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2734 17 Avenue SW,
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+15878858911
editorial-office@sciformat.ca

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EFFICACY AND SAFETY OF LOW-DOSE TOPICAL ATROPINE FOR THE PREVENTION OF MYOPIA PROGRESSION IN CHILDREN: A SYSTEMATIC REVIEW

Wiktoria Żelazna
Medical University of Silesia, 40-055 Katowice, Poland
ORCID ID: 0009-0001-8185-4846

Kalina Światlak
Medical University of Silesia, 40-055 Katowice, Poland
ORCID ID: 0009-0007-9406-6519

Justyna Trzaskalik
Medical University of Silesia, 40-055 Katowice, Poland
ORCID ID: 0009-0006-8466-0402

Jakub Sokołowski *(Corresponding Author, Email: czjaslo@gmail.com)*
Medical University of Silesia, 40-055 Katowice, Poland
ORCID ID: 0009-0008-7031-5311

Monika Leśniak
Medical University of Silesia, 40-055 Katowice, Poland
ORCID ID: 0009-0004-1400-1263

ABSTRACT

Background: Myopia poses a significant global health challenge. Preventing childhood axial elongation is essential for reducing the lifetime risk of severe ocular complications. Low-dose topical atropine (≤ 0.05%) is a promising intervention, but its optimal concentration and long-term safety profile remain debated.
Aim: To systematically evaluate the efficacy (changes in spherical equivalent refraction [SER] and axial length [AL]) and safety of low-dose topical atropine in slowing childhood myopia.
Materials and methods: A systematic search of the PubMed database was conducted on July 8, 2026, following the PRISMA guidelines. Out of 103 identified records, 46 studies (including 36 randomized controlled trials) evaluating pediatric patients (<18 years) treated with atropine (≤ 0.05%) versus placebo or standard care were included.
Results: Results: Most studies demonstrated a significant deceleration in SER progression and AL elongation with low-dose atropine compared to placebo. Efficacy was dose-dependent, with 0.05% atropine showing superior clinical results over 0.025% and 0.01%, but also a more pronounced rebound effect after discontinuation. Active therapy effectively mitigated rapid progression (≥ 0.50 to 0.75 D/year). Adverse events were mild and transient; photophobia and accommodation paralysis were most common, while allergic conjunctivitis was primarily associated with the preservative benzalkonium chloride (BAK). Systemic complications were exceptionally rare.
Conclusion: Low-dose atropine is a highly effective and safe treatment option. Although a 0.05% concentration offers the highest efficacy, it carries a greater risk of rebound. Lower doses (such as 0.01%) provide an excellent safety profile and minimal rebound effect, ensuring high long-term compliance.

KEYWORDS

Low-Dose Atropine, Childhood Myopia, Myopia Progression, Axial Length, Safety, Rebound Effect

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1. Introduction

Myopia has become one of the fastest-growing causes of visual impairment worldwide and is now recognized as one of the most important global public health challenges. Epidemiological projections estimate that by 2050, nearly 50% of the world's population will be affected by myopia, while approximately 10% will develop high myopia, substantially increasing the risk of irreversible ocular complications, including retinal detachment, myopic macular degeneration, glaucoma, cataracts, and permanent vision loss [1]. Consequently, the socioeconomic burden associated with myopia is expected to increase considerably owing to rising healthcare costs, reduced quality of life, and productivity losses. In response to this rapidly growing prevalence, the International Myopia Institute (IMI) has identified childhood myopia control as one of the major priorities in contemporary ophthalmology and has emphasized the importance of early interventions aimed at reducing excessive ocular growth [2].

The development of childhood myopia is multifactorial and results from a complex interaction between genetic susceptibility and environmental influences. Although parental myopia remains one of the strongest predictors of disease development, environmental and behavioral factors have become increasingly important contributors to the current myopia epidemic. Prolonged near work, intensive educational demands, increased digital screen exposure, and insufficient time spent outdoors have all been associated with accelerated myopia progression [2–4]. In particular, a systematic review and meta-analysis demonstrated that increased outdoor activity is associated with a significantly lower risk of myopia onset and may also contribute to slowing disease progression [4]. These environmental factors are believed to alter retinal signaling pathways that regulate ocular growth, ultimately promoting excessive axial elongation. As axial length is the principal structural determinant of pathological myopia, preventing excessive axial elongation during childhood is considered essential for reducing the lifetime risk of vision-threatening complications [2,3].

