REVIEW

Controlling myopia progression in children and adolescents

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Abstract: Myopia is a common disorder, affecting approximately one-third of the US population and over 90% of the population in some East Asian countries. High amounts of myopia are associated with an increased risk of sight-threatening problems, such as retinal detachment, choroidal degeneration, cataracts, and glaucoma. Slowing the progression of myopia could potentially benefit millions of children in the USA. To date, few strategies used for myopia control have proven to be effective. Treatment options such as undercorrection of myopia, gas permeable contact lenses, and bifocal or multifocal spectacles have all been proven to be ineffective for myopia control, although one recent randomized clinical trial using executive top bifocal spectacles on children with progressive myopia has shown to decrease the progression to nearly half of the control subjects. The most effective methods are the use of orthokeratology contact lenses, soft bifocal contact lenses, and topical pharmaceutical agents such as atropine or pirenzepine. Although none of these modalities are US Food and Drug Administration-approved to slow myopia progression, they have been shown to slow the progression by approximately 50% with few risks. Both orthokeratology and soft bifocal contact lenses have shown to slow myopia progression by slightly less than 50% in most studies. Parents and eye care practitioners should work together to determine which modality may be best suited for a particular child. Topical pharmaceutical agents such as anti-muscarinic eye drops typically lead to light sensitivity and poor near vision. The most effective myopia control is provided by atropine, but is rarely prescribed due to the side effects. Pirenzepine provides myopia control with little light sensitivity and few near-vision problems, but it is not yet commercially available as an eye drop or ointment. Several studies have shown that lower concentrations of atropine slow the progression of myopia control with fewer side effects than 1% atropine. While the progression of myopic refractive error is slowed with lower concentration of atropine, the growth of the eye is not, indicating a potentially reversible form of myopia control that may diminish after discontinuation of the eye drops. This review provides an overview of the myopia control information available in the literature and raises questions that remain unanswered, so that eye care practitioners and parents can potentially learn the methods that may ultimately improve a child's quality of life or lower the risk of sight-threatening complications.

Keywords: myopia control, children, review, atropine, orthokeratology, soft bifocal contact lenses

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Introduction

Myopia, also known as nearsightedness, is caused by an increase in eye length or corneal curvature and this condition causes light from distant objects to focus in front of the retina. Light focused in front of the retina results in blurry vision while looking at far away objects but clear vision while looking at close objects.

Myopia affects approximately one-third of the US population,[1] but the prevalence ranges from as low as 3% for Sherpa in Nepal[2] to over 90% in Taiwan University students.[3] In general, the prevalence of myopia is highest in Asian children,[4–7] followed by Hispanic, and then black and white children.[6,7] Some studies report a greater proportion of myopic females,[8–11] but others report a similar prevalence between sexes.[12–14] Myopia typically develops at approximately 8 years of age and progresses through 15 or 16 years of age,[15,16] and the average rate of progression is approximately 0.50 D (diopter) per year.[17–20]

Although myopia is a prevalent disease, little is known about the risk factors that lead to the development and progression of myopia. Genetics appear to play a role in determining a child's refractive error status. The risk of becoming myopic increases with the number of myopic parents,[21–23] monozygotic twins have significantly stronger correlation of refractive error than dizygotic twins,[24,25] and genetic factors are more responsible for variability in refractive error than environmental factors.[26,27] However, no single chromosomal locus has been consistently associated with myopia.[28–38] While near work has long been suspected to be a risk factor for myopia, few studies have found a strong correlation with either the onset or progression of myopia.[21–23,39–41] However, spending more time outdoors has been shown to decrease the likelihood of becoming myopic,[22,42–46] but does not slow down the progression of myopia.[41,47] Some schools in Taiwan were randomly assigned to encourage outdoor activities during recess, while other schools maintained their normal routine during recess. In the schools that encouraged more outdoor activities during recess, only 8.4% of children became myopic, compared to 17.7% in the schools that maintained their normal recess activities ($P<0.001$). However, the myopic children who were encouraged to spend time outdoors during recess progressed in myopia at the same rate as those who maintained their typical recess activities ($P=0.18$).[47]

