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ORIGINAL RESEARCH

Investigation into the Therapeutic Efficacy and Inflammatory Modulatory Effects of the Combined Use of 0.01% Atropine Eye Drops and Orthokeratology Lenses in the Management of Myopia Among Adolescent Patients

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Objective: To evaluate the therapeutic efficacy and inflammatory modulatory effects of combined 0.01% atropine eye drops and orthokeratology (OK) lenses in controlling myopia progression among adolescent patients.

Methods: This retrospective study analyzed clinical data from 90 adolescent patients (90 eyes) with myopia treated from April 2021 to June 2023. Patients were divided into two groups: control group (n=45, treated with OK lenses alone) and observation group (n=45, treated with OK lenses combined with 0.01% atropine). Baseline and 1-year post-treatment measurements included refractive status, axial length (AL), corneal parameters, ocular surface indices, tear film stability, endothelial cell morphology, inflammatory cytokine levels in tears, and incidence of adverse events.

Results: After 1 year, both groups showed myopic progression, but the observation group exhibited significantly less axial elongation (0.12 ± 0.08 mm vs 0.21 ± 0.09 mm; $p < 0.001$) and smaller increases in refractive error ($p < 0.001$). Corneal curvature and central corneal thickness were also significantly lower in the observation group ($p < 0.05$). The pupil diameter increased more in the observation group ($p = 0.002$), consistent with atropine's pharmacologic effect. Ocular surface damage was less severe, with lower OSDI ($p = 0.002$) and staining scores ($p < 0.001$). Tear film stability was better preserved, as reflected by higher NIBUT and TBUT values ($p < 0.05$). No significant differences in endothelial cell density or hexagonality were observed ($p > 0.6$). Tear cytokine levels (IL-1β, IL-6, TNF-α) increased in both groups but were significantly lower in the observation group (all $p < 0.01$). The incidence of adverse reactions was low and comparable between groups ($p = 0.235$), with no severe events reported.

Conclusion: The combination of 0.01% atropine eye drops with orthokeratology lenses is more effective than orthokeratology alone in controlling myopia progression and mitigating ocular surface inflammation in adolescents, without increasing adverse effects.

Keywords: adolescents, myopia, orthokeratology lenses, 0.01% atropine eye drops, inflammatory response, effect

Introduction

Myopia is the most common refractive error among adolescents. With changing modern lifestyles and increased academic burdens, the incidence of myopia has risen dramatically, reaching epidemic proportions globally. The World Health Organization (WHO) estimates that half the world's population may be myopic by 2050, with high myopia affecting nearly 10%, highlighting a significant public health burden.[1,2] According to relevant epidemiological data, the prevalence of myopia in adolescents has reached over 70% in many regions, making it a major global public health challenge.[2,3] The rapid progression of myopia not only affects visual quality but may also lead to severe ocular complications, such as retinal detachment, cataracts, glaucoma, and even blindness.[3,4] Emerging evidence suggests

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that inflammatory pathways may play a role in scleral remodeling and axial elongation, a key pathological feature of myopia progression.[5] Therefore, controlling myopia progression in adolescents, particularly preventing axial length elongation, remains a critical focus in refractive correction research.

Orthokeratology (Ortho-K) lenses represent a non-surgical refractive correction method. They utilize customized rigid gas-permeable contact lenses worn overnight to temporarily reshape the cornea, enabling clear daytime vision without glasses or contact lenses.[4,6] Ortho-K lenses are effective in slowing adolescent myopia progression, particularly by controlling axial length growth, and offer higher compliance and safety compared to traditional spectacles and soft contact lenses.[5,7,8] Consequently, they have become a mainstay treatment option. However, long-term Ortho-K lens wear can be associated with side effects such as discomfort, dry eye symptoms, and corneal staining in some patients.[7,9] The integrity and stability of the tear film and ocular surface are crucial factors influencing the safety, comfort, and efficacy of Ortho-K lens wear; disruptions can contribute to inflammation, discomfort, and potential complications.[10,11] To optimize treatment outcomes and mitigate adverse effects, researchers have explored combining Ortho-K with pharmacological agents.

Atropine, a non-selective muscarinic antagonist widely used in ophthalmology, inhibits ciliary muscle contraction and modulates intraocular pressure.[8,12] Low-concentration atropine eye drops (0.01%) are recognized as an effective and safe treatment for controlling myopia progression. Previous studies[9,13,14] have demonstrated that 0.01% atropine effectively slows axial length elongation and refractive error worsening. Beyond its antimuscarinic effects, atropine exhibits anti-inflammatory properties. It is known to suppress the release of inflammatory cytokines (eg, IL-6, TNF-α) and matrix metalloproteinases (MMPs) in ocular tissues, potentially mitigating inflammation associated with contact lens wear and myopia progression itself.[15,16] Therefore, investigating the combined application of Ortho-K lenses and 0.01% atropine presents a promising strategy. However, there is a paucity of clinical trials specifically evaluating the combined effect of these two modalities on ocular inflammatory markers and tear film stability in adolescents.[17] This study retrospectively analyzed the clinical data of 90 adolescent myopia patients to explore the therapeutic efficacy and inflammatory modulatory effects, particularly its impact on tear film and ocular surface factors, of combining 0.01% atropine eye drops with Ortho-K lenses, aiming to provide more optimized and comprehensive strategies for clinical myopia control.

