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Slowing Myopia Progression in European Children with Cylindrical Annular Refractive Elements (CARE)- Zeiss or Hoya- or Use of Atropine Eye Drops: A Comprehensive Review

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ABSTRACT

Several studies have been carried out during the last decade with the purpose of evaluating the efficacy of myopia control spectacle lens (DIMS) at slowing the progression of myopia in populations of European children in comparison with 0.01% atropine eye drops or a combination of the two methods (Figure 1). The following comprehensive review focuses on presenting the results of these studies and on examining the statistical accuracy of their measurements. Most of the studies analyzed included participants aged 6-13 years old with typically high spherical equivalent refractive error (SE) from -0.75 D to -5.00 D that were randomly selected and divided into groups. Three categories of patients could be distinguished: those wearing single vision (SV) spectacle lens and those wearing CARE and CARE S spectacles. Cycloplegic SE and axial length were measured at 6-months intervals. The general findings of their research can be summarized in the conclusion that CARE and CARES spectacle lenses can slow myopia progression (statistically significant result) compared to single vision lenses. Finally, eye disorders such as strabismus, cataracts or myopia, are prevalent in many genetic syndromes e.g. Fragile X syndrome, Marfan's, Prader Willi syndrome, therefore a special screening process should be modulated in this population group. In other words, the syndromes mentioned above constitute distinct risk factors for the acceleration of myopia in young adults.

Abbreviations: SV: Single Vision; SER: Spherical Equivalent Refraction; AL: Axial Length; PPSL: Peripheral Plus Spectacles; SVLs: Single Vision Spectacles; MFSCL: MULTIFOCAl SoE Contact Lenses; LDA: Low-Dose; tDCS: Transcranial Direct Current Stimulation; TMS: Transcranial Magnetic Stimulation; VR: Virtual Reality; EK: Exposure Keratopathy; ITT: Intention-To-Treat; SER: Spherical Equivalent Refraction; DIMS: Defocus Incorporated Multiple Segments

Figure 1: A European child wearing spectacle lenses to slow down myopia progression.

Introduction

Different epidemiological studies have shown that myopia is an established risk factor for a number of ocular pathologies, including cataract, glaucoma and retinal detachment (Flitcroh 2012). Although myopia-related complications can occur irrespective of age and degree of myopia (Dhakal 2018), the excessive axial elongation associated with higher degrees of myopia causes biomechanical stretching of the outer coat of the eye, increasing the risk of sight-threatening pathologies such as posterior staphyloma and myopic maculopathy (Saw 2005; Verkicharla 2015). A meta-analysis of population studies reporting blindness and visual impairment due to myopic maculopathy (Fricke 2018), estimated that in 2015, approximately 10 million people had visual impairment due to myopic macular degeneration, of whom 3 million were blind. Although the sight-threatening pathologies associated with myopia usually occur later in life, the underlying myopia develops during childhood and therefore interventions to reduce the progression of myopia have the potential to reduce future visual impairment [1]. Refractive errors, particularly myopia, are increasing globally (especially in young children and adolescents) prompting extensive research into the deceleration or even interception of its rapid evolution and progression. This study examines children aged between 5-16 years old and aims in evaluating the efficacy of different methodology's application in slowing down myopia progression.

The results are contextualized using existing literature to strengthen interpretation and relevance. A significant key point to consider is the association between systemic parameters and refractive errors in children and adolescents. According to several studies findings myopic individuals tend to have higher body mass index and diastolic pressure measurements compared to their emmetropic counterparts. This observation lines with the assumption that elevated BMI can lead to increased BP, which may subsequently raise IOP, potentially affecting ocular anatomy and contributing to refractive errors such as myopia. On the other hand, intraocular pressure and systolic blood pressure measurements do not differ significantly between case and control groups. According to some studies, intraocular pressure was significantly higher in females, potentially due to hormonal influences or differences in corneal biomechanics. Even normal range IOP can increase glaucoma risk in myopic individuals, underscoring the importance of routine monitoring. As a fact, early-life metabolic influences can lead to more prominent variations in weight and BMI among younger adolescents. During this age period, the interaction among refractive errors, IOP, BP, and BMI becomes increasingly complex due to the physiological changes of puberty, shifts in metabolism and modifications of daily habits. Emerging studies have shown that adolescents with refractive errors often exhibit higher values of IOP, BP and BMI compared to their emmetropic counterparts.

Overall, these trends support the integration of cardiovascular and ocular assessments in early myopia screening and prevention strategies. Combined therapy (which translates into use of atropine drops and application of spectacle lenses in a child simultaneously) is more effective in controlling or slowing down low and initial stages of myopia in younger children. The decision-making strategies are greatly relied on the age of the child, more specifically, the time limit of 4-5 years is the most determining period for intervention, since the greatest part of refractive error measurements have been established by this age. This comprehensive review examines the progression of myopia in children and adolescents aged between 6-18 years and follows the evolution of the disease after applying 0.01% eyedrops in both eyes, DIMS (Hoya, MiyoSmart) spectacles and combined atropine and DIMS or single-vision spectacle lenses. By gathering different and diverse data from studies who have observed this evolution with measurements of key outcome variables like cycloplegic autorefraction, spherical equivalent refraction (SER) and axial length (AL), it arrives at valid conclusions concerning the advancement of myopia in this age group and it estimates in a retrospective manner the efficacy of each treatment methodology.

Most of these studies use the time spectrum of three, six and twelve months as more representative and appropriate for following up these cases and for evaluating the outcome of myopia evolution after receiving the three options of therapy mentioned before. For this purpose, real life examples from children with myopia that visited the General Pediatric Hospital in Athens during September 2024 and June 2025 are taken into consideration, a fact that raises the validity scores of results, increases the accuracy and reinforces the reproducibility of the study.

Review

Definitions and Classifications: Thresholds for Myopia, High Myopia, Hyperopia, Astigmatism, and Emmetropia

The aim of recommending thresholds for myopia and high myopia within the IMI white paper by defining and classifying this entity is to promote consistency in reporting and to aid study comparisons and meta-analyses. Recent research of population refraction data that included 41 studies with over a million participants in China reveals an interesting pattern, as shown in Figure 2. Most studies use the IMI definitions of ≤−0.5 diopters (D) for myopia and ≤−6.0 D for high myopia. Even though there was good consensus on the threshold values of −0.5 D for myopia and −6.0 D for high myopia, there was a disagreement as to whether to use ≤ or < within the definition. For hyperopia, there was clear preference for a threshold of SE ≥2.0 D (prevalence figure amongst the studies examined). Reports for astigmatism showed even more variability, with a threshold of SE ≥0.75 D being the commonest (Figure 2) [2]. In school-aged children, pre-myopia is gaining interest with increased attention to early implementation

of myopia control. In this age group, refraction typically changes over several years, with slow myopic shifts in hyperopes and more rapid myopic shifts in myopes, however emmetropia can be a transient state [3]. While many studies have attempted to predict myopia onset, identifying future myopes in their pre-myopic phase offers the prospect of early intervention.

Identification of predictive factors of progression into myopia will allow a more precise definition of pre-myopia. That, in turn, will help to separate young pre-myopes from stable emmetropic peers. Detailed longitudinal studies offer the best prospect of understanding the dynamics of myopia development from the pre-myopic phase. As noted in the 2021 digest, there are several large ongoing trials targeting the pre-myopic phase with interventions such as atropine, and results from a recent small trial indicate that this represents a valid therapeutic approach, but larger and more definitive studies are required [4].

