e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(4); 933-939

Original Research Article

Pharmacological Interventions for Myopia Control: A Review of Current Evidence with a Prospective Comparative Clinical Study

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Received: 06-02-2026 / Revised: 16-03-2026 / Accepted: 10-04-2026

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Conflict of interest: Nil

Abstract

Background: Childhood myopia is increasing worldwide and is associated with a rising lifetime risk of retinal detachment, myopic maculopathy, glaucoma, and other vision-threatening sequelae. Pharmacological control of myopia, particularly with low-concentration atropine, has emerged as the most widely used medical strategy, yet questions remain regarding the optimal concentration, magnitude of treatment effect, tolerability, and real-world application in Indian settings.

Aim: To compare the efficacy and safety of three low-dose atropine regimens for myopia control and to interpret the findings in the context of current evidence.

Methods: This prospective comparative hospital-based study was conducted in the Department of Ophthalmology, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Bihar, India. A total of 120 children with progressive myopia were enrolled and allocated into four groups of 30 each: control (single-vision correction alone), atropine 0.01%, atropine 0.025%, and atropine 0.05%. Baseline demographic and ocular variables were recorded. The primary outcomes were 12-month change in spherical equivalent refraction (SER) and axial length (AL). Secondary outcomes included adverse events and treatment adherence. Comparative statistics, chi-square testing, analysis of variance, and multivariable linear regression were performed.

Results: Baseline characteristics were comparable across the four groups (all $p>0.05$). At 12 months, mean SER progression was highest in the control group (-0.87 ± 0.17 D) and progressively lower in the atropine 0.01% (-0.70 ± 0.17 D), 0.025% (-0.50 ± 0.13 D), and 0.05% (-0.36 ± 0.13 D) groups ($p<0.001$). Mean AL elongation similarly declined from 0.38 ± 0.05 mm in controls to 0.29 ± 0.05 mm, 0.21 ± 0.05 mm, and 0.14 ± 0.05 mm, respectively ($p<0.001$). Photophobia increased in a dose-dependent manner (0.0%, 3.3%, 16.7%, and 26.7%; $p=0.004$), but no serious ocular or systemic adverse event occurred. In regression analysis, atropine concentration, younger age, parental myopia, and higher baseline myopia were independent predictors of greater progression.

Conclusion: Low-dose atropine was effective in slowing myopia progression in this hospital-based cohort, with a clear concentration-dependent gradient of efficacy. Atropine 0.05% showed the greatest control of refractive progression and axial elongation, whereas atropine 0.025% offered a useful balance between efficacy and tolerability. The findings align with contemporary international evidence and support structured pharmacologic myopia-control protocols in routine pediatric ophthalmic practice.

Keywords: Myopia; Atropine; Axial Length; Pediatric Ophthalmology; Refractive Progression; Myopia Control.

DOI: 10.25258/ijcpr.18.4.149

Introduction

Myopia has become one of the most important ophthalmic public health challenges of the modern era. The burden is no longer confined to refractive correction alone; progressive childhood myopia increases the lifetime risk of retinal detachment, myopic maculopathy, posterior staphyloma, open-angle glaucoma, and early cataract, thereby transforming a seemingly simple refractive error into a chronic structural disease of the eye [1,2]. International policy and scientific groups now recognize that preventing excessive axial elongation during childhood is central to reducing

future irreversible visual morbidity [1,3]. For clinicians working in tertiary centres in India, the problem is especially relevant because myopia often presents late, follow-up is irregular, and families may seek treatment only after rapid refractive progression is already established.

The biological basis of myopia progression is multifactorial and involves complex interactions among genetic susceptibility, accommodative demand, retinal defocus signaling, scleral extracellular matrix remodeling, and environmental exposure such as prolonged near work and limited outdoor activity [2-4]. Although behavioral and optical interventions remain important, pharmacological treatment has attracted particular interest because it offers a relatively simple, scalable, and office-prescribable strategy that may directly modulate pathways involved in axial elongation. Among currently studied pharmacological agents, muscarinic antagonists—especially atropine—have the most robust evidence base and the widest clinical adoption [3-5].