Higher amounts of myopia increase the risk of ocular complications such as glaucoma,[48–51] cataracts,[52–55] and retinal detachment and atrophy.[56–60] Due to these sight-threatening complications and the high worldwide prevalence, research scientists have attempted many methods to reduce the progression of nearsightedness, including undercorrection of myopic refractive error,[61,62] bifocal or multifocal spectacles,[17,18,63–65] gas permeable contact lenses,[19,66] topical pharmaceutical agents,[67–73] orthokeratology contact lenses,[74–79] and soft bifocal contact lenses.[80–83]

Undercorrection of Myopia

Myopes read more[84,85] and scholastically perform better[86,87] than emmetropes or hyperopes, so accommodative effort and myopia may be associated. Myopic patients also have a higher accommodative lag than emmetropic patients,[88–91] and the lag of accommodation focuses light behind the retina during near work, potentially acting as a putative cue for increased myopia progression. Undercorrection of myopia reduces accommodative effort and accommodative error (lag), and hence is thought to slow myopia progression. In actuality, undercorrecting a child's refractive error either increases[62] or has no effect on myopia progression,[61] and so undercorrection does not slow myopia progression.

Bifocal or multifocal spectacles

A great deal of research has examined the effect of bifocal or multifocal spectacles on myopia progression.[17,18,63–65] These glasses allow children to clearly see far away objects through the top portion of the spectacle lens. The bottom portion of the lens contains the reading power, which may control myopia progression by reducing or eliminating the accommodative effort or error associated with myopia.[88–91] When compared to single vision lenses, bifocal or multifocal lenses slow the progression of myopia, but the difference in progression rates is typically not clinically meaningful.[17,18,64,65] Even myopic children believed to benefit most from bifocal or multifocal spectacle myopia control – those with esophoria (the resting position of the eyes is too close to the nose) and accommodative lag – do not exhibit clinically meaningful slowing of myopia progression.[17,65] The most promising method of bifocal spectacle myopia control was reported by Cheng et al.[63] They provided executive top bifocal spectacles and base-in prisms to children with progressing myopia and showed that the progression slowed by 51% over 3 years. The base-in prism did not result in additional treatment effect, but it is unknown whether they found a stronger treatment effect than other bifocal or multifocal spectacle myopia control studies because they utilized an executive top bifocal spectacle lens or because they only enrolled progressing myopes, which allowed for better myopia control.[63]

