Special Issue

IMI Prevention of Myopia and Its Progression

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The prevalence of myopia has markedly increased in East and Southeast Asia, and pathologic consequences of myopia, including myopic maculopathy and high myopia-associated optic neuropathy, are now some of the most common causes of irreversible blindness. Hence, strategies are warranted to reduce the prevalence of myopia and the progression to high myopia because this is the main modifiable risk factor for pathologic myopia. On the basis of published population-based and interventional studies, an important strategy to reduce the development of myopia is encouraging schoolchildren to spend more time outdoors. As compared with other measures, spending more time outdoors is the safest strategy and aligns with other existing health initiatives, such as obesity prevention, by promoting a healthier lifestyle for children and adolescents. Useful clinical measures to reduce or slow the progression of myopia include the daily application of low-dose atropine eye drops, in concentrations ranging between 0.01% and 0.05%, despite the side effects of a slightly reduced amplitude of accommodation, slight mydriasis, and risk of an allergic reaction; multifocal spectacle design; contact lenses that have power profiles that produce peripheral myopic defocus; and orthokeratology using corneal gas-permeable contact lenses that are designed to flatten the central cornea, leading to midperipheral steeping and peripheral myopic defocus, during overnight wear to eliminate daytime myopia. The risk-to-benefit ratio needs to be weighed up for the individual on the basis of their age, health, and lifestyle. The measures listed above are not mutually exclusive and are beginning to be examined in combination.

Keywords: myopia, pathologic myopia, high myopia, atropine, contact lenses, orthokeratology, myopic macular degeneration, myopia-associated optic neuropathy

Investigative Ophthalmology & Visual Science

Parallel to the process of urbanization, in combination with a pronounced intensification of education and marked reduction in time spent outdoors, the prevalence of axial myopia has profoundly increased over the last three decades globally in the younger generations, in particular in East and Southeast Asia.[1–3] The prevalence of myopia ranges from about 3% among school children in Sub-Sahara African countries to approximately 80% to 90% among senior high school students in parts of East and Southeast Asia.[4–6] Because axial elongation is the main risk factor for the development of pathologic complications of myopia in adulthood, it may be foreseen that a relatively large number of presently young myopic individuals may develop pathology related to myopia later in life.[1–3,7–9] Pathologies including myopic maculopathy and high myopia-associated optic neuropathy are already now among the most frequent causes of irreversible vision loss and blindness in East Asia.[1,10,11] In some individuals, axial elongation can continue beyond the fifth decade of life.[7] Axial elongation is accompanied by thinning of the choroid and sclera, being most marked at the posterior pole.[12] In addition, there is enlargement and misalignment of the optic nerve head with elongation and thinning of the lamina cribrosa; shifting and enlargement of Bruch´s membrane opening resulting in the development of parapapillary gamma zone and delta zone; rotation of the optic disc; glaucoma-like (or glaucomatous) and nonglaucomatous optic nerve damage; development of lacquer cracks and secondary Bruch´s membrane defects in the macular region, first in the extrafoveal area and eventually in the foveal region; development of scleral staphylomata; and occurrence of myopic macular choroidal neovascularization and subsequent scar formation in the fovea (Fuchs' spot).[9,13–15] Besides longer axial length and continuing axial elongation, older age is an important risk factor for the development of myopic pathology.[7,8] In some studies, female sex was an additional risk factor.[7,8]

Procedures are therefore warranted to prevent the development of high myopia and subsequent pathology and also to reduce the economic burden caused by uncorrected and pathologic myopia. The measures that can be taken for the prevention of the development of myopia and for the reduction of the progression of myopia include public health interventions, a pharmacological approach with the topical application of low-dose atropine eye drops, and optical measures including multifocal spectacles and multifocal contact lenses that can have aspheric or discrete dual-focus designs, and orthokeratology (OK). Besides the vision reduction–associated problems of high myopia and pathologic myopia, one may also take into account a public health-related aspect to controlling myopia, particularly in the low- and middle-income countries where uncorrected myopia, because of a lack of access to glasses, is still a major challenge. These topics will be addressed in the present review, updating and translating a previous comprehensive review of clinical trials on myopia control.[16]

