Myopia is a common condition that has traditionally been regarded as benign, although it has long been known that high myopia, generally classified as greater than -6D, carries a significant risk for sight-threatening pathology. Common complications associated with high myopia include early onset cataract, glaucoma, retinal detachment, myopic maculopathy and choroidal neovascularization, etc.¹ ² However, a recent study of risk factors reinforced the fact that all myopes carry an increased risk of such complications, with the risk increasing with the magnitude of myopia.³ The prevalence of myopia is increasing worldwide, especially in developed east and south-east Asian countries such as Singapore, Taiwan, China, Japan and Korea. Urban areas of these countries are impacted most, with studies reporting prevalence figures as high as 80-90% in high school children, 10-20% of whom have high myopia.⁴ In the US, the prevalence of myopia has also shown a dramatic increase from 24% in 1986 to over 40% in 2010, affecting approximately 18 million people, according to the National Eye Institute.⁵ By 2030, that number is expected to increase to more than 30 million people. The incidence of high myopia in the US has also risen significantly, further increasing the number of people at risk of potential irreversible vision loss. All these numbers add up to make myopia one of the leading causes of blindness worldwide as well as a major economic burden. As eye care practitioners, it is important to keep up to date with current research and treatment options available for our patients at risk of developing myopia, especially high myopia.

Risk factors for rapid myopia progression

Numerous ongoing studies are attempting to identify the factors contributing to the development and progression of myopia. What is clear so far is that multiple factors are involved. Genetics are likely to play a role, as suggested by studies reporting that children with either one or two myopic parents are more likely to develop myopia compared to children without myopic parents.⁶ ⁷ Nonetheless, it is also plausible that the behavioral traits that caused myopia in the parents are passed on to their children. Specifically, since children are likely exposed to similar lifestyles and environments to their parents, it is difficult to separate environmental and genetic influences. As a result, caution needs to be exercised in interpreting the results of genetic studies. Genome-wide association studies represent a more direct approach for identifying the genetic contribution to myopia, with more than 20 loci linked to refractive error development in recent studies.⁸ However, these loci collectively explain less than 5% of the variation seen in refractive errors within populations, suggesting extremely low penetrance of identified genes. These results also imply that complex genetic-environmental interactions play a critical role in the development and progression of myopia.
Although there is little doubt that myopia has a strong genetic component, there is overwhelming epidemiological evidence demonstrating the critical influence of environmental factors on emmetropization and myopia development. Similar results from various population studies involving different ethnicities point to outdoor activities serving as a strong and independent protective factor. Children who spend more time outdoors are less likely to become myopic than children who spend less time outdoors, after adjusting for the amount of time spent indoors. However, the nature of this protective effect is not well understood; the intensity and/or the specific spectral distribution of outdoor lighting, hormonal changes associated with outdoor activities, and optical defocus factors are those under consideration as the source of this protective effect.

It has been speculated that increased encounters of hyperopic defocus in close-up (indoor) environments contribute to myopia progression. Despite evidence from animal models suggesting a causal link between hyperopic imposed defocus and myopia development, clinical epidemiological studies investigating the role of near work on myopia progression have not consistently shown a strong association. Nonetheless, one study reported that although myopia was not significantly associated with the total amount of time spent with near work, close reading distance (<30 cm) and continuous reading (>30 min) were independently associated with greater odds of having myopia. This suggests that the intensity of near work rather than its total duration may be a more important contributing factor in the development of myopia. It should also be noted that most studies to-date have relied on questionnaires for such data, which may not accurately capture the key environmental factors.

In summary, it is evident that the development and progression of myopia is significantly influenced by genetic predisposition as well as environmental factors, and that the interactions between these factors are extremely complex. Unlike cases such as congenital color blindness where the individual’s genes directly lead to the manifestation of the condition, in most cases of myopia, genetic abnormalities likely only increase one’s susceptibility to developing myopia when exposed to provocative environmental risk factors.

**Treatment options for progressive myopia**

In managing myopia, the goal is to not only provide patients with clear vision, but to also slow the rate of axial length elongation in still progressing myopes. In doing so, one is minimizing the risk of subsequent ocular complications, which may lead to permanent vision loss.