Gas permeable contact lenses

Alignment-fit gas permeable contact lenses worn during the day slowed myopia progression in early studies, but all those studies suffered from study design issues such as unequal loss to follow-up, enrollment of subjects outside of the expected age of progression, and lack of randomization.[92–95] Two more recent randomized clinical trials showed that gas permeable
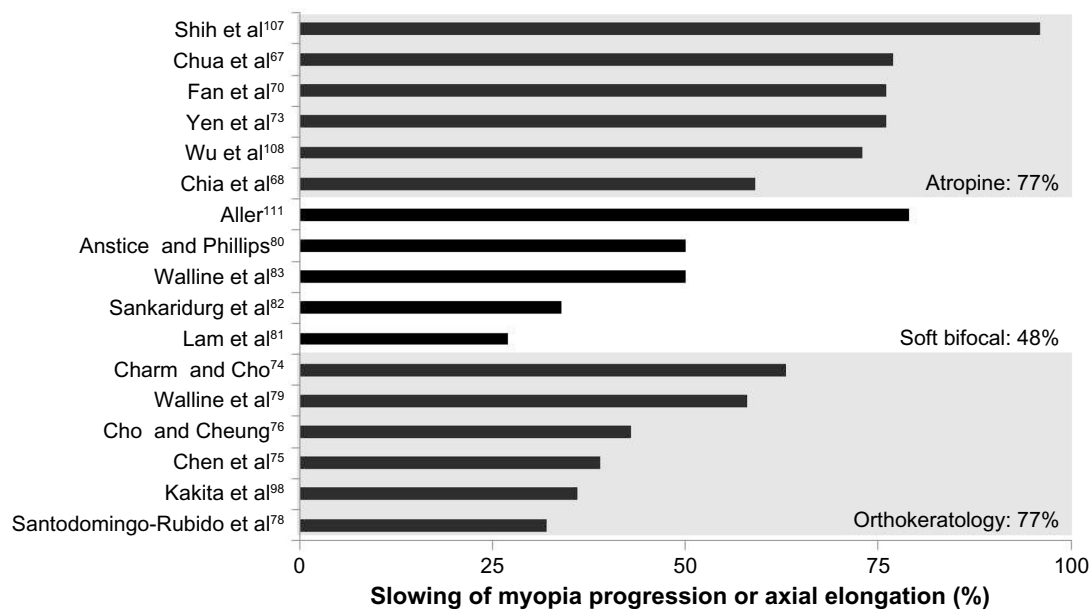
Figure I Percent slowing of myopia progression by atropine, soft bifocal, or orthokeratology contact lenses in controlled studies published in the literature.
Notes: Percent slowing is calculated as the difference in progression between the experimental and control group, divided by the progression of the control group. The overall average for each type of correction is the simple mathematical average of the percent slowing for each study in that type of correction. Axial elongation was used when available, but myopia progression was used if axial elongation was not available.

contact lenses do not slow the growth of the eye.[19,66] Although Walline et al reported significantly slower myopia progression in the gas permeable contact lens group, they found no difference in the eye growth.[19] The treatment effect was mostly due to the differences in corneal curvature at the end of the study. Because corneal curvature changes are temporary, the slowed myopia progression is unlikely to be permanent, so the authors concluded that children should not be fitted with gas permeable contact lenses solely to slow the progression of myopia.[19]

In order to be considered clinically meaningful, a myopia control modality should slow the progression by approximately 50%, according to most myopia control grant applications. Only three modalities are currently considered to be at least close to this level of myopia control: orthokeratology contact lenses, soft bifocal contact lenses, and topical pharmaceutical agents (Figure 1).

Orthokeratology contact lenses

Orthokeratology contact lenses are worn overnight to flatten the central cornea and temporarily reduce the amount of myopia. Orthokeratology contact lenses provide clear vision without the need for vision correction during the day, and they also reduce myopic progression (Table 1).[74–79,96–98] These contact lenses are thought to slow myopia progression optically. Light that focuses in front of the retina (myopic blur) acts as a putative signal to slow the eye growth.

Orthokeratology contact lenses correct central refractive error while leaving peripheral myopic blur, which acts as a putative cue to slow the progression of myopia.[98–100] Because these contact lenses are worn overnight, they are associated with an increased risk of microbial keratitis, which may be as high as wearing soft contact lenses overnight.[101]

Orthokeratology contact lenses slow axial length growth compared to single vision gas permeable contact lenses,[96] single vision soft contact lenses,[79] and single vision spectacles.[74–76,97,98,102] The first randomized clinical trial of orthokeratology myopia control demonstrated significantly slower mean (± standard deviation) axial elongation in children wearing orthokeratology lenses (0.36 ± 0.24 mm) than children wearing single vision spectacles (0.63 ± 0.26 mm, $P<0.01$).[76]

Soft bifocal contact lenses

Soft bifocal contact lenses are typically worn by patients 40 years old or older to provide clearer vision while reading. Soft bifocal contact lenses with a center distance design (reading portion outside the central contact lens) also slow myopic progression by creating myopic defocus in the periphery,[103] which acts as a putative signal to slow the eye growth. However, these lenses are worn during the day and fitted more commonly than orthokeratology contact lenses. Several nonrandomized, controlled clinical trials have shown the myopia control benefit of soft bifocal contact lenses.[80–83]

Table 1 Axial elongation of orthokeratology contact lens wearers compared to controls

