

Treatment Procedures for Prevention of Myopia Progression

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Abstract

Hypertension, myopia is a common refractive error that continues to affect an increasing number of people worldwide and is expected to impact approximately 50% of the world's population by 2050. Higher levels threaten vision, potentially leading to visual impairment or blindness. This review aims to examine the most recent approaches for preventing or slowing myopia progression, such as atropine, progressive lens spectacles, bifocal glasses, soft bifocal contact lenses, orthokeratology contact lenses and more outdoor activities. In a few children, orthokeratology has been demonstrated to diminish the elongation of the axial length of an affected eye and slow the progression of myopia at a modest rate. The most effective treatment for the progression of myopia is atropine. Furthermore, there is a link between the prevalence of myopia and the amount of time spent outdoors. The possible prevention of myopic progression using bifocal or Progressive Addition Lenses (PAL), either as spectacles or contact lenses, is also discussed. In addition to the approaches mentioned in this review, various regulatory and technological care options offer promising solutions to manage myopia progression. This review concludes that there is a need to customize treatment approaches for every patient, as revealed in the literature. Likewise, it is necessary to look into the delineation of the long term consequences of such approaches as well as the optimal timing for interventions.

Keywords: European Eye Epidemiology (E3); Progressive Addition Lenses (PAL); Myopia; Hypertension; Microbial keratitis

Introduction

Spontaneous Myopia, or nearsightedness, is the most prevalent refractive error in the world and is expected to impact around 50% of the world's population by the year 2050 [1]. Asian countries report the highest number of patients with myopia. For example, the latest estimates of the prevalence of myopia in South Korea and China are about 80% [2]. In Taiwan, 25 years ago, 84% of people between 16 and 18 years old were determined to be myopic [3]. In a one year survey of school based communities of children and teenagers in China, myopia was shown to be prevalent among 33.6% of first graders and 54% of seventh graders [4]. About 90% of Chinese adolescents and adults were affected with myopia [5]. Another study revealed that myopia was prevalent in Shanghai among 94.9% of university students and 96.9% of graduate students and 19.5% of all myopic students had high myopia [6]. Concurrently, a report from the European Eye Epidemiology (E3) consortium based on a population analysis reported that the incidence of myopia is also rising significantly in Western countries, with substantial variability between age groups, culminating in the 25 year old subgroup having a rate of myopia 46% higher than the 75 year old subgroup, which had just 15% of individuals affected [7]. Higher myopia levels are related to conditions that threaten vision, such as retinal detachment, cataracts, macular degeneration and glaucoma. These pathologies are the primary causes of vision deficiency and blindness [8]. Over the past decade, there has been a higher awareness of molecular biological processes that evaluate refractive error, This further supports the concept that environmental exposure and genetic predisposition interact dynamically, contributing to the development of myopia [9].

Literature Review

The aim of this review is to discuss updates in potential strategies

to prevent or slow the progression of myopia, including orthokeratology contact lenses, atropine, more outdoor. This review aims to examine the most recent approaches for preventing or slowing myopia progression, such as atropine, progressive lens spectacles, bifocal glasses, soft bifocal contact lenses, orthokeratology contact lenses and more outdoor activities.

Orthokeratology contact lenses

Orthokeratology involves the use of rigid gas permeable contact lenses worn overnight to temporarily reshape the cornea, providing clear daytime vision. Additionally, studies have demonstrated its effectiveness in slowing the progression of myopia [10,11]. Orthokeratology studies commonly utilize axial length elongation as a surrogate marker for myopia progression, rather than relying on changes in equivalent spherical refractive error. Axial elongation is a critical endpoint, as the majority of sight threatening complications associated with myopia are linked to excessive eyeball growth. Different studies have shown a 30%–71% decrease in axial elongation relative to regulation [12,13].

