ORIGINAL ARTICLE

10.2478/AMB-2026-0053

PHARMACOLOGICAL, OPTICAL, AND COMBINED APPROACHES TO MYOPIA CONTROL IN BULGARIAN CHILDREN: A LONGITUDINAL STUDY

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Abstract. *This study presents different treatments, including both medication and glasses, that affect the progression of myopia in children over time. A total of 250 children aged 6 to 16 were evaluated for a period of 36 months. For the purpose of the study, four groups were formed: one group of pediatric patients receiving low-dose atropine (0.01%), another group wearing defocus-modifying glasses, a third group receiving both treatments, and a control group with no treatment. Key biometric indicators, such as axial length, spherical equivalent, and best-corrected visual acuity, were measured at the start of the study and after that every six months. Non-parametric statistical methods were used to compare changes within each group over time and to identify differences between groups. The protocol achieved high data completeness and showed significant changes within the groups ($p<0.001$). Clear differences between groups appeared after 12 months. The results suggest that combining atropine and defocus lenses is most effective in slowing myopia progression while maintaining good vision.*

Key words: *myopia control, pediatric ophthalmology, defocus lenses, atropine 0.01%*

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Received: *01 November 2025;* ***Accepted:*** *06 November 2025*

INTRODUCTION

Myopia has emerged as one of the most prevalent vision disorders in children worldwide, particularly in urban populations [1, 2]. Epidemiological studies indicate that by 2050, nearly half of the global population may be affected, with the most dramatic increase observed in East and Southeast Asia [1, 3]. Recent studies also indicate an upward trend in myopia prevalence across Europe. Data from the Northern and Central European populations suggest a prevalence rate between 20% and 30% in school-aged children, with higher rates observed in

urban areas [4]. In Bulgaria, population-based data remain limited, but emerging clinical observations indicate a rising trend, particularly in children living in metropolitan regions, such as Sofia, but also in Pleven [5, 6]. Local reports from school screening programs and outpatient clinics reveal increasing numbers of myopic children, often presenting at earlier ages [7]. This shift underscores the urgent need for evidence-based, scalable interventions that can be implemented within national school health systems and ophthalmic care pathways [8].

Growing evidence supports the use of pharmacological and optical interventions for slowing axial elongation and refractive progression [9, 10]. Low-dose atropine (typically 0.01%) has been shown to reduce myopic progression with minimal side effects [11, 12]. Optical solutions, such as defocus-modifying spectacle lenses or orthokeratology, aim to control peripheral retinal defocus, thereby inhibiting ocular growth [13, 14, 15]. However, long-term comparative studies evaluating these approaches – alone and in combination – are limited by inconsistent methodology and follow-up [16, 17].

The rising prevalence of pediatric myopia presents a public health challenge due to its strong association with increased risk of retinal detachment, glaucoma, and other ocular pathologies later in life [18, 19]. Early onset and faster progression in school-age children highlight the need for effective interventions. While low-dose atropine and peripheral defocus-modifying lenses have each demonstrated efficacy independently, evidence for their combined, long-term application remains scarce. This study aims to describe a reproducible and scalable methodology for comparative assessment of these approaches [17, 20].

MATERIALS AND METHODS

This prospective, observational, longitudinal study was conducted over 36 months. Ethical approval was obtained and informed consent was secured from all participants or their guardians. The study adhered to the tenets of the Declaration of Helsinki.

A total of 250 children aged 6 to 16 years were enrolled and allocated into four groups: (1) Atropine 0.01%, (2) Defocus spectacle lenses, (3) Atropine + Defocus combination, and (4) untreated controls. Inclusion criteria were applied to ensure an “otherwise healthy eye” for each participant. Both eyes were initially analyzed, but because no statistically significant differences were observed between them, the analysis presented here focuses on the right eye.

Measurements were taken every six months (baseline, 6, 12, 18, 24, 30, 36 months) and included axial length (AL), spherical equivalent (S.E.), and best-corrected visual acuity (BCVA). AL was measured using the IOLMaster (Carl Zeiss Meditec), a non-contact optical biometer employing partial coherence interferometry for high precision and repeatability. Refractive error (S.E.) was determined under cycloplegia using an autorefractometer. Visual acuity was measured with a standard Snellen chart under consistent lighting conditions.

Statistical analyses were conducted using SPSS (version 20.0). Normality of distributions was assessed using the Kolmogorov-Smirnov test. Inter-group comparisons were performed using the non-parametric Kruskal-Wallis test, while intra-group changes over time were evaluated using the Friedman test. Significance was accepted at $p<0.05$. Additionally, ChatGPT (OpenAI, 2024) was used during the manuscript preparation phase to assist with structure optimization, clarity, and language refinement, under full author supervision.