Reference	Study design	Study duration (years)	Control method	Mean change (±SD) in axial length (mm)	
				Orthokeratology	Control
Charm and Cho[74]	Randomized clinical trial	2	Single vision spectacles	0.19±0.21	0.51±0.32
Chen et al[75]	Self-selected prospective	2	Single vision spectacles	0.31±0.27	0.64±0.31
Cho et al[76]	Randomized clinical trial	2	Single vision spectacles	0.36±0.24	0.63±0.26
Hiraoka et al[97]	Self-selected retrospective	5	Single vision spectacles	0.99±0.47	1.41±0.68
Kakita et al[98]	Self-selected retrospective	2	Single vision spectacles	0.39±0.27	0.61±0.24
Santodomingo-Rubido et al[78]	Self-selected prospective	2	Single vision spectacles	0.47	0.69
Swarbrick et al[96]	Randomized, contralateral crossover	1	Spherical gas permeable contact lenses	0.02±0.09 mm in first 6 months	0.04±0.06 mm in first 6 months
Walline et al[79]	Prospective, historical controls	2	Soft contact lenses	0.25±1.02	0.57±1.12

Abbreviation: SD, standard deviation.

Overall, soft bifocal contact lenses slow the progression of myopia in children by nearly 50%, which is similar to orthokeratology contact lenses (Table 2).

Topical pharmaceutical agents

Topical pharmaceutical methods to control myopic progression in children are anti-muscarinic eye drops that are used in routine eye care to dilate the pupil and reduce or eliminate accommodation. Atropine is a broad spectrum anti-muscarinic agent and side effects include temporary sensitivity to light and unclear vision at near. Pirenzepine affects only M1 anti-muscarinic receptors, which are less concentrated in the iris and ciliary body, and hence does not dilate the pupil or reduce accommodation as much as atropine.

Although the specific myopia control mechanism of anti-muscarinic agents is unknown, studies show both pirenzepine and atropine are very effective at reducing myopic eye growth in children (Table 3).[70,71,73,104–108] However, atropine is rarely prescribed due to the side effects, and pirenzepine is not approved by the US Food and Drug Administration (FDA) for myopia control, nor is it commercially available.

Lower concentrations of atropine may provide clinically meaningful myopia control while minimizing side effects.[68,69,71,107] Chia et al randomly assigned myopic children to 0.5%, 0.1%, and 0.01% atropine eye drops.[68] Over 2 years, myopia progressed −0.30±0.60 D for the 0.5% group, −0.38±0.60 D for the 0.1% group, and −0.49±0.63 D for the 0.01% groups. All were significantly slower than the historical placebo control group. There was no difference between the groups in terms of best-corrected distance visual acuity, but the subjects with higher concentration of atropine had worse near visual acuity while wearing correction for distance vision. Subjects in this investigation were told that if they had trouble reading at near, they could request for reading glasses to help them see more clearly; 70% of children on 0.5% atropine, 61% of children on 0.1% atropine, and only 6% of children on 0.01% atropine requested the glasses to improve near vision.[68] Although myopic progression was slowed by the lower concentration of eye drops, axial elongation of the eye was not.[69] This result is puzzling and suggests that the myopia control may be due to changes in crystalline lens curvatures secondary to reduced tonic accommodation while the eyes are at rest. In fact, 1 year after discontinuation of the various concentrations of atropine eye drops, the most

Table 2 Changes in refractive error with soft bifocal contact lenses compared to single vision contact lens wearers

Reference	Study design	Study duration	Control method	Mean (± SE) spherical equivalent cycloplegic refractive error	
				Soft bifocal contact lens	Control
Anstice and Phillips[80]	Randomized, crossover	20 months	Single vision contact lens	Period 1: −0.44±0.33 Period 2: −0.17±0.35	Period 1: −0.69±0.38 Period 2: −0.38±0.38
Lam et al[81]	Randomized clinical trial	2 years	Single vision contact lenses	−0.59 D	−0.80 D
Sankaridurg et al[82]	Prospective matched design	1 year	Single vision spectacles	−0.57 D	−0.86 D
Walline et al[83]	Prospective matched design	2 years	Single vision contact lenses	−0.51±0.06	−1.03±0.06

Abbreviations: SE, standard error; D, diopter.

