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Myopia progression in children and adolescents: impact of COVID-19 pandemic and current and future control strategies

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Abstract. Myopia is a significant and growing public health problem with typical onset or progression during childhood adolescence. High myopia has lifelong impact on ocular health and socio-economic aspects of patients 'lives. COVID-19 lockdown resulted in demonstrable increase in incidence and progression rate of myopia in children and adolescence. Low dose atropine and Orthokeratology contact lenses appear to be most effective in slowing down myopia progression. Rebound progression after stopping both modalities were reported. Defocus modifying spectacle lenses and contact lenses are less effective but possibly better tolerated. (www.actabiomedica.it)

Key words: Adolescents, myopia, atropine, contact lenses, mydriatics, eyeglasses

Introduction

Myopia is the commonest and the fastest growing condition in the world with the highest prevalence of 50% reported in South East Asia. It has a tremendous effect on ocular health with significant socioeconomic impact. High myopia is defined as myopia more than -6.0 diopters. Pathologic myopia is a term that refers to myopia associated adverse, structural complications of myopia (1,2). Both are associated with significantly higher risk of ocular complications including rhegmatogenous retinal detachment, primary open angle glaucoma, myopic choroidal neovascular membrane, myopic choroidal atrophy, macular atrophy, myopic traction maculopathy and dome-shaped macula (2).

The rate of myopia progression represented by peak ocular axial length and spherical equivalent was found to correlate with peak height in Singaopore Cohort Study of the Risk Factors for Myopia and thus adolescent years represent a window of opportunity to control myopia progression. In this article, we will discuss the effects of COVID-19 home schooling and associated increase in screen time on the progression of myopia as well current control strategies and future avenues for control.

Magnitude of problem, visual and socioeconomic effects

Myopia impacts 30% of the world's population and is projected to impact 50% of the world's population in 2050 (3). In a cross-sectional study of the Dutch population, the risk of uncorrectable vision impairment was 3.8% and 39% by 75 years of age in individuals with myopia (-0.5 to -6.0 D) and those with high myopia (-6.0 D or worse) respectively (4, 5).

It is estimated based on a model of risk of visual impairment as a function of myopia level that the risk of myopic maculopathy, open-angle glaucoma, posterior subcapsular cataract, and retinal detachment increases with each additional 1 D of myopia

by 58%, 20%, 21%, and 30% respectively. An individual with -3 D myopia is expected to have a mean of 4.42 years of visual impairment compared to a mean of 9.56 years with -8 D myopia (6).

Uncorrected myopia-related vision impairment resulted in loss of productivity as percentage of gross domestic product of 1.35%, 1.3%, and 1.27% in Southeast Asia, South Asia, and East Asia respectively (7, 8).

The cost of myopia correction with spectacles contact lenses and refractive surgeries varies in different countries. A systematic review reports such cost per capita to be ranging from $14-26, $56 and $199 in the USA, Iran and Singapore respectively (9).

The impact of COVID-19 pandemic and quarantine on rate of myopia progression

An inverse relationship between progression of myopia and time spent outdoors is well-documented (10-12). Spending 200 minutes or more weekly outdoors with exposure to moderate light intensity (greater then 1000 lux) was found to be protective against myopia in schoolchildren aged 6 to7 yrs. Additionally, Wen et al. (13) reported near work at distance less than 20 cm is associated with increased risk of myopia in a study of 86 Chinese children of mean age 10.1 ± 0.48 years.

Xu et al. (14) reported the effects of COVID-19 quarantine on six-month myopia progression on a random sample of 12,013 chines schoolchildren aged 7 to 18 year. Myopia progression increased by approximate 1.5 times from -0.23 D before the quarantine to -0.343 D after the quarantine (P: < 0.001). The myopia incidence rate increased from 8.5% to 13.62% over the same period (P: < 0.001). The authors reported students' online time to be significantly positively associated with increased myopia incidence and progression, whereas outdoor activity time was significantly negatively associated with incidence and progression of myopia.

Ma et al. (15) reported the short-term effect of more time spent indoors and screen time on myopic progression during the COVID-19 home quarantine on 201 Chinese myopic children aged 7 to 12 years. There was a significantly greater change in spherical equivalent a (-0.98 ± 0.52 D) at four month-follow up visit compared to baseline (-0.39 ± 0.58 D; P < 0.001). Children using television and projectors had significantly less myopic shift than those using digital devices. More time spent on digital screens but not less outdoor times correlated with myopia progression.