Increased Time Spent Outdoors

Since the landmark studies by Jones and colleagues[17] and by Rose and associates[18,19] and others, it has become apparent that the amount of time spent outdoors is a significant parameter associated with the development of myopia in school children.[5–16,20–38] The Sydney Myopia Study showed that exposure to more than two hours of time spent outdoors daily was associated with a reduced odds of myopia, even in children who engaged in high levels of near work.[19] Subsequently, interventional studies revealed that increasing the amount of time spent outdoors decreased the incidence of myopia in children.[20,21] A meta-analysis of the existing literature published in 2012 estimated that the odds of developing myopia were decreased by 2% for each additional hour of time spent outdoors per week.[22] A meta-analysis published in 2017 reported that increased time spent outdoors reduced the incidence of myopia with a risk ratio of 0.54 to 0.57 for high versus low time spent outdoors in clinical trials and longitudinal cohort studies, and an odds ratio of 0.96 per hour spent outdoors in cross-sectional investigations, but it had no effect in reducing the progression of myopia in children who were already myopic at baseline.[23] The most recent review concluded that more time spent outdoors helped in slowing down the change of axial length, as well as in reducing the risk of myopia.[38] In a school-based trial performed in Guangzhou, China, 12 schools with altogether 1903 children in Grade 1 (mean age, 6.6 years) were randomized to an intervention group (with a compulsory 40-minute outdoor class at the end of each school day, and parents were asked to encourage outdoor activity outside after school hours), or into a control group (without adjustment of the outdoor activity schedules). After a follow-up of three years, the incidence of myopia was significantly lower (30.4% vs. 39.5%), and the change in refractive error was slightly lower (1.42 diopters vs. 1.59 diopters) in the intervention group than in the control group. However, a recent study revealed a potential rebound effect that occurred within three years after stopping of a one-year program with 30 minutes of daily outdoor jogging.[24] Including only children who were myopic at baseline of the study, the intervention was associated with a slight increase in myopia progression.

In Taiwan, school-based efforts to reduce myopia started by improving room lighting and table height, encouraging distance gaze and ocular exercises, and performing intervals of near work of 39 minutes followed by 10 minutes of break. These procedures, however, were not associated with a reduction in the incidence and prevalence of myopia; in fact, despite these measures, the prevalence of myopia continued to increase year by year. Only after the education policy specified increased outdoor time of at least 80 minutes per day did the myopia incidence decrease from 17% to 8%, with a reduction in the myopic shift from 0.38 diopters to 0.25 diopters.[21] This measure was more effective in children before the onset of myopia.

The underlying reasons why increased time spent outdoors is linked to a lower myopia incidence have not completely been elucidated so far, but proposed reasons include factors such as higher light intensities, variations in the chromatic light composition, differences in dioptric topographies, less near work, and a decrease in the accommodative demand.[20,39–45] The idea of a protective effect of an increased outdoors time against myopia development was based on evidence from animal studies, including primates, that brighter light produced more dopamine release from the retina and that dopamine and dopamine agonists slowed axial elongation, which is the structural basis of axial myopia.[1,46–48] This hypotheses was then tested and confirmed in animal models of myopia, with increased light intensity able to completely block the development of experimental myopia, without changing any other parameter.[1,46–48]

Investigative Ophthalmology & Visual Science

Differences in the designs of the clinical studies on the amount of time spent outdoors make their comparison difficult. The statistically significant effect of a prolonged time spent outdoors on the reduction of myopia progression showed a considerable variation between the studies; however, the safety of the intervention, because of its noninvasiveness, should make a prolongation of outdoors time a measure of first choice for parents in the education of their children and for public health policies of governments.

It is also worth mentioning that not only the accumulative time spent outdoors but also how it is combined right after sustained near work may be of potential importance in delaying the onset, as well as slowing down the progression of myopia. An animal study has suggested that a brief period of plus defocus or bright light exposure right after a minus defocus treatment can be effective in negating the impact from the signals for developing or increasing myopia.[49]