Subjects and Methods

Study Subjects

A retrospective analysis was conducted on the clinical data of 90 adolescent myopic patients (90 eyes, all using left eye data) who were treated at our hospital from April 2021 to June 2023. Inclusion criteria: Age 8–18 years, no gender restriction, initial treatment; diagnosed according to clinical standards for adolescent myopia;[11] spherical refractive error between −1.0 and −6.0 D, with regular astigmatism < −1.50 D; best corrected visual acuity >1.0; normal fundus and anterior segment, intraocular pressure between 10–21 mmHg; central corneal thickness >0.45 mm, corneal curvature between 39.00–46.00 D; patients and their families provided informed consent and signed the relevant informed consent forms. Exclusion criteria: Patients not meeting the age requirement; patients with strabismus, amblyopia, keratitis, dry eye disease (defined as OSDI score >12, TBUT < 5 seconds, or Schirmer I test <5 mm/5 min), or other significant eye diseases; patients with allergic reactions or contraindications to the operations or medications used in this study; patients with a history of eye surgery; patients with psychiatric disorders and/or autoimmune diseases. Based on the treatment method, patients were divided into a control group (n=45, wearing corneal reshaping lenses) and an observation group (n=45, wearing corneal reshaping lenses combined with 0.01% atropine eye drops). As this was a retrospective study, randomization was not performed; group allocation was determined solely by the treatment regimen chosen and adhered to by the patient and their guardian after detailed counseling by the attending ophthalmologist. Consequently, masking (blinding) of participants and clinicians to the treatment group was not feasible. To account for potential confounding factors known to influence myopia progression,[14] available clinical records were reviewed for documentation of parental myopia history and average daily near work/screen time (>4 hours per day vs ≤4 hours).[15,16] Data on daily outdoor time, however, were inconsistently recorded in the clinical notes and thus not included in the analysis. The use of data from only the left eye per patient was implemented to ensure statistical independence of observations and avoid the correlation inherent in bilateral data from the same individual, a common methodological approach in ophthalmic studies.[17,18] This study was approved by the Changzhi People's Hospital Medical Ethics Committee (JSJZ24017), and the study strictly adhered to the ethical guidelines of

the Declaration of Helsinki. Written informed consent was obtained from the legal guardians of all underage participants, authorizing their participation and the use of their clinical data for research purposes.

Methods

All patients underwent routine ophthalmic examinations and cycloplegic refraction. Based on these evaluations, the control group was treated with corneal reshaping lenses. The lenses used were Japanese Alpha corneal reshaping lenses (registration number: Guo Zhu Jin 20163221583). Trial lenses were selected according to the corneal topography's flat K-value and E-value. After tear stabilization, dynamic and static judgments were made under a slit lamp, adjusting the trial lenses based on lens position, fluorescein staining, and mobility, until the patient was satisfied and comfortable The prescription was collected from the trial lenses, and patients were instructed to wear the lenses for 8 hours at night, removing them in the morning, and to continue wearing them for 1 year, with monthly follow-up visits. In the observation group, 0.01% atropine eye drops were applied in combination with corneal reshaping lenses. The corneal reshaping lens usage followed the same protocol as the control group. Patients were instructed to use 0.01% low-concentration atropine eye drops 30 minutes before wearing the lenses each night. The eye drops were prepared by the hospital pharmacy department by mixing atropine sulfate injection (Tianjin Jinyao Pharmaceutical Co., Ltd., National Drug Approval No. H12020383) and sodium hyaluronate eye drops (Zhuhai Yisheng Biopharmaceutical Co., Ltd., National Drug Approval No. H20183333) in a specified ratio (1:100 dilution to achieve 0.01% atropine concentration). The compounded formulation was prepared under aseptic conditions in batches sufficient for 1 month per patient, stored at 4°C in opaque bottles, and dispensed with clear instructions to patients regarding cold storage and a 28-day discard policy after opening, in accordance with standards for extemporaneous ophthalmic preparations.[19] One drop was applied each time, with a frequency of once daily. After instillation, the lacrimal sac was gently pressed for 10 minutes to facilitate drug absorption and reduce systemic side effects. Follow-up in the observation group was consistent with the control group.

Observation Indicators

Refractive Effect Indicators

Refraction, corneal curvature, axial length (AL), central corneal thickness (CCT), and pupil diameter (PD) were measured before treatment and after 1 year of treatment. Refractive error: Measured using a retinoscope after cycloplegia, with results expressed as equivalent spherical power. Corneal curvature: Measured using a CSO corneal topography device. AL: Measured with an anterior segment optical biometer. CCT: Measured with an anterior segment optical biometer. PD: Measured using a CSO corneal topography device.

Ocular Surface Indicators

The ocular surface disease index (OSDI)[12] was used to evaluate the severity of ocular surface disease before treatment and after 1 year. The scale includes three dimensions: "ocular symptoms", "visual function", and "environmental triggers", with 12 items in total. Each item is scored from 0 to 4, with a total score range of 0–48. Higher scores correlate with greater severity of ocular surface disease. After 1 year, the ocular surface staining score[13] was also assessed, with grading based on the severity of conjunctival (using the Oxford Scheme) and corneal (using the NEI/Industry Workshop scale) staining, ranging from 0 to 5 points per region, with higher scores indicating more severe staining.

Tear Film Indicators

Non-invasive tear film breakup time (NIBUT) and tear breakup time (TBUT) were measured before treatment and after 1 year. NIBUT: Measured with a comprehensive ocular surface analyzer. TBUT: Measured by fluorescein staining paper. The patient was instructed to blink three times and then gaze straight ahead, after which slit-lamp cobalt blue light was used to observe the tear film and record the first tear film breakup time. The test was repeated three times, and the average value was taken.

Corneal Endothelial Cell Indicators

Corneal endothelial cell density (CD) and hexagonal cell percentage (HEX) were measured before treatment and after 1 year using a specular microscope (Konan Noncon ROBO, Japan), with the values measured three times and averaged.

Inflammatory Factor Indicators

Tear samples (20 μL) were collected before treatment and after 1 year from the lateral canthus using calibrated glass microcapillary tubes without topical anesthesia, avoiding reflex tearing. Samples were immediately frozen at −80°C. Enzyme-linked immunosorbent assay (ELISA) kits (R&D Systems, Minneapolis, MN, USA) were used according to the manufacturer's instructions to detect interleukin-1β (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α) levels. All samples were analyzed in duplicate, and the mean value was used.

