

## Original Research Article

# Effect of sodium hyaluronate eye drop on tear film stability and tear secretion in patients with rigid gas-permeable contact lens-associated xerophthalmia

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## Abstract

**Purpose:** To evaluate the impact of sodium hyaluronate eye drops on tear film stability and tear secretion in patients suffering from rigid gas-permeable contact lenses (RGPCL)-associated xerophthalmia.

**Methods:** 88 patients treated at Shangrao Aier Eye Hospital, China with RGPCL-associated xerophthalmia were enrolled in this study from May 2021 to May 2022. They were randomly and equally divided into two groups: a study group (treated with sodium hyaluronate eye drops) and a control group (treated with meibomian gland massage). Tear secretion parameters (lacrimal river width, Schirmer I test (S1t), tear fluid lysozyme content), tear film stability indicators (tear film break-up time, tear film thickness, corneal fluorescein staining score), ocular surface disease index (OSDI), therapeutic effect and incidence of adverse reactions were compared between the two groups.

**Results:** Following the treatment, study group exhibited significantly improved tear secretion compared to control group ( $p < 0.05$ ). Similarly, tear film stability indicators significantly improved in study group after treatment, accompanied by a reduction in corneal fluorescein staining score ( $p < 0.05$ ). Although both groups showed decreased OSDI scores after treatment, the reduction was more substantial in study group. Additionally, the therapeutic effect and incidence of adverse reactions were superior in study group compared to control group.

**Conclusion:** The use of sodium hyaluronate eye drops in the treatment of patients with RGPCL-associated xerophthalmia enhances tear secretion, and improves tear film stability and therapeutic outcomes, leading to a reduction in ocular surface disease index and the incidence of adverse reactions. However, this treatment strategy warrants a large-scale clinical trial prior to application in clinical practice.

**Keywords:** Sodium hyaluronate eye drop, Rigid gas-permeable contact lens, Xerophthalmia, Tear film stability

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## INTRODUCTION

With evolving learning methods, lifestyle changes and the widespread use of electronic devices, the prevalence of myopia in China is

steadily rising, and the onset age is decreasing. Consequently, there is a growing trend of younger individuals using corneal contact lenses (CL) [1]. CLs are essential medical devices used for correcting vision and refractive

errors and are employed globally by over 140 million people. Correspondingly, complications arising from CL usage are on the rise, including eye surface infections, conjunctivitis and dry eye syndrome [2]. Among these, dry eye syndrome is the most prevalent complication among CL wearers, leading to symptoms such as eye dryness, fatigue, burning and a sensation of foreign objects. These symptoms significantly impact the daily lives and work efficiency of affected individuals [2]. In clinical practice, dry eye is often managed with artificial tears or meibomian gland massage. Meibomian gland massage involves the discharging of blocked lipids from the meibomian gland after a hot compress and subsequent eye massage [3]. This method unclogs the meibomian gland ducts, enhances tear film stability and improves meibomian gland function. However, relying solely on this approach for an extended period is not always effective and is also time-consuming [4]. Sodium hyaluronate eye drops, a type of artificial tears mainly composed of components found in human tears, possess strong water-retaining properties [5]. These eye drops alleviate dryness and irritation symptoms, smoothen the corneal surface and enhance the stability of the tear film-cellular interface, thus improving visual function [6]. This study investigates the clinical efficacy of sodium hyaluronate eye drops in treating dry eye syndrome related to hard, breathable corneal contact lenses (RGPCL).

## METHODS

### General information

The study included 88 patients diagnosed with dry eye syndrome related to rigid gas-permeable corneal contact lenses (RGPCl), who were treated at Shangrao Aier Eye Hospital, China between May 2021 and May 2022. The patients were randomly divided into a study group and a control group, each comprising 44 cases. In the study group, there were 27 males and 17 females, aged between 14 and 26 years, with an average age of  $21.58 \pm 2.64$  years. The length of time the patients wore glasses ranged from 8 to 25 months, averaging  $16.59 \pm 3.42$  months, and the diopter ranged from -0.79 to -5.96 D, with an average of  $-3.47 \pm 1.46$  D. Control group consisted of 26 males and 18 females, aged 15 to 26 years, with an average age of  $21.58 \pm 2.64$  years. The length of time the patients wore glasses ranged from 8 to 25 months, averaging  $16.59 \pm 3.42$  months, and the diopter ranged from -0.79 to -5.96 D, with an average of  $-3.47 \pm 1.46$  D. The two groups had similar gender distribution, age, length of time the patients wore