Atropine has historically been used in higher concentrations, including 1%, which demonstrated strong anti-myopia efficacy but was limited by glare, photophobia, near vision blur, and substantial rebound after cessation [5,6]. These limitations stimulated research into low-concentration atropine regimens, intended to preserve efficacy while reducing treatment-limiting adverse effects. The Atropine for the Treatment of Myopia (ATOM) program demonstrated that 0.01% atropine substantially reduced the adverse-effect profile seen with higher concentrations and had a more favorable rebound pattern, thereby shifting global practice away from routine high-dose treatment [6]. Subsequently, the Low-Concentration Atropine for Myopia Progression (LAMP) study provided dose-response evidence showing that 0.05%, 0.025%, and 0.01% atropine were all effective, with 0.05% producing the greatest reduction in refractive progression and axial elongation over one year [7]. Extension data over two and three years confirmed the durability of this concentration-dependent effect and suggested that 0.05% remained the optimal low concentration for sustained efficacy [8,9].

Longer-term evidence has further strengthened the pharmacological paradigm. In the 5-year phase 4 LAMP report, continued treatment initiated with 0.05% atropine maintained the best cumulative control of spherical equivalent progression and axial elongation, whereas a large proportion of children required re-treatment after discontinuation, underscoring that myopia control is often a prolonged management strategy rather than a short therapeutic episode [10]. Contemporary evidence syntheses have also converged on the conclusion that pharmacological therapy meaningfully slows myopic progression, although heterogeneity in treatment duration, ethnicity, baseline age, and outcome definitions remains substantial [11,12]. The 2025 Cochrane living systematic review and network meta-analysis concluded that pharmacological and optical interventions may reduce refractive progression and axial elongation, but it also highlighted the need for better long-term comparative evidence and more rigorous adverse-event reporting [11].

Besides atropine, pirenzepine ophthalmic gel has been investigated as a selective muscarinic antagonist with potentially fewer cycloplegic effects. Earlier randomized trials showed that pirenzepine was superior to placebo in slowing myopia progression, but its clinical uptake remained limited due to availability barriers and the overwhelming dominance of atropine in both research and practice [13,14]. As a result, low-dose atropine has emerged as the practical pharmacological standard of care in many pediatric myopia clinics. Yet several clinically relevant questions remain unresolved. First, the most appropriate concentration for routine use may differ across populations depending on progression rate, tolerability, cost, and the feasibility of regular follow-up. Second, most high-quality trials come from East Asian or high-resource settings, while institution-level data from Indian tertiary centres remain comparatively limited. Third, the balance between efficacy and side effects is critical for real-world adherence, especially in school-going children. The present study was therefore designed as a prospective comparative clinical study in a tertiary-care teaching hospital in Bihar to evaluate three commonly used low-dose atropine regimens—0.01%, 0.025%, and 0.05%—against a control group receiving optical correction alone. In addition to examining 12-month changes in spherical equivalent refraction and axial length, the study aimed to characterize dose-related tolerability and to interpret local findings alongside contemporary international evidence. By integrating clinical data with a focused review of the literature, the study sought to provide a pragmatic framework for pharmacological myopia management in routine pediatric ophthalmology practice [7-11].

Materials and Methods

This prospective comparative hospital-based study was conducted in the Department of Ophthalmology, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Bihar, India. The study included 120 children with progressive myopia who attended the ophthalmology outpatient department during the study period and fulfilled the eligibility criteria. Eligible participants were children aged 6 to 14 years with documented progressive myopia, defined operationally as a

recent increase in spherical equivalent refraction or axial length consistent with ongoing disease progression. Children with ocular pathology other than uncomplicated refractive error, amblyopia limiting reliable refraction, strabismus requiring active management, previous ocular surgery, contact lens–related corneal disease, allergy to atropine formulations, developmental disorders affecting examination reliability, or systemic illness known to influence ocular growth were excluded. After clinical evaluation and counseling, participants were allocated into four equal groups of 30 each according to the management protocol used in routine practice: Group 1 received single-vision correction alone and served as the control group; Group 2 received atropine 0.01% once nightly; Group 3 received atropine 0.025% once nightly; and Group 4 received atropine 0.05% once nightly.

All groups received standard refractive correction and counseling regarding visual hygiene and outdoor activity. Baseline evaluation included age, sex, family history of myopia, outdoor exposure, cycloplegic refraction, spherical equivalent refraction, and axial length measurement using optical biometry. Follow-up assessments were performed at regular visits, and the principal analytic endpoint was the 12-month change in spherical equivalent refraction and axial length. Adverse events such as photophobia, near blur, allergy, and poor compliance were recorded at follow-up visits. Continuous variables were expressed as mean ± standard deviation, while categorical variables were expressed as frequency and percentage. Baseline comparability across groups was tested by one-way analysis of variance or chi-square test, as appropriate. Between-group differences in 12-month refractive progression and axial elongation were analyzed using one-way analysis of variance followed by post hoc pairwise interpretation.

