Journal of Clinical Pharmacology and Therapeutics

ISSN: 2766-8347

Research Article

A Novel Approach: Enhancing Adolescent Myopia Control with Orthokeratology and Atropine

*Yingying Yang, Zhigang Xiao, Jing Ouyang and Yan Guo**

Department of Ophthalmology, Hunan Children's Hospital, China

Abstract

Myopia is a growing concern in adolescents worldwide. This retrospective case study evaluated the efficacy of combining 0.01% atropine with orthokeratology lenses to control myopia progression in children. Results from 33 patients showed a significant reduction in axial length growth with the combined treatment, without notable changes in UCVA and IOP. Significant improvements were seen in TBUT and pupil diameter. Age was identified as a key factor affecting myopia control effectiveness. The study supports the safe and effective use of orthokeratology lenses and atropine synergy, particularly in younger patients.

Keywords: Orthokeratology lenses; 0.01% atropine; Adolescent myopia; Axial length growth; Myopia control; Retrospective case study; Visual acuity

Highlights

1. The Study introduces a novel approach combining orthokeratology and atropine for adolescent myopia control.
2. The Study demonstrates a significant reduction in axial length growth with the combined treatment.
3. The Study identifies age as a key factor influencing the efficacy of myopia control using ortho-atropine.
4. The Study highlights the safety and effectiveness of orthokeratology lenses combined with 0.01% atropine.
5. The Study provides new insights for improving myopia diagnosis and treatment strategies in adolescents.

Introduction

Myopia, particularly in the adolescent demographic, has emerged as a formidable challenge in public health globally [1]. World Health Organization data indicate an escalating trend in the prevalence of myopia, projecting that by 2050; nearly half of the global population will be myopic [2]. The implications of myopia extend beyond compromised visual health and quality of life; it predisposes individuals to more severe ocular conditions such as retinal detachment and glaucoma, particularly in cases of high myopia [2]. These complications can potentially lead to profound vision loss, even culminating in blindness [3]. Consequently, the prevention and management of myopia, especially in the high-risk adolescent period, have become pivotal areas of focus in ophthalmologic research [2].

Corneal reshaping lenses, a non-surgical approach to correcting refractive errors, function by altering the curvature of the cornea [4]. Utilizing specially designed rigid gas-permeable contact lenses overnight facilitates unaided clear vision during daytime hours, obviating the need for glasses or contact lenses [5]. Recent investigations indicate that orthokeratology not only enhances vision but also effectively curbs the progression of myopia in adolescents [6]. Nonetheless, the efficacy of corneal reshaping lenses in myopia control, particularly in relation to axial elongation, varies among individuals and warrants further enhancement [4].

Atropine has been widely employed for long-term myopia management [7]. Initial strategies involved high concentrations of atropine, which were marred by numerous side effects [8]. Recent research has shifted focus towards low-concentration atropine, such as 0.01% atropine, for myopia control [9,10]. This low-dose approach has demonstrated considerable success in decelerating axial elongation of the eye with markedly fewer side effects [11]. However, the solitary use of low-dose atropine may offer limited efficacy, suggesting that its combination with other myopia control methodologies could represent a promising avenue for research [12].

Despite the individual effectiveness of corneal reshaping lenses and low-dose atropine in myopia management, comprehensive research on their concurrent application remains absent [4]. Thus, this study is dedicated to examining the effectiveness of integrating orthokeratology with 0.01% atropine in adolescent myopia control. Our rigorous investigation into the combination of orthokeratology lenses and low-concentration atropine is grounded in clinical observations of actual axial changes. This research contributes significantly to identifying more efficacious strategies for myopia control and lays the groundwork for tailored myopia treatments. By analyzing variables such as age, gender, initial myopia degree, and familial myopia history, we aim to enhance the understanding and prediction of myopia progression trends in adolescents, thereby facilitating more informed and effective treatment strategies in clinical practice.

Materials and Methods

Subjects

All participants underwent comprehensive screening prior to receiving orthokeratology lens treatment, including anterior

Citation: Yang Y, Xiao Z, Ouyang J, Guo Y. A Novel Approach: Enhancing Adolescent Myopia Control with Orthokeratology and Atropine. J Clin Pharmacol Ther. 2024;5(1):1053.