RESULTS

A total of 250 children were enrolled, with a balanced distribution across the four study groups. Table 1 summarizes the baseline demographic characteristics stratified by intervention group: Atropine, Defocus, Atropine + Defocus, and a Healthy control group.

The mean age of participants ranged from 9 to 11 years across groups, with a pooled mean of 10.0 years (SD 1.5). Age distribution was comparable, though the control group was slightly older on average. Gender distribution was balanced, with 53.2% females and 46.8% males overall. Family history of myopia showed that approximately half of the participants (49.6%) had one myopic parent, while 14.8% had both parents affected. These characteristics suggest a well-distributed sample in terms of age, sex, and familial risk, providing context for understanding the genetic background of the participants without skewing the group composition.

Axial Length Progression

Figure 1 illustrates the mean AL over time across the four groups. All groups exhibited progressive axial elongation, with the control group showing the most pronounced growth. The combined Atropine+Defocus group had the slowest rate of elongation throughout the 36-month period – mean initial axial length 24.51 mm (Fig. 1).

Table 1. Baseline demographic characteristics of study participants by group

Sample characteristic		Atropine	Defocus	Atropine + Defocus	Healthy control group	All
		n = 82 (32.8%)	n = 54 (21.6%)	n = 41 (16.4%)	n = 73 (29.2%)	n = 250 (100%)
Age (years)	Mean (SD)	9 (1.6)	10 (1.5)	9 (1.6)	11 (1.4)	10 (1.5)
	max	12.6	13.3	12	14.2	14.2
	min	6	6.2	6.2	8	6
Gender	Female	40 (48.8%)	33 (61.1%)	23 (56.1%)	37 (50.7%)	133 (53.2%)
	Male	42 (51.2%)	21 (38.9%)	18 (43.9%)	36 (49.3%)	117 (46.8%)
Family history	no	25(30.4%)	18(33.3%)	19 (46.3%)	27 (36.9%)	89 (35.6%)
	1 parent	43 (52.4%)	28 (51.8%)	17 (41.4%)	36 (49.3%)	124 (49.6%)
	2 parents	14 (17%)	8 (14.8%)	5 (12%)	10 (13.6%)	37 (14.7%)

Variable distributions are reported as n (%) unless otherwise specified

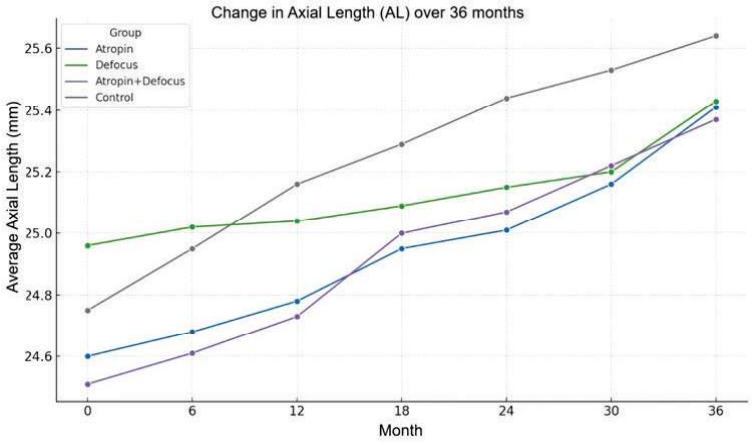

Fig. 1. Change in Axial Length (AL) over 36 months

At the 36-month follow-up, axial elongation of the right eye (OD) was evident in all groups. The control group recorded the highest mean axial length of 25.64 mm, indicating the fastest ocular growth. In contrast, the combination therapy group (Atropine + Defocus) exhibited the lowest axial length at 25.37 mm, followed closely by the Atropine (25.41 mm) and Defocus (25.43 mm) groups. The intergroup differences were statistically significant (Kruskal-Wallis $H = 8.00$, $p<0.05$), confirming the efficacy of intervention strategies in slowing axial growth. These results support the use of combination therapy as the most effective option for controlling axial elongation over time.

Refractive Error Progression (S.E.)

Figure 2 presents the change in S.E. over time. A consistent negative shift was observed in all groups, representing the progression of myopia. The rate of progression was fastest in the control group and slowest in the combined therapy group. Notably, the Atropine and Defocus groups alone also exhibited reduced progression compared to controls.