glasses, and refractive index ( $p > 0.05$ ), indicating their comparability. The study was approved by the Shangrao Aier Eye Hospital Ethics Committee (approval no. 202105LL-001). All procedures were carried out in accordance with the declaration of Helsinki [7]. Participants were briefed about the study's purpose, methods, risks and benefits. They participated voluntarily and provided informed consent. The privacy and security of participants' personal information were protected and all research data was anonymized.

### Inclusion criteria

Participants were included if they met the diagnostic criteria for dry eye syndrome [8], were aged between 15 and 26 years and were of both genders. They also should not have received any treatment related to dry eye before their inclusion in the study. All patients willingly participated in the study and provided informed consent.

### Exclusion criteria

Patients with other eye conditions such as conjunctivitis and dacryocystitis, a history of eye surgery, eye injuries, mental or cognitive disorders, non-cooperation with treatment, and had major organ lesions, such as of heart and lungs, were excluded from the study.

### Treatment procedures

#### Control group

The procedure involved disinfecting a glass rod (Taizhou Kangzhida Experimental Equipment Co., Ltd., Taizhou, China, model: 88) and gently massaging the tarsal conjunctival surface of the patient. Simultaneously, gentle pressure was applied to the eyelid surface with a cotton swab, massaging the upper eyelid from top to bottom and the lower eyelid in the same manner. The massage was repeated with moderate pressure to avoid causing any harm to the eyelids. After the massage, any secretions were wiped away. This massage therapy was administered approximately three times a week, with each session lasting 5 - 10 mins. The treatment duration spanned 2 months.

#### Study group

Patients in study group were treated with 0.3 % sodium hyaluronate eye drops (Qilu Pharmaceutical Co., Ltd., National Drug Approval No. H20133263). These eye drops were instilled onto the surface of the

patient's eyes, with 1 – 2 drops administered per application and at a frequency of four times a day. This treatment regimen was sustained for 2 months.

### Evaluation of parameters/indices

#### Tear secretion

Comparison of tear width, Schirmer I test (Sl<sub>t</sub>) and tear lysozyme content before and after treatment in both groups was performed. Tear width was measured using the slit lamp examination method, recording the liquid level height of tears at the junction of the corneal surface light band and the lower eyelid edge light band. Sl<sub>t</sub> was determined by placing tear-detection filter paper on the patient's lower eyelid, closing the eyes for 5 min, and measuring the wetting length of the filter paper. Tear lysozyme content was assessed using the photoelectric turbidimetric method with a test kit from Shanghai Xige Biotechnology Co., Ltd.

#### Tear film stability

Comparisons of tear film break-up time (BUT), tear film thickness and corneal fluorescein staining score (FL) were made before and after treatment. Sodium fluorescein solution was instilled into the patient's eye and BUT was calculated as the time ratio from the last blink to the appearance of black spots after multiple eye rotations under narrow cobalt blue light. Corneal fluorescein staining was scored from 0 to 3 (0 = no staining, 1 = mild, 2 = moderate and 3 = severe).

#### Eye surface disease index

The OSDI scale, encompassing eye symptoms, visual function, and environmental stimuli, was utilized to assess the eye surface disease index before and after treatment. The scale ranged from 0 to 48 points, with higher scores indicating greater severity of eye surface disease.

#### Treatment effect

Treatment efficacy was evaluated based on established standards. Categories included recovery (complete disappearance of symptoms and normal levels of BUT and Sl<sub>t</sub>), significant improvement (significant symptom relief and increased BUT and Sl<sub>t</sub> levels), effective (symptom relief and increased BUT and Sl<sub>t</sub> levels with minimal secretion), and ineffective (no

change in symptoms, BUT and Sl<sub>t</sub> levels, with obvious secretions). The total effective rate was calculated.