Current strategies for myopia control include pharmacological treatment, optical interventions, and behavioral modifications. Among these approaches, low-dose topical atropine has emerged as the most extensively investigated pharmacological strategy for slowing myopia progression in children. Although atropine is traditionally known as a nonselective muscarinic receptor antagonist producing cycloplegia and mydriasis, accumulating evidence indicates that its antimyopic effects extend beyond accommodation paralysis. Experimental and clinical studies suggest that atropine may modulate retinal neurotransmission, influence dopamine-mediated retinal signaling, affect scleral extracellular matrix remodeling, and regulate ocular growth pathways responsible for axial elongation [2]. Importantly, the use of low atropine concentrations substantially reduces treatment-related adverse effects while maintaining clinically meaningful efficacy, making long-term therapy more acceptable for pediatric patients.

The efficacy of low-dose atropine has been confirmed in several landmark randomized clinical trials. The Atropine for the Treatment of Myopia (ATOM) studies demonstrated that 0.01% atropine effectively slowed myopia progression while producing fewer adverse effects and a smaller rebound phenomenon after treatment cessation than higher concentrations [5]. More recently, the Low Concentration Atropine for Myopia Progression (LAMP) study provided robust evidence of a dose-dependent treatment response. The initial randomized clinical trial demonstrated that 0.05% atropine produced the greatest reduction in both spherical equivalent (SER) progression and axial elongation compared with 0.025%, 0.01%, and placebo [6]. Three-year follow-up data further confirmed the superior efficacy of continuous treatment with 0.05% atropine and highlighted the importance of maintaining therapy to minimize disease progression, while also demonstrating that treatment cessation may result in a rebound effect, particularly in younger children [7]. More recently, long-term observational data have confirmed the sustained effectiveness and acceptable safety profile of low-doseatropine during prolonged treatment, supporting its role as a cornerstone of modern myopia control strategies [8].

Despite the rapidly expanding evidence base, several important clinical questions remain unresolved. Although numerous clinical studies have evaluated different low-dose atropine regimens, uncertainty persists regarding the optimal concentration that provides the best balance between efficacy and safety, the appropriate duration of treatment, long-term tolerability, rebound after treatment cessation, and the applicability of current findings to populations beyond those predominantly represented in Asian clinical trials [5,7,8]. Furthermore, substantial heterogeneity among published studies with respect to atropine concentration, participant characteristics, follow-up duration, treatment protocols, and reported adverse events complicates the direct comparison of outcomes and limits the development of universally accepted clinical recommendations. These limitations highlight the need for a comprehensive synthesis of the available evidence to better define the efficacy and safety profile of low-dose topical atropine for childhood myopia control.

Therefore, the aim of the present systematic review is to comprehensively evaluate the efficacy and safety of low-dose topical atropine in slowing myopia progression in children. Specifically, we summarize the current evidence regarding its effects on spherical equivalent refraction, axial length elongation, and treatment-related adverse events across different atropine concentrations while identifying the regimen that provides the most favorable balance between therapeutic efficacy and safety.

2. Research materials and methods

To investigate the impact of low-dose topical atropine on the prevention of myopia progression, a systematic literature search was conducted on July 8, 2026, using the PubMed electronic database.

The following search query was applied.

(("Atropine"[Mesh] OR "atropine"[Title/Abstract] OR "low dose atropine"[Title/Abstract]) AND ("Myopia"[Mesh] OR "myopia progression"[Title/Abstract] OR "short-sightedness"[Title/Abstract]))

As a result of applying this strategy, 108 records were identified. The results were exported to the Rayyan platform, which is dedicated to literature review management and analysis. Using this platform, five duplicates were identified and removed after manual verification by our research team. This process allowed for the identification of 103 unique articlesthat qualified for the next selection stage.