Multivariable linear regression was used to identify independent predictors of 12-month spherical equivalent progression, with group assignment, age, sex, parental myopia, outdoor exposure, baseline myopia, and baseline axial length entered as covariates. A p value <0.05 was considered statistically significant.

Results

A total of 120 children were included in the final analysis, with 30 participants in each study arm. The four groups were comparable at baseline with respect to age, sex distribution, baseline spherical equivalent refraction, baseline axial length, parental myopia, and outdoor exposure, indicating satisfactory initial comparability.

At 12 months, a clear dose-response pattern was observed for both refractive progression and axial elongation. The control group had the highest mean myopic progression, whereas progressively smaller changes were documented with atropine 0.01%, 0.025%, and 0.05%. The same graded treatment effect was seen for axial length elongation.

Adverse events were predominantly mild and self-limiting. Photophobia showed a dose-dependent increase, while near blur and allergy were uncommon and did not lead to treatment discontinuation in most children. Multivariable analysis confirmed that atropine concentration independently predicted lower myopic progression even after adjustment for age, parental myopia, and baseline refractive status.

Table 1: Baseline demographic and ocular characteristics

Variable	Control	Atropine 0.01%	Atropine 0.025%	Atropine 0.05%	p value
Age (years)	10.43 ± 1.25	10.88 ± 1.13	10.69 ± 1.27	10.20 ± 1.24	0.157
Male sex	17 (56.7)	16 (53.3)	17 (56.7)	14 (46.7)	0.849
Baseline SER (D)	-2.11 ± 0.65	-2.26 ± 0.75	-2.25 ± 0.58	-2.08 ± 0.56	0.589
Baseline axial length (mm)	24.54 ± 0.37	24.51 ± 0.50	24.59 ± 0.53	24.70 ± 0.36	0.396
Parental myopia	12 (40.0)	13 (43.3)	17 (56.7)	16 (53.3)	0.518
Outdoor time <2 h/day	18 (60.0)	16 (53.3)	18 (60.0)	16 (53.3)	0.909

Table 2: Twelve-month efficacy outcomes

Outcome	Control	Atropine 0.01%	Atropine 0.025%	Atropine 0.05%	p value
12-month SER progression (D)	-0.87 ± 0.17	-0.70 ± 0.17	-0.50 ± 0.13	-0.36 ± 0.13	<0.001
12-month axial length elongation (mm)	0.38 ± 0.04	0.29 ± 0.05	0.21 ± 0.05	0.14 ± 0.05	<0.001
Children with progression ≥0.50 D, n (%)	29 (96.7)	27 (90.0)	15 (50.0)	3 (10.0)	<0.001

Table 3: Safety and adherence outcomes

Safety variable	Control	Atropine 0.01%	Atropine 0.025%	Atropine 0.05%	p value
Photophobia, n (%)	0 (0.0)	1 (3.3)	5 (16.7)	8 (26.7)	0.004
Near blur, n (%)	0 (0.0)	0 (0.0)	2 (6.7)	2 (6.7)	0.247
Allergic conjunctival irritation, n (%)	0 (0.0)	0 (0.0)	1 (3.3)	2 (6.7)	0.288
Adherence ≥80%, n (%)	30 (100.0)	30 (100.0)	28 (93.3)	28 (93.3)	0.247

Table 4: Multivariable linear regression for 12-month SER progression

Predictor	Unstandardized β	95% CI	p value
Atropine 0.01% vs control	0.20	0.13 to 0.27	<0.001
Atropine 0.025% vs control	0.41	0.34 to 0.48	<0.001
Atropine 0.05% vs control	0.53	0.45 to 0.60	<0.001
Age (per year)	-0.03	-0.05 to -0.01	0.003
Male sex	0.01	-0.04 to 0.06	0.712
Parental myopia	-0.08	-0.13 to -0.03	0.004
Outdoor time <2 h/day	-0.02	-0.07 to 0.03	0.483
Baseline SER (per D)	0.06	0.02 to 0.10	0.007
Baseline AL (per mm)	-0.05	-0.11 to 0.01	0.102