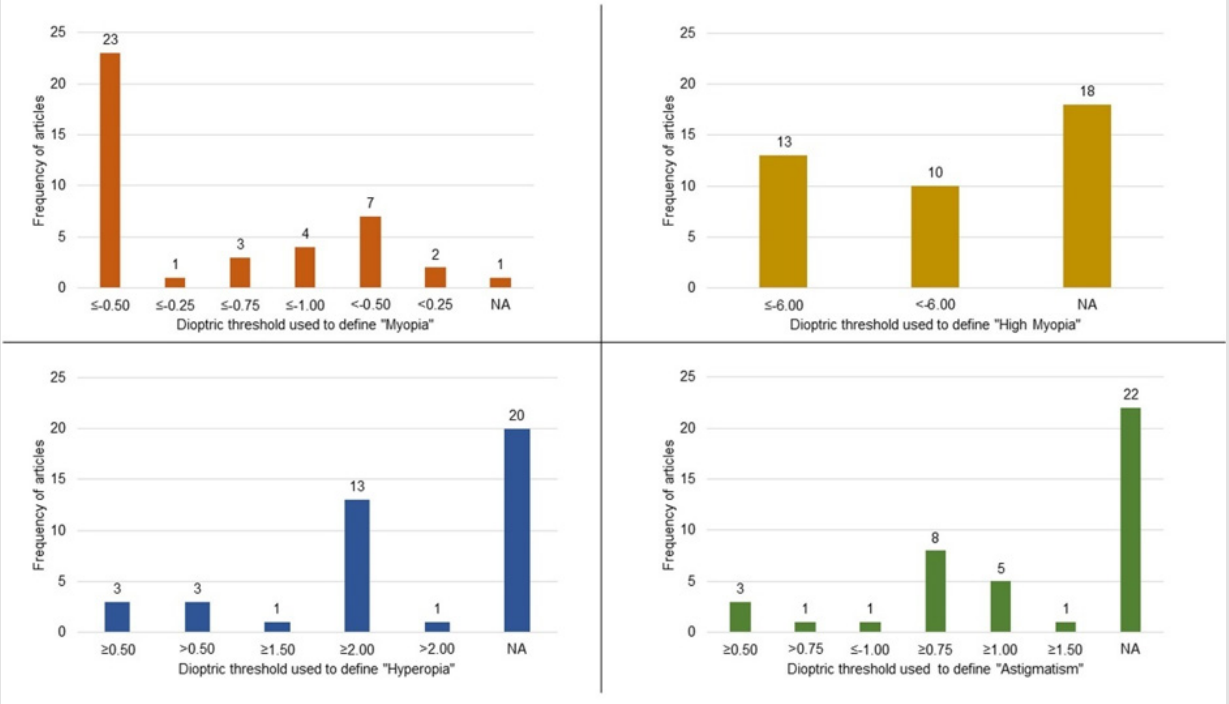

Figure 2: Criteria used to define myopia, high myopia, hyperopia, and astigmatism in 41 studies as extracted from Tang, et al. [7] NA, not available [4].

The Structural Consequences of High Myopia

As far as retinal complications are concerned, both myopic maculopathy and myopic macular degeneration are common and almost interchangeably used. Modern technology such as ultra-widefield optical coherence tomography provides new insights into the scleral complications of pathologic myopia. While refractive error, AL, and age remain the strongest predictors for the development of pathologic myopia, identification of other modifiable risk factors for sight loss would be very valuable. IMI Myopia Definition: A refractive error in which rays of light entering the eye parallel to the optic axis are brought to a focus in front of the retina when ocular accommodation is relaxed. This usually results from the eyeball being too long from front to back but can be caused by an overly curved cornea and/or a lens with increased optical power. It also is called near-sightedness (Figure 3).

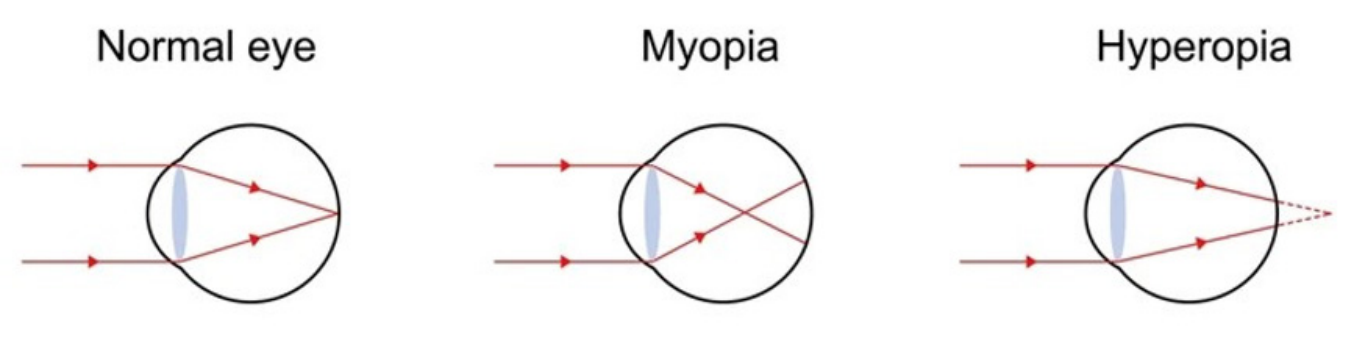

Figure 3: Normal eye, myopic eye and hyperopic eye, comparison and schematic representation of the three conditions.

The term degenerative high myopia remains the principal diagnostic term for myopic complications in the ICD-11 classification listed under "Disorders of the Retina" and is defined as follows:

"Macular lesions occurring in people with myopia, usually high myopia, causing a decrease of the best corrected visual acuity and comprising myopic chorio-retinal atrophy, myopic choroidal neovascularization and myopic retinoschisis."

Other pending definitions within the ICD-11 include new codes that reflect some specific retinal complications of myopia, such as the following:

9B76.1 Myopic maculopathy

9B76.2 Myopic traction maculopathy

9B76.3 Macular hole in high myopia

9B76.4 Retinal detachment in high myopia

Within the ICD-11, degenerative high myopia is categorized as a retinal condition but fails to capture the sight-threatening complications of high myopia such as posterior staphyloma and myopia-associated optic neuropathy. Optic nerve conditions such as glaucomatous optic neuropathy are listed under the category of "Disorders of the Visual Pathways or Centers" [4].

Purpose

According to Green et al., every narrative review constitutes an efficient attempt of retrieving condensed and "filtered" information gathered by scientific articles but can also include accumulation of patient data from routine (uncontrolled) clinical practice. Reviews constitute a useful tool for medical researchers in different ways. Each review can assist in refining a study hypothesis and in identifying pitfalls to avoid in the conduct of trials, providing precious aid in the projects of future researchers. Via the exploitation of critical thinking, they can lead to new insights, justify future research directions and essentially contribute to the enrichment and expanding of scientific knowledge in a specific field of interest. The constructed hypothesis of this current scientific review is evaluating the efficacy of different interventions for myopia control in children aged 6-13 years old (atropine eye-drops, use of spectacle lenses or both). The extraction of conclusions takes place by analyzing a satisfactory number of relevant, recently published studies and by providing real-life examples focused on this subject of interest. The different types of intervention aiming at slowing down myopia progression are summarized below: multifocal spectacles, peripheral plus spectacles (PPSL), under-corrected single vision spectacles (SVLs), multifocal SoE contact lenses (MFSCL), orthokeratology, rigid gas-permeable contact lenses (RGP); or pharmacological interventions (including high- (HDA), moderate (MDA) and low-dose (LDA) atropine, pirenzipine or 7-methylxanthine. These types of interventions were compared with inactive controls using a 6-to-36-month interval follow up, for enhanced assessment of results.

Methodology

Navigation on diverse electronic databases such as PubMed, Semantic Scholar and the Cochrane Database of Systematic Reviews unveiled a variety of scientific articles on this field. When searching the most current and relevant literature, the following keywords were used: myopia control in European children, use of spectacle lenses, use of atropine eye drops, combination of the two methods. Afterwards, a data extraction procedure took place via analysis and critical discussion of the articles selected, and subsequently the most useful information about each investigation was unveiled. Interventions to slow progression of myopia can be grouped into three broad categories: optical, pharmacological and environmental (Wildsoet 2019). Optical interventions include a variety of spectacle and contact lens designs. Spectacles are the least invasive and most accessible method for potentially slowing myopia [1]. Clinical trials have demonstrated that newer spectacle lens designs incorporating multiple segments, lens lets, or diffusion optics exhibit good efficacy [4-11]. Spectacle options include refractive under-correction, customized spectacle lenses, as well as bifocal and progressive addition designs. Soft multifocal and approved myopia control contact lenses are increasingly being used for myopia management in children (Efron 2020). Cen-

tre-distance soft multifocal lens designs incorporate a central zone that contains the distance correction with peripheral regions of the lens containing increased positive power (myopic defocus).

