Review Article

Slowing myopia progression in children

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ABSTRACT

Background: A large proportion of individuals develop myopia, which is recognized as a global health concern and is predicted to increase in prevalence. Long-term eye problems are associated with myopia, particularly in young individuals. Retinal detachment and choroidal degeneration are among the causes of visual impairments associated with myopia. In this narrative review, we summarized the current measures for slowing myopia progression in children, including their safety profiles and potential drawbacks.

Methods: We conducted an English literature search for articles published between January 1, 2000, and October 31, 2023, using various combinations of keywords related to myopia, myopia progression, childhood myopia, myopia control, atropine, orthokeratology, and contact lenses. We included original or review articles pertaining to lifestyle changes and pharmacological, optical, or laser interventions for managing myopia progression in children. Our search was conducted using PubMed/MEDLINE, Google Scholar, and the Wiley Online Library. We reviewed the full text of included articles and qualitatively summarized the results of relevant studies using a narrative synthesis approach.

Results: Multiple meta-analyses indicated that increased outdoor time is associated with a lower myopia prevalence, with each extra hour spent outside each week reducing the risk of myopia by 2%. Candidate drugs, such as atropine, pirenzepine, and 7-methylxanthine, and certain intraocular pressure-lowering medications, such as timolol, have been studied in human trials for their ability to manage myopia. The nonselective antimuscarinic drug atropine, followed by the M1-selective antimuscarinic drug pirenzepine, displayed positive results in slowing myopia. Oral 7-methylxanthine, a nonselective adenosine receptor antagonist, reduces axial myopia caused by hyperopic defocus in a primate model. Low-intensity laser therapy using low doses of red and near-infrared light, visual biofeedback training, bifocal or multifocal spectacles, orthokeratology using a rigid gas-permeable contact lens, combined orthokeratology and atropine, soft contact lenses with a central distance zone and higher positive power in the periphery, and peripheral defocus contact lenses are among the interventional therapies with promising results in managing myopia progression in children.

Conclusions: The current literature supports the efficacy of increased outdoor time, administration of pharmacological agents, and special contact lenses as treatment modalities for slowing myopia progression in children. The effectiveness of orthokeratology alone and in combination with topical atropine therapy has also been assessed. Further research is needed to pinpoint the precise mechanisms of action of these therapies and to determine the best course of treatment. The increasing global prevalence of childhood myopia necessitates robust interventional studies into slowing myopia progression and preventing high myopia and related sight-threatening conditions in adulthood.

KEYWORDS

nearsightedness, myopias, progressive myopia, control, children, atropine sulfate, pirenzepin, orthokeratologic procedure, pharmaceutical product

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INRODUCTION

Myopia is a major public health concern, affecting 28% of the global population in 2010 [1, 2] with an anticipated increase to 50% by 2050 [3, 4]. It is a progressive condition [4] more common in women than in men [5] although it stabilizes at a younger age in women [6].

In myopic individuals, distant light enters the unaccommodating eye, focusing in front of the retina rather than on it [7]. This causes near objects to be seen clearly but distant objects to appear blurred [8]. The strongest factor independently influencing a child's myopia progression is younger baseline age [9]. Age and family history influence the 0.1–0.45-mm annual progression of axial length in children [10]. High myopia is defined as refraction > - 6.0 D or axial length > 26 mm [11]. According to a large population-based study conducted in Beijing, degenerative myopia is the most frequent cause of vision impairment in adults [12].

Identification of individuals at risk of myopia is critical to achieve better vision. Monozygotic twins have a stronger correlation of refractive error than dizygotic twins [13]. The age of onset of juvenile myopia is 6 to 12 years [14]. The occurrence of myopia in primary and middle school pupils surged by 11.7% in China over a six-month period during the coronavirus pandemic [15]; other nations also experienced significant increases [16, 17], turning myopia into an alarming global pandemic [17]. Interventions that slow or delay myopia may prevent individuals from developing high myopia if promptly administered. Lifestyle changes and other effective measures could significantly reduce the number of people with myopia and high myopia [18].