Similarly, Zhang et al. (16) studied the effects of COVID-19 pandemic on children aged 6-8 years in Hong Kong compared to a cohort of pre-COVID-19 cohort. The study reported reduced time spent outdoors and increased screen time from 1.2±1.1 to 0.41±0.90 hours/day and 2.4 ± 2.3 to 6.8 ± 4.4 hours/day (P:< 0.001) respectively. The authors estimated 1-year incidence of myopia at 27.6%, 26.4% and 25.8% for 6, 7 and 8-year-olds in the COVID-19 cohort, respectively, compared to 16.76%, 15.42% and 14.66%for 6, 7 and 8-year-olds in the pre-COVID-19 cohort (P: 0.03).

Similar results were reported by Mohan et al. (17) in India. The annual progression of myopia ≥1 D occurred in 45.9% of children during the pandemic compared to 10.5% in the year prior to COVID-19 in a study conducted in a tertiary center in India. Multivariate analysis found rapid progression in pre-COVID-19 and sun exposure <1 h/day (P: < 0.00001) to be independent risk factors for rapid myopia progression.

Myopia prevention

Numerous modalities were devised for myopia control. These include both optical and pharmacologic interventions. In this review, we will focus on the interventions that were studied the most and are commercially available.

a. Atropine

Atropine is an anticholinergic agent that causes loss of accommodation and mydriasis when applied topically to the eye. The mechanism of action of atropine on myopia progression is unclear. Initially hypothesized to happen through its effect on accommodation, animal research suggests an effect on axial length through a direct effect on retina or sclera (18).

Atropine 1% was shown to be effective in slowing down myopia progression in comparison to

cyclopentolate but high dropout rate was reported due to associated side effects namely mydriasis and loss of accommodation (19).

A study by Shih et al. (20) reported the outcome of atropine concentrations 0.5%, 0.25% and 0.1% administered in children from 6 to 13 years of age for 2 years compared to a control group. No myopia progression was noted in 61%,49% and 42% of the 0.5%, 0.25% and 0.1% groups, respectively compared to 8% of the controls. A dose dependent effect was noted on myopia progression with mean progression in diopter per year 0.04 ± 0.63, 0.45 ± 0.55, and 0.47 ± 0.91 and 1.06±0.61 in the 0.5% atropine group, 0.25% atropine group, 0.1% atropine group and control groups respectively.

The Atropine Treatment of Myopia 1 (ATOM1) study evaluated the effect of atropine 1% as well on Asian children aged 6-12 years with myopia of -1.0-6.0 diopters for 2 years. Atropine-treated eyes progressed by only 0.28±0.92 D with axial length elongation of 0.02±0.35 mm compared to significantly more progression in placebo eyes with 1.20±0.69 D and 0.38±0.38 mm in spherical equivalent and axial length respectively (21).

A rapid catchup in myopia progression in the 1 year washout period in the atropine 1% treated eyes with myopia progression of 1.14 ± 0.80 D over 1 year, whereas the progression in placebo-treated eyes was 0.38 ± 0.39 D. Nevertheless, atropine treated eyes had less myopia than control eyes at the end of the three-year study period with progression of 0.46 ± 0.26 D/year and 0.5 ± 0.30 D/year for the atropine1% and control groups, respectively (P:0.043). No effect of amplitude of accommodation and near visual acuity was noted at the conclusion of the study (22).

The ATOM2 study enrolled 400 Asian children aged 6 to 12 years with myopia of 2.0 D or worse and were randomized to receive atropine 0.01%, 0.1% and 0.5% once nightly for 2 years followed by a one year washout period. Children who progressed by 0.50 diopters in at least 1 eye were restarted on atropine 0.01% for a further 24 months. A dose dependent reduction in myopia progression was noted in the first 2 years of the study but by the end of the first 3 years, atropine 0.01% was associated with the least rebound myopia resulting in the atropine 0.01% being the most effective with myopia progressing by 1.15 ± 0.81D, 1.04 ± 0.83 D, and 0.72 ± 072 D in the atropine 0.5%, 0.1%and 0.01%, respectively. This result persisted at the conclusion of the 5 year study duration as well with less increase in myopia and axial length in the 0.01% group (-1.38±0.98 D; 0.75±048 mm) compared with the 0.1% (-1.83±1.16, P:0.003; 0.85 ± 0.53, P:0.144) and 0.5% (-1.98±1.1 D, P:< 0.001; 0.87 ± 049 mm, P: 0.075). Notably, photopic pupil dilation was the least with the 0.01% atropine (0.74 mm, compared with 2.25 and 3.11 mm in the 0.1% and 0.5% groups, respectively). Loss in accommodation or near visual acuity was also the least and not clinically significant in the 0.01% group (4.6 D, compared with 10.1and 11.8 D in the 0.1% and 0.5% groups, respectively) (23).