Table 3 Effects of pharmaceutical agents on myopia progression compared to control groups

Reference	Study design	Study duration (years)	Treatment method	Control method	Mean change (±SD) in myopia progression (D)	
					Treatment	Control
Fan et al[70]	Interventional control	1	1% atropine	No treatment	+0.06±0.79	−1.19±2.48
Lee et al[71]	Retrospective, case–control	1	0.05% atropine	No treatment	−0.28±0.26	−0.75±0.35
Shih et al[107]	Randomized clinical trial	2	0.5%, 0.25%, 0.1% atropine	0.5% tropicamide	0.5%: +0.04±0.63 0.25%: −0.45±0.55 0.1%: −0.47±0.91	−1.06±0.61
Siatkowski et al[105]	Randomized clinical trial	2	2% pirenzepine	Placebo	−0.58±0.53	−0.99±0.68
Tan et al[106]	Randomized clinical trial	1	2% pirenzepine	Placebo	−0.47±1.02	−0.94±0.99
Wu et al[109]	Retrospective case–control	3	0.1% atropine	No treatment	−0.31±0.26	−0.90±0.30
Yen et al[73]	Randomized clinical trial	1	1% atropine; 1% cyclopentolate	Saline	Atropine: −0.22±0.54 Cyclopentolate: −0.58±0.49	−0.91±0.58

Abbreviations: SD, standard deviation; D, diopter.

effective myopia control was provided by 0.01% atropine,[69] presumably because the accommodative tonus returned to normal, negating the stronger myopia control effect due primarily to changes in tonic accommodation. In a separate study, 0.025% atropine was found to reduce the onset of myopia from 54% to 21% (P=0.016).[110]

The most effective myopia control was provided by topical pharmaceutical agents, but they are rarely prescribed due to the side effects. While lower concentrations provide clinically meaningful myopia control, the mechanism may be at least partially due to temporary changes in tonic accommodation and may not lead to permanent decreases in myopia progression.

Conclusion

Of all the methods studied to slow the progression of myopia, topical pharmaceutical agents, orthokeratology contact lenses, and soft bifocal contact lenses were found to be the most effective, commercially available modalities. However, none of them is approved by the FDA to slow the progression of myopia. Topical pharmaceuticals are not used frequently due to the side effects, primarily photophobia and reduced near vision and accommodation, but there is potential for myopia control with fewer side effects using lower concentrations. Orthokeratology contact lenses and soft bifocal contact lenses slow the myopic progression of myopia in a similar manner, so the best modality should be determined by the eye care practitioner and parent, based on the lifestyle of the specific child. Bifocal and multifocal spectacles is statistically significant in slowing the myopia progression, but do not provide a clinically meaningful effect; however, the latest randomized clinical trial using executive top bifocal

spectacles on progressing myopes exhibited a clinically meaningful slowing of myopia progression. Undercorrection of myopia and gas permeable contact lenses were not found to slow the progression of myopia in children.

Although we have answered many questions about slowing of myopia progression in children, many questions remain to be answered. For example, will soft bifocal contact lenses with the reading portion in the center of the contact lenses also slow myopia progression? Will the implementation of both optical (soft bifocal or orthokeratology contact lenses) and pharmacologic (atropine) myopia control methods provide better myopia control than either one alone? Can we permanently reduce the risk of myopia onset using these myopia control methods? What happens to myopia progression once the myopia control modalities are discontinued? Far more research needs to be conducted to answer these important questions so that we can optimize eye care for children and potentially prevent or maintain lower amount of myopia, which may reduce the risk of sight-threatening complications.

Disclosure

The authors report no conflicts of interest in this work.

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