### Incidence of adverse reactions

Occurrence of adverse reactions, such as eyelid inflammation, itching, congestion and irritation, was recorded and analyzed. The incidence rate was calculated.

### Statistical analysis

Statistical analysis was performed using SPSS 22.0 software. The  $\chi^2$  test, rank sum test for rank data, and t-test for measurement data (mean  $\pm$  standard deviation) were applied, with statistical significance set at  $p < 0.05$ .

## RESULTS

#### Tear secretion

In study group, tear river width significantly increased from  $0.13 \pm 0.03$  mm to  $0.32 \pm 0.09$  mm ( $p < 0.001$ ), Sl<sub>t</sub> improved from  $5.36 \pm 2.24$  mm/5 min to  $8.24 \pm 2.46$  mm/5 min ( $p < 0.001$ ), and tear lysozyme content rose from  $0.68 \pm 0.19$  g/L to  $1.38 \pm 0.41$  g/L ( $p < 0.001$ ) after treatment. Similarly, control group also exhibited significant improvements in tear river width (from  $0.14 \pm 0.04$  mm to  $0.26 \pm 0.07$  mm,  $p < 0.001$ ), Sl<sub>t</sub> (from  $5.39 \pm 2.26$  mm/5 min to  $7.18 \pm 2.34$  mm/5 min,  $p < 0.001$ ) and tear lysozyme content (from  $0.72 \pm 0.21$  g/L to  $1.05 \pm 0.32$  g/L,  $p < 0.001$ ) after the treatment.

Also, comparison between the two groups showed no significant difference in tear river width before and after treatment ( $p = 0.188$ ). However, study group exhibited a significantly higher improvement in Sl<sub>t</sub> compared to control group ( $p = 0.001$ ). Additionally, study group showed a more substantial increase in tear lysozyme content compared to control group ( $p < 0.001$ ) (Table 1 and Figure 1).

#### Tear film stability

In study group, tear film thickness increased significantly from  $18.53 \pm 2.64$  mm to  $26.33 \pm 3.39$  mm ( $p < 0.001$ ) and tear film break-up time (BUT) improved from  $4.72 \pm 1.08$  seconds to  $9.61 \pm 1.63$  seconds ( $p < 0.001$ ) after treatment. Corneal fluorescein staining score (FL) decreased significantly from  $2.06 \pm 0.23$  to  $0.84 \pm 0.16$  ( $p < 0.001$ ).

**Table 1:** Comparison of tear secretion between two groups of patients (n=44)

Group	Tear river width (mm)		Slt (mm/5 min)		Tear lysozyme content (g/L)	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Study	0.13±0.03	0.32±0.09*	5.36±2.24	8.24±2.46*	0.68±0.19	1.38±0.41*
Control	0.14±0.04	0.26±0.07*	5.39±2.26	7.18±2.34*	0.72±0.21	1.05±0.32*
T	1.327	3.491	0.063	2.071	0.937	4.209
P-value	0.188	0.001	0.950	0.041	0.351	<0.001

\*P < 0.05 vs. before treatment

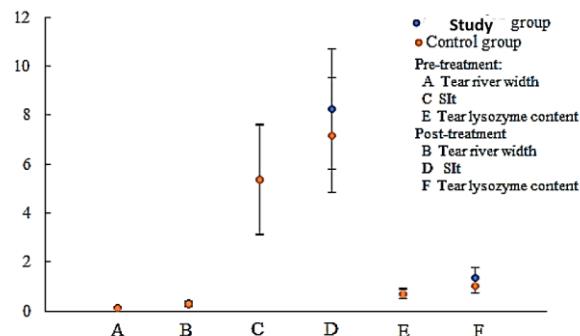
**Table 2:** Comparison of tear film stability between two groups of patients (n=44)

Group	Tear film thickness (mm)		BUT (s)		FL (score)	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Study	18.53±2.64	26.33±3.39*	4.72±1.08	9.61±1.63*	2.06±0.23	0.84±0.16*
Control	18.72±2.68	24.23±3.24*	4.65±1.06	8.83±1.48*	2.04±0.21	1.01±0.18*
T	0.335	2.971	0.307	2.350	0.426	4.682
P-value	0.738	0.004	0.760	0.021	0.671	<0.001

