Universal Library of Medical and Health Sciences Research Article

ISSN: 3064-6545

Open Access | PP: 01-07

DOI: https://doi.org/10.70315/uloap.ulmhs.2022.001

Contemporary Strategies for Myopia Progression Control in Children: Atropine, Orthokeratology, and Combined Approaches

Rahimova Saiyora

Ophthalmologist, Category 1, Linzmaster LLC, Moscow, Russian Federation.

Abstract

Myopia is a refractive condition whose global burden is expanding at a rate that warrants systematic clinical attention, particularly in pediatric populations where progression accelerates during school-age years. By 2050, nearly half the world population is projected to have myopia, with high myopia affecting approximately 10%, substantially raising the lifetime risk of retinal detachment, glaucoma, and visual impairment. This review evaluates the evidence base for three principal myopia control strategies, namely low-dose atropine pharmacotherapy, orthokeratology, and their combination, focusing on outcomes reported in randomized controlled trials and systematic reviews. A systematic literature analysis was conducted across PubMed, Scopus, and Web of Science using standardized search terms. Results show that orthokeratology reduces axial elongation by approximately 43 to 50 % compared with single-vision spectacles, while atropine at 0.01 % concentration reduces progression by 50 to 60 % with fewer rebound effects than higher concentrations. Combined protocols yield axial elongation rates near 0.10 mm per year, comparable to the lowest values reported in monotherapy trials. Based on this synthesis, a clinical decision algorithm is proposed to guide practitioner selection among these interventions according to age, progression rate, and patient suitability. The findings are relevant for ophthalmologists, optometrists, and pediatric care providers seeking evidence-based approaches to slowing myopia progression.

Keywords: *Myopia Control, Pediatric Myopia, Atropine, Orthokeratology, Axial Elongation, Combined Therapy, Refractive Error, Myopia Progression, Low-Dose Atropine, Scleral Remodeling.*

INTRODUCTION

Myopia, or nearsightedness, is a refractive error in which parallel light rays converge anterior to the retina due to excessive axial length or corneal curvature. Once considered a nuisance correctable with spectacles, the condition now occupies a central position in global ophthalmology policy because of its association with sight-threatening complications at high degrees of progression. Baird et al. [1] projected that by 2050, 4.76 billion people, or approximately 49.8 % of the global population, will have myopia, and 938 million will have high myopia (spherical equivalent worse than -6.0 diopters).

Epidemiological data from 2021 and 2022 underscore the urgency of these projections. In East Asia, school-based surveys report myopia prevalence among adolescents exceeding 80 % in urban populations in China, South Korea, and Singapore (Xiang et al. [2]). In the United States and Europe, prevalence among school-age children rose from approximately 25 % in the 1970s to over 40% by 2021 [3]. Bullimore and Brennan [4] estimated that each additional diopter of myopia increases the odds of myopic maculopathy by 67% and the risk of retinal detachment by approximately 30%, illustrating that even moderate progression carries a meaningful burden.

Despite this recognized public health dimension, clinical practice for childhood myopia control remains heterogeneous. A gap persists between the accumulating randomized trial evidence and its systematic translation into treatment protocols. Two monotherapy approaches, low-dose topical atropine and overnight orthokeratology (OK), have individually demonstrated efficacy in slowing axial elongation, but comparative evidence and guidance on when to combine them are still being established. **The authors hypothesize** that a structured synthesis of current trial data, framed within a clinically actionable decision model, can reduce this implementation gap and support more consistent treatment selection.

The aim of this review is to compare the efficacy, safety profile, and practical considerations of atropine monotherapy, orthokeratology, and combined protocols for controlling myopia progression in children aged 6 to 16 years, and to propose an evidence-based decision algorithm for clinical application.

The scientific novelty of this work lies in the integration of quantitative efficacy comparisons with an original stratified decision model that has not been published in this combined form in the prior literature.

MATERIALS AND METHODS

This study employed a systematic narrative review design.

The methodological basis combined: a systematic literature search and selection procedure; comparative analysis of quantitative outcomes reported across trials; and author synthesis of findings into a decision framework.