2.1. Participants

The research inclusion criteria were structured based on the PICOS framework (population, intervention, comparison, outcome, and study design) in accordance with the PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses). The selected articles aimed to answer the following research question: "What is the clinical efficacy and safety profile of low-dose atropine (≤0.05%) compared with placebo or standard care in slowing the progression of myopia in children and adolescents?".

The main inclusion criteria were as follows: (1) clinical, cohort, or case-control studies; (2) a pediatric population aged <18 years with a confirmed diagnosis of myopia; (3) documented low-dose topical atropine treatment; (4) inclusion of a control group consisting of myopic children and adolescents receiving placebo or standard care; (5) measurement of spherical equivalent refraction (SER) and/or axial length (AL) changes during treatment; and (6) reporting of adverse event rates and incidence of rapid myopia progression.

The exclusion criteria were as follows: (1) literature reviews, meta-analyses, and case reports; (2) preclinical studies conducted on animal models, as well as works covering adult populations or premyopic patients; and (3) studies evaluating only combined therapies within study cohorts or high-dose atropine (≥0.5%).

2.2. Data collection and analysis

The literature selection process was carried out in multiple stages, strictly following PRISMA guidelines. Initially, a four-person team of independent reviewers assessed the titles and abstracts of 103 articles, examining their compliance with the main objective of the study. To ensure maximum objectivity and minimize systematic error, this stage was conducted independently on the Rayyan platform. Studies that failed to meet the basic assumptions of the PICOS protocol were excluded. The next step involved an independent full-text assessment of the remaining publications by all four authors, based on detailed inclusion and exclusion criteria. Potential disagreements and conflicting assessments were subjected to joint analysis and discussed until a final consensus was reached. Forty-six studies were included in this systematic review. Of these, 36 were randomized controlled trials (RCT).

2.3. Data Extraction

The following data were extracted from the qualified publications: DOI number, first author's name, year of publication, study type, follow-up period, number of participants in the study and control groups, mean age of participants, atropine dosage and administration protocol, type of placebo used within the control cohort, baseline SER (diopters) and AL (mm), mean changes in SER and AL over the study period with standard deviation, presence of fast myopia progression (defined as myopic shift exceeding 0.50 to 0.75 diopters per year), and adverse events (including photophobia, cycloplegia, hypersensitivity reactions, and systemic complications).

3. Research results

3.1. Spherical equivalent refraction changes

Twenty of the forty-six included studies were characterized by a 1-year follow-up period (ranging from 6 months up to 5 years). The predominant atropine dosing regimen included one drop into each eye once daily.

Most studies demonstrated a deceleration in myopia progression within the study cohort compared to the placebo group [6, 9, 12, 16-23, 26, 28, 37, 38, 40, 42, 43, 47, 48, 49, 52, 53]. Notably, six studies reported differences in the mean change in spherical equivalent refraction (SER) depending on the atropine concentration (0.05% vs. 0.025% vs. 0.01%), highlighting the superior clinical efficacy of the highest dose [6, 10, 11, 14, 15, 32]. Furthermore, Chia et al. [24] demonstrated that while low doses of atropine (0.01% and 0.005%) were effective in inhibiting myopia progression and axial length (AL) elongation, the effect of a 0.0025% microdose did not differ significantly from that of placebo. Concurrently, 0.01% atropine therapy was effective among highly myopic patients (greater than -5.00 D) [19].

Two studies have indicated the presence of a significant rebound effect [11, 31] and accelerated progression of myopia following treatment cessation or dose reduction, which was most pronounced at higher concentrations (0.05%). Conversely, an RCT by Lougham et al. [13] and a crossover trial by Wei et al. [39] demonstrated that this effect does not occur after discontinuation of the 0.01% dose.

However, it should be emphasized that the WA-ATOM RCT [25], conducted in children aged 6–16 years (mean age 11.2±1.1), revealed that 0.01% atropine mildly decelerated myopia progression only during the first 18 months. The cumulative outcomes of the study cohort (n = 104) and control cohort (n = 49) after 2 years of treatment and 1 year of observation were ultimately convergent, as discontinuation of the drug induced a significant rebound effect. Similar results in terms of SER and AL measurements after 24 months were also reported by Lee et al. [46], although the authors noted the potential for attrition bias within the placebo group.