Adverse Reaction Incidence

Adverse reactions, including allergic reactions (eg, conjunctival hyperemia, itching, eyelid swelling), photophobia, diagnosed conjunctivitis or keratitis (by slit-lamp examination), persistent foreign body sensation (>1 week), and significant pupil dilation (>6mm in photopic conditions), were recorded prospectively by the medical staff at our hospital during each monthly follow-up visit and documented in the patient record. The severity of adverse events was graded as mild (transient, no intervention), moderate (required intervention or temporary discontinuation), or severe (discontinued treatment, required medical therapy).[20]

Statistical Analysis

GraphPad Prism 8 software was used for charting; SPSS 23.0 software was used for data processing. For count data, the results are expressed as percentages (%) and analyzed using the chi-square test or Fisher's exact test, as appropriate. For measurement data, results are expressed as mean ± standard deviation (mean ± SD). Normality of data distribution was assessed using the Shapiro–Wilk test. Homogeneity of variance was assessed using Levene's test. Independent sample *t*-tests were used for normally distributed comparisons between two groups, and the Mann–Whitney *U*-test was used for non-normally distributed data. Paired *t*-tests or Wilcoxon signed-rank tests were used for comparisons within the same group before and after treatment, depending on data distribution. A formal power calculation was not performed a priori for this retrospective study. However, the sample size (n=45 per group) is comparable to or larger than those used in similar published studies investigating combination myopia control therapies.[21,22] A P value <0.05 was considered statistically significant.

Results

Comparison of Clinical Data

There were no significant differences between the control group and the observation group in terms of gender, age, equivalent spherical degree, intraocular pressure, parental myopia history, or high near work/screen time ($P > 0.05$), indicating comparability. See Table 1.

Comparison of Correction Effect Indicators

After one year of treatment, the refractive degree, AL, and PD of both groups increased compared to before treatment, while corneal curvature and CCT decreased. The refractive degree, corneal curvature, AL, and CCT of the observation group were significantly lower than those of the control group after one year of treatment, and the PD of the observation group was higher ($P < 0.05$). The mean axial length (AL) increase in the observation group (0.12 ± 0.08 mm) was 42.9% lower than in the control group (0.21 ± 0.09 mm) ($P<0.001$), a difference considered clinically significant for myopia control based on established thresholds.[23] The observed pupil dilation (PD) in the observation group (+0.55 ± 0.23 mm) aligns with known antimuscarinic effects of atropine,[24] though remained within physiological ranges. See Table 2.

Table 1 Comparison of Clinical Data ($\bar{x} \pm s$, n[%])

	Control (n=45)	Observation (n=45)	t/x^2	*P*
Gender	–	–	0.400	0.526
Male	25 (54.55)	22 (47.73)	–	–
Female	20 (45.45)	23 (52.27)	–	–
Age (years)	13.57±2.46	13.39±2.58	0.338	0.735
Equivalent Spherical Degree (D)	−1.65±0.72	−1.61±0.74	0.259	0.795
Intraocular Pressure (mmHg)	15.86±3.13	16.01±2.97	0.233	0.816
Parental Myopia History, n (%)	31 (68.9%)	33 (73.3%)	0.214	0.643
High Near Work/Screen Time, n (%)	29 (64.4%)	27 (60.0%)	0.185	0.668

Table 2 Comparison of Correction Effect Indicators ($\bar{x} \pm s$)

	Control (n=45)	Observation (n=45)	*t*	*P*	95% CI for Difference
Refractive Degree (D)	–	–	–	–	
Before treatment	−2.17±0.12	−2.18±0.14	0.363	0.716	−0.06 to 0.04
1 year after treatment	−2.58±0.20[a]	−2.41±0.16[a]	4.452	<0.001	0.09 to 0.25
Corneal Curvature (D)	–	–	–	–	
Before treatment	42.37±1.15	42.32±1.21	0.200	0.841	−0.63 to 0.77
1 year after treatment	40.11±1.63[a]	38.87±1.19[a]	4.121	<0.001	0.67 to 1.81
AL (mm)	–	–	–	–	
Before treatment	25.35±0.27	25.31±0.33	0.629	0.530	−0.09 to 0.17
1 year after treatment	25.56±0.18[a]	25.43±0.22[a]	3.067	0.002	0.05 to 0.21
CCT (μm)	–	–	–	–	
Before treatment	568±43	565±45	0.323	0.747	−16.0 to 22.0
1 year after treatment	545±42[a]	528±34[a]	2.110	0.037	1.1 to 32.9
PD (mm)	–	–	–	–	
Before treatment	5.86±0.44	5.84±0.42	0.220	0.825	−0.19 to 0.23
1 year after treatment	6.13±0.38[a]	6.39±0.40[a]	3.161	0.002	−0.42 to −0.10

Note: [a]Indicates P < 0.05 compared to pre-treatment within the same group.

Comparison of Ocular Surface Indicators

After one year of treatment, both groups exhibited increased Ocular Surface Disease Index (OSDI) scores compared to baseline. However, the observation group showed significantly lower post-treatment scores than the control group (Control: 18.2 ± 4.3 vs Observation: 15.6 ± 3.8; P = 0.002), with a mean difference of 2.6 points (95% CI: 1.1–4.1). Additionally, corneal staining scores were significantly lower in the observation group (1.8 ± 0.7) compared to the control group (2.6 ± 0.9; P < 0.001), indicating improved ocular surface integrity in patients receiving combination therapy. See Figure 1A and B.

Comparison of Tear Film Indicators

Following treatment, both Non-Invasive Break-Up Time (NIBUT) and traditional Tear Break-Up Time (TBUT) decreased in the two groups. However, the decline was significantly less in the observation group, indicating better tear film stability. The observation group demonstrated longer NIBUT values (10.6 s; 95% CI: 9.7–11.5) compared to the control group (9.7 s; 95% CI: 8.9–10.5; P = 0.016). Similarly, TBUT was higher in the observation group (10.0 s; 95% CI: 9.2–10.8) than in the control group (9.3 s; 95% CI: 8.6–10.0; P = 0.038). The between-group differences (approximately 0.9–1.3 seconds) suggest clinically meaningful preservation of tear film function. See Figure 2A and B.