In addition, it is possible that increased time spent outdoors in combination with physical activity will promote a healthier lifestyle in children and adolescents and reduce obesity and other disorders.[50] Combining the delay of myopia onset with the prevention of excessive body weight could lead to better emotional health and lower levels of depression, anxiety and stress. Risks of outdoors need to be considered such as increased sun exposure and skin cancers as well as exposure to pollution. Positive examples of public health policy are the Singaporean early childhood agency organizing preschool children to have one hour of outdoor time daily, the regulations by the Taiwanese authorities, and China, where the amount of homework for schoolchildren has been reduced and where a policy has been started to increase compulsory time outdoors.[51] Reductions in homework could be more related to a decrease in the amount of near work than to an increase in the time spent outdoors, because there may be some cultural emphasis on the avoidance of sun exposures, particularly for girls. Encouraging children to spend more time outdoors may be an appropriate strategy also for very young children, because data from Singapore showed that 10% of the children in Singapore have developed myopia already by the age of 6 years, with the mean age of myopia onset at 8.5 years.

Pharmacological Measures

In the first randomized, placebo-controlled trial of atropine for myopia control, Yen and colleagues[52] reported in 1989 that the progression of myopia was least marked in the group with application of 1% atropine eye drops for one year (myopia progression: −0.22 ± 0.54 diopters/y), followed by the group with application of 1% cyclopentolate eye drops (−0.58 ± 0.49 diopters/y), and a control group with application of placebo eye drops (−0.91 ± 0.58 diopters/y).[52,53] Because photophobia and near blur were severe side effects, the results of the study were not translated into clinical practice. Ten years later, Shih and associates[54] found in a randomized, controlled trial that the progression of myopia after two years was least pronounced in a study group with 0.5% atropine eye drops (−0.04 ± 0.63 diopters/y), followed by the atropine 0.25% group (−0.45 ± 0.55 diopters/y), and the atropine 0.1% eye drop group (−0.47 ± 0.91 diopters/y).It was most marked in the control group with the application 0.5% tropicamide eye drops, (−1.06 ± 0.61 diopters/y).[54] Limitations of the study by Shih et al.[54] were the lack of biometry for the measurement of axial length and the lack of a placebo control group. In the ATOM (Atropine for the Treatment of Childhood Myopia)-1 Study, conducted by Chua and colleagues[55] in 2006, the mean progression of myopia was significantly lower in the 1% atropine group (−0.28 ± 0.92 diopters/2 y) than in the eyes receiving placebo eye drops (−1.20 ± 0.69 diopters/2 y). Axial length, as measured sonographically, remained unchanged (−0.02 ± 0.35 mm/2 y) in the study group with 1% atropine, although there was a significant ($P <$ 0.001) axial elongation in the placebo control group (0.38 ± 0.38 mm/2 y).[55]These differences resulted in a 77% reduction in the mean progression of myopia compared with placebo treatment over two years of treatment. The limitation of the study design was that the high concentration atropine was associated with a marked rebound effect after the application of the eye drops was stopped.[56] At one year after cessation of the treatment, myopia progressed by −1.14 ± 0.8 diopters/y in the study group and by −0.38 ± 0.39 diopters/y in the control group.[56] In other randomized controlled trials, a concentration of atropine of 0.5% or 1% was associated with a relatively high antimyogenic effect (myopia control) and a relatively high rate of side effects, namely mydriasis and decrease in the amplitude of accommodation.[53,57,58]

Subsequently, the ATOM2 study published in 2012 revealed that lower concentrations of atropine eye drops, such as 0.5%, 0.1%, and 0.01%, were associated with a two-year progression of myopia by −0.30 ± 0.60 diopters, −0.38 ± 0.60 diopters, and −0.49 ± 0.63 diopters, respectively, and with an axial elongation of 0.27 ± 0.25 mm, 0.28 ± 0.28 mm, and 0.41 ± 0.32 mm, respectively.[59] The side effect of the atropine concentrations of 0.5%, 0.1%, and 0.01% was an increase in pupil size by 3.11 mm, 2.42 mm, and 0.91 mm, respectively. The amplitude of accommodation was less affected with the lower atropine concentration and was reduced by 3.6 D, 6.0 D, and 11.7 D with atropine of 0.01%, 0.1%, and 0.5%, respectively.[60,61] The rebound effect was considerably smaller in the group with 0.01% atropine eye drops than in the 0.1% and 0.5% groups. After one year of wash-out from atropine eye drops, myopia progressed by −0.87 ± 0.52 D, −0.68 ± 0.45 D, and −0.28 ± 0.33 D in the atropine 0.5%, 0.1%, and 0.01% groups, respectively. In a parallel manner, the amount of axial elongation during the wash-out phase was 0.26 ± 0.23 mm, 0.24 ± 0.21 mm, and 0.19 ± 0.18 mm, respectively.[60] Taking the two years of treatment and the third year of wash-out together, the overall progression of myopia was the smallest in the 0.01% atropine group (−0.72 ± 0.72 D).[60] The limitation of the ATOM-2 study was the lack of a placebo control group. It has to be taken into account that the 0.01% atropine group of the ATOM-2 study did not differ markedly in the amount of axial elongation from the historical placebo group of the ATOM-1 study (0.41 vs. 0.38 mm/2 y).[58,59] However, based on the ATOM-2 study, the application of 0.01% atropine eye drops has become widely used as a medical prevention of myopia progression.[61–63]