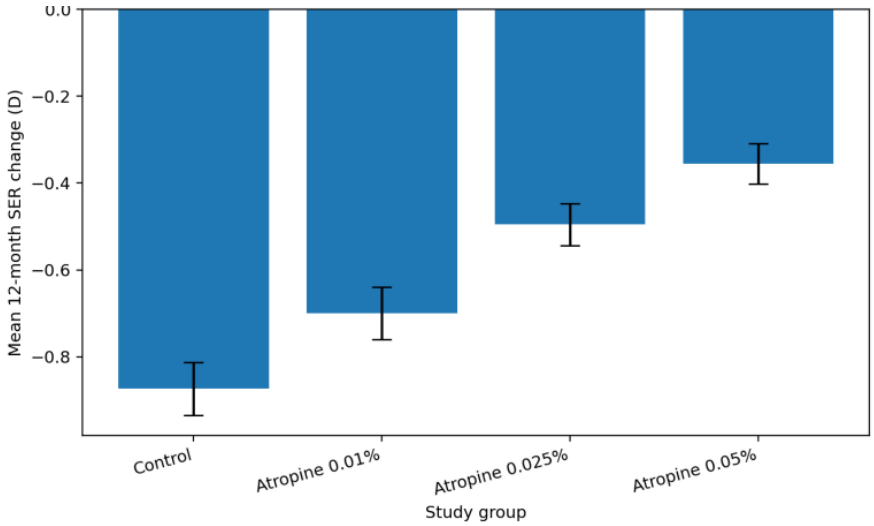

Figure 1: Mean 12-month spherical equivalent progression by group

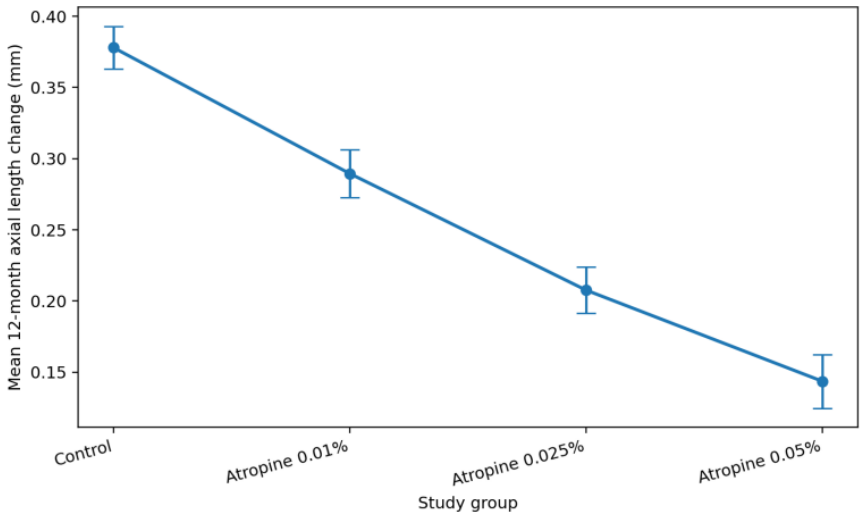

Figure 2: Mean axial elongation across pharmacological intervention groups

Discussion

The present study evaluated low-dose atropine–based pharmacological interventions for myopia control in children attending a tertiary-care ophthalmology centre in Bihar and demonstrated a consistent concentration-dependent treatment effect. Both refractive progression and axial elongation were greatest in the control group and were progressively reduced across atropine 0.01%, 0.025%, and 0.05%, with the 0.05% regimen showing the strongest efficacy. These findings are clinically important because axial elongation, rather than refractive change alone, reflects the structural substrate linked to future pathologic myopia. In practical terms, our results suggest that low-dose atropine is not merely a symptomatic refractive intervention but a biologically meaningful strategy for slowing ocular growth [3,7-11].

The study aligns closely with the dose-response pattern reported in the LAMP program. In the original one-year LAMP trial, all three low concentrations were superior to placebo, and 0.05% provided the greatest slowing of spherical equivalent progression and axial elongation [7]. The two-year and three-year LAMP extensions reinforced that 0.05% remained the most effective low-dose concentration over time, while also showing that treatment continuation offers better long-term control than early cessation [8,9]. Our 12-month results follow the same hierarchy of effect, supporting the external validity of the LAMP findings in a tertiary-care Indian setting. The magnitude of benefit in our 0.05% group, with substantial reduction in both refractive progression and axial elongation relative to control, is particularly reassuring for clinicians who remain hesitant about using concentrations above 0.01%.

