058-2026; Huinuode Biotechnology Co., Ltd., Qingdao, China) had been applied as a generous, even layer to the external periocular skin with the eyes closed and had not been instilled into the eye. The formulation contained water, sodium hyaluronate, and sodium chloride. A 10 × 10 cm wound dressing or steam eye mask had been placed over the application area to limit drying. The preparation had remained in place for more than 2 hours or overnight and had been used once daily for seven consecutive days. The records described only external periocular application, and no conclusions regarding direct ocular use or use with contact lenses were made.

2.2 Retrospective outcome extraction

Available records contained study-specific 0–10 ratings, informed by numerical rating-scale principles,[4] that were retrospectively extracted and summarized descriptively for this case series. Ocular discomfort/pain/itch, ocular fatigue, and reduced perceived visual brightness had been participant-reported. Ocular/palpebral conjunctival appearance, lateral canthal wrinkles, upper-eyelid thickness, and palpebral fissure enlargement had been investigator-rated by visual observation; periocular tissue softening had been investigator-rated by visual observation and tactile palpation. For ocular discomfort/pain/itch, ocular fatigue, reduced perceived visual brightness, ocular/palpebral conjunctival findings, lateral canthal wrinkles, and upper-eyelid thickness, 0 indicated absence of the finding and 10 indicated the greatest severity on the case-specific scale. Palpebral fissure enlargement and periocular tissue softening had been recorded as changes from baseline; baseline was defined as 0, and higher post-use scores indicated a greater observed

change. Ocular discomfort/pain/itch and ocular fatigue had been recorded before use, approximately 20 minutes after the first application, and after seven applications. The remaining outcomes had been recorded before use and after seven applications. One rating per individual was available at each applicable time point. Values are reported as mean ± standard deviation (SD). Because this was a retrospective uncontrolled case series of seven individuals, no inferential statistical testing was performed. The records were also reviewed for documented unexpected ocular or periocular reactions during product use.

3 RESULTS

Ocular discomfort/pain/itch decreased from 3.14 ± 0.89 before use to 0.42 ± 0.53 at 20 minutes and 0.00 ± 0.00 after seven applications. Ocular fatigue decreased from 2.85 ± 0.69 to 0.28 ± 0.48 at 20 minutes and 0.00 ± 0.00 after seven applications. At day 7, the score for reduced perceived visual brightness decreased from 1.85 ± 0.69 to 0.00 ± 0.00, the ocular/palpebral conjunctival composite from 3.14 ± 0.37 to 0.00 ± 0.00, right lateral canthal wrinkles from 1.57 ± 1.13 to 0.71 ± 0.48, and right upper-eyelid thickness from 2.14 ± 0.37 to 0.00 ± 0.00. In contrast, right palpebral fissure enlargement and periocular tissue-softening/improvement scores increased from 0.00 ± 0.00 before use to 2.85 ± 0.69 after seven applications (Table 2).

Table 2: Descriptive 0-10 outcome scores recorded during prior periocular use of 10% 35-kDa hyaluronan gel (n = 7)

Outcome (0-10 score)	Before use	20 min after first use	After seven applications
Ocular discomfort or pain/itch	3.14 ± 0.89	0.42 ± 0.53	0.00 ± 0.00
Ocular fatigue	2.85 ± 0.69	0.28 ± 0.48	0.00 ± 0.00
Reduced perceived visual brightness	1.85 ± 0.69	Not recorded	0.00 ± 0.00
Ocular/palpebral conjunctival composite	3.14 ± 0.37	Not recorded	0.00 ± 0.00
Right lateral canthal wrinkles	1.57 ± 1.13	Not recorded	0.71 ± 0.48
Right upper-eyelid thickness	2.14 ± 0.37	Not recorded	0.00 ± 0.00
Right palpebral fissure enlargement	0.00 ± 0.00	Not recorded	2.85 ± 0.69
Periocular tissue softening	0.00 ± 0.00	Not recorded	2.85 ± 0.69

Note: Values are mean ± SD. "Not recorded" indicates that no value was available in the existing records at the 20-minute time point. For ocular discomfort/pain/itch, ocular fatigue, reduced perceived visual brightness, ocular/palpebral conjunctival findings, lateral canthal wrinkles, and upper-eyelid thickness, lower scores indicate improvement. For palpebral fissure enlargement and periocular tissue softening/improvement, higher scores indicate greater post-use change.