To address the limitations of the ATOM-2 study, the Low-concentration Atropine of Myopia Progression study was recently conducted.[64] In children aged four to 12 years and with a myopic refractive error of ≥−1.0 diopter, the daily application of atropine 0.05%, 0.025%, 0.01%, and placebo eye drops resulted, after one year, in a change of refractive error by −0.27 ± 0.61 D, −0.46 ± 0.45 D, −0.59 ± 0.61 D, and −0.81 ± 0.53 D, respectively, with corresponding changes in axial length of

0.20 ± 0.25 mm, 0.29 ± 0.20 mm, 0.36 ± 0.29 mm, and 0.41 ± 0.22 mm, respectively.[64] The application of 0.01% atropine eye drops decreased myopia progression by 27%, although this trend did not reach the level of statistical significance for the reduction in axial elongation. In the two-year follow up report of the Low-concentration Atropine of Myopia Progression study, the mean myopic refractive error progression was 0.55 ± 0.86 D, 0.85 ± 0.73 D, and 1.12 ± 0.85 D in the 0.05%, 0.025%, and 0.01% atropine groups, respectively ($P = 0.015$, $P < 0.001$, and $P = 0.02$, respectively, for pairwise comparisons), with mean axial length changes of 0.39 ± 0.35 mm, 0.50 ± 0.33 mm, and 0.59 ± 0.38 mm ($P = 0.04$, $P < 0.001$, and $P = 0.10$, respectively).[65] Compared with the first year of follow-up, the second-year efficacy of 0.05% atropine eyes drops and 0.025% atropine eye drops remained similar ($P > 0.1$) and improved slightly in the 0.01% atropine group ($P = 0.04$).In children in the placebo group of phase 1 who were switched to 0.05% atropine eye drops in phase 2, the myopia progression decreased significantly in terms of myopic refractive error (myopic refractive error change of 0.18 D in the second year versus 0.82 D in the first year; $P < 0.001$) and axial elongation (axial elongation of 0.15 mm in the second year versus 0.43 mm in the first year; $P < 0.001$).The authors concluded that over a follow-up of two years, the efficacy of 0.05% atropine eye drops was double that of the 0.01% eye drops with respect to the reduction of myopic progression, and that the 0.05% atropine concentration was the optimal concentration among the studied atropine concentrations for slowing the progression of myopia.[65]

In a recent Cochrane review, Walline and colleagues[66] summarized that children receiving atropine eye drops, pirenzepine gel, or cyclopentolate eye drops as compared to children receiving placebo eye drops showed a significant, 1-year reduction in the increase of myopic refractive error (1.00 D [95% confidence interval {CI}, 0.93–1.07], 0.31 D [95% CI, 0.17–0.44], and 0.34 D [95% CI, 0.08–0.60], respectively). In a similar manner, axial elongation was less pronounced for children treated with atropine (−0.35 mm; 95% CI, −0.38 to −0.31) and pirenzepine (−0.13 mm; 95% CI, −0.14 to −0.12) than for those treated with placebo. Walline and associates concluded that antimuscarinic topical medication was effective in slowing the progression of myopia in myopic children. The use of pirenzepine eye drops as a myopia reduction therapy was, however, abandoned, and the pirenzepine eye drops are no longer available as a treatment option.