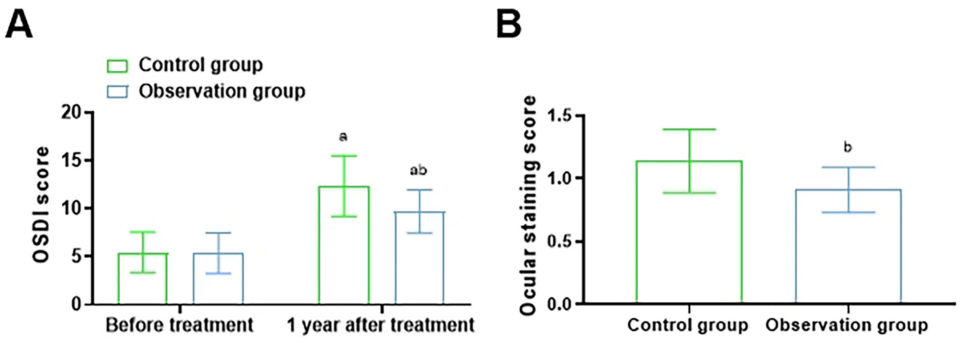

Figure 1 Comparison of Ocular Surface Indicators ($\bar{x} \pm s$, Score).
Notes: (**A**) OSDI Score; (**B**) Ocular Surface Staining Score. a indicates P < 0.05 compared to pre-treatment within the same group; b indicates P < 0.05 compared to the control group at the same time point.

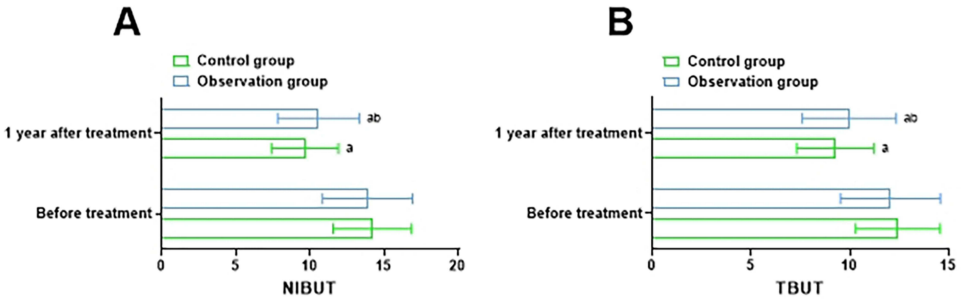

Figure 2 Comparison of Tear Film Indicators ($\bar{x} \pm s$, s).
Notes: (**A**) NIBUT; (**B**) TBUT. a indicates P < 0.05 compared to pre-treatment within the same group; b indicates P < 0.05 compared to the control group at the same time point.

Comparison of Corneal Endothelial Cell Indicators

There were no statistically significant differences between groups in changes to corneal endothelial cell density (CD) or hexagonality percentage (HEX) after treatment. CD decreased slightly in both groups (Control: −10.7 cells/mm²; 95% CI: −45.2 to 23.8 vs Observation: −11.0 cells/mm²; 95% CI: −49.1 to 27.1; P = 0.982). Similarly, HEX showed minor reductions (Control: −0.58%; 95% CI: −2.1 to 0.9 vs Observation: −0.93%; 95% CI: −2.4 to 0.5; P = 0.674). These changes were minimal and fell within the range of normal physiological variation, indicating no clinically significant endothelial cell loss. See Figure 3.

Comparison of Inflammatory Factor Indicators

Analysis of tear fluid inflammatory markers revealed that although both groups showed post-treatment increases in pro-inflammatory cytokines, the observation group exhibited significantly smaller elevations. The mean increases in IL-1β, IL-6,

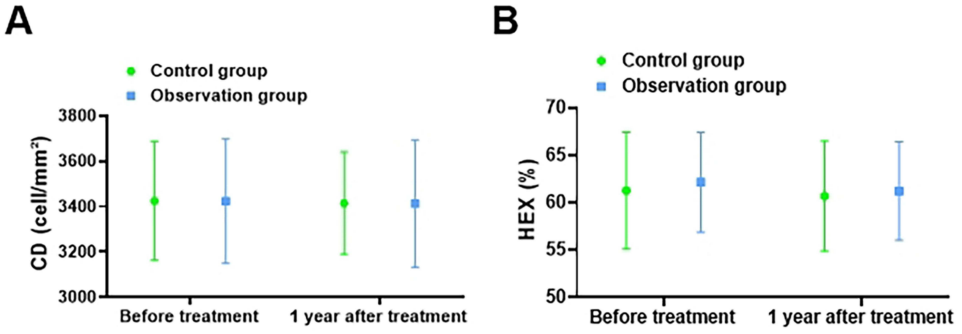

Figure 3 Comparison of Corneal Endothelial Cell Indicators ($\bar{x} \pm s$).
Notes: (**A**) CD; (**B**) HEX.

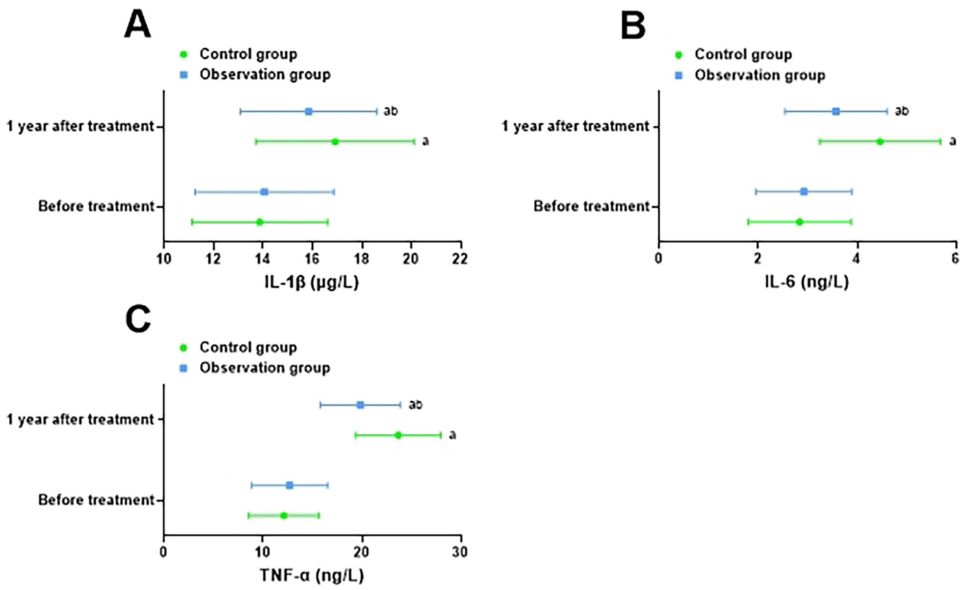

Figure 4 Comparison of Inflammatory Factor Indicators ($\bar{x} \pm s$).
Notes: (**A**) IL-1β; (**B**) IL-6; (**C**) TNF-α. a indicates P < 0.05 compared to pre-treatment within the same group; b indicates P < 0.05 compared to the control group at the same time point.