The absence of a statistically significant difference between the treatment and control groups was also reported by Chia et al. [31], Hansen et al. (at both 1- and 3-year follow-ups) [29, 30], and Chan et al. [50]. However, the latter emphasized the impact of baseline retinal function (measured via mfERG) on treatment efficacy.

3.2. Axial length changes

In most studies, the direction of changes in axial length was consistent with that of SER [6, 9, 10, 12, 13, 17-23, 26, 27, 31, 32, 34, 36, 40, 42, 43, 47, 48, 51, 52, 53]. Similarly, analyses have indicated a more pronounced clinical effect with higher concentrations of atropine [10, 11, 14, 15, 32]. Furthermore, Hieda et al. [41] noted that the benefit in terms of AL elongation achieved during 2 years of 0.01% atropine treatment was sustained for 1 year post-therapy, in contrast to the observed changes in the SER. A crossover study also found no rebound effect on the inhibition of AL elongation [43]. Concurrently, the WA-ATOM RCT reported similar conclusions for AL changes as for SER [25], while several studies noted only statistically non-significant differences in AL changes between the study cohort and placebo group [29, 30, 38, 50].

3.3. Fast myopia progression

Myopia progresses most rapidly in children aged 7–10 years. To mitigate this progression and monitor changes in visual acuity, researchers have increasingly utilized low-concentration atropine eye drops. Rapid progression, clinically defined as a myopic shift exceeding 0.50 to 0.75 diopters (D) per year, has been reported in 31 of 46 evaluated studies. Indeed, in several trials, a documented progression of ≥0.5 D in preceding years served as a primary eligibility criterion for patient enrollment [6, 9, 16, 17, 19-25, 35, 36, 38, 43, 49, 50, 53].

Furthermore, age remains the most critical risk factor for rapid progression and rate of myopic shift [14]. Recent data confirm that administering 0.01% atropine to pre-myopic children significantly delays the onset and progression of this condition. Trajectory analyses have also established a clear link between choroidal thinning and axial elongation, demonstrating that children with rapid choroidal thinning exhibit accelerated eyeball elongation.

Atropine at a 0.01% concentration effectively inhibits axial elongation, the primary anatomical driver of myopia, by blocking the muscarinic receptors in the retina and sclera. In contrast to higher concentrations, 0.01% atropine achieves this therapeutic effect without causing clinically significant cycloplegia (accommodation paralysis) or mydriasis (pupil dilation). Consequently, pediatric patients can comfortably read, study, and perform their daily activities without experiencing photophobia.

However, discontinuing therapy often triggers a rebound effect, resulting in the resurgence of rapid myopic progression and necessitating reintroduction of the drug. A strong association was observed between treatment cessation in the third year and the recurrence of rapid progression; as many as 87.9% of children (94 out of 107) who discontinued the drops exhibited a rebound of ≥0.50 D/year, requiring the reinitiation of treatment in Phase 4. A younger age was strongly correlated with a higher risk of rapid recurrence [10]. Long-term, multi-year analyses confirm that while treatment discontinuation leads to accelerated progression (particularly in younger cohorts), the cumulative therapeutic benefit achieved during the first two years of therapy is still partially preserved compared to that in untreated controls [11].

3.4. Safety and side effects

Throughout the reviewed clinical trials, mild side effects associated with low-dose atropine were observed in subsets of patients. The most prevalent adverse event reported in pediatric cohorts was photophobia, which was documented in 27 of 46 studies [6, 10-15, 19-21, 23, 24, 27, 29-33, 33, 40-42, 44-51, 49, 51, 52]. This phenomenon stems from the temporary paralysis of the pupillary sphincter muscle, which leads to mydriasis and subsequent excessive light entry into the eye, particularly in bright environments. The second most common side effect was cycloplegia (accommodation paralysis), driven by the antagonistic action of atropine on muscarinic receptors within the ciliary body [6, 10-15, 20, 24, 41, 44-49,52]. Blocking these receptors impairs the eye's ability to focus on near objects, resulting in near-vision blurriness.