Figure 1: Available right ocular and periocular photographs of the 68-year-old male participant before product use (A) and after seven applications (B). The photographs show differences in palpebral fissure appearance, periocular tissue appearance, and ocular and palpebral conjunctival redness; they were not obtained under a validated standardized photographic protocol.

These quantitative changes were accompanied by changes in the available paired clinical photographs. In the 68-year-old male participant shown in Figure 1, the before-use photograph of the right eye showed a relatively narrow palpebral fissure, mild upper-eyelid puffiness near the lash line, a relatively tense periocular appearance, and visible ocular/palpebral conjunctival redness, swelling, and congestion. After seven applications, the palpebral fissure

appeared larger, the surrounding periocular tissue appeared softer and less tense, and the conjunctival redness, swelling, and congestion appeared less prominent (Figure 1).

In the same participant, the before-use open-eye photographs showed a relatively thick-appearing right upper eyelid, multiple lateral canthal wrinkles, and a relatively tense periocular appearance. After seven applications, the upper eyelid appeared less thick and less puffy, the lateral canthal wrinkles appeared less prominent, and the periocular appearance appeared more relaxed. Similar changes in upper-eyelid fullness and lateral canthal wrinkling were observed in the paired closed-eye photographs (Figure 2). These observations were not supported by direct measurements of eyelid thickness, palpebral fissure dimensions, or wrinkle severity. No product-related adverse events, unexpected ocular/periocular reactions, or discontinuations were documented in the available records during the 7-day observation period.

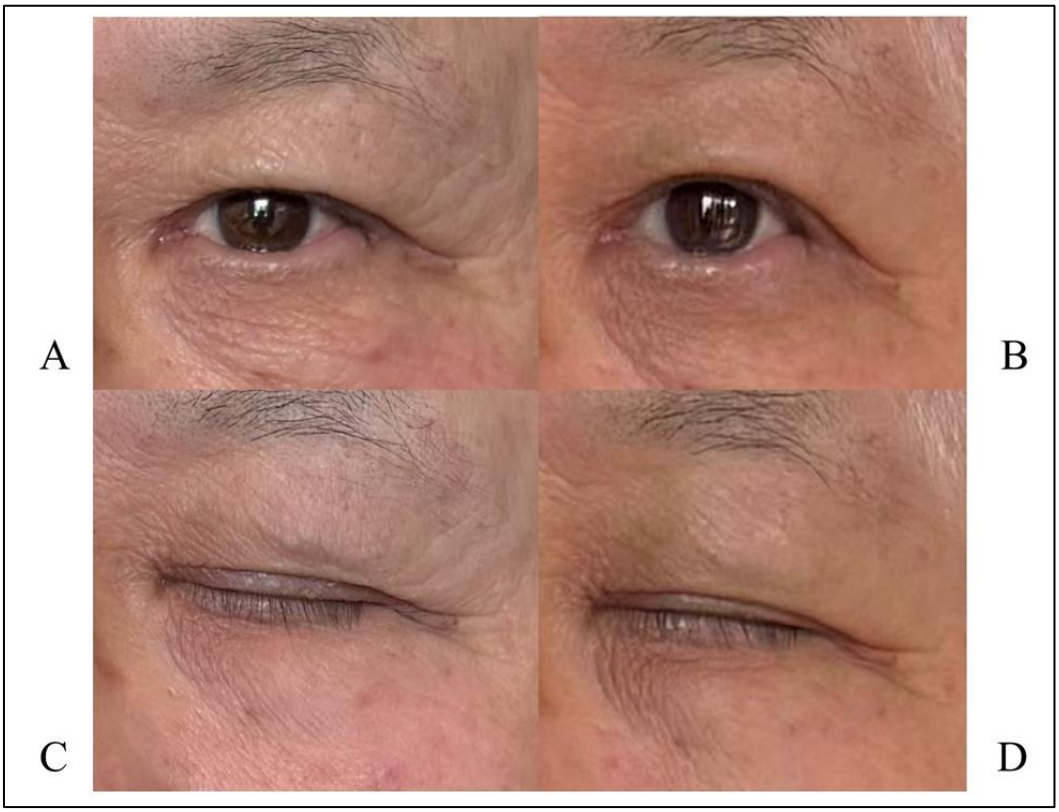

Figure 2: Available right periocular photographs of the 68-year-old male participant before product use and after seven applications: open-eye views before use (A) and after use (B), and closed-eye views before use (C) and after use (D). The photographs show differences in upper-eyelid fullness, lateral canthal wrinkles, and overall periocular appearance; they were not obtained under a validated standardized photographic protocol.