**Topical atropine as an anti-myopia drug therapy:** Topical atropine has demonstrated the greatest efficacy among all anti-myopia treatments investigated in clinical trials. For example, one two-year study observed a 77% reduction in mean progression of myopia compared to placebo treatment with 1% atropine eye drops applied daily. However, the adoption of this atropine treatment protocol has not been wide-spread due to a high incidence of ocular side effects. Common side effects of 1% topical atropine include mild to moderate discomfort, as well as glare and blurred near vision associated with atropine’s mydriatic and cycloplegic actions; long-term use also carries a risk of allergic reactions. Perhaps of greater concern is the finding of a significant rebound effect after cessation of treatment with 1% topical atropine, i.e., increased myopia progression relative to eyes previously receiving the placebo treatment. Nonetheless, the absolute myopia progression after three years was still significantly lower in the group receiving the atropine treatment compared with the placebo group. Also, the effect of the atropine treatment on accommodation was not permanent; after cessation of the atropine treatment, amplitudes of accommodation and near visual acuity returned to pretreatment levels.

**Orthokeratology as an anti-myopia optical therapy:** One optical treatment showing great promise as a myopia control therapy is Orthokeratology (OrthoK). OrthoK makes use of a reverse-geometry gas-permeable lens that is specially designed to reshape the cornea with overnight wear to allow clear vision throughout the day without the need for spectacle or contact lens corrections. For this reason, it is traditionally

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prescribed to low to moderate myopes. However, based on promising findings from a number of small-scale studies, first in East Asian countries, OrthoK is increasingly being used for the purpose of myopia control. Converging evidence from clinical trials based in Asia, Europe and in the US suggest that the rate of progression can be reduced by approximately 50% as measured by axial length changes with OrthoK compared to progression in those wearing single vision soft lenses and/or spectacles.22,23,24 As an explanation for this myopia treatment effect, it has been hypothesized that the reshaping of the central and paracentral corneal regions by OrthoK creates relative myopic defocus on peripheral retinal regions, thereby slowing eye elongation. While OrthoK lens wear reduces on-axis myopia by flattening the central cornea, the paracentral cornea steepens, producing a relative myopic shift off-axis.25,26 Consistent with these corneal effects, in myopic children, off-axis (peripheral) refractive errors are reported to be more hyperopic relative to on-axis refractive errors. Simulation of such effects in animal studies using lenses designed to impose peripheral myopic defocus, a known “stop signal” to axial elongation, also slows progression of myopia.27,28

**Multifocal soft contact lenses as an alternative anti-myopia optical therapy:** Distance center multifocal soft contact lens (MFSCL) designs, like OrthoK lenses, also appear to slow myopia progression. Clinical trials investigating their myopia-controlling effects were fewer in number and generally smaller in scale than those involving OrthoK lenses, likely contributing to the much greater variability in published outcomes. Nonetheless, the overall anti-myopia effects from MFSCL appear to be similar to those reported for OrthoK treatment,29,30 which may not be surprising given that both designs produce similar (myopic) shifts in peripheral defocus.31 Interestingly, MFSCL with center near designs also appear to be effective in controlling myopia (unpublished data), perhaps reflecting interactions between lens and ocular aberrations, which are known to influence the optimal state of focus of the eye.32

Although it has been consistently demonstrated in various animal models that myopic defocus, imposed with positive lenses, prevents the development and progression of myopia, clinical trials investigating the effects of bifocal (BF) and progressive addition (PAL) spectacles lenses on myopia progression have generally yielded disappointing, typically clinically insignificant results.33,34,35 Poor compliance with BF and/or PAL treatments may be one contributing factor, given that most children have little incentive to look down through the near add during near work. However, other optical differences between the various multifocal spectacle lens designs and MFSCL and OrthoK designs may be more important in explaining their relatively poor treatment efficacy. Specifically, the total area of the positive defocus imposed by BF and PAL spectacle lenses is relatively limited and also gaze-dependent in both cases. Neither is true for OrthoK and MFSCL lenses. Evidence supporting this interpretation comes from a study using high set executive BF lenses, which also reported improved efficacy compared to typical multifocal spectacle lens studies.36

A common clinical practice, especially in Asia, is to undercorrect myopia when prescribing single vision spectacles in the hope of slowing down myopia progression. A handful of small retrospective and prospective studies on this topic have reported mixed results. However, the most recent of these studies, a 2-year prospective randomized controlled trial, found that undercorrection produced more rapid myopia progression and axial elongation compared to full correction.37 Nonetheless, the results of this study are difficult to interpret due to the use of variable amounts of undercorrection; the prescription of each subject was undercorrected by the amount which allowed them to maintain 20/40 visual acuity in each eye, which averaged +0.75 D overall. Just how such treatments affect the retinal defocus experience during near work is also yet to be investigated but possibly relevant. Potentially valuable insights will be provided by the Full Correction and Undercorrection of Myopia Evaluation Trial (FUMET), a larger randomized, double-blind, controlled trial that is currently underway in China. FUMET is designed to determine the efficacy of spectacle undercorrection by +0.50 D as a myopia control treatment option.38 However, pending the results of FUMET, undercorrection of myopia is not advised as a myopia control strategy.