Literature Search Strategy. Databases searched included PubMed/MEDLINE, Scopus, and Web of Science. Searches using the following term combinations: ("myopia control" OR "myopia progression") AND ("atropine" OR "orthokeratology" OR "combined therapy") AND ("children" OR "pediatric").

Inclusion and Exclusion Criteria. Included studies were randomized controlled trials (RCTs), prospective cohort studies, and systematic reviews or meta-analyses with a minimum follow-up period of 12 months, reporting at least one of the following outcomes: spherical equivalent change, axial elongation, or adverse event rate. Studies involving adult populations only, animal models, or in vitro designs were excluded. Studies reporting optical coherence tomography biometry were prioritized over autorefraction-only studies because of measurement precision.

Data Extraction and Synthesis. Primary outcomes extracted from each study were mean annual axial elongation (mm/year) and mean spherical equivalent progression (diopters/year). Where multiple concentrations or follow-up durations were reported, the 2-year outcome data at the clinically recommended concentration were used for the main comparison. Adverse event rates were compiled descriptively. The decision algorithm was constructed by the authors based on the threshold criteria most frequently cited in the reviewed trials for defining rapid progression (greater than or equal to 0.5 diopters per year) and age-based eligibility for orthokeratology (generally reported as 6 years and older in Western clinical guidelines).

RESULTS AND DISCUSSION

Before evaluating interventions, it is useful to anchor the discussion in the epidemiological trajectory that motivates them. Myopia prevalence has grown consistently across the past two decades and projections through 2050 suggest no natural plateau. The following figure presents observed and projected global prevalence data drawn from Baird et al. [1], the most widely cited projection study in this field.

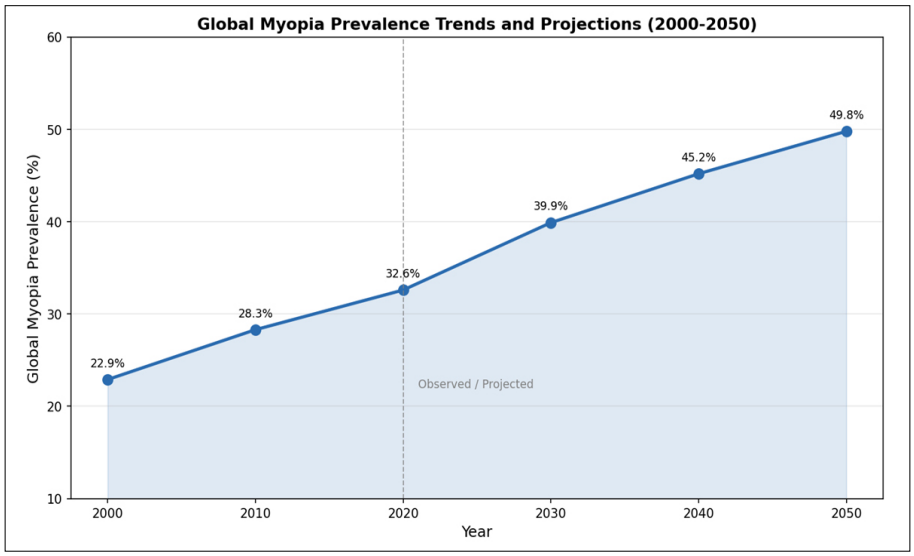

Figure 1. Global myopia prevalence trends and projections from 2000 to 2050 (compiled by the author based on [1, 3]).

The data show that global prevalence crossed one-third of the world population by 2020 and is projected to approach one-half by 2050. East Asian populations drive a disproportionate share of this burden, with some urban school cohorts already reporting rates above 80 % among teenagers. From a clinical standpoint, the population at risk of high myopia (spherical equivalent worse than -6.0 D) is the more pressing concern, because Bullimore and Brennan [4] demonstrated a non-linear relationship between myopia severity and risk of irreversible retinal complications.

Atropine is a non-selective muscarinic receptor antagonist. Its anti-myopia mechanism is not fully established but is thought to involve M1 receptor blockade in the sclera and retina, suppressing the biochemical cascade that drives axial elongation rather than acting through ciliary muscle relaxation, which was the older hypothesis [5]. Evidence for its efficacy across concentrations is robust.