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Publisher Name: Medtext Publications LLC

Manuscript compiled: May 10th, 2024

***Corresponding author:** Yan Guo, Department of Ophthalmology, Hunan Children's Hospital, No.86, Ziyuan Road, Changsha 410007, Hunan Province, China, Tel: +86-13786199535

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segment biomicroscopy, fundus examination, non-cycloplegic refraction, visual acuity, and corneal topography. Spherical or toric design orthokeratology lenses were fitted in both eyes. For initial lens selection, flat K and corneal eccentricity were used to determine the alignment curve radius. A suitable contact lens for the eye and corneal topography was established based on the fluorescein pattern. Over-refraction alignment planes were ordered for the lenses. Follow-ups occurred at 1 day, 1 week, 1 month, 3 months, and then every 3 months thereafter.

At each follow-up, detailed examinations were conducted for each participant, including Uncorrected Visual Acuity (UCVA), computerized optometry, slit-lamp microscopy, corneal fluorescein staining, TBUT, corneal topography, Intraocular Pressure (IOP), axial length, pupil diameter, and lens fitting assessments.

When axial length change of ≥ 0.25 mm was observed in any eye at the 6-month follow-up, 0.01% atropine eye drops were administered in conjunction with informed consent from patients and families. The method involved applying 0.01% atropine drops to both eyes 15 minutes before wearing orthokeratology lenses each night. The same examinations were continued at subsequent follow-ups.

Patients were excluded if they (1) experienced ocular inflammation or keratitis leading to discontinuation for over two weeks, (2) required orthokeratology lens parameter adjustments due to poor fitting (3) were undergoing other myopia control treatments such as phototherapy, (4) had atropine allergies or contraindications, (5) had systemic or autoimmune diseases, or (6) displayed poor compliance with follow-up schedules.

Observational indicators

1. UCVA was measured using a standard logarithmic visual acuity chart at 5 m and recorded as LogMAR for analysis.
2. Axial length was measured using an IOL Master, repeated five times, and averaged.
3. Tear Film Break-Up Time (TBUT) was determined by lightly touching the upper conjunctiva with a moistened fluorescein strip, instructing the patient to blink 3-4 times for even distribution, and observing under cobalt blue light on a slit lamp immediately upon eye opening. The time to the first appearance of a dry spot on the cornea was recorded as TBUT.
4. IOP was measured using a TOPCON non-contact tonometer, repeated three times, and averaged.
5. Photopic pupil diameter was measured under consistent lighting conditions using a Sirius corneal topographer, repeated three times, and averaged.

Statistical methods

Data were analyzed using SPSS 26.0 software. Quantitative data, conforming to normal distribution as per the Kolmogorov-Smirnov test, were presented as mean ± standard deviation (x ± s). One-way ANOVA was used to examine data changes over time, and paired t-tests assessed changes pre-and post-combined treatment. Influential factors were analyzed using Spearman correlation, with significant variables included in Logistic regression analysis. A P-value of <0.05 was considered statistically significant.

Results

Demographic and baseline characteristics of participants

A total of 33 patients (65 eyes) were ultimately included in the study, comprising 16 males and 17 females. The age range of the patients extended from 8 to 14 years, with an average age of 9.85 years. Among these, 21 patients were under the age of 10, and 12 were aged 10 years or older. At the initiation of orthokeratology lens wear, 29 patients had an equivalent spherical lens range of -1.00D to -3.00D, while 4 patients fell within the -3.00D to -5.00D range.

The dot-line graph depicted in Figure 1 illustrates the changes in axial length of participants using orthokeratology lenses before and after the addition of low-concentration atropine. In the six-month visit prior to combination therapy, the average axial change ± Standard Deviation (SD) was 0.30 ± 0.10 mm. Post combination therapy, this change was recorded as 0.08 ± 0.15 mm on average. As demonstrated in Table 1, there was a significantly reduced axial length growth post combination therapy compared to the period prior, with a notable difference between the two groups (t=10.590, P<0.001).

The axial length growth post combination therapy was calculated as the difference in axial length between post-treatment with orthokeratology lenses in conjunction with 0.01% atropine and post-treatment with only orthokeratology lenses.