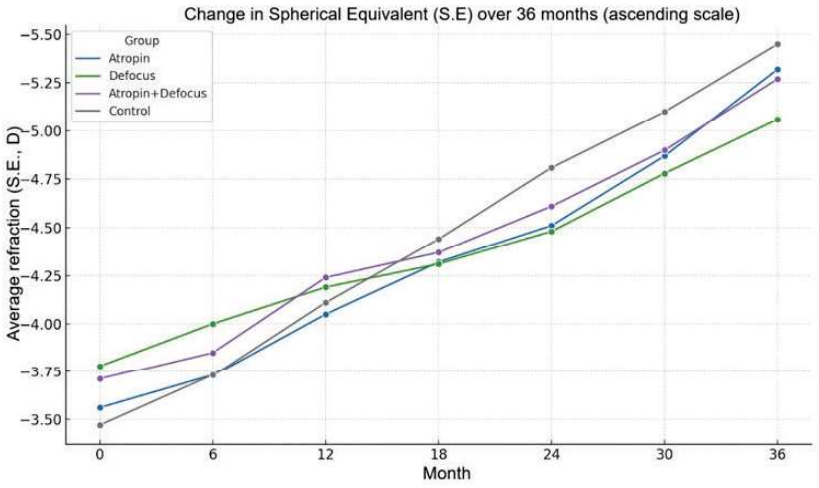

Fig. 2. Refractive Error Progression (S.E.)

Refractive error progression in the right eye, as measured by S.E., followed a similar pattern to axial length elongation. The control group showed the steepest decline, ending at −5.45 D, followed by the Atropine (−5.32 D), Atropine + Defocus (−5.27 D), and Defocus (−5.06 D) groups. Despite relatively small numerical differences between the intervention groups, statistical analysis revealed significant inter-group variation (Kruskal-Wallis H = 8.00, $p<0.05$). These results demonstrate a measurable slowing of myopic progression with treatment, especially with the combined therapy approach.

Visual Acuity Outcomes

Figure 3 shows the BCVA trends over time. The intervention groups maintained higher levels of visual acuity compared to the control group, with statistically significant differences emerging after 12 months. Visual acuity was best preserved in the Defocus group by the end of follow-up.

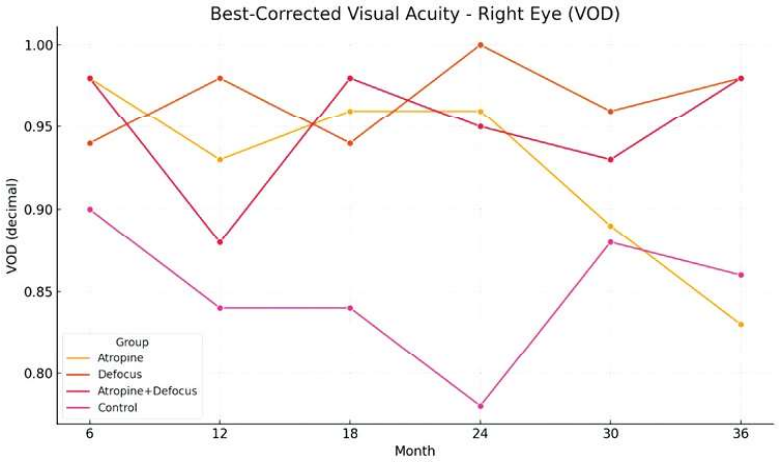

Fig. 3. BCVA trends over time

At month 36, best-corrected visual acuity in the right eye (VOD) was best preserved in the Defocus and Atropine + Defocus groups (both 0.98). The control group showed a modest decline (0.86), while the Atropine group had the lowest acuity (0.83). Inter-group differences were statistically significant (Kruskal-Wallis H = 8.00, $p<0.05$), indicating that optical and combined interventions not only slowed refractive changes, but also helped maintain functional visual outcomes over time.

DISCUSSION

Myopia is not only a refractive error, but also a progressive disease that can lead to sight-threatening complications, such as retinal detachment, choroidal neovascularization, myopic maculopathy, glaucoma, and cataract [21, 22, 23].

Multiple risk factors have been implicated in the development and progression of myopia. These include genetic predisposition (e.g., parental myopia), environmental influences, such as reduced time spent outdoors, increased near work (e.g., prolonged screen use and reading), and poor ambient lighting [24, 25]. Recent studies also highlight the influence of urbanization, socioeconomic status, and educational pressure as contributors to earlier onset and faster progression of myopia in children [2, 26]. Children are particularly vulnerable, with early onset linked to higher risk of high myopia later in life. Addressing these modifiable risk factors is a cornerstone of preventive pediatric ophthalmology. Interventions promoting increased outdoor activity, optimized classroom lighting, and limiting excessive screen exposure are being explored as low-cost, scalable public health measures [27].