A one-year study of the effect of orthokeratology on myopia progression utilized a contralateral eye design, which was believed to eliminate conflicting variables. Children between the ages of 7 and 13 years who had myopic anisometropia were given an orthokeratology contact lens for their affected eye only. Researchers reported a decrease in the elongation of the axial

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length of the affected eye [14]. Traditionally, orthokeratology lenses have been designed with a spherical geometry. However, recent advancements have focused on the development of toric designs to effectively treat astigmatism. Zhang, et al., studied myopic progression in children with myopia and moderate to high astigmatism to evaluate the effects of toric *versus* spherical orthokeratology lens designs [15]. Orthokeratology lens wearers had a 55.6% lower chance of axial elongation than the spherical intervention group.

Despite evidence supporting orthokeratology as effective in myopia control, it is necessary to consider other factors before pursuing this intervention. Microbial keratitis risk stands as the greatest concern when it comes to overnight contact lens wear. Infectious keratitis has been documented in orthokeratology contact lens wearers, as reported in case studies and series [16]. A recent systematic review of clinical profiles related to orthokeratology-associated infectious keratitis revealed that the majority of cases occurred in patients under 18 years of age, with an average onset after 19.4 months of lens use. The prevalent pathogens included *Pseudomonas aeruginosa*, *Acanthamoeba* and coagulase negative *Staphylococcus spp.*, representing 36.4%, 32.4% and 6.9%, respectively [17].

Another point to consider is the rebound effect observed following orthokeratology discontinuation. It has been said that discontinuing lens wear is related to faster axial length elongation compared to controls and those who wear orthokeratology lenses continuously. Additional investigation of this rebound effect, as well as studies to determine the ideal duration of orthokeratology treatment to obtain maximum myopic control, are required [10].

Based on the suggestion of Cheung et al., it is likely that young children between 6 and 9 years of age with rapid myopic progression (defined as an increase in axial length of 0.20 mm per 7 months or spherical equivalent of 1 diopter per year) are candidates for orthokeratology [12]. They recommend conducting an observational trial period to evaluate the patient's rate of myopic progression before initiating orthokeratology as an intervention.

Atropine

Applying atropine is the best intervention towards combating myopia progression, despite being invasive [18]. There is wide use of atropine in Taiwan, China and Singapore to inhibit myopia *via* instilling it into the eyes in the evening. SHIH et al., were able to treat 186 children of ages between 6 and 13 years using 0.5%, 0.25% and 0.1% atropine within 2 years and they discovered that 0.5% atropine had the best effectiveness [19]. Further, for the 3% of atropine, 61%, 49% and 42%, respectively, of the children did not exhibit myopic progression, while 4%, 17% and 33% exhibited speedy myopic progression. Atropine Treatment of Myopia 2 (ATOM2) study in Singapore carried out by Chia et al., involved the treatment of 400 children between ages 6 to 12 years using 0.5%, 0.1% and 0.01% atropine within 2 years [20]. According to the study report, there were declines in myopia progression of about 75%, 67% and 58% for the three concentrations. The mean axial length increase was recorded as 0.27 mm, 0.28 mm and 0.41 mm for the respective

concentrations. Notably, the side effects of 0.01% atropine on pupil size and accommodation were minimal compared to those observed with 0.1% and 0.5% concentrations. Chia et al., carried out a follow up study that involved the treatment of 400 children with 0.5%, 0.1% and 0.01% of atropine in year 1, followed by all of them using 0.01% [21]. They observed an increasing refraction and axial elongation to be the least in children who received 0.01% atropine (-1.38 D/0.75 mm relative to -1.83 D/0.85 mm and -1.98 D/0.87 mm, respectively) after five years.

A 2023 meta analysis demonstrated that combining atropine with orthokeratology significantly outperformed monotherapy in reducing axial elongation. This finding highlights the potential advantages of integrating pharmacological and optical therapies for more effective myopia control [22].

Time spent outdoors

According to research, there is correlation between an increase in time spent outdoors and a decrease in prevalence of myopia [23]. Pärssinen, et al., conducted a longitudinal study to investigate the factors associated with the development of high myopia, defined as six diopters spherical equivalent, from childhood to adulthood [24]. Their findings revealed an inverse correlation between time spent outdoors and myopic progression in children, but no significant correlation in adults. However, the researcher reported the time spent outdoors using a questionnaire and it can bring about recall bias. In addition, the researchers carried out a longitudinal study instead of a randomized clinical trial and they performed the assessment of relationship instead causality.

