Interventions To Slow The Progression Of Myopia

Myopia (commonly termed nearsightedness or shortsightedness) has increased in prevalence around the world. In addition to genetic factors, there now exists evidence of numerous environmental factors that contribute to myopia development. It is well-known that the common forms of childhood myopia are due to axial elongation (i.e., a longer eyeball). As a result of renewed research activity on myopia, it is clear that some forms of early intervention slow the axial elongation process and thus the potential amount of myopia. In a small percentage of myopes, the elongation process becomes "pathologic" and is associated with an increased risk of cataract, glaucoma, retinal detachment, strabismus (heavy eye syndrome) and myopic maculopathy[1]. Additionally, functional deficits when myopia is uncorrected along with impacted career choices can occur. It is not clear at this time if the new interventions can prevent or reduce these complications, although, there are sound hypothetical reasons to believe they do. In this Consensus Statement all the interventions we have described are based on studies that have shown statistical and clinical significance.

What Does Not Work or Has Minimal Effect

Undercorrection: Data from prospective clinical trials suggest that undercorrection of myopia either increases or has no effect on myopia progression[2-7]. Undercorrection does not slow myopia progression and should no longer be advocated.

Pin hole glasses: No Effect.

Blue light blocking glasses: No Effect.

Bifocal glasses: Randomized, clinical trials in the US, Finland, and Denmark showed no significant slowing of myopia with bifocals alone[8-11]. The only promising results of 39% reduction were reported by Cheng et al in a group of Chinese Canadian children but these have not been corroborated in other studies[12].

Progressive addition spectacle lenses: The use of progressive addition lenses (PALs) has produced relatively small treatment effects[13-17]. The correction of myopia evaluation trial (COMET, a multicenter, randomized, double-masked clinical trial), concluded that the overall adjusted 3-year treatment effect was statistically significant but not clinically meaningful[18]. The 3-year treatment effects decreased even further after 5 years[19, 20]. Overall, multifocal lenses (bifocal spectacles or progressive addition lenses) yielded small effect in slowing myopia progression.

Peripheral plus/defocus correcting spectacle lenses: Although it was hypothesized that hyperopic defocus experienced by the retinal periphery may drive further axial elongation, aspheric spectacle lens designs developed to reduce the relative peripheral hyperopic defocus did not lead to a significant decrease in the rate of myopia progression or axial elongation[21-23]. There was also no benefit found in positively aspherized PALs (PA-PALs) which combined a peripheral defocus correction with a progressive addition zone to reduce lag of accommodation during near work and hyperopic defocus in the peripheral retina when looking through the distance portion of the lens[24]. Please note that newer lens designs which still tackle peripheral defocus are discussed below and do appear to work.

Day time single vision soft contact lenses/rigid gas permeable contact lenses: There was little or no effect in reduction of myopia progression and axial length elongation in children wearing single vision contact lenses or rigid gas-permeable contact lenses[25-32].

What Appears To Work

Behavioral Interventions

Increased time spent outdoors:

While evidence from all the initial studies[33,34] to the latest ones[35,36] suggests that increased outdoor time is effective in preventing the onset of myopia, it is still unclear whether outdoor time is effective in slowing progression in eyes that are already myopic; some studies showing that it does[36] and others that it does not[35]. Studies of children aged 6-8 yrs. confined indoors during the COVID pandemic-related lockdown showed a significant myopic shift[37-39]. The advice then is that if parents have myopia and the child does not, at least 2 hours[34] daylight exposure will help prevent the onset of myopia. Even if myopia onset has occurred 2 hours daylight exposure is a small behavioral change that might be helpful. *[Also see WSPOS Sunlight Exposure & Children's Eyes Consensus Statement]*.

Reduced time on Smartphones/Near Digital Devices/Near Tasks:

In a systematic review and meta-analysis looking at all relevant published data between 1989 and 2014, it was suggested that more time spent on near work tasks was associated with a higher risk of myopia; the odds of myopia increased by 2% for every one diopter-hour of near work per week[40]. Using objective measures of near work and light intensity, a working distance of <20 cm regardless of light intensity, has been shown to be a risk factor for myopia progression[41]. Not only might near task work be implicated with increased myopia but so might increased smartphone use [40]. In a comparison of home-based work done on a smartphone or tablet laptop, versus a television or projector during the enforced COVID-19 lockdown, the latter showed less myopic shift in 7 to 12-year-old children compared to those using smartphones or tablets. Perhaps even more importantly, near task in dim light has also been shown to be a possible risk factor for myopia progression[40]. However, a recent systematic review and meta-analysis[42] concluded with the interpretation that smart device exposure might be associated with an increased risk of myopia. Whether it is the use of digital devices per se or the behavioral change because of them is unclear.