This is achieved by either a gradual increase in power towards the periphery or using concentric peripheral zones of alternating myopic defocus and distance correction [1]. Orthokeratology principles are considered to be the main component of myopia control in children. In pediatric practice, orthokeratology is used in cases of amblyopia, latent amblyopia and accommodative dysfunctions. As a fact, its application usually leads to esotropia disappearance or regression and orthophoria restoration. In milder cases, esophoria can be corrected after applying orthokeratology through turning myopia into hyperopia. According to a study published by Lawrenson JG, et al. in Cochrane Database of Systematic Reviews 2021, Orthokeratology (ortho-K) involves the use of specialized rigid contact lenses that are worn during sleep to change the topography of the cornea to reduce myopic refractive error and also manipulate peripheral retinal defocus to slow eye growth. Safety remains a concern because of the risk of sight threatening microbial keratitis and there is also the possibility of regression or rebound after discontinuation of lens wear or change to an alternative refractive intervention (VanderVeen 2019) [1]. Low concentration atropine eye drops (0.01 or 0.05%) are considered another effective means of slowing down myopia progression in children.

Antimuscarinic agents can halt myopia advancement through a non-accommodative mechanism that interferes with eye-growth regulatory pathways that arise in the retina and are related to the sclera via the retinal-pigment epithelium and choroid [1]. Therefore, the use of low concentration eye drops can reduce the rate of axial elongation and myopia aggravation in children and adolescents (Figure 4) [2]. The protective effect of increased time outdoors on myopia development is thought to be related to the higher light intensity of sunlight and possibly its spectral composition (French 2013). Light levels have been shown to influence refractive development in animal models (Smith 2012). Higher light intensities stimulate retinal dopamine production, which is thought to inhibit axial elongation (Feldkaemper 2013) [1]. Several studies have been carried out, arriving at statistically significant conclusions regarding combined therapy vs monotherapy in young individuals struggling with this disease. In general terms, combined therapy is more effective in low initial myopia and younger kids. Moreover, it should be considered an option for children under monotherapy with noticed progression. In general terms, it is a valuable alternative in children with fast progression and risk of high myopia development. Therefore, practitioners should be kept updated and well informed to apply the most appropriate individualized treatment and effectively monitor progression of the disease.

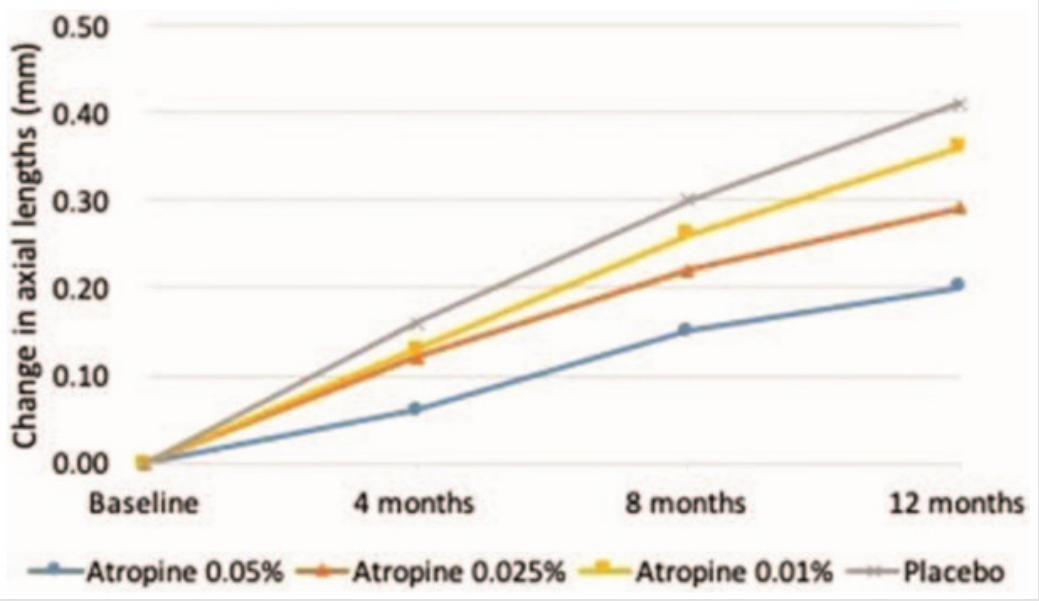

Figure 4: Change in axial length (AL) over one year [2].

This review aims to inspire the exploitation of flexible and creative ideas in managing these cases. An increase in refractive error measurement of more than -2 Diopters in one year is considered the limit for requirement of treatment initiation with atropine drops to slow down myopia progression in the age group mentioned above. It is important to take into account the normal hyperopic refraction (usually +1.5 D) that characterizes this patient's population. The role of astigmatism should not be neglected in selecting the right treatment and in prescribing the correct spectacle lenses. Multifocal ortho-K lenses with an aspheric central zone can be used for hyperopic correction.

The most popular optical interventions for myopia progression interception on a worldwide scale are:

A. Defocus Incorporated Multiple Segments (DIMS) Lenses. The DIMS lens design includes a central optical zone for correcting refractive error and multiple segments with constant myopic defocus (+ 3.50 D) around the central zone. This enables clear central vision providing myopic defocus simultaneously [12-14].

B. Highly Asperical Lens lets Lenses. Another new lens design incorporates (highly) aspherical lens lets. Spectacles with aspherical lens lets were more effective in slowing axial growth compared to single vision lenses [14].

C. Diffusion Optics Technology Lenses (DOT), Cylindrical Annular Refractive Element (CARE) Lenses, and Shamir Myopia Control (SMC) Lenses. The CARE lenses were recently patented as myopia control lenses. Developed by researchers at Wenzhou Medical University, these lenses generate blur signals on the retina by induction of high-order aberrations. These lenses comprise a central optical area providing full correction and a control area featuring numerous micro cylinders arranged in concentric circles. The SMC lens involves a central vertical aperture, known as the central vertical canal, designed to correct distance refractive error. The outer region of the lens features a power profile with a comparatively higher positive power than the central aperture, resulting in peripheral defocus [14].

D. Soft Contact Lenses for Myopia Control. There is an increasing use of different bifocal and multifocal soft contact lenses (SCL) and approved myopia control lenses for managing myopia in children. Several studies investigating the effects of different SCL exist and effects of slowing myopia progression by 30–45% and AL by 31–51% over 24 months with bifocal SCL have been reported [49, 161–163]. In children with faster myopia progression, effectiveness may improve with increased wear time, and with lens designs possessing higher hyperopic power in the mid-periphery (up to 6 D) [14].

E. Orthokeratology. Orthokeratology (OK) lenses are rigid gas-permeable contact lenses worn during sleep to alter corneal topography. Typically, modern OK lenses are designed to incorporate four zones: a central optic zone for flattening the central cornea and refractive correction, the reverse zone with a steeper curvature, the alignment zone (usually aspherical or tangent) for lens centration, and the peripheral zone. Myopia control with OK is primarily based on the hypothesis of inducing myopic defocus on the peripheral retina, but further research is necessary to understand the precise mechanism responsible for OK effectiveness. Several clinical studies have demonstrated the effectiveness of various OK lens designs in inhibiting myopic progression. Meta-analyses have shown a 30–60% reduction in myopia progression rate with OK lenses compared to controls using SV spectacles over 1–2 years of treatment [14].