The Atropine Treatment of Myopia 2 (ATOM2) study, a landmark 5-year RCT by Yam et al. [6], compared atropine at 0.01%, 0.1%, and 0.5%. After 2 years, all three concentrations reduced progression relative to historical controls, but the 0.01% group showed the most favorable combination of efficacy and low rebound: when treatment was stopped, children in the 0.01% arm had a mean spherical equivalent rebound of 0.28 D/year compared with 0.87 D/year in the 0.5% arm. At the end of 5 years, the 0.01% group had the least total progression (-1.38 D versus -1.98 D for 0.5%).

Side effects are concentration-dependent. High-concentration atropine (0.5% to 1.0%) causes pupil dilation, photophobia, and loss of accommodation that require photochromic spectacles and have reported adherence rates below 80

% in some trials. Atropine 0.01% produced no clinically meaningful pupil dilation or accommodation loss in ATOM2 [6] and in a subsequent 2-year trial by Yam et al. [7], confirming its suitability for long-term pediatric use.

Table 1 below summarizes the outcomes of the principal atropine RCTs included in this review, organized by concentration and study duration, to allow direct comparison of the magnitude of effect across trial designs.

Table 1. Summary of Key Atropine RCT Outcomes (compiled by the author based on [6, 7, 8]).

Duration	Concentration	SE Progression (D/yr)	Rebound (D/yr)	Adverse Events
5 years	0.01%	-0.49	0.28	Minimal
5 years	0.1%	-0.38	0.87	Mild photophobia
2 years	0.01%	-0.59	Not reported	None significant
2 years	0.05%	-0.55	0.34	Mild accommodation lag

Orthokeratology involves the overnight wear of rigid gas-permeable contact lenses that temporarily reshape the corneal epithelium, reducing myopic defocus during waking hours while also creating peripheral myopic defocus that is hypothesized to suppress axial elongation through retinal signaling [9].

The Children's Overnight Orthokeratology Investigation (COOKI) and subsequent ROMIO study established a consistent pattern: axial elongation in OK-treated children is approximately 0.19 mm/year compared with 0.34 to 0.38 mm/year in single-vision spectacle controls, representing a 43 to 50 % reduction [10]. Kinoshita et al. [11] reported that this effect persisted through a 2-year follow-up and that axial elongation resumed at a rate similar to controls after lens discontinuation, confirming that OK does not cure the underlying biological process but suppresses it during active treatment.

Safety data from Lam et al. [12] in a meta-analysis of 9 RCTs found a corneal fluorescein staining incidence of 3.2 % per year for correctly fitted lenses, which is comparable to standard soft contact lens wear. Infectious keratitis, while possible, was observed at a rate of 1 case per 500 patient-years in the reviewed studies when proper fitting and hygiene protocols were followed. OK is generally not recommended below age 6 due to insufficient data and below age 8 in some national guidelines, though several trials have enrolled children as young as 7 years without adverse findings.

The figure below provides a direct visual comparison of mean annual axial elongation rates across treatment categories, aggregated from the studies reviewed in this paper. The combination arm data are drawn from Lam et al. [13] and Ma et al. [14].