and TNF-α were lower in the observation group compared to the control group (IL-1β: +1.79 pg/mL vs +3.05 pg/mL, P < 0.001; IL-6: +0.65 pg/mL vs +1.63 pg/mL, P = 0.003; TNF-α: +7.16 pg/mL vs +11.58 pg/mL, P < 0.001). These findings suggest that the combination therapy may provide better control of subclinical ocular surface inflammation. See Figure 4.

Comparison of Adverse Reaction Incidence

The overall incidence of adverse reactions did not differ significantly between groups (P=0.235). Most events were mild (80.0% control, 85.7% observation). One case of moderate keratitis in the observation group resolved with temporary discontinuation. Severe adverse reactions requiring treatment discontinuation did not occur. See Table 3.

Table 3 Comparison of Adverse Reactions (n[%])

Adverse Reaction	Control Group (n=45)		Observation Group (n=45)		P-Value
	n	%	n	%	
Allergic Reaction					
Mild	0	0	1	2.2	1
Photophobia					
Mild	3	6.7	4	8.9	0.5
Conjunctivitis					
Mild	1	2.2	1	2.2	1
Keratitis					
Moderate	0	0	1	2.2	1
Foreign Body Sensation					
Mild	1	2.2	0	0	1
TOTAL	5	11.1	7	15.6	0.235
By Severity:					
Mild	4/5 (80.0%)		6/7 (85.7%)		1
Moderate	1/5 (20.0%)		1/7 (14.3%)		1
Severe	0	0	0	0	–

Notes: Fisher's Exact Test used for comparisons; Total incidence comparison by χ^2-test.

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Discussion

Orthokeratology lenses are rigid contact lenses specifically designed for myopic patients. Their unique nighttime wear method temporarily alters the shape of the cornea by flattening its curvature, which helps to reduce myopia.[24] This process not only effectively slows down the axial length growth but also improves vision, allowing patients to go without glasses or contact lenses during the day.[25] Clinical studies[26] have shown that for juvenile myopic patients with refractive errors between −1.00 and −6.00 D, orthokeratology lenses can significantly reduce the rate of axial length growth and have a stabilizing effect on peripheral refractive shift, which helps prevent further myopic progression. On the other hand, atropine eye drops help slow myopia progression by affecting the retina and scleral axial elongation. The mechanism of action involves the blockade of muscarinic receptors and stimulation of α2-adrenergic receptors, intervening in the process of axial elongation.[27] Previous clinical studies[28,29] have shown that 0.01% atropine is an effective myopia control drug with almost no side effects, and it can reduce approximately 70% of myopia progression. However, despite the effectiveness of 0.01% atropine eye drops in controlling myopia progression, using this medication alone cannot fully prevent the onset of myopia and needs to be combined with other vision correction methods. Recent studies[30,31] suggest that the combined use of low-concentration atropine with orthokeratology lenses provides better myopia control than either treatment alone. The results of this study are consistent with previous findings, further confirming that this combination therapy achieves more positive clinical effects in several aspects when compared to monotherapy.

The progression of myopia is often accompanied by an increase in AL, and an increase in PD is believed to slow down AL growth.[32] Studies[33] have shown that orthokeratology lenses are significantly more effective than traditional single-vision lenses in controlling AL growth. In this study, after one year of treatment, the increase in axial length in the observation group was significantly lower than that in the control group, while the increase in PD was significantly higher than that in the control group ($P<0.05$). This phenomenon can be explained by the mechanism of action of orthokeratology lenses. Orthokeratology lenses apply continuous mechanical pressure on the cornea, flattening its central curvature, which reduces myopia and delays axial elongation. The change in peripheral refractive power, especially the increase in PD, may be related to the structural adjustments in the cornea and the peripheral refractive changes caused by the orthokeratology lenses, which help slow further axial elongation. Additionally, the combined use of low-concentration 0.01% atropine eye drops may also play an important role in controlling axial elongation. Although the mechanism of 0.01% atropine is not yet fully understood, studies[34] suggest that it may help slow axial growth by improving the morphology of the sclera, promoting increased scleral thickness, and enhancing the thickness of the nerve fiber layer.

The treatment effectiveness of myopia in adolescents largely depends on patient compliance, which is closely related to ocular comfort. In this study, the OSDI score after one year of treatment was higher than before treatment in both groups, indicating that wearing orthokeratology lenses increased ocular discomfort. However, the OSDI score of the observation group after treatment was significantly lower than that of the control group, suggesting that the combined treatment of orthokeratology lenses and 0.01% atropine eye drops alleviated ocular discomfort. This improvement may be closely related to the components and mechanism of action of 0.01% atropine eye drops. Not only does 0.01% atropine help control myopia progression, but its formulation also contains polyethylene glycol, which is widely used in ophthalmic medications to relieve burning, stinging, and dryness, thereby increasing comfort for glasses or contact lens wearers.[35] Experimental studies confirm that PEG-based lubricants enhance corneal epithelial barrier function by upregulating tight junction proteins (ZO-1, occludin) and reducing desquamation.[36] Furthermore, the observation group showed significantly lower ocular surface staining scores compared to the control group, further supporting the advantage of combined therapy in reducing ocular discomfort. Ocular surface staining scores typically reflect the health status of the cornea and conjunctiva, and lower staining scores indicate less ocular surface damage.[37] The reduction in ocular surface staining scores in the observation group may be due to the alleviation of mechanical stimulation caused by orthokeratology lenses through 0.01% atropine eye drops.