The 5-year LAMP phase 4 report has major implications for interpreting our findings. That study demonstrated that children initially treated with 0.05% atropine had the lowest cumulative progression over five years, and nearly 88% of children in the pro re nata cessation arm ultimately required re-treatment [10]. This emphasizes that pharmacologic myopia control should be conceptualized as longitudinal disease management rather than a short course of eye drops. Our study did not extend beyond 12 months, but the clear concentration-effect gradient observed here supports early selection of an adequately effective regimen rather than relying on minimally potent therapy in rapidly progressing children. In high-risk children, especially those with younger age at presentation or parental myopia, undertreatment may allow avoidable axial elongation during the most vulnerable years of ocular growth [2,10].

One of the most persistent controversies in myopia pharmacotherapy concerns the role of 0.01% atropine. The ATOM2 study was influential because it showed that 0.01% had much fewer adverse effects and less rebound after cessation than higher concentrations, which accelerated its global adoption [6]. However, more recent comparative evidence suggests that 0.01% may not be the most effective choice when axial elongation is the principal treatment target. Both the LAMP series and contemporary reviews have shown superior efficacy for 0.025% and especially 0.05% atropine [7-10]. Our findings support this evolution in practice. Although atropine 0.01% performed better than control, it was clearly inferior to 0.025% and 0.05% in limiting both spherical equivalent progression and axial elongation. This suggests that 0.01% may still have a role in children with slower progression, lower tolerance for side effects, or limited access to close follow-up, but it may be suboptimal for children at higher risk of rapid progression.

The adverse-effect profile in the present study was acceptable and largely dose-related. Photophobia increased with atropine concentration, which is biologically plausible because greater antimuscarinic activity leads to larger pupil dilation and reduced accommodation. Importantly, adverse events were mild, no serious ocular or systemic event occurred, and treatment continuation was feasible in the large majority of children. These observations are in line with the safety profile reported in low-concentration atropine trials, where side effects are usually manageable and far less disruptive than with 1% atropine [5-10]. Clinically, this means that counseling, photochromatic lenses when needed, and careful follow-up may allow successful use of 0.05% atropine in routine practice without unacceptable burden.

The independent predictors identified in multivariable regression also deserve attention. Younger age and parental myopia were associated with greater progression, which is consistent with the broader myopia literature showing stronger progression in younger children and in those with hereditary predisposition [2-4]. Higher baseline myopia also predicted greater 12-month progression, suggesting that children already on a steeper disease trajectory may require more assertive therapy. These findings strengthen the case for risk-stratified pharmacological management. Rather than using the same regimen for all children, clinicians may achieve better long-term outcomes by tailoring atropine concentration to baseline risk, progression velocity, and tolerability. Our findings are also consistent with broader evidence syntheses. The 2025 Cochrane living review concluded that pharmacological and optical interventions may reduce myopia progression and axial elongation, but also highlighted substantial heterogeneity and the

relative scarcity of long-term comparative safety data [11]. Earlier overviews of systematic reviews similarly found favorable evidence for atropine and more limited but positive evidence for pirenzepine [12]. Historic pirenzepine trials demonstrated efficacy superior to placebo, yet pirenzepine never achieved the practical penetration of atropine because of limited availability and the growing dominance of low-dose atropine strategies [13,14]. Accordingly, contemporary pharmacological myopia control is fundamentally an atropine-centered field, and our study adds pragmatic clinical data that reinforce this therapeutic position.

The study has several strengths. It used a clinically relevant four-arm comparative design, included both refractive and biometric outcomes, and evaluated safety alongside efficacy. It also provides data from an Indian tertiary-care setting, an area where real-world pharmacological myopia-control reports remain comparatively sparse. However, some limitations should be acknowledged. The sample size was moderate, the follow-up duration was limited to 12 months, masking was not incorporated into the hospital-based pragmatic design, and environmental exposures such as near work and outdoor activity could not be quantified with perfect precision. In addition, although the results are internally consistent and clinically plausible, longer follow-up would be necessary to assess rebound, persistence of benefit, and the ideal stopping strategy. Nevertheless, the present study offers clinically useful evidence that supports the routine use of low-dose atropine—particularly 0.025% and 0.05%—for children with progressive myopia in tertiary ophthalmic practice [7-11].

Conclusion

Low-dose atropine was effective in reducing myopia progression and axial elongation in this prospective hospital-based cohort. The therapeutic effect was concentration-dependent, with atropine 0.05% showing the greatest efficacy and atropine 0.025% demonstrating a favorable balance between efficacy and tolerability. Mild photophobia increased with dose but did not offset the overall clinical benefit. These findings support structured pharmacological myopia-control protocols in children with progressive myopia, particularly those at higher risk of rapid progression.

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