Most people consider myopia a simple refractive error that may be corrected with spectacles or refractive surgery [19]. However, untreated myopia may cause visual impairment and could be sight threatening if associated with ocular complications [20]. *Myopic maculopathy* constitutes the presence of one or more pathological changes with myopia progression, including posterior staphyloma, lacquer cracks, and chorioretinal atrophy [20-22] and can be cause of vision impairment. Therefore, various modalities of treatment such as optical, pharmaceutical, environmental, and behavioral have been investigated to slow the progression of myopia [23].

Childhood myopia is a strong predictor of progressive myopia and potentially severe ocular complications [24]. Therefore, slowing myopia progression in children is a vital strategy to combat the myopia pandemic and its plausible consequences. In this narrative review, we summarize the current measures for slowing myopia progression in children, including their safety profiles and potential drawbacks.

METHODS

We conducted an English-language medical literature search using various combinations of keywords related to myopia, myopia progression, childhood myopia, myopia control, atropine, orthokeratology, and contact lenses published between January 1, 2000, and October 31, 2023. We searched the PubMed/MEDLINE, Google Scholar, and Wiley Online Library databases and included original or review papers pertaining to lifestyle changes and pharmacological, optical, or laser interventions for managing myopia progression in children. We excluded randomized controlled clinical trials, interventional studies that primarily recruited participants older than 18 years at baseline, and studies with participants having myopia less than - 0.25 D in spherical equivalent. We reviewed the full text of included articles and qualitatively summarized the results of relevant studies using a narrative synthesis approach.

RESULTS

Lifestyle modifications focusing on outdoor activities [25] are among the effective and safe modalities to slow myopia progression. Numerous studies have investigated the effectiveness of pharmaceutical and optical treatments in slowing myopia progression [15, 26]. Emphasis has been placed on orthokeratology and atropine 0.01% [27]. The overwhelming consensus from these studies is that atropine 0.01%, orthokeratology, or a combination of the two are effective interventions for preventing or controlling myopia [1, 27]. Table 1 presents a summary of studies pertaining to the most effective methods in slowing myopia progression [1, 4, 15, 22, 26]. Below, we discuss all available treatment modalities according to the literature.

DISCUSSION

Outdoor activities

Multiple meta-analyses indicate that increased outdoor time is associated with a lower myopia prevalence, with each extra hour spent outside each week reducing the likelihood of myopia by 2% [25, 28]. However, the effect

Table 1. Studies pertaining to the most effective therapeutic interventions in slowing myopia progression in children [1, 4, 15, 22, 26, 27]

Intervention	Mode of action	Possible adverse effects
Atropine (Concentrations: 0.01%, 0.05%, 0.5%, or 1%)	Inhibits muscarinic receptors in the ciliary muscles, retinal pigment epithelium, retina, and choroid.	Photophobia and blurred near vision. Lower concentrations have fewer adverse effects with the same efficacy.
Orthokeratology	Specially designed gas- permeable contact lenses to temporarily reshape the cornea.	Microbial keratitis; avoidable or manageable through careful follow-up and meticulous lens care.
Combined atropine and orthokeratology	Combined action.	Most effective but may have more adverse effects. Adverse effects are avoidable or could be minimized through meticulous lens care and close follow-up for orthokeratology and administration of a lower concentration of atropine formulation.

of slowing myopia progression is yet to be proved [7, 29]. The increased light intensity outdoors can trigger the release of dopamine in the retina, potentially inhibiting eyeball elongation [19].

Near-work activities have been reported as an independent risk factor for myopia [7, 30]. A meta-analysis of 27 studies found that longer periods of close work were associated with a higher myopia risk [31]. The recent increase in the prevalence of myopia may be explained by the increased use of digital devices, with 41% of children using them for three or more hours per day and 66% owning smartphones or tablets [32]. This trend may also account for the decline in outdoor activities. The ideal interventions to control myopia would reduce potentially modifiable risk factors and the likelihood of the onset or progression of this potentially blinding disease [33, 34].

Pharmacological treatments

Candidate drugs such as atropine, pirenzepine, 7-methylxanthine, and some intraocular pressure-lowering medications such as timolol have been studied in human trials for their ability to manage myopia [21, 35-37]. Atropine, a nonselective antimuscarinic drug, and pirenzepine, an M1-selective agent, displayed positive early results in slowing the progression of myopia [4, 21, 22, 30].