Tear film stability is an important factor affecting ocular health, and NIBUT (Non-invasive Breakup Time) and TBUT (Tear Breakup Time) are commonly used indicators for evaluating tear film stability. In this study, both NIBUT and TBUT were significantly lower after treatment in both groups, suggesting that tear film stability had changed during the treatment. Possible reasons for this include: (1) direct contact of orthokeratology lenses with the cornea reduces the

oxygen supply to the corneal surface during blinking, which affects the distribution and flow of tear fluid, leading to decreased tear film stability;[38] (2) the wearing of orthokeratology lenses may directly impact the tear film structure, especially the thickness of the lipid layer, thereby worsening tear film function; (3) orthokeratology lenses may inhibit corneal sensory nerves, resulting in reduced blink activity, which negatively impacts tear film stability.[39] However, the observation group showed significantly longer NIBUT and TBUT than the control group, indicating that the combined treatment had certain advantages in improving tear film stability. This improvement may be due to: (1) 0.01% atropine, through its effect on neurotransmitter release, helping maintain the structural integrity of corneal epithelial cells; (2) 0.01% atropine eye drops also contain polyethylene glycol, which includes hydroxypropyl guar gum. After binding with inorganic salt ions, this forms high molecular weight gel compounds that can create a long-lasting lubricating film on the ocular surface, maintaining ocular moisture; (3) polyethylene glycol eye drops also promote the proliferation of goblet cells on the ocular surface,[40] as demonstrated in murine dry eye models where PEG increased MUC5AC expression by 40% compared to controls.[41]

The use of orthokeratology lenses, especially during the night, has garnered significant attention due to its impact on the cornea. Since these lenses directly contact the cornea and apply constant mechanical pressure while being worn during sleep, this unique usage pattern could potentially affect the corneal structure and function. Of particular concern is the health and function of the corneal endothelial cells. However, there is no unified conclusion in current research regarding whether orthokeratology lenses have adverse effects on endothelial cells after long-term or short-term use. This study observed that, in patients treated with orthokeratology lenses combined with 0.01% atropine eye drops for one year, both CD and HEX values decreased post-treatment. However, the inter-group comparison before and after treatment showed no significant changes, and no treatment-related abnormalities were observed. These results suggest that wearing orthokeratology lenses in combination with low-concentration atropine eye drops has a negligible impact on corneal endothelial cell function.

Regarding inflammatory responses, this study found that the levels of inflammatory factors such as IL-1β, IL-6, and TNF-α were significantly higher in both groups after one year of treatment compared to pre-treatment levels. This phenomenon may be related to the mechanical pressure effect caused by wearing orthokeratology lenses. The lens's compression might increase the osmotic pressure of the tear fluid, thus activating ocular immune responses and triggering a series of inflammatory reactions.[42] Clinically, this mild elevation in inflammatory markers—though statistically significant—remains within sub-clinical ranges and has not been associated with symptomatic ocular surface disease in our cohort. Similar transient cytokine increases have been reported in OK lens wearers without clinical sequelae, suggesting an adaptive response rather than pathological inflammation.[43] Importantly, no patients developed sight-threatening complications (eg, microbial keratitis) during the study period, supporting the safety profile of combined therapy despite biomarker fluctuations. Additionally, long-term use of orthokeratology lenses may lead to structural changes in the cornea, further affecting the stability of the ocular surface and promoting an increase in inflammatory factor levels. However, the observation group had significantly lower IL-1β, IL-6, and TNF-α levels after one year of treatment compared to the control group. This difference may be attributed to the effect of low-concentration atropine eye drops. The 0.01% atropine eye drops contain polyethylene glycol, which can effectively repair cell membranes and help restore the normal physiological functions of damaged cells. Polyethylene glycol also has certain antioxidant properties, which can alleviate oxidative stress in the eye and inhibit inflammation caused by orthokeratology lenses. Furthermore, 0.01% atropine eye drops may reduce the release of local inflammatory factors by inhibiting the activation of phagocytic cells. Therefore, the combined use of 0.01% atropine eye drops may mitigate the inflammatory response caused by wearing orthokeratology lenses. In terms of safety, there were no statistically significant differences in the adverse reaction rates between the two groups during treatment ($P > 0.05$), suggesting that the combination of orthokeratology lenses and 0.01% atropine eye drops is safe. This result aligns with previous related studies and provides strong support for the clinical application of this combined treatment method in adolescent myopia control.

Limitations

Despite offering valuable clinical data, this study has several limitations. First, it is a retrospective analysis without a randomized controlled trial (RCT) design, which introduces the possibility of selection bias and confounding factors. Although strict inclusion criteria were applied to reduce interference, future studies should validate the effectiveness and safety of combination therapy through prospective, randomized trials. Second, the sample size was relatively small, involving only 90 adolescent

patients from a narrow age range, which may limit the generalizability of the findings. Expanding the study population to include different age groups and degrees of myopia would enhance the external validity. Third, the measurement of inflammatory biomarkers was limited by tear sample volume constraints (≤5 μL per collection), which prevented multiplex cytokine profiling and duplicate assays. Additionally, variability in tear collection methods (eg, capillary tubes vs Schirmer strips) and differences in assay sensitivity may influence cytokine quantification. Future studies should adopt standardized sampling protocols and include spike-and-recovery validation to improve data accuracy. Furthermore, this study mainly focused on clinical and biological endpoints such as refractive error, ocular surface changes, and inflammation, without assessing long-term outcomes like treatment adherence, patient-reported symptoms, or quality of life. Including such measures in future research would provide a more comprehensive understanding of treatment impact. Lastly, while low-concentration atropine is generally considered safe, the long-term effects on ocular tissues remain unclear. Future studies should investigate prolonged use, dose-dependence, and potential cumulative toxicity of atropine over extended follow-up periods.