The Low-Concentration Atropine for Myopia Progression (LAMP) study examined the effectiveness of atropine concentrations 0.05%, 0.025%, and 0.01% compared to placebo over 2 years in 438 children 4-12 years of age. After 1 year, the mean SE change was 0.27 ± 0.61 D, 0.46 ± 0.45 D, 0.59 ± 0.61 D, and 0.81 ± 0.53 D in the 0.05%, 0.025%, and 0.01% atropine groups, and placebo groups, respectively (P :< 0.001). A similar dose-dependent effect was noted after year 2 with mean spherical equivalent progression of 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. The study concluded that atropine 0.05% was the most optimum concentration for myopia control with no significant impact on accommodation or photopic pupillary dilation with the accommodation amplitude was reduced by 1.98 ± 2.82 D in the 0.05% concentration compared to 0.26 ± 3.04 D in the 0.01% concentration group (P:< 0.001). The photopic pupillary dilation increased by 1.0 ± 1.0 mm in the 0.05% atropine group and 0.23 ± 0.46 mm in the 0.01% atropine group (P :< 0.001) (24, 25).

Despite demonstrated effectiveness of low dose atropine in myopia control in Asian population, effectiveness in whites continues to be questionable. A Meta-analysis by Li et al (26) demonstrated greater effect in Asian population.

Polling et al. (27) studied the use of 0.5% atropine in white population. They reported 28% drop out of the study in one year due to photophobia (72%), followed by reading problems (38%), and headaches (22%). A reduction in myopia progression in patients

receiving treatment. Progression was noted to be 0.1 ± 0.7 D/year compared to 0.5D/year ± 0.6 (P: 0.03) in those not tolerating treatment.

A network meta-analysis reported 0.05% was comparable with high-dose atropine (1% and 0.5%) in effectiveness of controlling refraction change and axial elongation and had better side effects profile (28). The risk of vision loss with low dose atropine is very low but photochromic lenses and less commonly near add for light sensitivity and near vision blurring respectively may be needed (6). Cooper et al. (29) established the highest dose at which no significant light sensitivity or near vision blur was 0.02% in white eyes.

b. Orthokeratology

Orthokeratology is utilized for temporary correction of mild to moderate myopia by flattening the cornea. The Euclid-approved lenses aim to reduce -5.00 diopters (D) with astigmatism up to 1.5 diopters (D) and the Paragon CRT lenses are used to correct up to -6.0 diopters with astigmatism up 1.75 diopters. The use of these contact lens to control myopia progression is off-label (30).

Swarbrick et al. (31) utilized a within-subject cross-over trial where 32 patients were enrolled with ortho-K in one eye and RGP in contralateral eye for 6 months followed by switching lenses types between eyes after 2-3-week washout period for another 6 months. Patients were 8 to 16 years in age, of Asian ethnicity and had baseline myopia between 1 to 4 diopters. Myopia progression was less with Ortho-K in both six-month intervals but this reached statistical significance only in the second follow up suggesting possible rebound with ortho-K.

In the retardation of myopia in Orthokeratology (ROMIO) study Cho et al. (32) compared ortho-K to single vision glasses in 78 children from 6 to 10 years of age myopia between 0.50 and 4.00 diopters (D) for 2 years and noted the average axial elongation, at the end of 2 years, were 0.36 ± 0.24 and 0.63 ± 0.26 mm in the ortho-k and control groups respectively (P < 0.01) constituting a 43% reduction in axial length with ortho-K. Myopic progression more than 1 D/year was noted in younger age group (age range: 7-8 years) in both ortho-K and control group.

The Corneal Reshaping Influences Myopic Prescription Stability (CRIMPS) study examined retrospectively the use of ortho-K in 26 patients compared to right eyes of 30 controls in children and adolescents younger than 16 years of age. It reported complete arrest of myopia progression in 64% of ortho-K eyes for up to 8 years (33).

Comparable success was noted in high myopic children and early adolescents (aged 8 to 11 years) with spherical equivalent at least-5.75 diopters(D) compared to single vision lenses in controls. There was median increase in non-cycloplegic residual myopia by 0.13 D compared to increase in myopia by 1.0 D in control group. Nevertheless, the mean increases in axial length were 0.19 ± 0.21 mm in the PR ortho-k group and 0.51±0.32 mm in the control group (34).

Chen et al. (35) in the Myopia control using toric orthokeratology (TO-SEE) study reported 52% slower axial length elongation in 35 patients in ortho-K group compared to 23 controls in a non-randomized trial. The average axial elongation at the end of study was 0.31 ± 0.27 and 0.64 ± 0.31 mm in the ortho-k and control groups, respectively (P: < 0.001).