4 DISCUSSION

In this retrospective case series, topical periocular application of 10% high-concentration 35-kDa hyaluronic acid fragment for more than 2 hours or overnight, once daily for 7 consecutive days, was associated with improvements in ocular discomfort or fatigue, perceived visual brightness, palpebral fissure appearance, periocular tissue softness, ocular and palpebral conjunctival redness, swelling and congestion, lateral canthal wrinkles, and upper-eyelid thickness. Ocular discomfort and fatigue decreased markedly within 20 minutes after the first application and were rated 0 after seven applications, while perceived visual brightness and several periocular appearance-related outcomes also improved.

Of particular interest, ocular discomfort and fatigue were markedly relieved within only 20 minutes after the first application. Participants kept their eyes closed throughout product use, and the externally applied HA35 gel did not directly enter beneath the eyelid. We therefore hypothesize that such a rapid effect may not depend solely on tissue penetration but may involve rapidly responding transient receptor potential (TRP) channels. TRP channels participate in the rapid transmission of temperature, pain, itch, and other sensory signals.[5] Sensory-ion-channel research, including the discovery of TRPV1 and related sensory mechanisms, was recognized by the 2021 Nobel Prize in Physiology or Medicine.[5] Previous studies from our group also showed rapid relief of pain and pruritus with high-concentration HA35,[6,7] and electrophysiological work suggested modulation of TRPV1 and TRPA1 by HA35.[8] These

findings suggest that the rapid relief of ocular discomfort or fatigue observed here may involve TRPV1/TRPA1-related sensory pathways.

From the first day of overnight periocular application, two younger women who wore contact lenses daily reported marked reductions in contact-lens-associated dryness, redness, swelling, and itch. After seven applications, these symptoms had largely disappeared, suggesting that high-concentration HA35 may have potential value for discomfort associated with daily contact-lens use.

Perceived visual brightness also improved after seven applications. This subjective change may reflect improvement in the ocular surface and periocular tissue environment and may also have been influenced by pre-existing presbyopia, myopia, or refractive error. In addition, changes in ocular or periocular lymphatic drainage may have contributed to the observed improvement.[9]

Periocular tissue softness and palpebral fissure appearance improved after seven applications, consistent with the changes shown in the paired photographs. Ocular and palpebral conjunctival redness, swelling, and congestion also decreased markedly, which may indicate a local anti-inflammatory effect of topical high-concentration HA35. This effect may be related to TRPV1/TRPA1-associated signaling in local sensory and lymphatic tissues.[8,9]

Lateral canthal wrinkles decreased after seven applications, although baseline variability was relatively large because two younger women had few or no lateral canthal wrinkles. Upper-eyelid thickness also decreased markedly, with corresponding changes visible in the clinical photographs. This effect may be related to changes in periocular tissue swelling or subcutaneous tissue, consistent with previous case series reporting changes in facial subcutaneous fat following topical application or oral administration of high-concentration hyaluronic acid fragments.[3,10].

5 CONCLUSION

Topical periocular application of high-concentration 35-kDa hyaluronic acid fragment rapidly reduced ocular discomfort and fatigue and, after seven applications, improved perceived visual brightness, conjunctival redness and swelling, periocular tissue softness, palpebral fissure appearance, upper-eyelid thickness, and lateral canthal wrinkles. Two daily contact-lens users also reported relief of dryness, redness, swelling, and itch. These findings support the potential of HA35 as a topical preparation for periocular aesthetics and ocular comfort. However, larger prospective controlled studies with longer follow-up periods are warranted to further establish its efficacy, optimal application protocol, and long-term ocular and periocular safety.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

Disclosure of conflict of interest

Mizhou Hui is the applicant and inventor of patent application PCT/CN2026/097259 related to HA35. The authors are affiliated with Hynaut Laboratory, and the HA35 preparation described in this case series was manufactured by Huinuode Biotechnology Co., Ltd. The authors declare no other competing interests.

Statement of informed consent

Written informed consent for publication was obtained from all individuals included in this case series. The participant shown in Figures 1 and 2 also provided written consent for publication of the identifiable clinical photographs.

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