During the last years, several meta-analysis, observational, retrospective studies and reviews have been conducted for estimation of selection of the most correct treatment methodology and have efficiently arrived at valid conclusions regarding the factors that shape the final result, such as refraction (initial measurement less than -3.00 Diopters or deterioration in myopia more than 2 Diopters in one year), corneal shape (presence of astigmatism) and anatomical features (increased axial length). These elements should guide practitioners in choosing the right type of lenses in a child (individualized care) by taking into account all the available parameters as well as psychological aspects, and socioeconomic status of each case. In this endeavor, the exploitation of AI algorithms could prove to be beneficial. For instance, the detection of peripapillary atrophy by a CNN algorithm in fundus images could be a prognostic factor for disease advancement and should be included in the criteria for more aggressive medication. In this context, updated guidelines for individualized screening should be created, and AI should be implemented in this attempt to ameliorate and facilitate everyday clinical practice in this challenging medical field.

Results

Negative mean-differences (MDs) for changes in refractive error represent faster progression of myopia in the intervention group compared to progression in the control group. Measurement of refractive error is not an appropriate outcome in orthokeratology studies. Overnight wear of ortho-K lenses flattens the central cornea and temporally reduces refractive error. It is therefore not possible to assess the true progression of refractive error without ceasing lens wear for a period of time to allow the cornea to return to its pre-treatment state (Lawrenson JG, 2023) [1]. According to a study published in July 2012 by Santodomingo-Rubido, et al. orthokeratology contact lens wear reduces axial elongation in comparison to distance single-vision spectacles in children. In this study, sixty-one subjects were recruited between 2007 and March 2008. The effect of refractive correction and component of refraction were found to be significant ($P< 0.001$) together with their interaction (P0.05). The effect of time on actual axial length was found to be significant ($P<0.001$), but the effect of refractive correction on axial length was insignificant ($P= 0.22$). However,

the interaction between refractive correction and time was significant (P=0.05), the latter reflecting a greater increase in length over time in the SV group compared to the OK group. A study published by Li Fen et al in 2019 in Asia Pacific Journal of Ophthalmology, showed that atropine eye drops 1% conferred a strong efficacy on myopia control.

However, its use was limited by the side effects of blurred near vision and photophobia. ATOM 2 study evaluated 0.5%, 0.1%, and 0.01% atropine on 400 myopic children, and suggested that 0.01% is the optimal concentration with good efficacy and minimal side effects (Figure 5). Since then, the use of atropine eye drops has been transitioned from high-concentration to low-concentration worldwide [2]. Although higher atropine concentrations have been shown to be effective in retarding myopia progression in children, the higher incidence of side effects with higher doses, including cycloplegia (inhibition of accommodation) and pupil dilation (which causes blur for near vision and photophobia) limits its long-term use. Furthermore, a rebound effect after discontinuation of therapy is more pronounced with higher concentrations of atropine (Chia 2014). More recent studies have evaluated the efficacy of lower concentrations to reduce side effects and lessen the likelihood of rebound. The results of these studies have led to a renewed interest in the clinical application of low-dose atropine (e.g. 0.01% and 0.05%) for myopia control (Wu 2019). Other pharmacological agents that have been evaluated for myopia control include tropicamide, cyclopentolate, the selective M1 muscarinic antagonist, pirenzepine, and the oral adenosine antagonist, 7-Methylxanthine [1].

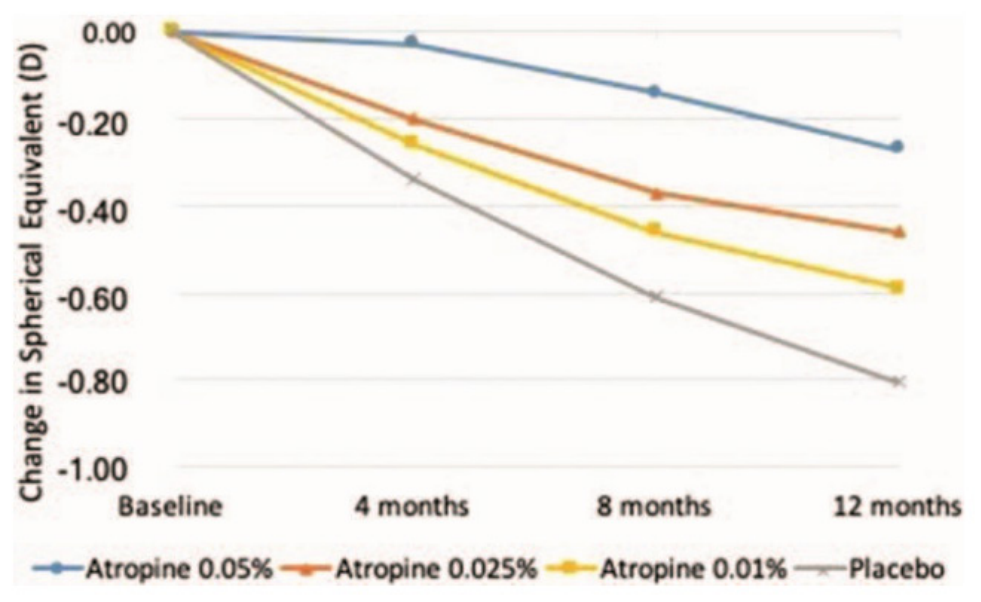

Figure 5: Change in spherical equivalent (SE) over one year [2].

Furthermore, evidence that more time spent on near work activities is associated with higher odds of developing myopia (Huang 2015), and the observation that increased time spent outdoors is protective against myopia, after adjusting for near work, parental myopia and ethnicity (Rose 2008), have raised the possibility that environmental or behavioral interventions could be effective for myopia control. Trials of school-based programs that promote outdoor activities, conducted in East Asia, have reported a lower incidence of myopia onset but no significant effect on progression following onset of myopia (He 2015; Wu 2018) [1]. Another aspect that must be mentioned is the issue of cost-effectiveness that needs to be addressed when selecting each methodology of intervention. According to a study published by Agyekum S et al. in 2023 at JAMA Network Open, outdoor activity, use of 0.05% eye drops, and orthokeratology principles are all cost effective measures for myopia control in children. Orthokeratology yielded the most promising results, achieving an ICER (Incremental cost-effectiveness ratio) of US $2376/AL reduction, followed by red light therapy (US $846/SER reduction) and HALs, US $448/SER reduction. The ICER of atropine 0.05%, was US $220/SER reduction, whereas the outdoor activity yielded the lowest results with a savings of US $5/SER reduction and US $8/AL reduction.

The next study worth mentioning was carried out by Liu X et al. in Acta Ophthalmologica and was published in January 2023. The purpose of the study was to assess the 1-year myopia control efficacy of a spectacle lens with annular cylindrical microstructures. A group of 118 consecutive eligible children aged 8-12 years with −1.00 D to −4.00 D of spherical component and <1.50 astigmatism was enrolled

between August 2020 and November 2020 at the Eye Hospital of Wenzhou Medical University. Participants were randomly assigned to wear cylindrical annular refractive element (CARE) (n = 61) or single-vision (n = 57) spectacle lenses. Cycloplegic autorefraction (spherical equivalent refraction [SER]) and axial length (AL) were measured at baseline and 6- month intervals. The results of the study are summarized below: Adjusted 1- year myopia progression was −0.56 D for CARE and −0.71 D for single-vision spectacle lenses. The difference in progression was 0.14 D (95% CI, −0.04 to 0.32) for CARE vs single vision. Adjusted 1- year eye growth was 0.27 mm for CARE and 0.35 mm for single vision. The difference in eye growth was 0.09 mm (95% CI, −0.15 to −0.02) for CARE vs single vision [3]. In other words, among children with myopia, treatment with cylindrical annular refractive element spectacle lenses significantly reduced the rate of axial elongation over 1 year compared with single-vision spectacle lenses (Figure 6).