**Vision therapy for myopia control:** Finally, vision therapy primarily focused on improving accuracy and/or facility of accommodation has also been used empirically as an anti-myopia treatment. However, results of clinical studies investigating such effects have been equivocal.39

**Clinical Recommendations**

Based on currently available evidence, OrthoK and MFSCL treatments are the most clinically viable options for myopia control, considering their significant efficacy and minimal long-term ocular side effects. Neither carry a greater risk of infection/adverse events than other daily wear or extended wear contact lenses,40,41 and furthermore, both options can easily be integrated into clinical practice. Children to consider fitting with these lenses are those who have progressed in their myopia by a diopter or more in one year and are mature enough to handle the insertion, removal, and care of their lenses independently or with very little parental help. Other factors to consider are age and level of myopia, and patient and parent motivation. Ideally, patients should adhere to anti-myopia treatment until stabilization of their myopia, which can take several years, even extending into early adulthood depending on their life choices.

In a practice setting, very few extra supplies and equipment are needed to provide these contact lens treatment options.
OrthoK requires a trial fitting set and a topographer is also essential to the fitting and follow-up process. Once the cornea has undergone reshaping, eyes are left with minimal refractive error, making it nearly impossible to detect mild myopic progression. Thus, in order to monitor progression, an IOL-master or LENSTAR, which allow noncontact monitoring of axial length changes with high precision, is absolutely critical. For success in OrthoK fitting, completion of a certificate training process is also recommended. MFSCL require less investment. The Biofinity multifocal contact lens is a good option for children because of its center distance design; it offers better distance vision than near center designs, and has high oxygen permeability. It also comes with a few add options. Considerations in the initial add power selection include the current rate of progression, ocular posture at near (in the CONTROL study, near fixation disparities were neutralized), as well as best correctable distance acuity, etc. Although changes in refractive error offer a more valid measure of progression in MFSCL than in the case of OrthoK, the purchase of an IOLmaster or LENSTAR is strongly recommended to obtain axial length data as an independent measure of myopia control; this data also represents a valuable teaching tool for patients.

The appropriate selection for individual patients of OrthoK versus MFSCL is a multifactorial decision, based on the severity of baseline myopia, corneal curvature and asphericity, daily activities of the patients and financial and time investment, etc. OrthoK requires frequent follow-ups, especially during the fitting process, which may extend over a couple of months. There is also an upper limit to the amount of myopia that can be corrected with OrthoK, of around -6 D, with substantial individual variations. In general, with higher levels of baseline myopia, i.e., greater than -4 D, corneal reshaping effects also tend to decrease more quickly over the course of the day, increasing the likelihood of fluctuating vision and slight distance blur at night. On the other hand, fitting MFSCL is relatively straightforward and is less limited by the severity of myopia. However, many parents may be uncomfortable letting their children wear such contact lenses away from their guidance and monitoring during the day at school. Regardless of the modality selected, providing contact lens treatments to children for myopia control requires a comprehensive understanding of the treatment – its potential benefits, risks and limitations, with thorough patient/parent education being of paramount importance.

The long-term potential beneficial effects of OrthoK and MFSCL on myopia progression strongly outweigh the potential risks associated with contact lens wear. Both treatments can be expected to reduce myopia progression by 50% on average compared to single vision correction options. Importantly, the anti-myopia effects from both modalities appeared to be without significant rebound progression should the treatment be discontinued before myopia has stabilized, in contrast to the case of topical 1% atropine treatment.

What role does topical atropine have in the clinical management of myopia? Because of the adverse ocular side effects and rebound effects reported for 1% topical atropine, its use is not advised. However, 0.02% topical atropine has recently been shown to be without significant effects on accommodation and pupil function; given the latter observation and findings of significant control effects with doses as low as 0.01%, it seems reasonable to consider the off-label use of topical low dose atropine (0.01-0.02%) in rapidly progressing myopes and/or those for whom contact lenses treatments are not a viable option. Nightly instillation, just before bed, will also ensure that any effects on pupil and accommodation are minimized during the day. The services of a formulation pharmacy will be required to obtain a suitable product.

Although further research needs to be done to obtain better understanding of the causes of myopia progression, the above treatment options for controlling progression warrant more wide-spread use in clinical practice. With early intervention, eye care practitioners can have a positive impact on the future of patients’ vision, minimizing their risk of pathological complications and permanent vision loss.
REFERENCES