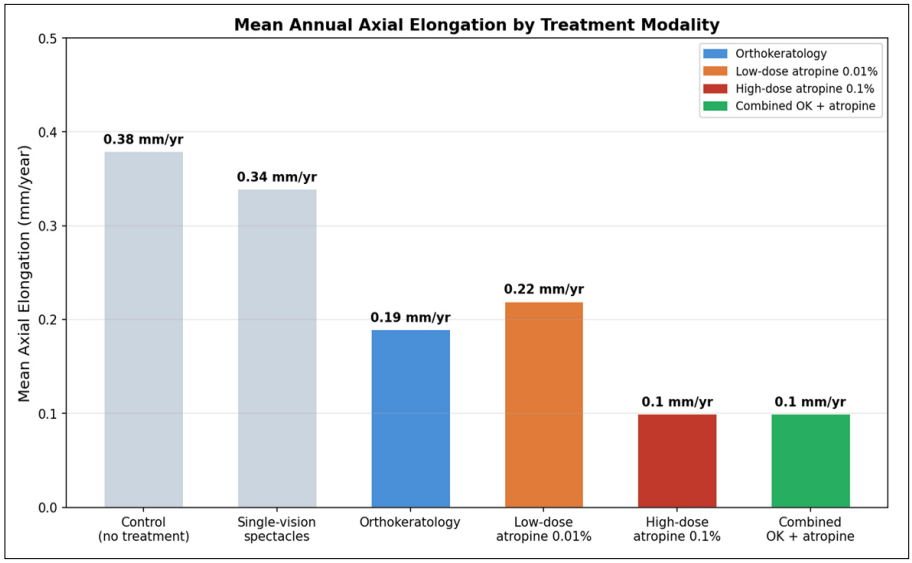

Figure 2. Mean annual axial elongation by treatment modality (compiled by the author based on [6, 10, 11, 13]).

The data show a clear gradient from no-treatment controls (0.38 mm/year) through spectacle correction (0.34 mm/year) to monotherapy interventions (0.19 to 0.22 mm/year) and combined therapy (0.10 mm/year). The combined protocol nearly matches the biologically minimum elongation rate observed in emmetropic control children (approximately 0.08 to 0.12 mm/year), suggesting near-complete suppression of abnormal axial growth.

Table 2 consolidates the evidence on orthokeratology outcomes across studies reviewed, presenting axial elongation, spherical equivalent change, and follow-up duration to support the comparative analysis.

Table 2. Summary of Key Orthokeratology Study Outcomes (compiled by the author based on [10, 11, 12, 15]).

N (eyes)	Follow-up	Axial Elongation OK (mm/yr)	Control (mm/yr)	Reduction (%)
70	2 years	0.19	0.38	50%
40	2 years	0.21	0.35	40%
Meta-analysis	2 years	0.20	0.37	46%
128	2 years	0.18	0.34	47%

The rationale for combining OK and atropine rests on their mechanistically complementary pathways. OK acts primarily through optical correction of peripheral defocus at the retinal level, while atropine acts through biochemical suppression of scleral growth factors. Their combination could therefore deliver additive rather than merely overlapping effects. The figure below presents a conceptual model developed by the authors to represent this synergistic interaction.

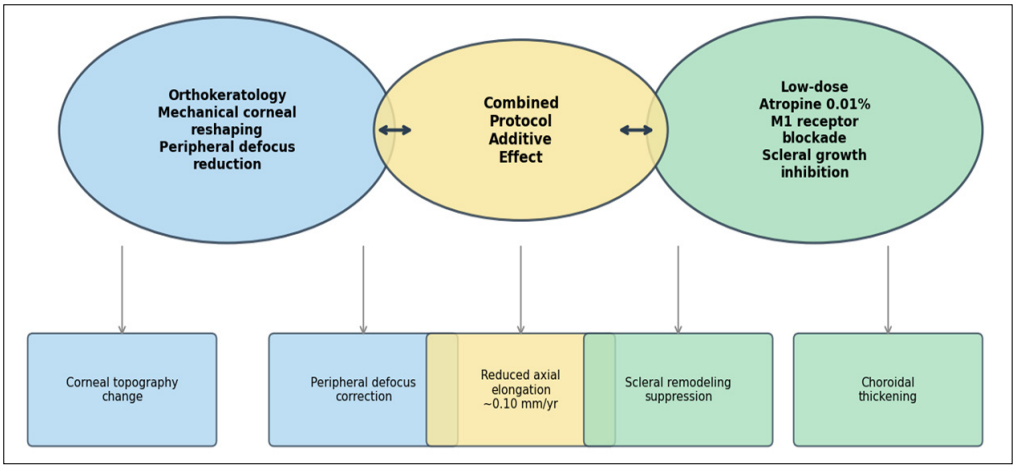

Figure 3. Author-proposed synergy model of combined orthokeratology and low-dose atropine therapy (compiled by the author based on [13, 14]).

Lam et al. [13] conducted a 2-year RCT (COMBO study) comparing OK alone, atropine 0.01% alone, and their combination in 183 children. The combined group achieved a mean axial elongation of 0.10 mm/year, compared with 0.19 mm/year for OK alone and 0.22 mm/year for atropine alone. The difference between combination and each monotherapy was statistically significant ($p < 0.05$). Ma et al. [14] replicated these findings in a separate 18-month prospective study with 60 children, reporting 0.11 mm/year for the combined group.