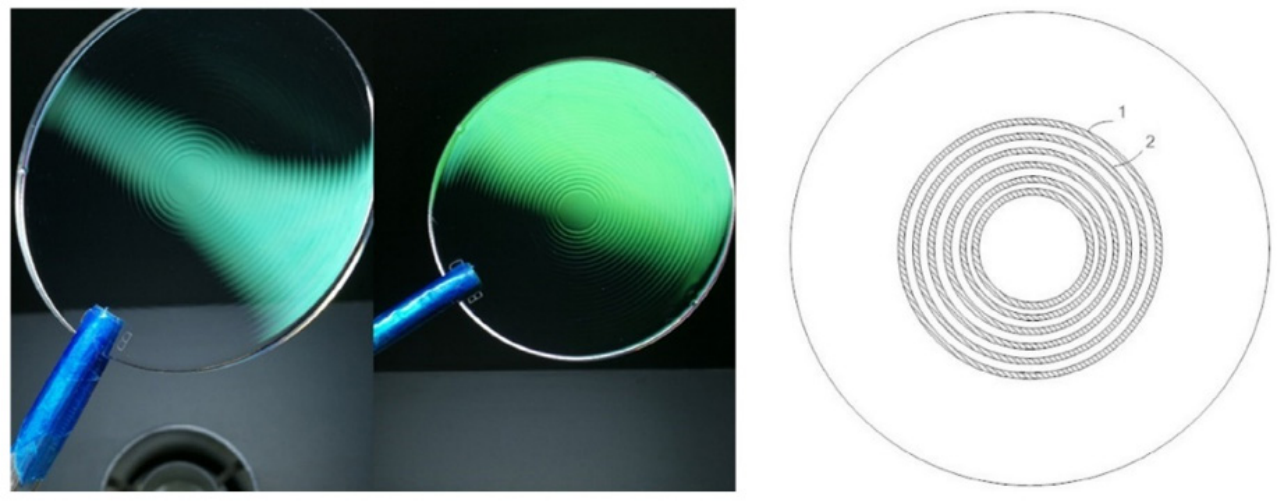

Figure 6: The physical picture of the patented lens (the left). Within the specific aperture range of the lens, the annular micro- cylinder array is centered on the geometric center of the lens (1- the occupied area with annular micro- cylinders, and 2- the spacing of two adjacent micro-cylinders) (the right) [3].

A study published by Nucci Paolo, et al. on February 2020 on Plos One was conducted in order to evaluate the efficacy of myopia control spectacle lens (DIMS) at slowing down myopia in a population of European children in comparison with 0.01% atropine and combined DIMS and atropine. The researchers followed a prospective controlled observational methodology to formulate reliable results. Participants aged 6-18 years old were allocated, according to patient/parent choice, to receive 0.01% atropine eyedrops, DIMS (Hoya, MiyoSmart) spectacles, combined atropine & DIMS or single vision spectacle lenses (control group). The scientists arrived at statistically significant results ($p<0.001$) regarding combined approach's (DIMS and atropine) effectiveness and successfulness at reducing myopia progression and axial elongation in this population group. A key point of this research that must be highlighted is the exclusion of children with concomitant ocular pathologies (e.g. genetic syndromes) from the study, a fact that raised the validity index and contributed to generalizability of conclusions. The selection criteria used in this experiment-masked, non-randomized study are cited in Table 1 [5]. Another study relevant to this subject was conducted by Tan Q, et al. in 2023. The researchers investigated whether combining 0.01% atropine with orthokeratology (AOK) has a better effect in retarding axial elongation, compared with orthokeratology alone (OK) over two years.

Table 1: Selection criteria used by the researchers for the study construction.

Inclusion Criteria	• Children or adolescents aged 6–18 years • Italian orEuropean ethnicity • Myopia with SER from -0.50D to -4.00D • Astigmatism fewer than 2.50DC • Anisometropia less than 1.25D
Exclusion criteria	Genetic syndromes suspected (e.g., Stickler, Marfan etc.) Other eye diseases (such as glaucoma, juvenile cataracts or retinal abnormalities, any form of strabismus) Myopia progression in the last year of less than 0.50D SER in either eye

The authors implemented the steps of the following methodology: recruitment of 96 Chinese children with myopia that were randomized into two groups (AOK and OK, 1:1 ratio). Axial length (the primary outcome), and secondary outcomes (e.g. pupil size and choroidal thickness) were measured at 1-month and at 6-monthly intervals after treatment initiation. The results were more promising for the combined therapy group, since they exhibited statistically slower axial elongation (adjusted mean 0.17 mm vs 0.34 mm, P < 0.001), larger increase in mesopic (0.70 mm vs 0.31mm, P ¼ 0.003) and photopic pupil size (0.78 mm vs 0.23 mm, P < 0.001), and greater thickening of the choroid (22.6 μm vs 9.0 μm, P < 0.001) than OK subjects that followed monotherapy over two years. Except for a higher incidence of photophobia in the AOK group (P = 0.006), there were no differences in the incidence of any other symptom or adverse events between the two groups. Slower axial elongation was associated with a larger increase in the photopic pupil size and a greater thickening in the choroid in the AOK group. The researchers used the standard error deviation as a statistical index to reinforce the validity of measurements and therefore the study's reliability. The scientists used intention-to-treat (ITT) analysis that included all subjects that received randomization, using linear mixed models.

In ITT analyses baseline parameters (age, sex, SER, pupil size, the amplitude of ac accommodation, and choroidal thickness), changes in parameters over two years (e.g. axial length, pupil sizes, amplitude of accommodation, and choroidal thickness), cycloplegic SER, and UVA, were compared between the two groups of subjects. They also used per-protocol (PP) analyses in which data from subjects who completed the 2-year study were included; the normality of the data was explored using the Kolmogorov-Smirnov test; after a normal distribution was confirmed, unpaired t-tests were used to compare baseline age, SER, pupil size (mesopic and photopic), the amplitude of accommodation, and choroidal thickness between the two groups [15]. Another recent study worth mentioning was carried out by Parida S, et al. in July 2025. The researchers conducted a prospective case-control interventional study in the department of ophthalmology at a tertiary Eye Care Centre in Eastern India. The primary goal of the study was to evaluate the effect of low dose atropine (0.01%) on choroidal thickness in children with myopia progression and to compare the rate of myopia progression in cases (patients treated with low dose atropine0.01%) versus controls (patients treated with placebo eyedrop) in terms of changes in spherical equivalence, axial length, BCVA and choroidal thickness at presentation and subsequent follow ups.

In terms of methodology, a total of 87 children aged 5-16 years with bilateral progressive myopia were recruited and randomly assigned into 2 groups. Spherical equivalence, axial length (AXL), and choroidal thickness (sub-foveal and at 1500 and 3000 microns nasal and temporal to fovea) were documented at baseline,1 month,3 months and 6 months.44 children in group A received treatment with once-daily dosing of atropine at bedtime, while 43 children in group B received a placebo eyedrop. The results unveiled the fact that children receiving atropine drops showed a significant increase in overall choroidal thickness at 3 and 6 months [11+/-9.67 and 18+/-13.43 microns, respectively], which showed a significant correlation with the decrease progression of myopia (in terms of spherical equivalence and axial length). The scientists made comparisons of their results with previous literature documentations on this subject of interest and included in their research an examination of the possible underlying pathophysiological mechanisms of atropine's way of action. For this reason, they highlighted the substance's effect on pre-junctional M2 and M4 muscarinic receptors located at the cholinergic-nitrergic nerve endings within the choroid. These receptors are crucial for regulating the cerebral nitric oxide signaling pathway, which in turn controls the dilation of blood vessels in the eyes. This mechanism contributes to changes in choroidal thickness, which is believed to influence ocular growth.