Conclusion

The combined treatment of 0.01% atropine eye drops and orthokeratology lenses effectively improves myopia correction outcomes, enhances ocular surface health and tear film stability, and reduces inflammatory responses, without increasing the risk of adverse reactions. This approach offers a safe and efficacious strategy for the comprehensive management of adolescent myopia and holds meaningful clinical application value. Future studies should continue to evaluate its long-term effects through larger, prospective investigations.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Public Health Ophthalmology Branch of Chinese Preventive Medicine Association. 儿童青少年近视防控公共卫生策略分期专家共识 [Expert consensus on stages of public health strategies for myopia prevention and control in children and adolescents]. *Zhonghua Yu Fang Yi Xue Za Zhi*. 2023;57(6):806–814. Chinese. doi:10.3760/cma.j.cn112150-20221002-00955
2. Singh H, Singh H, Latief U, et al. Myopia, its prevalence, current therapeutic strategy and recent developments: a review. *Indian J Ophthalmol*. 2022;70(8):2788–2799. doi:10.4103/ijo.IJO_2415_21
3. He XG, Zhang X, Xu X. [Orderly promoting myopia screening, refractive archives establishment, and the closed-loop management of myopia prevention and control for children and adolescents]. *Zhonghua Yu Fang Yi Xue Za Zhi*. 2021;55(4):551–555. Wolof. doi:10.3760/cma.j.cn112150-20201208-01435
4. Qian DJ, Wang C, Zhong H, et al. [Epidemiology and the risk factors of myopia among children and youths in Yunnan province]. *Zhonghua Yu Fang Yi Xue Za Zhi*. 2021;55(4):465–470. Wolof. doi:10.3760/cma.j.cn112150-20200521-00765
5. Lyu YY, Wu JJ, Guo W, et al. [Clinical observation and analysis on the effect of orthokeratology in myopic anisometropic children]. *Zhonghua Yu Fang Yi Xue Za Zhi*. 2021;55(4):471–477. Wolof. doi:10.3760/cma.j.cn112150-20210203-00119
6. Jiang DD, Zhao CP, Ding WZ, et al. [The role of peripheral retinal defocus in myopia progression]. *Zhonghua Yan Ke Za Zhi*. 2024;60(6):541–546. Hausa. doi:10.3760/cma.j.cn112142-20231024-00173
7. Xu XL, Lin X, Zhao LH, et al. [Long-term prevention and control effects of orthokeratology lenses designed for small treatment zones on children and adolescents with myopia]. *Zhonghua Yan Ke Za Zhi*. 2023;59(6):444–451. Hausa. doi:10.3760/cma.j.cn112142-20220929-00476
8. Sun XX, Zhang Y, Chen YG. [Correlation between the increase in corneal higher-order aberrations and the control of children's myopic anisometropia after wearing orthokeratology lenses]. *Zhonghua Yan Ke Za Zhi*. 2022;58(4):250–258. Hausa. doi:10.3760/cma.j.cn112142-20210715-00337
9. Chen Y, Xiong R, Chen X, et al. Efficacy comparison of repeated low-level red light and low-dose atropine for myopia control: a randomized controlled trial. *Transl Vis Sci Technol*. 2022;11(10):33. doi:10.1167/tvst.11.10.33
10. Huang Z, Chen X-F, He T, et al. Synergistic effects of defocus-incorporated multiple segments and atropine in slowing the progression of myopia. *Sci Rep*. 2022;12(1):22311. doi:10.1038/s41598-022-25599-z
11. Chiang ST, Turnbull PRK, Phillips JR. Additive effect of atropine eye drops and short-term retinal defocus on choroidal thickness in children with myopia. *Sci Rep*. 2020;10(1):18310. doi:10.1038/s41598-020-75342-9
12. Public Health Ophthalmology Branch, and Preventive Medicine Association. 中国儿童青少年近视防控公共卫生综合干预行动专家共识 [Chinese expert consensus on comprehensive public health intervention for myopia prevention and control in children and adolescents]. *Zhonghua Yi Xue Za Zhi*. 2023;103(38):3002–3009. Chinese. doi:10.3760/cma.j.cn112137-20230613-00996
13. Li J, Ye QQ, Luo XH, et al. [Effect of binocular accommodation and vergence function examinations and interventions on subjective discomfort of dry eye]. *Zhonghua Yi Xue Za Zhi*. 2021;101(32):2519–2524. Danish. doi:10.3760/cma.j.cn112137-20210331-00788
14. Liu SW, Zhao YH, Ma J, et al. [Efficacy evaluation of 0.05% cyclosporine A and 0.1% tacrolimus eye drops in the treatment of severe dry eye associated with chronic graft-versus-host disease]. *Zhonghua Yan Ke Za Zhi*. 2023;59(10):805–813. Hausa. doi:10.3760/cma.j.cn112142-20221112-00585
15. Zhang XJ, Zaabaar E, French AN, et al. Advances in myopia control strategies for children. *Br J Ophthalmol*. 2025;109(2):165–176.
16. Yang Y, Xiao Z, Ouyang J, Guo Y. A novel approach: enhancing adolescent myopia control with orthokeratology and atropine. 2024.
17. Xiao L, Lv J, Zhu X, et al. Therapeutic effects of orthokeratology lens combined with 0.01% atropine eye drops on juvenile myopia. *Arquivos brasileiros de oftalmologia*. 2023;87:e2022–0247. doi:10.5935/0004-2749.2022-0247