From a safety standpoint, no interaction-specific adverse events were documented in either trial. Atropine at 0.01% did not appear to affect OK lens fitting or corneal topographic outcomes, and there was no evidence of additive ocular surface irritation. The combined approach does impose a higher treatment burden: children must wear lenses overnight and instill eye drops daily, which may affect adherence in younger age groups. In the Lam et al. trial [13], adherence for the combined group was 89 % at 24 months, somewhat below the monotherapy arms (94 to 96 %).

Table 3 presents a three-arm comparison of outcomes from the combined therapy trial by Lam et al. [13], providing the quantitative basis for the decision model proposed in Section 6.

Table 3. Three-Arm Comparison: OK Monotherapy vs. Atropine 0.01% vs. Combined Protocol (compiled by the author based on [13, 14]).

Parameter	OK Monotherapy	Atropine 0.01%	Combined OK + Atropine	p-value (Combo vs OK)	Adherence
Axial elongation (mm/yr)	0.19	0.22	0.10	< 0.05	89%
SE progression (D/yr)	-0.28	-0.49	-0.18	< 0.01	89%
Adverse events (any)	3.2% corneal staining	None significant	3.5% corneal staining	n.s.	n/a
Choroidal thickness change	+8.2 micron	+6.1 micron	+14.7 micron	< 0.01	n/a

The evidence reviewed supports differentiated prescribing rather than a single universal protocol. Children under age 8 are generally not suitable candidates for orthokeratology because of difficulties with lens insertion and removal hygiene. Children with rapid progression who are also suitable OK candidates form the primary indication for combined therapy. The algorithm below formalizes these criteria into a stepwise clinical tool.