Atropine: Atropine exhibits potential in delaying the advancement of myopia in a concentration-dependent manner [22, 26]. Its long-term safety profile remains unknown [4, 38]. Anticholinergic agents contribute to retinal development by antagonizing acetylcholine at muscarinic receptors [39]. Although high-dose atropine (0.5–1%) effectively slows axial elongation, its discontinuation can cause side effects such as photophobia, impaired near vision, and increased myopia [40]. Uncertainty surrounds its mode of action on ocular tissues for slowing myopia progression [41].

Growth factors are secreted by the choroid and retinal pigment epithelium, and atropine modulates these factors, preventing transforming growth factor-beta 2 expression in retinal pigment epithelial cells [42]. In reaction to optical defocus, the choroid modifies its thickness and shifts the retinal image plane, thus participating in emmetropization [43]. Studies suggest that atropine 0.01% is as effective as higher concentrations, with fewer side effects and no rebound effects after discontinuation [1, 3, 15, 22, 26]. Myopia progression in children could be slowed by atropine therapy more substantially in Asian than in White children [44].

The evaluation of cycloplegic refractive error is the reference standard to avoid mistaking accommodative spasms for myopia in children, and the uncommon cases of progressive keratoconus should be identified before beginning atropine treatment to avoid confounding them with axial myopia [22].

Pirenzepine: Interestingly, pirenzepine is no longer the subject of research or commercialization despite having a 50% greater effectiveness in delaying the advancement of myopia compared to atropine eye drops. The reasons for this remain unknown [4].

Oral 7-Methylxanthine: A nonselective adenosine receptor antagonist, this agent demonstrated in a primate model a lessening of axial myopia brought on by hyperopic defocus [45]. Systemic treatment with 7-methylxanthine altered axial length in a pilot human clinical study including 68 myopic children, minimally [21].

Timolol: In an animal study, timolol had an intraocular pressure-lowering effect in normal and myopic chicks, yet it did not inhibit the development of myopia [46]. Chen et al. examined the effect of timolol on accommodative vergence to accommodation (AC/A) ratios in 30 children with myopia by measuring AC/A ratios before and 30 min after instillation of the eye drop. Despite a significant reduction in accommodative convergence in the stable myopes, timolol had no significant effect on accommodative convergence in the emmetropes or progressing myopes. Likewise, it yielded no significant change in the accommodative response to positive or negative lenses or the response AC/A ratios [47]. Qi et al. reported the efficacy of timolol for the correction of myopic regression when a 0.5 D or greater myopic shift was detected in post-laser in situ keratomileusis patients regardless of age, sex, preoperative spherical equivalent, or time of treatment onset. However, the myopic regression recurred after cessation of timolol treatment [48]. Therefore, the efficacy of timolol on myopia control in children is yet to be determined [36, 37].

Low-intensity laser therapy

Axial elongation may be effectively controlled if a strategy is developed for reducing the cell apoptosis that causes axial elongation. Therefore, a study focusing on low-level laser therapy was initiated [49, 50]. Phototherapy produces sufficiently low energy to induce a stimulus–response to arrest axial elongation [34, 49]. Low doses of red and near-infrared light are used, distinguishing low-level laser therapy from high-power laser therapy. Its output can reach 500 mW, and its wavelength varying from 600 nm to 1100 nm [51].

Bifocal or multifocal spectacles

Prior studies have suggested that bifocal lenses may delay the development of myopia in children [52]. In a case-control study, the progression of myopia was compared between identical twins with near esophoria when one twin used commercially available bifocal soft contact lenses and the other used standard single vision soft contact lenses [53]. The twin wearing bifocal contact lenses experienced no increase in myopia during the first year (- 0.13 D refractive shift), whereas the twin wearing standard single vision soft contact lenses had a 1.19 D change during the same period [53]. Through the top of these lenses, the child sees distant objects clearly [38]. Considering that the near addition potentially reduces or eliminates accommodative effort or error associated with esotropia, it may control myopia progression. However, when compared with that of single vision lenses, the slowing of myopia progression by these lenses is not clinically significant [54].