Near work tasks are a part of daily education in today's world[43]. Whether taking a break from near tasks is protective for the development of myopia, is unclear. However, preventing children from reading in dim light, especially at night in their beds, may be protective. For children being home schooled, early evidence suggests that using televisions or projectors & increasing the viewing distance, at the very least having a viewing distance of more than 20 cm, also appears protective.

Optical Treatment

Spectacle Lenses:

There are a number of relatively new lenses, but the two with most data available at the moment are the D.I.M.S. & H.A.L. lenses.

Defocus-Incorporated Multisegment (D.I.M.S.) Spectacle lenses: This dual-focus spectacle lens consists of a central distance optical zone with diameter of 9 mm, surrounded by an annular mid peripheral zone that includes multiple (396) small round segments about 1.03 mm in diameter with a +3.50 diopters add power, to simultaneously allow clear central vision and introduce myopic defocus in the peripheral retina. In a two-year double-masked randomized trial that included 183 myopic Chinese children (93 DIMS group/90 Control group) 8 to 13 years of age, the myopia control effect was 50%. The 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 (0.21 ± 0.02 mm vs. 0.55 ± 0.02 mm)[44]. Although the subsequent 3-year study showed that the myopia control effect was sustained in the third year in children who had used the DIMS spectacles in the previous 2 years and was also shown in the children switching from SV to DIMS lenses, the study was not randomized[45]. The myopia control effect of DIMS lenses was better in children with baseline hyperopic relative peripheral refraction (RPR) than those with myopic RPR[46]. Moreover, in temporal and nasal gaze conditions, visual acuity with DIMS lens decreased by 0.23±0.19 logMAR compared to single vison (SV) lens. A decrease in contrast sensitivity in the DIMS lenses only in the nasal and temporal gaze conditions and of only −0.12±0.20 and −0.18±0.20 logCS, respectively, corresponds to a defocus of about 0.5 dpt[47,48]. Mid-peripheral blurred vision was the main visual complaint, which was noticed only once or twice a day[49].

Highly Aspherical Lenslet (H.A.L.) Spectacle Lenses: 157 children aged 8–13 years with myopia of −0.75 D to −4.75 D were randomized to receive spectacle lenses with highly aspherical lenslets (HAL), spectacle lenses with slightly aspherical lenslets (SAL), or single-vision spectacle lenses (SVL). One-year results demonstrated 0.53 D (67%) and 0.33 D (41%) slowing of myopia progression, and 0.23 mm (64%) and 0.11 mm (31%) slowing of axial elongation with HAL and SAL[50]. After 2 years, the HAL and SAL lenses slowed myopia progression by 0.80 and 0.42 D, and axial elongation by 0.35 and 0.18 mm, respectively[51]. Myopia control efficacy of spectacle lenses with aspherical lenslets increased with lenslet asphericity. Low contrast visual acuity and reading was slightly reduced while high contrast visual acuity was unaffected when fixating through the periphery of the novel lens designs. Of

157 participants who completed each visit 54 were analyzed in the HAL group, 53 in the SAL group, and 50 in the SVL group. Mean 2-year myopia progression in the SVL group was 1.46 (0.09) D. Compared with SVL, the mean change in SER (spherical equivalent refraction) was less for HAL (by 0.80 [0.11] D) and SAL (by 0.42 [0.11] D; P ≤ .001). The mean increase in axial length was 0.69 (0.04) mm for SVL. Compared with SVL, increase in axial length was slowed by a mean of 0.35 (0.05) mm for HAL and 0.18 (0.05) mm for SAL (P ≤ .001). Compared with SVL, for children who wore HAL at least 12 hours every day, the mean change in SER (spherical equivalent refraction) was slowed by 0.99 (0.12) D and increase in axial length slowed by 0.41 (0.05) mm[52].

Contact Lenses:

There are two types of contact lens interventions: the Soft Multifocal Contact Lenses & Orthokeratology.