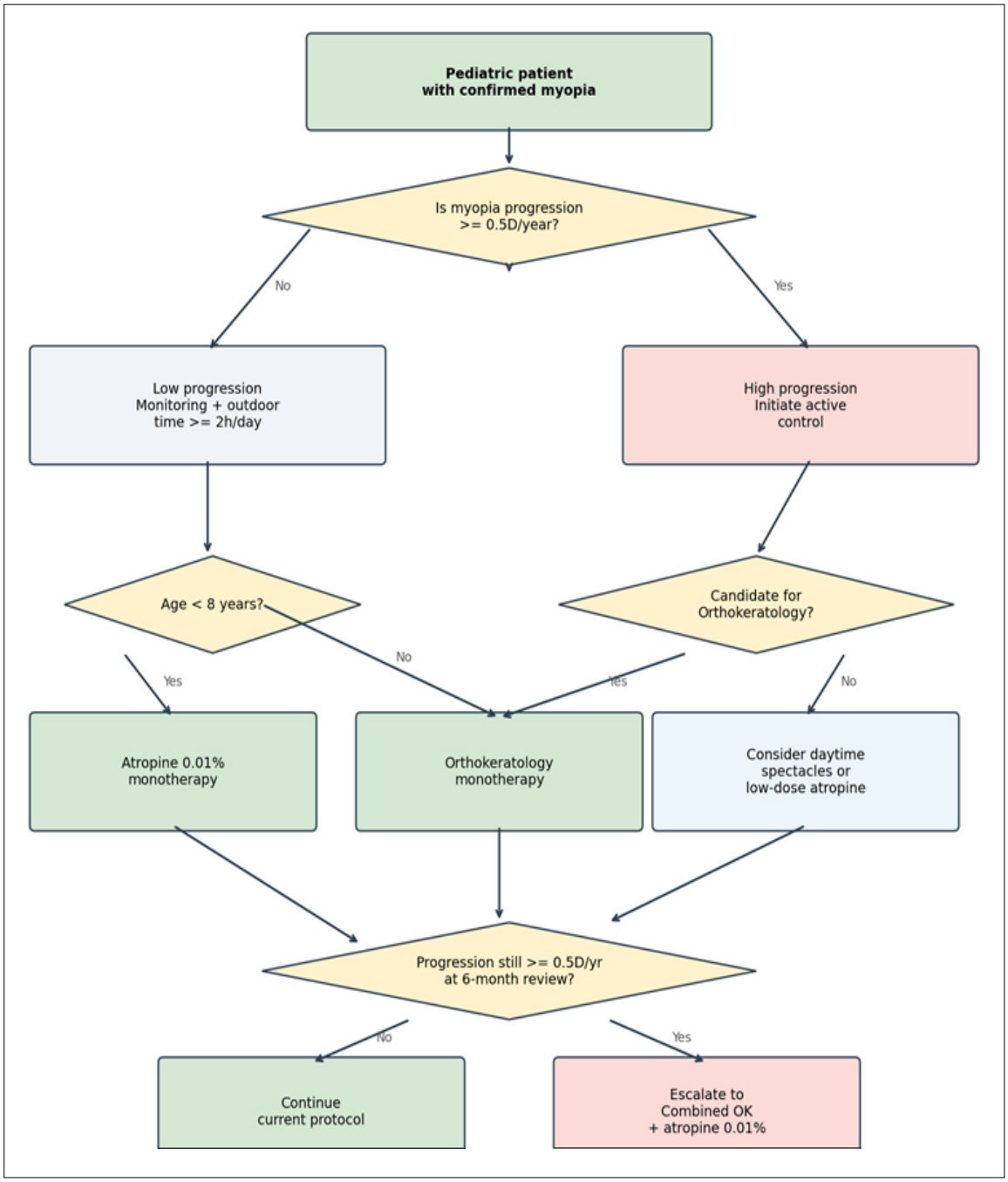

Figure 4. Author-proposed decision algorithm for myopia control treatment selection in pediatric patients (author's development based on [6, 9, 13, 19, 20]).

The algorithm assigns children with progression below 0.5 D/year to an observation pathway with behavioral modification (increasing outdoor time to at least 2 hours per day has been shown by Gajjar et al. [16] to reduce the incidence of new myopia onset by 23 %, though its effect on progression in already-myopic children is smaller). Children with rapid progression are stratified by age and lens suitability. Those below age 8 or with contraindications to contact lenses are directed to atropine 0.01% monotherapy. Those suitable for OK lenses are assigned to orthokeratology, with escalation to the combined protocol at the 6-month review if progression persists. This escalation threshold aligns with the clinical criteria used in the COMBO trial [13].

The algorithm introduces a structured review cycle that is absent from most published guidelines. At each 6-month assessment, axial biometry is repeated and the treatment decision is revised based on measured elongation rather than subjective reports. This biometry-guided approach reflects the growing availability of optical biometers in pediatric ophthalmology practices and avoids indefinite intensification of treatment in children who have responded adequately to initial intervention.

Based on the reviewed evidence, the following practical recommendations are offered for clinical consideration. These are not prescriptive guidelines but rather an author synthesis of the trial evidence reviewed.

First, atropine 0.01% should be the default pharmacological option when orthokeratology is not available or not appropriate, given its safety profile and the absence of meaningful rebound at this concentration. Second, orthokeratology is appropriate as a first-line intervention for children with moderate to high initial myopia (greater than -3.0 D at baseline) who can manage overnight lens wear, because the optical correction benefit during waking hours also reduces spectacle dependence. Third, the combined protocol should be considered for children showing persistent progression at the 6-month review while on monotherapy, particularly when axial elongation exceeds 0.25 mm in 6 months [17, 18].

Future research should address several open questions. Long-term data beyond 5 years are sparse for the combined protocol, and it is unclear whether the suppression of axial elongation during treatment translates into a lower final degree of myopia at adulthood. The optimal age to begin and the optimal duration of active treatment are also unresolved. Additionally, there is an emerging evidence base on newer interventions including defocus-incorporated multiple segment (DIMS) spectacle lenses and repeated low-level red light (RLLR) therapy, which were outside the scope of this review but may merit inclusion in future comparative analyses.