\*P < 0.05 vs. pre-treatment condition

**Table 3:** Comparison of eye surface disease index between two groups of patients

Group	Eye symptoms		Visual function		Environmental stimuli	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Study	16.97±1.58	7.63±1.67*	13.27±1.49	5.33±1.06*	10.03±1.09	4.17±0.92*
Control	17.05±1.61	8.97±1.82*	13.38±1.52	6.05±1.12*	9.97±1.07	4.82±0.98*
T value	0.235	3.598	0.343	3.097	0.261	3.208
P value	0.815	0.001	0.733	0.003	0.795	0.002

**Figure 1:** Comparison of the tear secretion between groups.

Similarly, in control group, tear film thickness increased significantly from  $18.72 \pm 2.68$  mm to  $24.23 \pm 3.24$  mm ( $p < 0.001$ ) and BUT improved from  $4.65 \pm 1.06$  seconds to  $8.83 \pm 1.48$  seconds ( $p < 0.001$ ) after treatment. Corneal fluorescein staining score decreased from  $2.04 \pm 0.21$  to  $1.01 \pm 0.18$  ( $p < 0.001$ ). When comparing the two groups, there were no significant differences in tear film thickness before and after treatment ( $p = 0.738$ ). However, study group demonstrated a significantly greater improvement in BUT compared to control group ( $p = 0.004$ ). Additionally, study group showed a more significant reduction in corneal fluorescein

staining score compared to control group ( $p < 0.001$ ), as shown in Table 2.

#### Ocular surface disease index (OSDI)

In study group, the Ocular Surface Disease Index (OSDI) scores significantly decreased from  $16.97 \pm 1.58$  to  $7.63 \pm 1.67$  for eye symptoms, from  $13.27 \pm 1.49$  to  $5.33 \pm 1.06$  for visual function and from  $10.03 \pm 1.09$  to  $4.17 \pm 0.92$  for environmental stimuli after treatment ( $p < 0.001$ ). Similarly, in control group, OSDI scores significantly decreased from  $17.05 \pm 1.61$  to  $8.97 \pm 1.82$  for eye symptoms, from  $13.38 \pm 1.52$  to  $6.05 \pm 1.12$  for visual function and from  $9.97 \pm 1.07$  to  $4.82 \pm 0.98$  for environmental stimuli after treatment ( $p < 0.001$ ). When comparing the two groups, there were no significant differences in OSDI scores for eye symptoms before and after treatment ( $p = 0.815$ ). However, study group showed a significantly greater improvement in OSDI scores for visual function ( $p = 0.001$ ) and environmental stimuli ( $p = 0.003$ ) compared to control group, as shown in Table 3.

#### Treatment effect

After treatment, the treatment effect of study group was better than that of control group ( $p < 0.05$ ), as shown in Table 4.

**Table 4:** Comparison of treatment effects between two groups of patients (n=44)

Group	Recovery	Apparent effect	Effective	Invalid	Total effective rate
Study group	26 (59.09)	10 (22.73)	7 (15.91)	1 (2.27)	43 (97.73)
Control group	18 (40.91)	9 (20.45)	10 (22.73)	7 (15.91)	37 (84.09)
Z/ $\chi^2$	2.200				4.950
P-value	0.028				0.026

**Table 5:** Comparison of adverse reaction rates between two groups of patients (n=44)

Group	Blepharitis	Pruritus	Congestion	Stimulation	Incidence rate
Study	0 (0.00)	1 (2.27)	0 (0.00)	1 (2.27)	2 (4.55)
Control	2 (4.55)	3 (6.82)	2 (4.55)	1 (2.27)	8 (18.18)
X <sup>2</sup>	4.062				
P-value	0.044				

### Incidence of adverse reactions

After treatment, the incidence of adverse reactions in study group was significantly lower than that in control group ( $p < 0.05$ ), as shown in Table 5.

