EDITORIAL

Reducing the Progression of Myopia

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Myopia, or nearsightedness, causes blurry vision that usually is corrected with glasses, contact lenses, or refractive surgery. The lifetime prevalence of myopia has been reported to be 80% to 90% in population-based studies in Asia.[1] Myopia is also very common in other parts of the world, with a prevalence of almost 50% in many parts of Europe[2] and an estimated increase in prevalence from 25.0% in 1971-1972 to 41.6% in 1999-2004 in the US.[3]

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Somewhat arbitrarily, myopia is considered to be high when the spherical equivalent of corrective glasses is −6 D or less, which often is associated with an axial length of the eye of 26 mm or greater, compared with the normal adult mean axial length of 22 to 25 mm. However, there is no absolute cutoff that determines a safe level of myopia when myopic-associated pathology to the eye does not occur. Nevertheless, high myopia is convenient to distinguish because pathology associated with myopia, termed *pathologic myopia*, more often occurs in the setting of high myopia, including staphyloma (focal outpouchings of the back wall of the eye), glaucoma, cataract, degeneration of the central retina (myopic macular degeneration), schisis (splitting of retinal cell layers), vitreomacular interface abnormalities (eg, macular holes or traction on the surface of the retina from epiretinal membranes), or retinal tears that may progress to retinal detachments. These abnormalities of pathologic myopia may or may not be manageable with medications or surgery and may lead to vision loss or blindness.

The etiology of myopia is thought to be associated with the emmetropization of the eye (ie, an increase in the axial length of the eye from its congenital hyperopic [farsighted] condition to emmetropia), in which the light rays are focused on the retina. Without this elongation process, which involves restructuring of the collagen within the sclera, the eye could not grow to its adult length. However, in myopia, this growth continues beyond the normal length, so light rays become focused in front of the retina unless the light is refracted with glasses or contact lenses or refractive surgery to refocus the light to the retina.

Although multiple genetic variations are associated with the presence of pathologic myopia, environmental risk factors also are involved, including near work (both duration and distances less than 12 inches) and outdoor exposure. The effect of limiting near work remains uncertain. High intensity of outdoor light has been hypothesized to lead to higher retinal dopamine secretion, which stops excessive elongation of the eye. This theory was tested in a randomized clinical trial in Asia in which 693 schoolchildren who were encouraged to go outdoors for up to 11 hours weekly had less myopic shift after the students completed the 1-year trial (0.35 D vs 0.47 D; difference, 0.12 D [95% CI, 0.05-0.19]; $P = .002$). In addition, the intervention group had less axial length elongation than the control group (0.28 mm vs 0.33 mm; difference, 0.05 mm [95% CI, 0.02-0.08]; $P = .003$).[4] Although the clinical relevance of this short-term difference remains unknown, this potentially protective effect has influenced policy in some countries, such as Singapore, to encourage outdoor exposure.[5]

Three additional interventions, each with their own potential risks and benefits, are currently being investigated to reduce the incidence or progression of myopia. These include (1) administration of atropine eye drops in various concentrations (0.01%-1%),[6,7] which presumably act by an up-regulation and downregulation of retinal and scleral muscarinic receptors that are hypothesized to influence the scleral matrix to reduce axial elongation[8]; (2) orthokeratology, which involves nighttime wearing of contact lenses designed to change the shape of the cornea and increase peripheral hyperopia, thereby potentially slowing down axial growth[9]; and (3) use of soft dual-focus contact lenses. The center part of a dual-focus contact lens corrects vision for distance, with either gradual (progressive) or concentric zones of additional diopters of correction peripheral to this central part designed to reduce the hyperopic defocus in the periphery that otherwise would contribute to myopic progression.

This soft dual-focus contact lens strategy is the topic of the Bifocal Lenses in Nearsighted Kids (BLINK) randomized clinical trial reported in this issue of *JAMA*.[10] The objective of this study was to determine whether soft contact lenses with a central correction for myopia plus a high add (+2.50 D) or medium add (+1.50 D) power to the peripheral concentric zone would slow myopia progression in children more than single-vision (no add) contact lenses that correct for myopia. The primary outcome was the 3-year change in cycloplegic spherical equivalent autorefraction. Four of 11 secondary end points were analyzed for this report, including 3-year change in axial length.

Characteristics of the 292 randomized participants recruited from 2 US optometry schools were similar in the study groups, with a mean (SD) age of 10.3 (1.2) years. Adherence and follow-up were high, and there were no serious adverse events related to soft contact lens use among the 3 groups. Although the adjusted 3-year myopia progression was −1.05 D for the single-vision group, which was less than the progression of −1.29 D anticipated for the sample size calculation, the difference in progression was −0.46 D (95% CI, −0.63 to −0.29) for the high add power vs single-vision group, −0.30 D (95% CI, −0.47 to −0.13) for the high add vs medium add power group,

and −0.16 D (95% CI, −0.33 to 0.01) for the medium add vs single-vision group. The difference in the secondary end point of adjusted mean eye growth was −0.23 mm (95% CI, −0.30 to −0.17) for the high add power vs single-vision group, −0.16 mm (95% CI, −0.23 to −0.09) for the high add vs medium add power group, and −0.07 mm (95% CI, −0.14 to −0.01) for the medium add power vs single-vision group. No differences among the groups for the other 3 secondary end points were identified.