While myopia control interventions offer significant benefits, they are not without associated risks. Low-dose atropine, though generally well tolerated, can cause side effects, such as photophobia, temporary anisocoria, blurred near vision, and allergic conjunctivitis, particularly at higher concentrations [28, 29]. Long-term safety remains an area of active investigation, especially concerning potential rebound effects upon cessation of treatment. Defocus-modifying spectacle lenses, although non-invasive and generally considered safe, may initially cause mild visual discomfort or adaptation issues, such as ghosting or blur at the periphery, particularly in children unaccustomed to lens design changes [30]. These effects are typically temporary and diminish with consistent wear. Therefore, careful patient education, regular follow-up, and appropriate approach are important to ensure optimal outcomes.

Nonetheless, the potential to prevent high myopia and its associated lifelong complications far outweighs the minor and manageable risks of these interventions, particularly when implemented within a supervised clinical setting [31].

The current study demonstrated that both pharmacological and optical interventions, especially when combined, significantly reduce the progression of myopia in children over a 36-month period. These findings are consistent with earlier studies showing the efficacy of low-dose atropine in slowing axial elongation and refractive error progression [32, 33]. The results from the CHAMP, ATOM-2, and LAMP trials have established 0.01% atropine as a safe and effective first-line

therapy for myopia control, particularly in Asian and Western pediatric populations [32, 33, 11].

Similarly, defocus-modifying spectacle lenses, such as DIMS (Defocus Incorporated Multiple Segments), have been shown to reduce myopia progression by inducing peripheral myopic defocus, a key mechanism in controlling axial growth [34, 35]. These lenses are especially suitable for younger children due to their ease of use and minimal impact on daily activities. Our findings further support their role as a standalone and adjunctive strategy.

Our results confirm that the combination of atropine and defocus therapy leads to the slowest progression in both AL and S.E., supporting previous reports of a synergistic effect [17, 36, 20]. This combination approach may offer enhanced efficacy through complementary mechanisms: atropine modulating biochemical signaling in the sclera and retina, and defocus lenses altering peripheral defocus to reduce axial elongation.

Notably, BCVA was better preserved in the intervention groups compared to the control group, highlighting not only refractive, but also functional benefits of active treatment. Preservation of visual acuity is a critical outcome, particularly in school-aged children, where optimal vision is directly linked to academic performance and psychosocial development.

Methodologically, this study benefited from its longitudinal design and rigorous standardization. High-precision AL measurements were obtained using non-contact partial coherence interferometry, while refractive error and visual acuity were assessed using consistent, protocoled methods. High participant retention and adherence to follow-up intervals further strengthened the reliability of intra- and inter-group comparisons. While the non-randomized design limits the ability to infer causality, the study reflects real-world conditions and provides a feasible model for clinical application.

This study provides a structured protocol for monitoring pediatric myopia interventions for control and highlights the advantages of the combined pharmacological and optical therapy potential. While the results we observe are promising, there are several limitations to be considered. The non-randomized design introduces the possibility of selection bias. Environmental factors, such as time outdoors, near work, or screen time, were not quantified. Furthermore, adherence to the intervention was not systematically monitored, which may have influenced the observed results. Future studies should incorporate randomization, behavioural monitoring, and objective adherence tracking to strengthen causal inference and applicability.

CONCLUSIONS

Our study supports the fact that a combination of atropine and defocus therapy results in the slowest progression in AL and S.E., which is also supported by recently published reports. Something very important is that the visual acuity was better maintained in the treated groups compared to controls, which highlights not only refractive, but also functional benefits.

Overall, this study contributes to the growing evidence supporting integrated myopia control strategies, particularly for school-aged children, where treatment compliance and regular monitoring can be more easily achieved. Integrated approaches can be effective in controlling myopia, especially in the examined age group, where it's easier to encourage good habits and keep track of progress. The integration of behavioural interventions, such as time outdoors and screen hygiene, with pharmacological and optical therapies may represent the most promising path forward in mitigating the global burden of myopia. Future research should look at how these strategies can be scaled within school health programs and examine their long-term impact on eye health, beyond just changes in refractive status, and investigate their cost-effectiveness, long-term safety, and impact on the quality of life.

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