Davis et al. (36) reported the outcome of the Stabilizing myopia by accelerating reshaping technique (SMART) study. The study enrolled 172 children in the ortho-K group and 110 children in the soft contact lens group who were followed over 3 years. Mean spherical equivalent change in myopia for the soft contact lens group was -1.0±0.58 diopters and -0.13 ± 0.62 diopters in the ortho-K group -0.13 ± 0.62 diopters (P:<0.0001). Both groups had similar high dropout rate of 32.5% and 33.6% in control and treatment groups respectively.

A systematic review and network meta-analysis reported ortho-K to be at least effective as low-dose atropine and that a combination of ortho-K and atropine to be synergistic (37).

Safety continues to be a concern with ortho-K given the potential of sight-threatening corneal infections. The risk of microbial keratitis in children wearing ortho-K lenses was reported as 13.9/10,000 patient-years compared to 1.2/10,000 in daily-wear corneal gas-permeable lens wearers (38, 39). A systematic review reported that the majority of infections resulting

from ortho-K lens to result from pseudomonas aeruginosa and acanthameba. Most of these infections resulted in corneal opacity and 10% of which required surgical interventions (40).

c. Multifocal and defocus modifying contact lenses

Multifocal contacts lenses are thought to reduce the progression of myopia by achieving myopic defocus on the peripheral retina thus reducing myopic progression.

A study by Walline et al. (41) reported the outcome of using multifocal contact lenses with +2.0 D add in 40 myopic children aged 8-11 years with -1.00-6.00 D myopia in comparison to historic controls. At 2 years, The adjusted mean ± standard error spherical equivalent progression of myopia at 2 years was -1.03 ± 0.06 D for the single-vision contact lens wearers and -0.51 ± 0.06 for the soft multifocal contact lens wearers (P:< 0.0001).

The BLINK (Bifocal Lenses in Near-sighted Kids) study was a randomized clinical trial including 294 children aged 7 to 11 years old with baseline myopia of -0.75 D to -5.00 D.

Children were randomized to using of 3 contact lenses: single vision, medium add power (+1.50 D) and high add power contact lenses (+2.50 D) over 3 years. Myopia progressed by -0.6 D, -0.89 d and -1.05 D in the high add power, medium add power and the single-vision lenses groups respectively. The difference was statistically significant for the high add power group (42).

Lam et al. (43) utilized 'Defocus Incorporated Soft Contact' (DISC) which was a custom-made bifocal soft contact lens of concentric rings design entailing a correction zone in the centre with a series of alternating defocusing and correction zones extending towards the periphery with 50:50 proportion. These were used in a 2-year double-blind randomised controlled trial of 221 children aged 8-13 years, with myopia between -1.00 and -5.00 D randomized to DISC or single vision contact lens. Only 128 children completed the study with equal drop out rate in both groups.

Myopia progression was slower in the DISC group 0.30 D/year; 95% CI -0.71 to -0.47 compared to progression 0.4 D/year; 95% CI -0.93 to -0.65 in the control group (P: 0.031). Although the difference was statistically significant, the difference is not clinically meaningful.

Similarly, experimental Dual-Focus (DF) soft contact lens with concentric treatment zones of 2.00 D simultaneous myopic retinal defocus during distance and near viewing in comparison to single vision contact lenses. Children wore the Dual focus lens in one eye and single vision lens in the fellow eye for 10 months and then swapped between eyes for more 10 months. the mean change in SER with DF lenses (-0.44 ± 0.33 D) was less than with SVD lenses (-0.69 ± 0.38 D; P: < 0.001) in the first 10 months and a similar effect was noted in the second ten-month interval. Visual acuity, contrast sensitivity and accommodation were not impacted in the eyes using Dual focus lenses (44).

The Misight® contact lens (CooperVision, Inc., Pleasanton, CA) is a dual focus contact lens tested in 53 myopic children 8-12 years of age with spherical equivalent between –0.75 to –4.00 D in a randomized controlled trial with 56 children using monofocal soft contat lens as control over 3 years. Less myopic progression was noted in the Misight® group by–0.73 D (59%) less in the test group than in the control group (–0.51 ± 0.64 vs. –1.24 ± 0.61 D, P: < .001 and axial length growth was also significantly less (0.30 ± 0.27 vs. 0.62 ± 0.30 mm in the Misight® vs controls respectively, P: < .001). Over 90% of the children described putting the lenses on the eye as "kind of easy" or "really easy" with no difference between intervention and control groups (45).

d. Bifocal and progressive addition spectacle lenses

The use of bifocals is based on the theory that hyperopic defocus resulting from hypo-accommodation during near work accelerates myopic progression.