Questions to be addressed in future studies include when to start the atropine therapy, the optimum dose of atropine eye drops, frequency and time of application (nightly, weekly), duration of treatment (up to what age), the potential rebound phenomenon after cessation of therapy including a potential tapering schedule for higher concentrations of atropine to address the rebound effect, current major issues about compounding the low-dose atropine medication, at which age the therapy can be stopped, long term effects including safety, the effect of ethnicity on the response to atropine, the mode of action of antimuscarinic eye drops, and others.

Optical Measures

The first studies applying optical interventions to prevent the progression of myopia were mainly focused on examining the effect of an undercorrection of the myopic refractive error and on the use of conventional bifocal spectacles. Studies, as summarized in recent Cochrane and systematic reviews, have shown, however, no strong evidence of benefits of an overcorrection or uncorrection of the myopic refractive error or of monovision.[66,67] In a similar manner, optical undercorrection of the myopic refractive error had no effect or showed the tendency to increase the progression of myopia. There was little or no difference between myopic progression of children wearing corneal, gas-permeable, single-vision contact lenses and children wearing single-vision soft contact lenses or children wearing bifocal soft contact lenses and children wearing single vision soft contact lenses.[66,67]

Studies including children wearing progressive addition lenses as compared to children wearing single-vision lenses suggested an advantage of a peripheral myopic defocus.[68–70] In a parallel manner, experimental studies revealed that in animals an imposed myopic defocus inhibited and an imposed hyperopic defocus promoted an enlargement of the globe.[39,71–76] The application of lenses with concentric dual-focus designs inhibited or reversed a myopic globe enlargement in the chicken, guinea pig, marmoset and rhesus monkey.[77–81] Induction of peripheral myopic defocus has consequently become the mainstay of a number of current myopia control strategies including multifocal soft contact lenses and OK.[16,41,82–89] Animal studies suggested that the sensory part of the presumed intraocular feedback mechanism governing the process of emmetropization is located in the peripheral and central retina.[39,76] Myopic eyes corrected with standard spectacles typically show a relative peripheral hyperopia. These observations led to the hypothesis that a peripheral hyperopic defocus may be the cause for further central axial elongation in myopic eyes, although a study by Mutti and colleagues[90] suggested that for every diopter of peripheral hyperopic defocus in children, myopia progression only increased by 0.02 D per year.[16,39,76] The optical measures include wearing of defocus incorporated multiple segments (DIMS) spectacle lenses, the application of concentric zone dual-focus soft contact lenses that provide simultaneous correction and myopic defocus, or the use of OK contact lenses.

Multifocal Spectacle Lenses

Aspheric spectacle lens designs initially developed to reduce the relative peripheral hyperopic defocus did not lead to a significant decrease in the rate of myopia progression.[91,92] Daily wear of newly developed DIMS spectacle lenses, however, was associated with a significant retardation of myopia progression and axial elongation in myopic children and the lenses were well tolerated.[84,93,] The DIMS lenses are custom-made plastic spectacle lenses with a central optical zone diameter of 9 mm, used for correcting distance refractive errors, and with an annular zone that includes multiple round segments about 1 mm in diameter with a +3.50 diopters add power.[84] Such an optical design simultaneously allows clear central vision and introduces, primarily over the peripheral retina, a myopic defocus. In a recently published, two-year double-masked randomized trial including 160 myopic Chinese children with an age of eight to 13 years, average myopic progression over two years was lower in the DIMS group (−0.41 ± 0.06 D) than in the control group wearing single-vision spectacle lenses (−0.85 ± 0.08 D).The mean axial elongation was also less in the DIMS group than in the single vision spectacle lens group

Investigative Ophthalmology & Visual Science

(0.21 ± 0.02 mm vs. 0.55 ± 0.02 mm).[83] Other spectacle lens designs such as the Zeiss MyoVision lens showed less efficacy.[94]