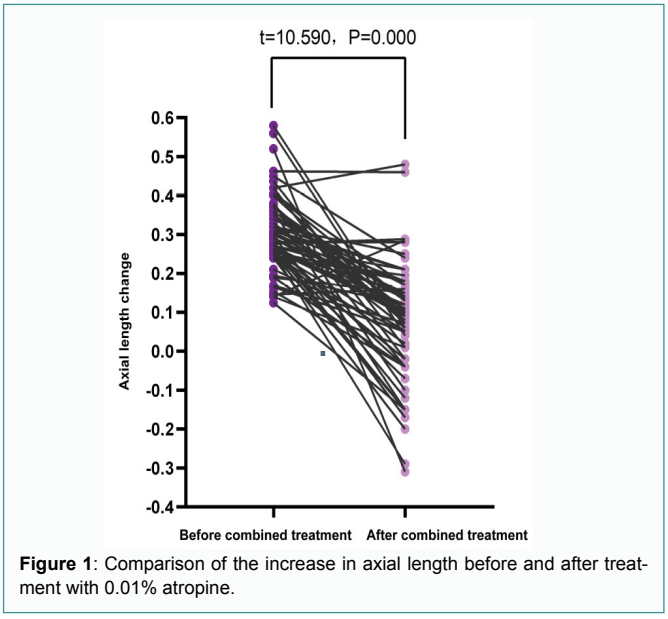

Figure 1: Comparison of the increase in axial length before and after treatment with 0.01% atropine.

Table 1: Comparison of the increase in eye axial length before and after the combined treatment of Orthokeratology with 0.01% atropine.

	Before combination therapy	After combined therapy
Eye axis growth	0.30 ± 0.10	0.08 ± 0.15
t	10.59	
P	<0.001	

Note: The increase in axial length before combined treatment refers to the difference between the axial length measured during the corneal reshaping lens follow-up examination at six months and the initial axial length.

Changes in UCVA, IOP, TBUT, and photopic pupil diameter

As indicated in Table 2 and Figure 2A, a statistically significant difference was observed between UCVA post-treatment with orthokeratology lenses combined with 0.01% atropine and the initial baseline visual acuity (F=349.107, P<0.001). However, a paired t-test comparing pre- and post-combination therapy visual acuity revealed no significant difference (t=-0.223, P=0.824). This suggests that orthokeratology lenses significantly improved patients' unaided visual

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acuity, and this improvement was not affected by the adjunctive use of 0.01% atropine.

Regarding IOP, as shown in Table 2 and Figure 2B, no significant differences were found between pre- and post-combination therapy readings compared to the baseline (F=0.491, P=0.613). Additionally, the paired t-test for IOP pre- and post-combination therapy revealed no statistically significant difference (t=-1.348, P=0.182). These results indicate that the combination therapy of orthokeratology lenses with 0.01% atropine did not impact patients' IOP.

As presented in Table 2 and Figure 2C, there was a statistically significant difference in TBUT when comparing pre- and post-combination therapy to the initial baseline (F=34.022, P=0.000). Furthermore, a paired t-test for TBUT showed a significant difference pre-and post-combination therapy (t=3.237, P=0.002), indicating a tendency for shortened TBUT following treatment.

Lastly, as detailed in Table 2 and Figure 2D, a significant difference was noted in photopic pupil diameter between pre- and post-combination therapy compared to the baseline (F=55.195, P=0.000). The paired t-test results for photopic pupil diameter pre- and post-combination therapy also showed a significant difference (t=-15.795, P=0.000), suggesting an increase in photopic pupil diameter following the treatment.

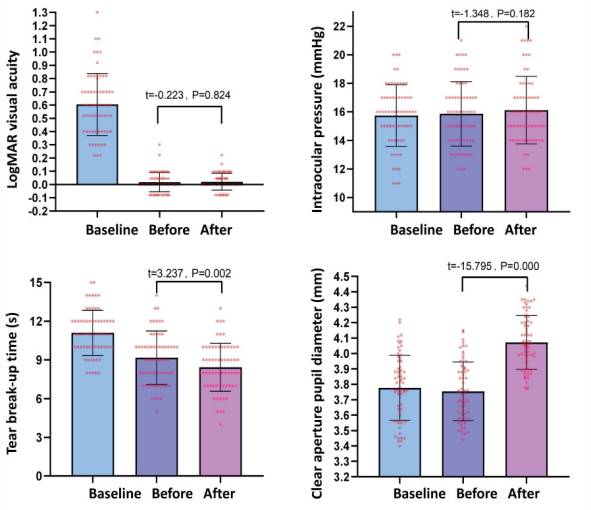

Figure 2: Changes in UCVA, IOP, TBUT, and Pupillary Diameter in Response to Combined Treatment.