Notably, higher concentrations of atropine have been linked to causing a rebound effect where myopia progression accelerates within a year after cessation of treatment. In contrast, lower concentrations are generally less likely to trigger this response. In a few words, low-dose atropine eyedrops influence myopia advancement in a non-accommodator manner by reducing disease's prevalence via haltering axial length elongation (secondary effect). Other techniques used to treat this condition are the application of progressive addition bifocal glasses/lenses, peripheral defocus altering lenses, other types of contact lenses (such as multifocal and orthokeratology) and additional time spent outdoors [16]. A schematic representation of the drug's mechanism of action is illustrated in Diagram 1.

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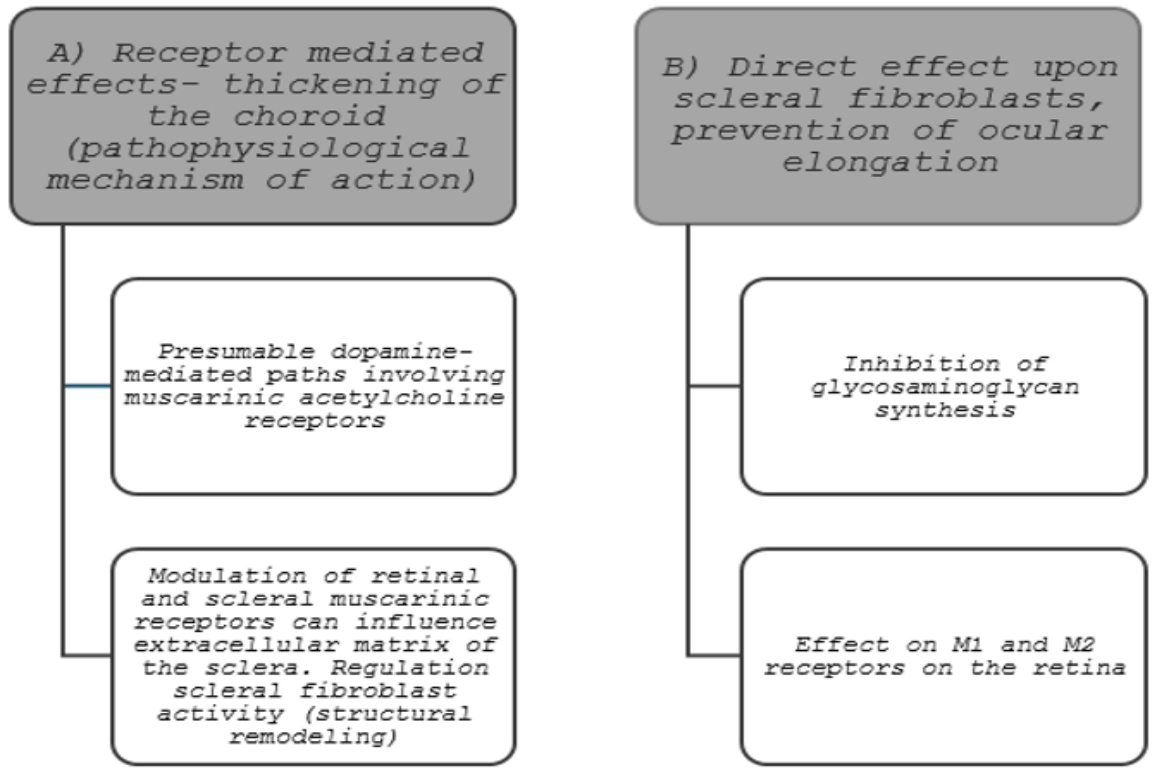

Diagram 1: The overall therapeutic effect of atropine can be postulated to be of a multifactorial nature with several of these biological processes included in its way of action [16].

Real life examples (paradigms) of interesting cases, unique patients with rare syndromes that were examined during scheduled evening or morning visits at the hospital, normal children with no concomitant anomalies who present for yearly ophthalmologic check-up and finally cases with diagnosed myopia (that require close monitoring and individualized protocols proposals).

A. A male patient aged 11.5 years old is diagnosed with pseudo myopia, hypermetropic refraction with a measurement of +1.50 grade after application of cycloplegic eye drops due to myopic adjustment/adaptation. Her examination took place on 23.05.2025. A recommendation was made for the avoidance of prolonged screen exposure during the day and the involvement in outdoor activities. Fundoscopic findings include whitening of the retina at a specific region in the periphery (1 o'clock) due to vitreous traction. The next re-examination was scheduled for 1-1.5 years.

B. A female patient aged 7 years old, with a history of congenital myopia was examined on 26.05.2025. Her visual acuity was 5/10 in the RE and 3/10 in the LE. Orthophoria was noticed for distant and close targets, normal eye movement and color perception. Her intraocular pressure measurement was 14 mmHg for both eyes and the cycloplegic refraction was: -12.00 -4.00 x 30° (OD) and -15.00 -3.00 x 130° (OS), indicative of high myopia and astigmatism. New glasses were prescribed based on these measurements, her fundus examination did not reveal any pathology (no myopic retinal alterations), whereas a recommendation for genetic testing was made. The next re-examination was scheduled in 8 months.

C. A male patient aged 6 years old, was examined during an evening appointment at the hospital in June 2025. He wore Lindberg glasses with mild hyperopic refraction, an esotropia of +15 Diopters was noticed in both eyes, with a visual acuity of 10/10 bilaterally and a normal eye movement. His cycloplegic refraction was: +2.00 spherical equivalent (OD) and +1.75 +0.50x 90° (OS). His fundus examination was normal. New glasses were prescribed due to a slight derogation from his previous glasses. A recommendation was made for instillation of atropine eye drops 1% to both eyes 30 minutes before applying his new glasses for the first time. The next examination was scheduled for 6 months follow-up (close monitoring protocol).

D. Two female patients (5 and 6 years old) present at an evening visit at the hospital, for their annual programmed ophthalmologic examination. An increase at spherical equivalent (myopic

refraction) greater than -0.75 each year was noticed. Due to their myopia progression, a decision was made by the physicians for initiation of atropine 0.01% and application of Zeiss clear view contact lenses. A recommendation was made to avoid excessive daily screen exposure (more than 1 hour per day) and the next examination was scheduled in 6 months.

E. A male patient aged 2.5 years old presents at the hospital for annual ophthalmological check-up. His cycloplegic refractometry is: +5.00 +0.50 x 180 (OD) and +4.00 +0.75 x105 (OS), indicative of hyperopia with upcoming astigmatism. Fundoscopy reveals the existence of myelinated retinal nerve fibers that led to the diagnosis of reverse Straatsma syndrome (amblyopic right eye). New glasses were prescribed after deducting +0.50 spherical equivalent from his cycloplegic refraction. Next examination was scheduled in 8 months.

F. A seven-year-old boy with a history of exophthalmos (globe prolapse) in the right eyes and ocular hypertonia due to the presence of bilateral glaucoma was examined during December 2024 on an evening hospital appointment. Orthoptic testing revealed divergent strabismus (exotropia) with accompanying high myopia. His cycloplegic refraction was: -4.75 -0.75 x 100 (OD) and -4.50 -1.40x 15 (OS). His IOP measurement was 30 mmHg in the RE and 27 mmHg in the left eye. Fundoscopy examination revealed a c/d ratio of 0.5 in the RE and 0.4 in the LE (normal value 0.3). New glasses were prescribed along with instructions for initiation of pharmaceutical treatment with Lumigan free 1 drop once daily, collyrium cos opt twice daily. Lastly, laboratory screening for thyroid disease and inflammation indexes (CRP, TSH, ft3, fT4, TRAb, anti-TPD, anti-Ty) were deemed necessary by the physicians. Next examination was scheduled in one-year interval.