Dual-Focus and MultiFocus Contact Lenses

More studies have been conducted on the efficacy of soft multifocal concentric zone contact lenses. These lenses have a center-distance design and include lenses with concentric rings as distinct zones of relative plus power and lenses with a gradient design, with increasing relative plus power toward the lens periphery. Soft multifocal contact lenses have been explored in several randomized controlled trials so far, which demonstrated a reduction in myopia progression of on average 36.4% and a decrease in axial elongation by 37.9%.[16,82,85,95–106] Notably, with the use of MiSight soft contact lens (clear center distance and concentric rings of relative plus power), the change in spherical equivalent refractive error over a 3-year period was −0.51 ± 0.64 vs. −1.24 ± 0.61 D (59% reduction) in the study group and control group, respectively.[101] Similarly, mean change in axial length was 0.30 ± 0.27 mm versus 0.62 ± 0.30 mm (52% reduction).[101] Based on the results of a multicenter, randomized, three-year clinical trial, the U.S. Food and Drug Administration approved the commercially available daily wear, single use multi-focal contact lens (MiSight; CooperVision Inc., Lake Forest, CA, USA) for use in slowing the progression of myopia in children.[101] In the study, the relative peripheral hyperopia at 30° and 40° nasal and 40° temporal to the fovea was significantly correlated with a reduction in the progression of myopic refractive error and the amount of axial elongation.[100]

The recent randomized clinical BLINK (Bifocal Lenses in Nearsighted Kids) study examined the efficacy of contact lenses with a central correction for myopia plus a high add (+2.50 diopter) or medium add (+1.50 diopter) power to the peripheral concentric zone as compared to single-vision (no add) contact lenses in 292 participants aged 10.3 ± 1.2 years with a mean spherical equivalent refractive error of −2.39 ± 1.00 D. The difference in the adjusted three-year myopia progression between the high add power group versus the single-vision group was −0.46 D (95% CI, −0.63, −0.29) and −0.23 mm (95% CI, −0.30, −0.17), between the high add power group versus the medium add power group was −0.30 D (95% CI, −0.47, −0.13) and −0.16 mm (95% CI, −0.23, −0.09), and between the medium add power group versus the single-vision group was −0.16 D (95% CI, −0.33, 0.01) and −0.07 mm (95% CI, −0.14, −0.01).[105,106]

Soft multifocal contact lenses slow the progression of myopia and growth of the eye, but questions remain about the optimum distribution of the refractive power across to maximize the slowing of myopia progression while not impacting functional vision, and whether, now that there is a regulatory-approved contact lens on the market, off-label use of repurposed multifocal presbyopic designs should stop.

Orthokeratology (OK)

OK is a technique whereby specially designed reverse-geometry corneal gas-permeable contact lenses are worn overnight to reshape the cornea by flattening of the corneal center and steepening the corneal mid-periphery.[39,41,107,108] Because the corneal surface typically keeps its reshaped form for at least the next day, OK corrects for myopic refractive error without the need to wear glasses or contact lenses during the day. The effect seems to occur from a redistribution of the multilayered corneal epithelium, leading to a central corneal epithelial thinning.[107] Subsequent studies, performed mostly on children and adolescents, suggested that OK may additionally slow myopic eye enlargement, potentially by a decrease in relative peripheral hyperopia caused by the steepening of the midperipheral corneal surface.[41,108–114] Two randomized controlled trials, the Retardation of Myopia in Orthokeratology (ROMIO) study by Cho and associates[41] and the HM-PRO study by Charm and Cho,[42] revealed that the axial elongation was reduced by 43% to 63%.[40,114] The reduction was more pronounced in younger, more rapidly progressing myopic children (age 7–8 years: 20% vs. 65% progression [control]) than in older children (age 9–10 years: 9% vs. 13% progression [control]).[40,41] Limitations of the ROMIO study were that about 27% of the participants in the intervention group did not finish the study. In another OK trial of children with a myopic refractive error of at least -5.75 D, the median increase in myopia after 2 years was 0.13 D in the study group and 1.00 D in the control group wearing spectacles.[41,115] Again, the drop-out rate of about 50% in the study was high. In a recent meta-analysis, the effect of OK was described to be modestly beneficial.[42] Extending the experiences gained with the application of spherical OK lenses for the therapy of myopia with low astigmatism, Chen and colleagues[114] conducted a study in which over a period of two years, toric OK lenses were used for therapy of myopia with moderate to high corneal astigmatism. They found that the axial elongation was reduced by 52% in the study group as compared to the control group with single vision spectacles. A Cochrane review and meta-analyses have confirmed that OK contact lenses are more effective than currently available single-vision contact lenses in slowing axial elongation.[65,115–119]