The Correction of Myopia Evaluation Trial (COMET) investigated the use of +2.0 Progressive Addition Lenses (PAL) compared to single vision lenses in slowing myopia progression. This was a multicenter, randomized, double-masked, controlled clinical trial study enrolled 469 children aged 6-11 years of ethnically diverse population. At year 3, a treatment

effect of 0.20 ± 0.08 D (P: 0.004) was noted but after 5 years of follow–up the adjusted progression of myopia (mean ± SE) was –1.97 ± 0.09 D in children wearing PALs and –2.10 ± 0.09 D in children wearing SVLs which was not statistically significant. Reduced accommodation (< 2.56 D for a 33 cm target) and near esophoria had a statistically significant treatment effect of 0.49 ± 0.24 D (P: < 0.05) (46).

Cheng et al. (47) compared the effect of +1.5 D executive style bifocal lenses with and without 3-Δ base-in prism in the near segment in a total of 135 Chinese-Canadian children aged 8-13 years in a randomized controlled trial and myopia progression over 3 years was an average (SE) of -2.06 ± 0.13 D for the single-vision lens group, -1.25 ± 0.10 D for the bifocal group, and -1.01 ±0.13 D for the prismatic bifocal group. The prismatic bifocal had a greater treatment effect in children with low lag of accommodation but no additional benefit over bifocals in children with high lag of accommodation (≥ 1.01 D).

A recent meta-analysis found the effect soft bifocal and progressive addition lenses to be comparable and that effect to be modest in myopia control (48).

e. Defocus incorporated multiple segment lenses

The 'Defocus Incorporated Multiple Segments' (DIMS) spectacle lenses aim at creating peripheral myopic defocus to slow down myopia progression. A 2-year double-masked randomized controlled trial was carried out in 183 Chinese children aged 8-13 years showed average progression in spherical equivalent over 2 years of -0.41 ± 0.06 D in the DIMS group and -0.85±0.08 D in the single vision lenses group respectively (49). The MiYOSMART® (Hoya Vision Care, Bangkok, Thailand) utilized this technology.

The design of Zeiss Myovision® lenses (Carl Zeiss AG, Oberkochen, Germany) was based on a controlled trial comparing single vision lenses and three novel lens designs aiming to reduce hyperopic defocus in 210 Chinese children aged 6 to 16 years. The lenses differed according to the size of the central optic zone and the amount of relative positive power in the periphery. There were no statistically significant differences observed in the rates of progression with the novel designs in comparison to control spectacle lenses but less progression was noted in younger children (6 to 12 years) with parental history of myopia (–0.68 D ± 0.47 D vs. –0.97 D ± 0.48 D) with lens type III compared with control spectacles. The study was designed to run for 2 years but was stopped after 1 year. The progression of myopia was significantly less in children and adolescents older then 12 years of age compared with younger children and the sample size, according to authors, did not allow to measure the effect of younger children reliably (50).

The Highly Aspherical Lenslets (HAL) utilize the concept of myopic defocus using 11 concentric rings formed by contiguous aspherical lenslets (around 1.1 mm in diameter). Bao et al (51) randomized 157 children 8–13 years of age with myopia of –0.75 D to –4.75 D to Highly

Aspherical Lenslets, Slightly Aspherical Lenslets and single vision lenses in the ratio of 1:1:1. At the end of 2 years, children who wore HAL at least 12 hours every day had less myopic progression by 0.99 ± 0.12 D, and less increase in axial length by 0.41±0.05mm compared to single vision lenses (5152).

A recent meta-analysis by Huang et al. (48) demonstrated moderate effectiveness of both peripheral defocus modifying contact lenses and spectacles but showed such contact lenses to have greater effect than spectacles in myopia control.

Conclusions

Myopia continues to be a significant public health problem. Quarantine and homeschooling during COVID-19 pandemic resulted in increased incidence and myopic progression among children and adolescents. Evidence supports offering both low dose atropine and orthokeratology as initial options for myopia control. Clinicians should be aware of the risk of rebound myopia following cessation of both treatment modalities. Possible limitations for widespread use of orthokeratology are the initial cost, limited availability of skilled practitioners for fitting and theoretical risk of vision-threatening infections. The inherent side effects of photosensitivity

and near vision blurring associated with low dose atropine potentially limits its wider spread use. Defocus incorporated multiple segment spectacle lenses and Dual focus soft contact lenses carry less side effects and appear to offer promising results but were not shown to be equally effective as atropine and ortho-K lenses.

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