However, other studies that use randomization and further quantifiable ways to assess outdoor time have obtained the same results. In Taiwan, Wu et al., carried out a multicenter randomized clinical trial towards the evaluation of the effectiveness of a school based program mandating an increase in time outdoors to control myopic progression [25]. The researchers used light meter recorders in quantifying outdoor time as well as light intensity augmented with questionnaire. The study demonstrated that a minimum of 11 hours of weekly outdoor exposure is effective in preventing myopic shift in baseline non-myopes and reducing the rate of myopia progression in baseline myopes, as measured by refractive error and axial length elongation. As for nonmyopes, they recorded a difference of 0.11 diopters in refractive error ($P \frac{1}{4}$ 0.02) as well as 0.03 millimeter in axial length elongation ($P \frac{1}{4}$ 0.02) between the intervention and control groups. The two myopes groups were different by 0.23 diopters ($P \frac{1}{4}$ 0.007) and 0.15 mm ($P \frac{1}{4}$ 0.02). Although the study outcomes were statistically significant, there was a small degree of difference between control and intervention groups such that they may be clinically irrelevant.

Xiong et al., identified a statistically significant protective effect of outdoor time on both incident and prevalent myopia [26]. The researchers conducted a systematic review and meta-analysis of existing literature on myopia and outdoor time, revealing a dose-dependent response. Increased outdoor exposure was associated with a reduced risk of myopia onset but showed no significant impact on the progression of pre-existing myopia. However, interpreting the outcomes of this meta-analysis requires caution due to the high heterogeneity among the analyzed studies.

Researchers are still evaluating the association between outdoor time and myopia in studies; examples include ongoing STORM and K-YAMS [27,28]. Overall, research trends suggest that increased time spent outdoors may offer protection against the onset of myopia. Similarly, it may help slow the progression of myopia in individuals already affected, though the impact is unlikely to be clinically significant. Therefore, encouraging outdoor activities should be considered as an adjunctive measure rather than a primary intervention for myopia control.

Bifocal and progressive lenses

The primary function of single vision spectacles and contact lenses is to correct refractive errors, including myopia. However, they are not typically prescribed as a means to control myopia progression [10].

A prevailing theory of myopic progression suggests that peripheral retinal hyperopic defocus serves as a driving factor for axial elongation [29]. Despite the correction of axial refractive error, animal studies indicate that hyperopic blur in the peripheral retina of myopic eyes promotes ocular growth and axial elongation, contributing to progressive myopia. Based on these findings, researchers propose that minimizing peripheral hyperopic defocus or inducing peripheral myopic defocus using bifocal or Progressive Addition Lenses (PAL) in spectacles or contact lenses may help prevent myopic progression.

Recently, Kang reviewed studies involving a comparison of spherical equivalent change from baseline following treatment using single vision spectacles, PAL and bifocal and prismatic bifocal lenses. Their analysis revealed that the majority of the reviewed studies demonstrated a statistically significant reduction in spherical equivalent progression with the use of Progressive Addition Lenses (PAL) and bifocal spectacles. Nevertheless, the studies recorded small numerical values such that they are negligible in terms of clinical significance, except for some population subgroups, like young children having parental myopia or esophoria, as well as one nonrandomized, unmasked trial which revealed that myopic control using bifocals improved by 50% [13].

Kanda et al., evaluated a novel spectacle lens design, MyoVision, which features an asymmetric central area with inferior extension for full refractive correction and additional positive peripheral power aimed at reducing peripheral hyperopia [30]. The study randomized myopic children aged 6 to 12 years, all of whom had at least one parent with myopia, to either MyoVision or single vision spectacle correction. After two years, the researchers found no statistically significant differences in spherical equivalent or axial elongation between the two groups. They suggested that this outcome could be attributed to the greater susceptibility of spectacles to misalignment between the line of sight and the optical axis of the lens during eye movements, compared to contact lenses. This misalignment, along with the elongated vertex distance in spectacles, may contribute to the difficulty in effectively correcting peripheral hyperopia.