With respect to any therapy applying contact lenses, in particular OK lenses, potential complications must be taken into account. The most severe one is microbial keratitis (although rare) whereas pigmented ring formation and altered corneal nerve pattern (fibrillary lines) have been reported to occur in OK wearers, but the latter appear to be reversible.[41,119–125] It has been estimated that the risk of microbial keratitis in children wearing OK lenses is 13.9/10,000 patient-years, as opposed to 7.7/10,000 in all OK wearers.[120] To put this into perspective, the estimated incidence of infectious keratitis in daily-wear corneal gas-permeable lens wearers is 1.2/10,000, whereas in extended-wear soft lens wearers, the incidence ranges from 13.3 to 19.5/10,000, suggesting that OK wear risk in children is similar to extended-wear soft contact lens wear.[126]

General Considerations and Limitations

When addressing the prevention of the development and progression of myopia, limitations have to be taken into account. There are many parts of the world where the prevalence of myopia has remained low so far and the prevalence of high myopia even lower. This situation raises the question of whether public health measures for the prevention of myopia progression are needed in these parts of the world as intensively as in other regions, such as in East Asia, although, however, prevention of any myopia reduces the burden for the individual. This may particularly be relevant for the hereditary forms of myopia for which a preventive measure has not yet been demonstrated. Prevention of

myopia may thus require quite different approaches depending on the individual circumstances and geographic regions. In general, continual review and regular updates are necessary for any overview of current possibilities and guidelines.[16,127,128] Furthermore, if the mechanisms underlying onset of myopia and myopia progression are not identical, their synergy and efficacy in different individuals need further exploration. Increased time spent outdoors is the only intervention known to reduce the onset of myopia, but, because both, myopia onset and myopia progression, depend on or are associated with axial elongation, potentially all approaches known to slow progression could also be applied to pre-myopes. In that context, it may also be taken into account that not all children will become myopic or highly myopic and that the final refractive error cannot yet precisely be predicted.[129] Conversely, delaying myopia onset is likely to slow progression, because progression rates seem to be largely age-dependent, and the available evidence suggests that if myopia onset can be delayed to the end of primary school, few children with a later onset of myopia will become highly myopic. It is important to note that most of the epidemiological data do not suggest that increased time outdoors slows progression, but the marked seasonal effects observed on myopia progression at least suggest that progression may be regulated in a way that is consistent with the known effects of educational pressures and time outdoors on the development of myopia.[130–132]

Because the various treatment modalities have not directly been compared with each other, one cannot state an order of treatment such as therapy of first choice or second choice.[133–135] Before specific guidelines about the choice of new treatments for an individual can be given, results from independent well-designed controlled longer-term studies should be obtained. With respect to the long-term sequelae of a therapy potentially applied to millions of children and adolescents, potential side effects of a pharmaceutical therapy, such as atropine, may not become apparent until several decades after its adoption. Considering that myopic children will require an optical correction regardless, an optical intervention such as spectacle or contact lens based, will not be an additional procedure, like atropine therapy. Other limitations of the available data are that most myopia control studies have been performed in Asia and in the United States, and on children or adolescents with an age of less than 18 years. There is almost no information available on the prevention or slowing of progression of myopia in adults, neither in the moderate myopia range or for high myopia. In terms of the reporting of the effect of the various treatment strategies, presenting the results as a percentage of a percentage may lead to the impression of a greater effect of the treatments than what really occurred in absolute terms. In the pharmacologic approach with the use of low-dose atropine eye drops, one has to consider that the availability of commercial atropine eye drop products can currently be limited in many regions. There is also marked individual variation in the myopic progression, caused by many different factors such as age of onset, heredity, parental myopia, near work, time spent outdoors, and others. Data tracking the refractive error of populations over their childhood years will assist practitioners in benchmarking an individual's risk of myopia and hence to make more informed choice of the benefits compared to any risks.[136]

In conclusion, there is consistent evidence of a benefit for the prevention of myopia development by the use of atropine eye drops, although the optimum concentration of atropine and the value of a combined use of atropine eye drops with optical devices are yet to be fully explored. There is also evidence of myopia control with soft multifocal contact lenses, OK, and a new type of multifocal spectacle. Information is constantly evolving, so one must stay abreast of studies published in the peer-reviewed literature for patients to benefit from the latest evidence-based practice.

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