Among the least frequently reported ocular complications was allergic conjunctivitis [6, 10-12, 29-31, 34, 40, 47, 51]. The primary link between eye drop administration and the onset of localized allergy is attributed to the preservative benzalkonium chloride (BAK). BAK exerts irritating and cytotoxic effects on both the tear film and ocular surface; consequently, long-term exposure frequently triggers delayed-type hypersensitivity reactions. Notably, allergic reactions were often observed at similar rates in both the active treatment and placebo groups, as both formulations utilized identical preservative systems. An immediate hypersensitivity reaction to the plant alkaloid itself is a far less common allergic manifestation that can precipitate contact dermatitis of the eyelids and acute conjunctivitis.

Finally, systemic complications severe enough to warrant hospitalization were exceptionally rare, being documented in only one of the analyzed studies [47], which underscores the robust systemic safety profile of low-dose atropine therapy in children.

4. Discussion

The present systematic review indicates that low-dose topical atropine can reduce childhood myopia progression, although the magnitude of the effect varies according to the atropine concentration, participant characteristics, and study methodology. In most studies, a slower progression of spherical equivalent refraction was accompanied by reduced axial elongation. The most consistent efficacy was observed with 0.05% atropine, whereas the effects of 0.01% atropine were heterogeneous. Treatment was generally well tolerated; however, uncertainty remains regarding the optimal concentration, duration of therapy, and risk of disease progression after discontinuation.

A concentration-dependent response was observed, which was one of the most consistent findings. In the first phase of the LAMP trial, 0.05% atropine provided greater control of SER progression and AL elongation than 0.025%, 0.01%, and placebo solutions [6]. This relationship was maintained in subsequent phases and secondary analyses of the LAMP program [10, 14, 15, 32]. Therefore, concentrations collectively classified as low doses should not be considered therapeutically equivalent, and findings obtained for 0.01% atropine should not be directly extrapolated to higher concentrations of atropine.

However, greater efficacy does not necessarily make 0.05% atropine optimal for every child. Higher concentrations may cause more pronounced changes in the pupil diameter and accommodation, leading to photophobia or near-vision difficulties. Although these effects are usually mild and do not result in treatment discontinuation, they may affect adherence during long-term therapy. Conversely, the favorable tolerability of 0.01% atropine is clinically relevant only if this concentration provides adequate control of disease progression in children. Therefore, the choice of concentration should balance efficacy, tolerability, and the feasibility of prolonged daily treatment.

The efficacy of 0.01% atropine was notably heterogeneous across the studies. Several studies have demonstrated significant reductions in SER progression and AL elongation [16, 19–23, 36, 43,52], whereas other trials have reported modest, inconsistent, or nonsignificant effects compared with placebo [25, 29, 30, 46, 50]. In the WA-ATOM study, the treatment effect was modest, and the differences between the atropine and placebo groups were attenuated during the washout period [25]. In the Danish trial, continuous treatment with 0.01% atropine did not produce a sustained benefit over placebo after two years of treatment and a subsequent one-year washout period [29, 30]. Limited efficacy was also observed in an Australian randomized trial [46]. In contrast, Chan et al. found that the response may depend on baseline electroretinal characteristics [50].

Differences in participant age, baseline progression, adherence, atropine formulation, follow-up duration, environmental exposure, and outcome assessment may contribute to the varying efficacy of 0.01% atropine. Although several Asian trials reported significant treatment effects, neutral or modest findings were observed in some European and Australian populations. These discrepancies should not be automatically attributed to ethnicity because geographical populations also differ in educational exposure, near-work intensity, time spent outdoors, age at myopia onset, and baseline progression. In addition, study protocols and atropine formulations were not uniform. Therefore, the present evidence does not allow the independent contribution of ethnicity or any other single factor to be established.

Age appears to modify treatment response. The LAMP analyses demonstrated that younger children generally had a poorer response to the same atropine concentration than older children [14]. Younger participants required 0.05% atropine to achieve a reduction in progression comparable to that observed in older children receiving lower concentrations. Residual progression during therapy should not necessarily be interpreted as a complete absence of effect, particularly in younger children with a high underlying progression rate. Nevertheless, such patients may require closer monitoring and, after adherence and measurement reliability have been verified, consideration of a higher concentration.