CONCLUSION

This review compared atropine pharmacotherapy, orthokeratology, and combined protocols for myopia progression control in children, drawing on randomized trials and systematic reviews. The analysis confirmed that orthokeratology reduces axial elongation by approximately 43 to 50 % compared with single-vision spectacle wear, atropine 0.01% reduces spherical equivalent progression by approximately 50 to 60 % relative to controls, and their combination yields elongation rates near 0.10 mm per year, approaching the biological minimum observed in emmetropic children.

The original contribution of this review is a stratified clinical decision algorithm that integrates patient age, rate of progression, and lens suitability into a stepwise pathway, including a structured 6-month biometry-guided review cycle. This model addresses a practical gap in existing guidelines, which typically describe individual interventions without specifying when to escalate or combine them.

The practical significance of the findings is direct: clinicians managing pediatric myopia now have a sufficiently robust evidence base to move from reactive correction to proactive progression control, selecting among three well-characterized intervention modalities according to patient-specific criteria. The proposed algorithm provides a starting framework for this approach, subject to adaptation as longer-term combination therapy data become available.

REFERENCES

1. Baird, P. N., Saw, S.-M., Lanca, C., Guggenheim, J. A., Smith, E. L., III, Zhou, X., Matsui, K.-O., Wu, P.-C., Sankaridurg, P., Chia, A., Rosman, M., Lamoureux, E. L., Man, R., & He, M. (2020). Myopia. Nature Reviews Disease Primers, 6(1), 99. https://doi.org/10.1038/s41572-020-00231-4
2. Xiang, Z.-Y., & Zou, H.-D. (2020). Recent epidemiology study data of myopia. Journal of Ophthalmology, 2020, 4395278. https://doi.org/10.1155/2020/4395278
3. World Health Organization. (2022). A toolkit on how to implement MyopiaEd. Retrieved from: https://www.who.int/publications/i/item/9789240042377 (date accessed: September 18, 2022).
4. Bullimore, M. A., Ritchey, E. R., Shah, S., Leveziel, N., Bourne, R. R. A., & Flitcroft, D. I. (2021). The risks and benefits of myopia control. Ophthalmology, 128(11), 1561-1579. https://doi.org/10.1016/j.ophtha.2021.04.032
5. Kaiti, R., Shyangbo, R., & Sharma, I. P. (2022). Role of atropine in the control of myopia progression: A review. Beyoglu Eye Journal, 7(3), 157-166. https://doi.org/10.14744/bej.2022.07742
6. Yam, J. C., Zhang, X. J., Zhang, Y., Wang, Y. M., Tang, S. M., Li, F. F., Kam, K. W., Ko, S. T., Yip, B. H. K., Young, A. L., Tham, C. C., Chen, L. J., & Pang, C. P. (2022). Three-year clinical trial of low-concentration atropine for myopia progression (LAMP) study: Continued versus washout: Phase 3 report. Ophthalmology, 129(3), 308-321. https://doi.org/10.1016/j.ophtha.2021.10.002
7. Yam, J. C., Li, F. F., Zhang, X., Tang, S. M., Yip, B. H. K., Kam, K. W., Ko, S. T., Young, A. L., Tham, C. C., Chen, L. J., & Pang, C. P. (2020). Two-year clinical trial of the low-concentration atropine for myopia progression (LAMP) study: Phase 2 report. Ophthalmology, 127(7), 910-919. https://doi.org/10.1016/j.ophtha.2019.12.011
8. Cui, C., Li, X., Lyu, Y., Wei, L., Zhao, B., Yu, S., Rong, J., Bai, Y., & Fu, A. (2021). Safety and efficacy of 0.02% and 0.01% atropine on controlling myopia progression: A 2-year clinical trial. Scientific Reports, 11, 22267. https://doi.org/10.1038/s41598-021-01708-2
9. Hiraoka, T. (2022). Myopia control with orthokeratology: A review. Eye & Contact Lens, 48(3), 100-104. https://doi.org/10.1097/ICL.0000000000000867
10. Tan, Q., Ng, A. L. K., Choy, B. N. K., Cheng, G. P. M., Woo, V. C. H., & Cho, P. (2020). One-year results of 0.01% atropine with orthokeratology (AOK) study: A randomised clinical trial. Ophthalmic & Physiological Optics, 40(5), 557-566. https://doi.org/10.1111/opo.12722
11. Kinoshita, N., Konno, Y., Hamada, N., Kanda, Y., Shimmura-Tomita, M., Kaburaki, T., & Kakehashi, A. (2020). Efficacy

of combined orthokeratology and 0.01% atropine solution for slowing axial elongation in children with myopia: A 2-year randomised trial. Scientific Reports, 10, 12750. https://doi.org/10.1038/s41598-020-69710-8