18. Wu H, Peng T, Zhou W, et al. Choroidal vasculature act as predictive biomarkers of long-term ocular elongation in myopic children treated with orthokeratology: a prospective cohort study. *Eye Vision*. 2023;10(1):27. doi:10.1186/s40662-023-00345-2
19. Tan Q. Combined atropine with orthokeratology in childhood myopia control (AOK)–a randomized controlled trial. 2021.
20. Ruan Y, Qian L, Chen S. Effect of combined use of orthokeratology and atropine eye drops on correction of myopia in young children, and its influencing factors. *Trop J Pharm Res*. 2022;21(11):2479–2485.
21. Pugazhendhi S, Ambati B, Hunter AA. Pathogenesis and prevention of worsening axial elongation in pathological myopia. *Clin Ophthalmol*. 2020;14:853–873. doi:10.2147/OPTH.S241435
22. National Academies of Sciences, Engineering, and Medicine. Current and emerging treatment options for myopia. In: *Myopia: Causes, Prevention, and Treatment of an Increasingly Common Disease*. National Academies Press (US); 2024.
23. Khanal S, Tomiyama ES, Harrington SC, et al. Childhood myopia part II: treatment mechanisms, emerging options, and considerations. *Invest Ophthalmol Visual Sci*. 2025;66(7):7. doi:10.1167/iovs.66.7.7
24. Gong G, Zhang BN, Guo T, et al. Efficacy of orthokeratology lens with the modified small treatment zone on myopia progression and visual quality: a randomized clinical trial. *Eye Vision*. 2024;11(1):35. doi:10.1186/s40662-024-00403-3
25. Ni NJ, Ma F-Y, Wu X-M, et al. Novel application of multispectral refraction topography in the observation of myopic control effect by orthokeratology lens in adolescents. *World J Clin Cases*. 2021;9(30):8985–8998. doi:10.12998/wjcc.v9.i30.8985
26. Ma W, Yang B, Wang X, et al. [Observational comparison of the safety and effectiveness of myopic children wearing defocus incorporated soft contact lenses or orthokeratology lenses]. *Sichuan Da Xue Xue Bao Yi Xue Ban*. 2023;54(1):181–185. Danish. doi:10.12182/20230160207
27. Chen XH, Xiong Y, Wang J-L, et al. [Prospective study on corneal safety evaluation of children/adolescents with low and moderate myopia after long-term orthokeratology]. *Sichuan Da Xue Xue Bao Yi Xue Ban*. 2021;52(6):1006–1010. Danish. doi:10.12182/20211160107
28. Tsai WS, Wang JH, Chiu CJ. A comparative study of orthokeratology and low-dose atropine for the treatment of anisomyopia in children. *Sci Rep*. 2020;10(1):14176. doi:10.1038/s41598-020-71142-3
29. Nucci P, Lembo A, Schiavetti I, et al. A comparison of myopia control in European children and adolescents with defocus incorporated multiple segments (DIMS) spectacles, atropine, and combined DIMS/atropine. *PLoS One*. 2023;18(2):e0281816. doi:10.1371/journal.pone.0281816
30. Loughman J, Lingham G, Nkansah EK, et al. Efficacy and safety of different atropine regimens for the treatment of myopia in children: three-year results of the MOSAIC randomized clinical trial. *JAMA Ophthalmol*. 2025;143:134. doi:10.1001/jamaophthalmol.2024.5703
31. Guo Y, Liu Y, Hu Z, et al. Efficacy and safety of 0.01% atropine combined with orthokeratology lens in delaying juvenile myopia: an observational study. *Medicine*. 2024;103(24):e38384. doi:10.1097/MD.0000000000038384
32. Zhao Q, Hao Q. Comparison of the clinical efficacies of 0.01% atropine and orthokeratology in controlling the progression of myopia in children. *Ophthalmic Epidemiol*. 2021;28(5):376–382. doi:10.1080/09286586.2021.1875010
33. Zhao Y, Yang B, Li X, et al. [Efficacy of combining highly aspherical lenslets spectacles with 0.01% atropine eye drops in myopia control]. *Sichuan Da Xue Xue Bao Yi Xue Ban*. 2024;55(5):1280–1287. Danish. doi:10.12182/20240960109
34. Lin L, Zhang X, Huang C, et al. Evaluation of retinal vascular density and related factors using OCTA in children and adolescents with myopia without maculopathy. *J Int Med Res*. 2023;51(1):3000605221150136. doi:10.1177/03000605221150136
35. Xia L, Zhao H, Wang Y. Effect of 0.01% Atropine on diopter and optic axis in adolescents and children with myopia. *J Pak Med Assoc*. 2023;73 (3):656–658. doi:10.47391/JPMA.6241
36. Sun Y, Sha Y, Yang J, et al. Collagen is crucial target protein for scleral remodeling and biomechanical change in myopia progression and control. *Heliyon*. 2024;10(15).
37. Guo L, Fan L, Tao J, et al. Use of topical 0.01% atropine for controlling near work-induced transient myopia: a randomized, double-masked, placebo-controlled study. *J Ocul Pharmacol Ther*. 2020;36(2):97–101. doi:10.1089/jop.2019.0062
38. Zheng N, Zhu SQ. Randomized controlled trial on the efficacy and safety of autologous serum eye drops in dry eye syndrome. *World J Clin Cases*. 2023;11(28):6774–6781. doi:10.12998/wjcc.v11.i28.6774
39. Zhu Q, Zhao Q. Short-term effect of orthokeratology lens wear on choroidal blood flow in children with low and moderate myopia. *Sci Rep*. 2022;12(1):17653. doi:10.1038/s41598-022-21594-6
40. Huang Z, Zhao W, Mao Y-Z, et al. Factors influencing axial elongation in myopic children using overnight orthokeratology. *Sci Rep*. 2023;13 (1):7715. doi:10.1038/s41598-023-34580-3
41. Xun Q, Mei W, Zhang X, et al. Frontiers of myopia research in the 21st century: a bibliometric analysis of the top 100 most influential articles in the field. *Medicine*. 2024;103(42):e40139. doi:10.1097/MD.0000000000040139
42. Lee SS, Lingham G, Clark A, et al. Choroidal changes during and after discontinuing long-term 0.01% atropine treatment for myopia control. *Invest Ophthalmol Vis Sci*. 2024;65(10):21. doi:10.1167/iovs.65.10.21
43. Lin HJ, Wei -C-C, Chang C-Y, et al. Role of chronic inflammation in myopia progression: clinical evidence and experimental validation. *EBioMedicine*. 2016;10:269–281. doi:10.1016/j.ebiom.2016.07.021