Despite the lack of persuasive evidence for peripheral myopic defocus spectacles for myopia control, unique design contact lenses could be promising. Past clinical trials show that spherical equivalent reduces by 20% to 72% and axial length

elongation is slowed down by 27% to 79% for contact lenses made to decrease peripheral hyperopic focus [13].

A recent two-year randomized trial conducted in Spain evaluated the effectiveness of MiSight contact lenses compared to single vision spectacles for myopia control in children aged 8 to 12 years [31]. MiSight lenses feature a large central zone designed for distance vision correction, surrounded by concentric rings with alternating distance and near powers to address myopia progression. The results of this study show that MiSight contact lenses reduce myopic progression by 39.3% and slow axial length elongation by 36% relative to controls.

Despite the necessity of further research on this topic, contact lenses made for peripheral hyperopic defocus could be promising for myopia control ahead, instead of spectacles.

Discussion

Managing myopia in forth coming years

Over the next decade, professionals treating myopic children will likely have a wide range of new regulatory and technological care options at their disposal. Several three-year clinical trials are currently underway in the US testing new types of spectacle lenses, such as low-concentration atropine. UK based research into how atropine can be used by optometrists is also ongoing and there is little doubt that there will be further innovation in several areas of treatment [32].

Unless pre-myopic patients and their parents are convinced that preventative measures will yield clear benefits to vision, they will likely refuse them. Some may believe that obtaining and wearing contact lenses will not provide a worthwhile return but may be more open to administering eye drops at night. Ongoing clinical trials are investigating the potential of low-dose atropine to delay the onset of myopia. Additionally, some practitioners may adopt this or other experimental therapies before the publication of final results. Furthermore, lifestyle factors are increasingly recognized as playing a significant role in myopia prevention. Multiple epidemiological studies demonstrate that the more time is spent outside, the lower the prevalence of myopia and there are clinical trials in progress investigating whether behavioral interventions aimed at encouraging individuals to spend more time outdoors will impact the incidence of myopia. Preliminary findings in this regard are promising; for example, a recent study of existing myopes found a decline in myopia progression and axial elongation by 0.23 D (95% CI: 0.06 to 0.39 D) and 0.15 mm (95% CI 0.02 to 0.28 mm), respectively, over a 12 month period as a result of spending more time outdoors. Encouraging this type of behavioral change is also of interest to optometrists in their capacity as primary care professionals, as it may help tackle childhood obesity and improve cardiovascular health [25].

As the refractive error has yet to be rectified, a proven optical therapy will be required whether atropine is used or not. If it is suspected that atropine is compromising near vision, the use of PALs or bifocals is recommended instead. Given the necessary residual accommodation, the two therapies, atropine and optical myopia control, may be used concurrently. In the case of younger children, overnight orthokeratology has been recommended, as the lenses are only used at home and parents can insert and

remove the lenses themselves. However, it should be noted that there is limited data on the outcomes of combined treatment and it remains unclear whether it is the pharmacological therapy or the increase in pupil size (which improves optical effects) that boosts effectiveness^[33].

Conclusion

As myopia becomes increasingly common across the world, the prevalence of high myopia, which can lead to vision loss, is also on the rise. To address this issue, there has been a significant investment in studies that aim to identify effective methods of myopic control. Some research has found that spending time in an outdoor environment can reduce the risk of developing myopia. In addition, optical solutions, such as wearing contact lenses that have been specifically created to reduce peripheral hyperopic defocus and orthokeratology, have also shown promising potential to reduce the rate of myopia development. However, of the various interventions that have been investigated, pharmacologic therapy involving the prescription of atropine has been most frequently researched and has been found to be the most effective means of controlling myopia. The outcomes of existing studies clearly show that treatment approaches should be specifically customized to the unique needs of each patient. Further studies are required to determine the long-term effects of treatment approaches and the optimal timing for interventions

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