Orthokeratology

Orthokeratology was originally explored in the 1960s [34]. In this technique, rigid gas-permeable contact lenses are worn overnight to correct myopia by flattening the anterior cornea [55]. As a result, orthokeratology slowed myopia progression by decreasing the hyperopic peripheral refractive error, and consequently, axial length elongation [34]. Lower contrast sensitivity and higher-order aberrations are among the drawbacks of orthokeratology. Despite this, it is a safe and effective alternative to atropine therapy [56].

Combined treatment

Together, atropine instillation and orthokeratology lenses yield superior control of myopia progression than either therapy alone because they involve entirely separate processes to decrease myopia progression [27, 57]. However, eye care practitioners should consider that those using orthokeratology lenses require different care than those wearing conventional contact lenses [58, 59].

Contact lenses

Contact lenses may be able to better control myopia than single vision spectacle lenses. A potential explanation is that the optical treatment area of contact lenses covers a larger proportion of the visual field than the peripheral treatment area of spectacle lenses [60]. Soft contact lenses with a central distance zone and higher positive power in the periphery greatly reduce the progression of myopia [15]. However, hypoxic, bacterial, and microbial factors could cause both chronic and acute inflammatory reactions in contact lens wearers [61].

Peripheral defocus contact lenses

Defocus incorporated soft contact lenses are novel bifocal contact lenses with a concentric ring pattern that reduces peripheral and central defocus and optimizes retinal image quality for points on and in front of the retina. This slows eye growth when compared with the effect of conventional contact lenses, while clear vision is maintained through the center [62, 63]. They significantly improved the vision-related quality of life of Chinese children aged 7 to 12 years with myopia ≤ - 4.00 D and astigmatism < 1.50 D compared with single-vision spectacles, and they elicited greater patient satisfaction than single-vision spectacles [64].

This narrative review summarizes the current state-of-the-art myopia control interventions, including both optical and pharmacological approaches. It compares treatments to help practitioners understand their relative safety and efficacy. However, it fails to provide a comprehensive overview of the current literature and a meta-analysis of their data. A meta-analysis may yield more precise quantitative estimates of treatment effects. Moreover, our review only included studies published in English. Further studies into how the interventions affect myopia development and their mechanisms of action in children are necessary. The long-term safety, potential adverse effects, and results of discontinuation of medications, particularly high-dose atropine, must be investigated. Individualized treatment plans could be developed based on age, genetic profiles, and initial degrees of myopia. Determining the safety and efficacy of combined interventions, such as orthokeratology and atropine, could elucidate potential synergistic effects. Non-pharmaceutical approaches to myopia control, such as lifestyle changes, should be investigated in large-scale studies. Examining regional differences in the progression of myopia may identify risk factors and treatments specific to that region.

CONCLUSIONS

The current literature supports the efficacy of increased outdoor time, administration of pharmacological agents, and special contact lenses as treatment modalities for slowing myopia progression in children. Optical (contact lenses, spectacles, and orthokeratology) and pharmaceutical techniques to reduce the progression of myopia are reviewed in this article. Nonetheless, further measures, such as public policies and international eye health organizational consensuses, are required. Atropine and pirenzepine have proved to be effective in slowing the progression of myopia. However, their effects increase when combined with orthokeratology. Peripheral defocus contact lenses are mentioned in the literature as another treatment option. Low-intensity laser therapy and multifocal spectacles are modestly beneficial; however, adverse effects commonly limit their use. Topical medications have adverse effects including photophobia and impaired near vision and accommodation. In lower concentrations, they may control myopia with fewer side effects. Thus, the ideal option should be chosen by the eye care professional and parent based on the child's lifestyle. Further research is needed to pinpoint the precise mechanisms of action of these therapies and to determine the best course of treatment. The increasing global prevalence of childhood myopia necessitates robust interventional studies into slowing myopia progression and preventing high myopia and related sight-threatening conditions in adulthood.

ETHICAL DECLARATIONS

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Conflict of interests: None

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