## DISCUSSION

This study has shown that after treatment the tear width, Slt and tear lysozyme content in study group were significantly higher than those in control group, indicating the effectiveness of sodium hyaluronate eye drops in improving tear secretion among patients with rigid gas-permeable corneal lens (RGPCL)-associated dry eye [9]. These findings align with previous research results by Okumura *et al* [10] and Son *et al* [11]. The rationale for this improvement lies in the ability of sodium hyaluronate eye drops to bind to fibronectin in the patient's eyes, stimulating mucin synthesis and consequently increasing lysozyme content in tears.

This effect has an impact on its antibacterial, antiviral and anti-inflammatory properties. Sodium hyaluronate, being a polymer compound, contains numerous water molecules, rendering it highly hydrophilic. It accelerates the growth rate of corneal epithelial cells and acts as a lubricant on the patients' eyelids [12]. Moreover, tears naturally contain mucin, which, through glycosylation, carries charges and forms hydrogen bonds with water molecules, thus enhancing the water retention ability of the patient's corneal surface. This process results in improved corneal moisturization [13].

The results of this study revealed significant improvements in tear film stability among patients treated with sodium hyaluronate eye drops. Study group specifically showed higher tear film break-up time (BUT), tear film thickness

and lower corneal fluorescein staining score (FL) compared to control group. This finding supports similar conclusions drawn in Vergés's research [14]. The effectiveness of sodium hyaluronate eye drops could be attributed to their viscoelastic properties as polysaccharide biomaterials. These properties provide excellent moisturization, helping to maintain eye moisture by reducing water loss and prolonging BUT [5]. Moreover, sodium hyaluronate eye drops facilitate the growth of corneal epithelial cells and enhance tear film structure and function, leading to increased tear film thickness. The linear structure of sodium hyaluronate molecules creates a network barrier around corneal epithelial cells, protecting against inflammatory and stimulating factors, thereby reducing inflammation-induced damage and providing protective effects on corneal and ocular surface epithelial cells [15].

Patients in study group exhibited lower Ocular Surface Disease Index (OSDI) scores and superior treatment efficacy compared to control group, supporting findings from Wen's research [6]. Sodium hyaluronate eye drops share physical and chemical properties with human tears and possesses remarkable water retention capabilities. They rapidly enhance eye surface wetness, reduce tear osmotic pressure and create a favorable microenvironment for eye surface cells [16]. Moreover, these eye drops swiftly form an artificial protective film on the eye surface, repairing tear film trauma and maintaining a moist state. This process enhances tear film stability, leading to improved treatment outcomes and reduced OSDI scores [17,18].

Furthermore, the study demonstrated a lower incidence of adverse reactions in study group compared to control group. This reduction is attributed to the superior water retention performance of sodium hyaluronate eye drops,

which enhances eye wetness, promotes tear film recovery and provides a protective barrier against external irritants. Consequently, the occurrence of adverse reactions is minimized.

This study's findings highlight the efficacy of sodium hyaluronate eye drops in enhancing tear film stability, reducing OSDI scores, improving treatment outcomes and lowering the incidence of adverse reactions among patients with rigid gas-permeable corneal lens-associated dry eye. These results corroborate previous research and underscore the significant potential of sodium hyaluronate eye drops as a therapeutic intervention in managing dry eye syndrome effectively.

### **Limitations of this study**

A major limitation associated with this study is the small sample size coupled with the fact that it was carried out in only one clinical setting.

## **CONCLUSION**

The application of sodium hyaluronate eye drops in the treatment of patients with rigid gas-permeable corneal lens (RGPCL)-related dry eye not only improves tear secretion and tear film stability but also enhances treatment effectiveness. Moreover, it significantly reduces patients' ocular surface disease index and the incidence of adverse reactions. These findings indicate the therapeutic potential of sodium hyaluronate eye drops in managing RGPCL-related dry eye. However, further large-scale clinical trials are required prior to application in clinical practice.

## **DECLARATIONS**

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### **Funding/Sponsorship**

None provided.

### **Conflict of Interest**

No conflict of interest associated with this work.

### **Contribution of Authors**

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

### **Ethical Approval**

The study was approved by the Shangrao Aier Eye Hospital Ethics Committee (approval no. 202105LL-001).

### **Availability of Data and Materials**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### **Use of Artificial Intelligence/Large Language Models**

None provided.

### **Use of Research Reporting Tools**

None provided.

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