Analysis of factors influencing rapid axial length growth in pediatric patients

To mitigate the impact of data redundancy on the analysis of correlational factors, only data from the right eyes were selected for analysis, encompassing a total of 33 eyes. The axial length growth prior to combination therapy was designated as the dependent variable, with age, gender, initial spherical lens degree, and parental history of myopia serving as independent variables. As illustrated in Table 3, the results of the Spearman correlation analysis indicated no significant correlation between pre-treatment axial length growth in children and variables such as gender, initial spherical lens degree, or parental history of myopia (P>0.05). However, a negative correlation was observed with age (P<0.05). As presented in Table 4 and Figure 3, subsequent incorporation of age into the Logistic regression analysis revealed that age was a significant factor influencing the effectiveness

Table 2: Comparison of the changes in UCVA, IOP, and TBUT before and after combined treatment of Orthokeratology with 0.01% atropine as compared to the initial baseline values.

	UCVA	IOP (mmHg)	TBUT (s)	BPD (mm)
Initial baseline data	0.61 ± 0.23	15.74 ± 2.16	11.09 ± 1.75	3.78 ± 0.21
Before combination therapy	0.02 ± 0.07	15.86 ± 2.26	9.17 ± 2.07	3.75 ± 0.19
After combined therapy	0.02 ± 0.06	16.12 ± 2.36	8.43 ± 1.86	4.07 ± 0.17
F	349.107	0.491	34.022	55.194
p	<0.001	0.613	<0.001	<0.001

Note: UCVA: Uncorrected visual acuity; IOP: Intraocular pressure; TBUT: Tear film break up time

Table 3: Correlation analysis between the increase in eye axial length prior to combined treatment with 0.01% atropine and the initial condition of pediatric patients.

Correlation	Gender	Initial Age	Initial Spherical Refraction	Parental Myopia
r	-0.045	-0.438	0.143	0.105
P	0.805	0.011	0.426	0.559

of myopia control (P<0.05). This analysis underscores the importance of considering age as a pivotal factor in strategies aimed at controlling myopia progression in pediatric patients.

Discussion

The escalating prevalence of myopia, particularly among children and adolescents, has emerged as a significant public health concern worldwide, impacting both physical and mental well-being [13]. Global statistics indicate a rise in myopia cases from 28% in 2010 to a projected 50% by 2050 [14]. Typically commencing in primary school, myopia's progression into adolescence significantly increases the likelihood of developing high myopia in adulthood. This escalation potentially augments the burden of high myopia-related diseases, such as cataracts, glaucoma, retinal detachment, and macular degeneration, leading to a notable increase in associated diseases [15]. Consequently, the importance of vision control, encompassing

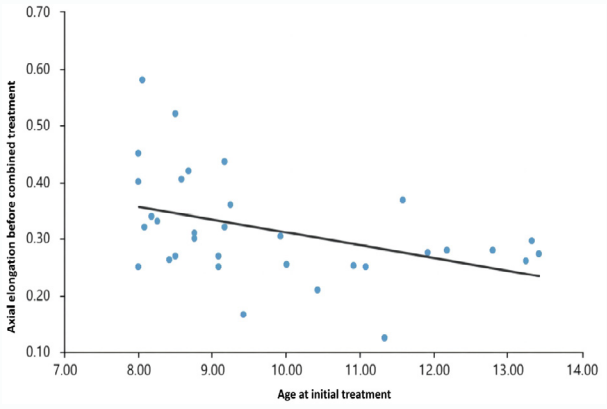

Figure 3: Scatter Plot Showing the Relationship between Age at Initial Treatment and Increase in Axial Length before Combined Treatment.

Table 4: Logistic regression analysis of the correlation between the increase in axial length before combined treatment with 0.01% atropine and the age at initial treatment.

	B	S.E.	t	P	OR	95%CI
Initial Age	-0.02	0.01	-2.59	0.02	0.18	-0.040~-0.005

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interventions to prevent or delay myopia onset and manage high myopia complications, is paramount in mitigating the visual impacts of myopia [16].