G. A female patient aged 6 years old with amblyopia (reduced vision in the right eye), a history of accommodative strabismus (esotropia) and inferior oblique muscle hyperfunction bilaterally presented on January 2025 at the hospital for a yearly ophthalmological assessment. Her visual acuity was 10/10 in the RE and 5/10 in the left eye without glasses and orthophoria was noticed while wearing her glasses. She was covering her right eye daily for 6 months. Her cycloplegic refractometry was: +6.50 +0.75 x 60 in the RE (10/10) and +7.50 +0.75x 130 in the LE (9/10). Her fundus examination did not reveal any pathology. Instructions were given for the application of atropine 1% collyrium in the RE (one drop once a week) and covering of the same eye 3-4 hours daily, measures aiming at increasing vision in the amblyopic eye. Next examination was programmed in 4 months. This is a typical example of hypermetropia with accompanying esotropia (fully accommodative strabismus) in a young child.

H. A female patient aged 15 years old, with decreased visual acuity wearing her glasses (5/10 RE, 8/10 LE) arrives for her annual ophthalmologic check-up. Her cycloplegic refraction is -3.75 -0.75 x 90 (OD, 10/10) and -3.25 -1.00x 75 (OS, 10/10). Her color perception and eye movement were within normal limits. New glasses (Zeiss clear view or Hoya Miyosmart) were prescribed, and a recommendation was made for use of atropine drops 0.01% bilaterally to slow down myopia aggravation. Fundus examination revealed myopic alterations (tessellation and areas of upcoming patchy atrophy at the periphery), however the optic nerves had clear boundaries, with no presence of papilledema or glaucomatous cupping. Nevertheless, a high level of suspicion should be kept for the development of sight-threatening complications such as retinal tears, retinal detachment or glaucoma.

I. A female aged twelve years old was examined on June 2025. She wore hyperopic refraction glasses and orthoptic testing revealed esotropia (+25 Diopters bilaterally without wearing her glasses). Her visual acuity was 5/10 in both eyes wearing her glasses and 7/10 binocularly. Orthoptic testing measurement showed esotropia with glasses (+10 Diopters) and her cycloplegic refraction was: +4.25 +1.25 x 60 (OD) and +4.50 +0.75 X 150 (OS). New glasses were prescribed based on this result. Slit lamp examination revealed the presence of a blue dot cataract bilaterally (Figure 7). Her fundus examination was normal. Re-examination was scheduled within one year.

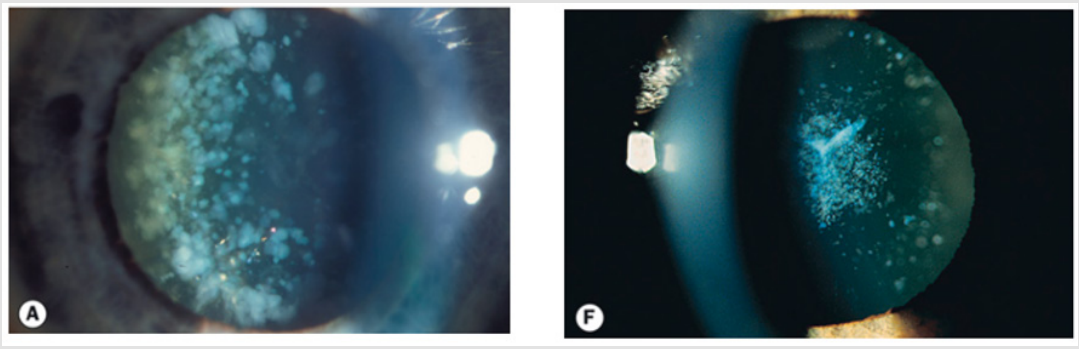

Figure 7: Blue dot cataract (congenital etiology) [7].

J. A female patient aged 6 years old was examined on May 2025 at the emergency department of the hospital. Her parents mentioned sleeping with open eyes (not proper closing). She wore glasses with a mild hypermetropia (+0.50 spherical equivalent, normal for her age) and astigmatism. Her orthoptic testing was normal for distant and close targets. Slit lamp examination showed spotted epitheliopathy of the cornea at the lower hours due to exposure keratopathy (EK) and palpebral papillae (allergic conjunctivitis) mainly in the right eye. A prescription for the application of eye gel plus every night in both eyes and collyrium cyclosporine 0.5% four times daily was decided. Re-examination was programmed in 6 months.

K. A female patient aged 11 years old, with a history of ROP was examined on May 2025. Her visual acuity was 2/10 (OD) and 5/10 (OS) and cover testing revealed exophoria for distant targets. Her cycloplegic refraction was -0.25 -2.75 x 10 (RE,10/10) and +1.00 -3.25 x 165 (LE, 7/10). New glasses (Zeiss clear view) were prescribed according to her cycloplegic measurements. Fundoscopy revealed protrusion of the optic discs bilaterally (IOP was 13 mmHg bilaterally, so benign intracranial hypertension was excluded) and laser spots due to ROP treatment. A recommendation was made for MRI brain and re-examination was programmed within 4-5 months.

Key Features, Stemming of Useful Messages and Information Through Daily Clinical Practice

Esotropia

(strabismus in a child) is usually accompanied by hypermetropic refraction due to shortening of axial length (anatomical bulb compression). In these cases, the full cycloplegic refraction is prescribed on glasses. On the other hand, exotropia is usually associated with myopic refraction measurements due to axial length elongation and scleral expansion. In such cases, we usually remove some degrees of adaptation before prescribing the new glasses (considering the occurrence of adaptation spasm phenomenon).

Diplopia

May be noticed at extreme eye positions due to the presence of phenomenon V in children with strabismus (usually exotropia). This is a normal phenomenon and does not require any further investigation in case of absence of nystagmus or amblyopia. Strabismus in children (especially exotropia), often co-exist with developmental disorders (e.g. Down syndrome) that require the initiation of speech therapy or ergotherapy. These children are usually autistic and need specialized management due to cooperation difficulties during the examination procedure.

Myopic Eyes

Run a greater risk of developing glaucomatous optic neuropathy (characterized by a c/d ratio greater than 0.6 on fundoscopy or cupping of the optic nerve), and they often appear with tilted optic disc (normal c/d ratio ≈0.3) on fundus examination. On the other hand, hypermetropic eyes appear with nasal protrusion of the optic disc on fundus examination. Eyes with high astigmatism usually present with asymmetry on pentagam corneal topography and run a higher risk of developing keratoconus after the age of four (eye rubbing, allergy/atopy background, genetic predisposition).

Straatsma Syndrome

Is a common pediatric disorder characterized by a triad of unilateral myelinated retinal nerve fibers, amblyopia and axial myopia (near-sightedness). On the contrary, reverse Straatsma syndrome constitutes a rare variant of SS, characterized by hyperopia, MRNF and amblyopia. Both conditions can lead to significant vision loss in the affected eye if not addressed properly. Extensive myelinated nerve fibers (Figure 8) can yield leukocoria. In such cases, the following conditions must be ruled out: retinoblastoma, coats disease, coloboma, cataract, ROP, PFV and FEVR. Moreover, myelinated nerve fibers can co-exist with high myopic astigmatism and anisometropic amblyopia. They may be found in 1% of eyes, and may be an isolated finding, or may be associated with other abnormalities such as neurofibromatosis and Gorlin syndrome. Branch retinal artery occlusion and cotton wool patches are two conditions that should be included in the differential diagnosis.