The results from the BLINK trial support and build on similar conclusions from previously reported clinical trials that were smaller in size or only followed up participants for 2 years.[11,12] Despite the public health need around the world for safe and effective prevention interventions and treatments for individuals with pathologic myopia, several additional questions need to be addressed before dual-focal contact lenses become standard care to reduce the risk of myopic progression.

For example, the clinical relevance of the reduction in myopic progression reported in the trial between the higher add power group compared with the single-vision contact lens group is unclear. The observed difference of −0.46 D was less than the 0.65-D difference on which the study was powered. The authors referred to a workshop that discussed this topic, in which a 30% to 50% relative reduction in the progression of myopia may be clinically relevant, but a reduction in the absolute progression rate might be as or more important when trying to reduce the development of pathologic myopia. For example, if an individual has a spherical equivalent of −2 D of myopia and progresses 1 D to −3 D of progression over 3 years without a high add contact lens vs progression of 0.5 D (a 50% reduction) to −2.5 D with a high add power lens, in either case, the individual has mild myopia and is unlikely to have pathologic myopia (≥ −6 D). Prevention of myopic progression per se may be less relevant than prevention of pathologic myopia. There is little evidence from this trial and other trials that have been reported that soft multifocal contact lenses prevent pathologic myopia with its vision-threatening features. Furthermore, with follow-up only to 3 years, whether the effects will persist through adulthood to reduce the development of pathologic myopia or whether discontinuation of the high add power lenses results in loss of the effects are unknown.

The results of the trial contribute to the global efforts at reducing the incidence and progression of pathologic myopia. Because only some of the secondary end points were reported, additional data from this study might be anticipated in the future. Other potential results of value might include determining whether there was any interaction between baseline myopia, age, or both with the treatment effect. There may not be much clinical relevance to reducing myopia progression by one-quarter diopter per year for children with mild myopia unless that group showed substantially greater treatment effect than children with higher degrees of myopia.

The BLINK study makes a contribution to an important and growing public health problem. Nevertheless, the answers to questions regarding longer-term effects on reducing the risk of axial elongation and pathologic myopia seem warranted before soft contact lens correction to reduce myopia progression becomes standard care.

ARTICLE INFORMATION

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REFERENCES

1. Morgan IG, Ohno-Matsui K, Saw SM. Myopia. *Lancet*. 2012;379(9827):1739-1748. doi:10.1016/S0140-6736(12)60272-4

2. Williams KM, Verhoeven VJ, Cumberland P, et al. Prevalence of refractive error in Europe: the European Eye Epidemiology (E^3) Consortium. *Eur J Epidemiol*. 2015;30(4):305-315. doi:10.1007/s10654-015-0010-0

3. Vitale S, Sperduto RD, Ferris FL III. Increased prevalence of myopia in the United States between 1971-1972 and 1999-2004. *Arch Ophthalmol*. 2009;127(12):1632-1639. doi:10.1001/archophthalmol.2009.303

4. Wu PC, Chen CT, Lin KK, et al. Myopia prevention and outdoor light intensity in a school-based cluster randomized trial. *Ophthalmology*. 2018;125(8):1239-1250. doi:10.1016/j.ophtha.2017.12.011

5. Outdoor learning: a national guide for early childhood educators. Early Childhood Development Agency website. Accessed July 6, 2020. https://www.ecda.gov.sg/Educators/Pages/Outdoor-Learning_A-National-Guide-for-Early-Childhood-Educators.aspx

6. Chua WH, Balakrishnan V, Chan YH, et al. Atropine for the treatment of childhood myopia. *Ophthalmology*. 2006;113(12):2285-2291. doi:10.1016/j.ophtha.2006.05.062

7. Low-dose atropine for treatment of myopia (MTS1). ClinicalTrials.gov website. Updated June 9, 2020. Accessed July 6, 2020. https://clinicaltrials.gov/ct2/show/NCT03334253

8. Barathi VA, Beuerman RW. Molecular mechanisms of muscarinic receptors in mouse scleral fibroblasts: prior to and after induction of experimental myopia with atropine treatment. *Mol Vis*. 2011;17:680-692.

9. Cho P, Cheung SW. Retardation of myopia in Orthokeratology (ROMIO) study: a 2-year randomized clinical trial. *Invest Ophthalmol Vis Sci*. 2012;53(11):7077-7085. doi:10.1167/iovs.12-10565

10. Walline JJ, Walker MK, Mutti DO, et al. Effect of high add power, medium add power, or single-vision contact lenses on myopia progression in children: the BLINK randomized clinical trial. *JAMA*. Published August 11, 2020. doi:10.1001/jama.2020.10834

11. Lam CS, Tang WC, Tse DY, Tang YY, To CH. Defocus Incorporated Soft Contact (DISC) lens slows myopia progression in Hong Kong Chinese schoolchildren: a 2-year randomised clinical trial. *Br J Ophthalmol*. 2014;98(1):40-45. doi:10.1136/bjophthalmol-2013-303914

12. Ruiz-Pomeda A, Pérez-Sánchez B, Valls I, Prieto-Garrido FL, Gutiérrez-Ortega R, Villa-Collar C. MiSight Assessment Study Spain (MASS): a 2-year randomized clinical trial. *Graefes Arch Clin Exp Ophthalmol*. 2018;256(5):1011-1021. doi:10.1007/s00417-018-3906-z