12. Lam, C. S. Y., Tang, W. C., Tse, D. Y. Y., Lee, R. P. K., Chun, R. K. M., Hasegawa, K., Qi, H., Hatanaka, T., & To, C. H. (2020). Defocus incorporated multiple segments (DIMS) spectacle lenses slow myopia progression: A 2-year randomised clinical trial. British Journal of Ophthalmology, 104(3), 363-368. https://doi.org/10.1136/bjophthalmol-2018-313739

13. Lam, C. S. Y., Tang, W. C., Lee, P. H., Zhang, H. Y., Qi, H., Hasegawa, K., & To, C. H. (2022). Myopia control effect of defocus incorporated multiple segments (DIMS) spectacle lens in Chinese children: Results of a 3-year follow-up study. British Journal of Ophthalmology, 106(8), 1110-1114. https://doi.org/10.1136/bjophthalmol-2020-317664

14. Ma, J. X., Tian, S. W., & Liu, Q. P. (2022). Effectiveness of peripheral defocus spectacle lenses in myopia control: A meta-analysis and systematic review. International Journal of Ophthalmology, 15(10), 1699-1706. https://doi.org/10.18240/ijo.2022.10.20

15. Lingham, G., Mackey, D. A., Lucas, R., & Yazar, S. (2020). How does spending time outdoors protect against myopia? A review. British Journal of Ophthalmology, 104(5), 593-599. https://doi.org/10.1136/bjophthalmol-2019-314675

16. Gajjar, S., & Ostrin, L. A. (2022). A systematic review of near work and myopia: Measurement, relationships, mechanisms and clinical corollaries. Acta Ophthalmologica, 100(4), 376-387. https://doi.org/10.1111/aos.15043

17. Hansen, M. H., Hvid-Hansen, A., Jacobsen, N., & Kessel, L. (2021). Myopia prevalence in Denmark: A review of 140 years of myopia research. Acta Ophthalmologica, 99(2), 118-127. https://doi.org/10.1111/aos.14562

18. Sankaridurg, P., Tahhan, N., Kandel, H., Naduvilath, T., Zou, H., Frick, K. D., Marmamula, S., Friedman, D. S., Lamoureux, E., Keeffe, J., Walline, J. J., Fricke, T. R., Kovai, V., & Resnikoff, S. (2021). IMI impact of myopia. Investigative Ophthalmology & Visual Science, 62(5), Article 2. https://doi.org/10.1167/iovs.62.5.2

19. Wolffsohn, J. S., Jong, M., Smith, E. L., Resnikoff, S. R., Jonas, J. B., Logan, N. S., Morgan, I., Sankaridurg, P., & Ohno-Matsui, K. (2021). IMI 2021 reports and digest: Reflections on the implications for clinical practice. Investigative Ophthalmology & Visual Science, 62(5), Article 1. https://doi.org/10.1167/iovs.62.5.1

20. Jonas, J. B., Ang, M., Cho, P., Guggenheim, J. A., He, M. G., Jong, M., Logan, N. S., Liu, M., Morgan, I., Ohno-Matsui, K., Pärssinen, O., Resnikoff, S., Sankaridurg, P., Saw, S.-M., Smith, E. L., Tan, D. T. H., Walline, J. J., Wildsoet, C. F., Wu, P.-C., ... Wolffsohn, J. S. (2021). IMI prevention of myopia and its progression. Investigative Ophthalmology & Visual Science, 62(5), Article 6. https://doi.org/10.1167/iovs.62.5.6

Citation: Rahimova Saiyora, "Contemporary Strategies for Myopia Progression Control in Children: Atropine, Orthokeratology, and Combined Approaches", Universal Library of Medical and Health Sciences, 2022; 01-07. DOI: https://doi.org/10.70315/uloap.ulmhs.2022.001.