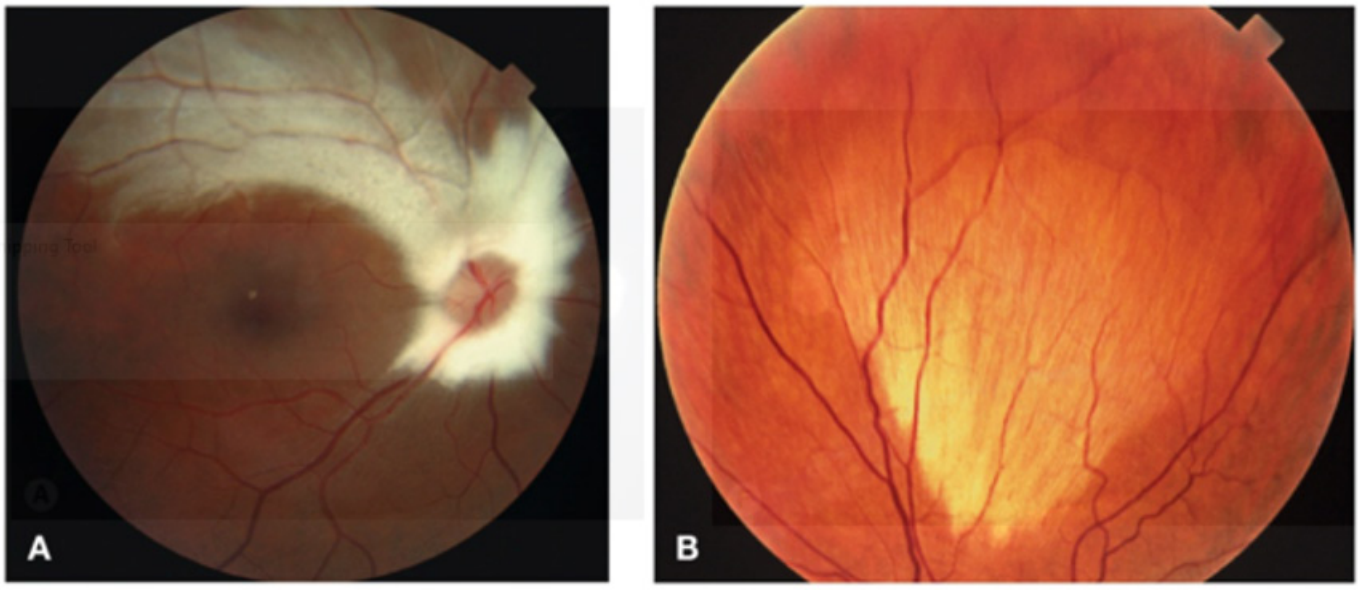

Figure 8: Myelinated nerve fibers:
A. Fundus Photograph with extensive feathery white myelination extending in all directions from the optic nerve
B. Myelinated nerve fibers superior to the optic nerve without direct connection to the optic nerve (Courtesy of William Tasman, MD) [6].

Amblyopia

"Lazy eye," is a common childhood vision disorder affecting 1% to 5% of children worldwide and as a fact it impairs visual acuity without visible eye abnormalities. If left untreated, this entity can lead to severe and irreversible loss of vision, which emphasizes the importance of early detection and intervention. Amblyopia develops due to visual deprivation, strabismus, or anisometropia. Strabismus disrupts binocular vision by causing eye misalignment. Consequently, it favors one eye while neglecting the other. Anisometropia creates a mismatch in visual perception due to differing refractive powers between the eyes. Visual deprivation, caused by conditions like ptosis or cataracts, obstructs vision in one eye and prevents proper sensory input. In all cases, the brain adapts by relying on the stronger eye, ultimately resulting in amblyopia. In the past, occlusion therapy-which involves patching the dominant eye to make the brain utilize the weaker eye-was a major component of amblyopia treatment.

Contemporary Management Guidelines for Amblyopic Eye Treatment

With the use of interactive smartphone apps and virtual reality (VR), which use both eyes to re-establish binocular integration, modern amblyopia treatment is progressing. In contrast to standard patching, these immersive techniques enhance sharpness and stereopsis by fostering visual coordination. According to research, they improve treatment compliance and could get around occlusion therapy's drawbacks [8-10]. Pharmacological and neuromodulation treatments are also part of the future for managing amblyopia, in addition to digital technology. Newer neuroenhancers have the potential to increase brain plasticity, although atropine drops are still a conventional treatment. Furthermore, visual processing may be improved by neuromodulation methods such as transcranial direct current stimulation (tDCS) and transcranial magnetic stimulation (TMS). The care of amblyopia is shifting toward more individualized and successful approaches with the use of sophisticated neuroimaging to guide treatment [11-13].

Conclusion

In general terms, combined treatments (orthokeratology with atropine 1% use) may enhance myopic outcomes in children compared to monotherapy (atropine 1% alone or orthokeratology alone). An interesting field to be discovered is Artificial Intelligence's application in optometry (i.e. myopia detection based on computer vision analysis of fundus images that involves a smart screening system and constitutes an objective, implementable, extensive, cost effective, patient friendly strategy). An example of the model's development highlights are CNNs based on YOLO-V8 that constitutes an easy-training (without coding experience) customizable algorithm. A key point that should be introduced and implemented in this patients' evaluation is axial length measurement (especially in high-risk cases), a non-negligeable risk factor that could essentially be used in predicting myopia progression in these cases. In a few words, a greater axial length (more than 26.5 mm) is considered to be associated with more rapid and aggressive myopia advancement in young children and adolescents.

References

1. Lawrenson JG, Shah R, Huntjens B, Downie LE, Virgili G, et al. (2023) Interventions for myopia control in children: A living systematic review and network meta-analysis. Cochrane Database of Systematic Reviews 2(2): CD014758.
2. Li F, JC Yam (2019) Low-Concentration Atropine Eye Drops for Myopia Progression. Asia Pac J Ophthalmol (Phila) 8: 360-365.
3. Liu X, Wang P, Zhu Xie, Muhan Sun, Minfeng Chen, et al. (2023) One- year myopia control efficacy of cylindrical annular refractive element spectacle lenses. Acta Ophthalmologica 101: 651-657.
4. Sankaridurg P, Berntsen DA, Bullimore MA, Pauline Cho, Ian Flitcroft, et al. (2023) IMI 2023 digest. Invest in Ophthalmology Visual Science (IOVS) 64(6): 7.
5. Nucci P, Lembo A, Schiavetti I, Shah R, Edgar DF (2023) A comparison of myopia control in European children and adolescents with defocus incorporated multiple segments (DIMS) spectacles, atropine, and combined DIMS/atropine. PLoS ONE 18(2): e0281816.
6. Leonard B, Nelson MD. Will's Eye Hospital, Color Atlas & Synopsis of Pediatric Ophthalmology (3rd Edn.).,.
7. Salmon JF, Kanski's Clinical Ophthalmology, A Systematic Approach, (10th Edn.)., Elsevier.
8. Li L, Xue H, Lai T, Ying Xue, Gang Luo, et al. (2022) Comparison of compliance among patients with pediatric amblyopia undergoing virtual reality-based and traditional patching method training. Front Public Health 10: 1037412.
9. Molina-Martín A, Leal-Vega L, de Fez D, Elena Martínez-Plaza, María Begoña Coco-Martín, et al. (2023) Amblyopia treatment through immersive virtual reality: A preliminary experience in anisometropic children. Vision (Basel) 7(2): 42.
10. Chan HS, Tang YM, Do CW, Horace Ho Yin Wong, Lily Yl Chan, et al. (2023) Design and assessment of amblyopia, strabismus, and myopia treatment and vision training using virtual reality. DIGITAL HEALTH 6: 9.
11. Chen AM, Cotter SA (2016) The Amblyopia Treatment Studies: Implications for Clinical Practice. Adv Ophthalmol Optom 1: 287-305.
12. Singh A, Nagpal R, Mittal SK (2017) Pharmacological therapy for amblyopia. Taiwan J Ophthalmol 7: 62-69.
13. Wu C, Gaier ED, Nihalani BR, Sarah Whitecross, Takao K Hensch, et al. (2023) Durable recovery from amblyopia with donepezil. Scientific Reports 13: 1-9.
14. Eppenberger LS, Grzybowski A (2024) Myopia Control: Are We Ready for an Evidence-Based Approach? Ophthalmol Ther 13: 1453-1477.
15. Qui Tan, Alex Lk Ng (2023) Combined 0.01% atropine with orthokeratology in childhood myopia control (AOK) study: A 2-year randomized clinical trial. Contact Lens and Anterior Eye 46(1).
16. Parida S, Das M, Dash S (2025) Effect of Low Dose Atropine on Choroidal Thickness in Children with Myopia Progression. Cureus 17(7): e88047.

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