Current myopia prevention and control strategies encompass various methods, including outdoor activities, corneal reshaping lenses, defocus soft contact lenses, multi-focal myopia control glasses, and low-concentration atropine [17]. While no single method guarantees complete efficacy, research suggests that a combination of optical and medicinal measures can effectively manage myopia. This effectiveness is likely due to their synergistic impact on myopia's pathogenesis through distinct pathways [2].

Orthokeratology lenses, recognized as the foremost optical method [18], control myopia by modifying corneal refractive power, reducing hyperopic defocus at the peripheral retina, and decelerating axial elongation of the eye [4]. Atropine, a non-selective acetylcholine receptor inhibitor, primarily influences M1 and M4 subtypes, effectively controlling myopia progression with minimal impact on the M3 subtype [19]. Atropine's mechanism in myopia control involves action on the scleral fibrous layer [20].

Recent international studies underscore the synergistic enhancement in myopia control through the combined use of orthokeratology lenses and 0.01% atropine [4,6,21]. However, initiating combined treatment is not always necessary, as myopia prevention and control should be tailored to each patient's specific condition [22]. Axial length and refractive error are primary indicators for assessing refractive status, with myopia development closely linked to axial length increase, exhibiting a negative correlation [23]. Studies indicate a significant reduction in axial elongation rate post-combined treatment [24], with evident effectiveness even in patients responding poorly to corneal reshaping lenses [25]. The potential mechanisms of combination therapy may involve atropine-induced pupillary dilation [26], suggesting that larger pupil size may enhance the effectiveness of orthokeratology lenses in myopia control [27].

The formulation of personalized myopia control plans requires consideration of factors such as age of onset, family history, and initial degree of myopia. Spearman correlation analysis in this study indicates no correlation between pre-treatment axial length increase and factors such as gender, initial spherical degree, and parental myopia ($P>0.05$). However, a negative correlation between axial length increase and age ($P<0.05$) suggests that younger children may experience faster axial length growth and a higher likelihood of poor response to corneal reshaping lenses. Thus, for younger children using corneal reshaping lenses, early combined use of 0.01% atropine therapy may enhance myopia control effectiveness [25]. This study also acknowledges the physiological axial elongation in patients under 12, emphasizing the need for future research to devise more effective myopia prevention and control methods based on different axial growth rates across age groups [28]. The potential influence of small sample sizes on the correlation between initial spherical power, parental myopia status, and response to orthokeratology warrants further investigation [29].

In conclusion, the combined use of corneal reshaping lenses and 0.01% atropine in adolescents synergistically enhances myopia control and is safe. Specifically, combination therapy significantly reduces axial elongation but does not statistically impact UCVA and IOP. Additionally, age is an important factor influencing myopia control effectiveness, negatively correlated with axial elongation. This study contributes to personalized treatment by evaluating the impact of different factors on treatment outcomes, aiding in the formulation of appropriate plans for various patients. While this research offers new insights for clinical practice, limitations such as small sample size, potential selection bias, and a short follow-up period necessitate further comprehensive research to optimize and confirm the effectiveness and applicability of this combination therapy.

While this study has yielded encouraging outcomes in managing adolescent myopia through the concurrent use of orthokeratology lenses and 0.01% atropine, it is important to acknowledge certain limitations. Firstly, the relatively modest sample size could potentially impinge upon the statistical robustness and the broader applicability of the findings. Secondly, the retrospective nature of the case study raises concerns about possible selection bias and confounding variables, which might compromise the precision of the conclusions drawn. Additionally, the limited duration of the follow-up period constrains a thorough evaluation of the long-term therapeutic efficacy and safety profile of the treatment. Future research directions should consider amplifying the sample size to bolster both the reliability and the external validity of the study's findings. Prolonging the duration of follow-up is crucial for a more comprehensive understanding of the long-term impacts and safety of the treatment. Engaging in multi-center collaborations could enhance the universality and practicality of the research, allowing for the formulation of more region-specific and population-tailored treatment recommendations. Moreover, there is a need to delve into and assess alternative combination therapy options to broaden the spectrum of effective myopia management strategies. In summary, despite this study introducing novel therapeutic avenues for clinical application, there remains a pressing need for more exhaustive and detailed research. Such research should aim to refine, validate, and expand upon the effectiveness and practicality of the combination therapy approach in myopia treatment.

Funding

This study was supported by Natural Science Foundation of Hunan Province (No. 2019JJ80042).

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