Pretreatment progression should also be considered when evaluating treatment effects. Several studies enrolled children with documented progression of at least 0.50 or 0.75 D/year. However, rapid progression was not consistently defined and was sometimes used as an eligibility criterion rather than an outcome. Consequently, the prevalence of rapid progression and proportion of responders cannot be directly compared across studies. Standardized definitions incorporating both annual SER progression and axial elongation will improve the comparability of future trials.

Changes in the AL were generally consistent with changes in the SER, supporting the effect of atropine on structural ocular growth. However, the outcomes were not consistently concordant. In the ATOM-J follow-up, post-treatment changes in SER and AL did not differ significantly between the previous atropine and

placebo groups, whereas the reduction in axial elongation achieved during treatment remained detectable after discontinuation [37,43]. The SER is influenced not only by the axial length but also by the cornea and crystalline lens. Changes in these structures may partly explain the differences between SER and AL outcomes, although their contributions remain uncertain [48,53]. Asexcessive axial elongation is associated with future myopia-related complications, AL should be assessed alongside cycloplegic SER whenever possible.

The rebound phenomenon remains uncertain. In the LAMP programme, children assigned to treatment withdrawal progressed more rapidly than those who continued therapy, with a greater rebound response among younger children and after higher concentrations [7,10]. In contrast, Hieda et al. did not find a significant difference in post-treatment SER progression or AL elongation between children previously receiving 0.01% atropine and placebo [37]. Wei et al. also reported no clinically relevant rebound after discontinuing 0.01% atropine [39]. Rebound is therefore not an inevitable consequence of withdrawal and may depend on concentration, age at cessation, previous treatment duration, and underlying progression.

The renewed progression after treatment withdrawal may represent either a true rebound or loss of the suppressive treatment effect. Without a concurrent untreated control group, these phenomena cannot be reliably distinguished. The high proportion of children requiring retreatment in the long-term LAMP follow-up demonstrates that clinically relevant progression may recur [10], but it does not prove a pharmacological rebound in all patients. Therefore, continued monitoring after treatment discontinuation is justified, particularly in younger children and those with a history of rapid progression.

The safety findings were generally reassuring. Photophobia, mydriasis, and reduced accommodative amplitude were the most frequently reported ocular effects [6,13,19,20,45,46,52]. These effects were generally mild. In MOSAIC2, blurred near vision and photophobia were more frequent among participants receiving 0.05% atropine during the third year than among participants following the other evaluated regimens, but these adverse effects did not result in treatment discontinuation [13]. Importantly, photophobia was also reported with 0.01% atropine and should not be considered absent at this concentration. In the study by Cui et al., photophobia in bright sunlight occurred with both 0.01% and 0.02% atropine but could usually be managed with sunglasses or a sun hat [52]. Pupil parameters may also return to baseline after treatment cessation [45].

Allergic conjunctivitis and other ocular surface reactions were less frequent. Similar rates in the active treatment and vehicle groups in some studies suggest that preservatives or other formulation components may have contributed to this. However, the available evidence does not establish benzalkonium chloride as the primary cause. No consistent signal of serious treatment-related systemic toxicity was identified; however, heterogeneous reporting, limited sample sizes, and relatively short follow-up periods do not allow for the exclusion of rare or delayed adverse effects.

These findings do not justify the identification of a single optimal concentration for all children in this age group. Atropine 0.05% demonstrated the most consistent efficacy, whereas 0.01% was better tolerated but produced a less predictable response. Treatment selection should consider age, baseline SER and AL, pre-treatment progression, response to therapy, adverse effects, and adherence. Persistent progression should prompt verification of adherence and measurement reliability before modifying the regimen. Treatment cessation should be followed by continuous observation.

Several limitations should be acknowledged. The search was restricted to PubMed, potentially omitting eligible studies indexed in other databases. Randomized and non-randomized studies were included in the same qualitative synthesis despite their different susceptibility to bias. The studies were also heterogeneous in concentration, formulation, dosing schedule, participant characteristics, follow-up duration, and outcome definitions. No meta-analysis was performed, and the absence of a formal risk-of-bias assessment limits the evaluation of the certainty of evidence. In addition, several publications represented subsequent phases or secondary analyses of the same trial programs, particularly LAMP, and should not be interpreted as independent patient populations.

In conclusion, low-dose topical atropine can reduce childhood myopia progression; however, its efficacy is concentration-dependent and heterogeneous. Atropine 0.05% provides the most consistent control of SER progression and axial elongation, whereas 0.01% is generally better tolerated but does not produce uniform responses. The risk of renewed progression after withdrawal appears to depend on the concentration, age, and natural course of myopia. Current evidence supports individualized treatment accompanied by regular assessment of cycloplegic SER, axial length, and tolerability and adherence. Further long-term randomized trials using standardized definitions of treatment response and rebound are required to determine the optimal duration of therapy and discontinuation strategies.

5. Conclusions

Low-dose topical atropine can reduce childhood myopia progression, although the magnitude and consistency of its effects vary according to the atropine concentration, participant characteristics, and study design. Most of the included studies reported slower spherical equivalent refractive progression during treatment than that with placebo or standard care. The response was generally concentration-dependent, with 0.05% atropine providing the most consistent control of SER progression in the study. Atropine 0.01% was effective in several studies, but modest or nonsignificant effects were also reported, indicating that its efficacy is not uniform across populations and in individual patients.

Changes in axial length generally followed the same direction as changes in SER, supporting an effect of atropine on structural ocular growth. Nevertheless, refractive and axial outcomes were not invariably concordant, emphasizing the importance of assessing both cycloplegic SER and AL when monitoring treatment response. Several studies have included children with previously documented rapid progression and reported reduced progression during atropine treatment. However, definitions of rapid progression varied from 0.50 to 0.75 D/year, and the designs of these studies differed. Therefore, the magnitude of the treatment effect in fast progressors cannot be compared directly across the available studies.

The risk of renewed progression after treatment withdrawal varied among the atropine concentrations and study populations. A more pronounced rebound was observed in some studies involving higher concentrations and younger children, whereas several trials did not demonstrate a clinically relevant rebound after the discontinuation of 0.01% atropine. Therefore, renewed progression should not be considered an inevitable pharmacological rebound. Nevertheless, continued monitoring after treatment cessation is necessary, particularly in younger children and those with a history of rapid progression.

Low-dose atropine was generally well tolerated by the patients. Photophobia, mydriasis, reduced accommodative amplitude, and blurred near vision were the most frequently reported ocular side effects. These adverse effects are usually mild and transient, although they are generally more pronounced at higher concentrations. Ocular surface reactions were reported less frequently, and the available evidence did not allow their cause to be attributed unequivocally to atropine, preservatives, or other formulation components. No consistent signals of serious treatment-related systemic toxicity were identified. However, heterogeneous adverse event reporting, limited sample sizes, and differences in follow-up duration preclude firm conclusions regarding rare or delayed complications.

Overall, 0.05% atropine demonstrated the most consistent efficacy in controlling both SER progression and axial elongation, whereas 0.01% was generally better tolerated but produced a less predictable therapeutic response. The available evidence does not support an optimal concentration for all children. Treatment should be individualized according to age, pretreatment progression, baseline SER and AL, response to therapy, adverse effects, and adherence. Further long-term randomized trials using standardized definitions of treatment response, rapid progression, and rebound are required to establish the optimal duration of therapy and the most appropriate discontinuation strategies.

Author Contributions:

Conceptualization, W.Ż, K.Ś.; methodology, K.Ś,, J.T, J.S, W.Ż and M.L; validation, K.Ś and W.Ż.; formal analysis, K.Ś, W.Ż; resources, K.Ś, J.T, J.S, W.Ż and M.L.; data curation,K.Ś, J.T, J.S, W.Ż, M.L; writing—original draft preparation, K.Ś, J.T, J.S, W.Ż. and M.L.; writing—review and editing, K.Ś; visualization, K.Ś, J.T, J.S, W.Ż and M.L.; supervision, K.Ś and W.Ż.; project administration, K.Ś and W.Ż .; funding acquisition, K.Ś, W.Ż. , J.T., J.S, M.L. All authors have read and agreed to the published version of the manuscript.

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