Soft Multifocal Contact Lenses: These soft multifocal concentric zone contact lenses have a centre-distance design and include lenses with concentric rings as distinct zones of relative plus power and lenses with a gradient design which has increasing relative plus power toward the lens periphery. Soft multifocal contact lenses have showed a reduction in myopia progression of on average 36.4% and a decrease in axial elongation by 37.9%[53-56]. One type is a large centre distance dual focus optical design with alternating correction zones and treatment zones. It is not a multifocal contact lens in the traditional sense of those prescribed for presbyopia. Use of this contact lens showed a change in spherical equivalent refractive error over a 3-year period in 144 children aged 8 to 12 was −0.51 ± 0.64 vs. −1.24 ± 0.61 D (59% reduction) compared to single vision contact lenses[57,58]. Similarly, mean change in axial length was 0.30 ± 0.27 mm versus 0.62 ± 0.30 mm (52% reduction). A recent publication showed that these dual-focus soft contact lenses continue to slow the progression of myopia in children over a 6-year period revealing an accumulation of treatment effect[59]. 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[60]. The randomized clinical BLINK (Bifocal Lenses in Near-sighted Kids) study examined the efficacy of contact lenses with a central correction for myopia plus a high add (+2.50 dioptre) or medium add (+1.50 dioptre) power to the peripheral 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[61]. The difference in the adjusted three-year myopia progression between the high add power group versus the single-vision group was −0.46 D and −0.23 mm, between the high add power group versus the medium add power group was −0.30 D and −0.16 mm and between the medium add power group versus the single-vision group was −0.16 D and −0.07 mm. Statistical significance was reached only for the high add group. Thus, the optimum distribution of the refractive power across to maximize myopia control while not impacting functional vision remains to be determined.

Orthokeratology: In overnight orthokeratology (OK) the patient wears reverse geometry contact lenses overnight to temporarily flatten the cornea and provide clear vision during the day without any glasses or contact lenses. Correction of myopia (up to −6 D sphere and -1.75 astigmatism) is achieved by central corneal epithelial thinning, midperipheral epithelial, and stromal thickening. Randomized clinical trials of orthokeratology myopia control demonstrated significantly slower axial elongation in children wearing orthokeratology lenses than children wearing single vision spectacles. In a recent meta-analysis, the effect of OK was described to be modestly beneficial[62-82]. The overall effect is 50% reduction in progression of myopia in 2 years with high drop-out rate in some studies. A few studies also suggest that relative treatment efficacy may decrease over time[66,83,84]. This applies to some extent to all myopia control treatments[85]. Research to understand the mechanism underlying myopia control effect of OK lens is ongoing although the hypothesis is a decrease in relative peripheral hyperopia caused by the steepening of the midperipheral corneal surface. Younger age groups and individuals with larger than average pupil size may have a greater effect with OK. Rebound can occur after discontinuation or change to alternative refractive treatment. Potential complications include microbial keratitis, pigmented ring formation and altered corneal nerve pattern (fibrillary lines). The estimated 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. This contrasts with the risk in daily-wear corneal gas-permeable lens wearers (1.2/10,000) and is fairly similar to the risk in extended-wear soft contact lens wear[86,87].

Pharmacological Treatment

Atropine Eyedrops:

Atropine blocks muscarinic receptors in a non-selective way. Muscarinic receptors are found in human ciliary muscle, retina and sclera. Although the exact mechanism of atropine in myopia control is not known, it is believed that atropine acts directly or indirectly on the retina or sclera, inhibiting thinning or stretching of the scleral, and thereby eye growth. Studies have shown some clinical effect on slowing the progression of myopia in children. The Atropine for the Treatment of Myopia studies (ATOM 1 and 2) were randomized, double-masked, placebo-controlled trials each involving 400 Singapore children[88-92]. The ATOM 1 study suggested 1% atropine eyedrops nightly in one eye over a 2-year period slowed myopic progression by 77% and reduced the axial length elongation (mean axial length increase of 0.39 mm in controls versus no growth in atropine group). In ATOM 1, 12.1 % of children (who tended to be younger and more myopic) had myopia progression of more than 0.5D after 1 year of treatment with atropine 1%. The ATOM 2 study demonstrated a dose-related response with 0.5%, 0.1% and 0.01% atropine slowing myopia

progression by an estimated 75%, 70% and 60% with spherical equivalent changes of 0.30 D, 0.38 D and 0.48 D, respectively over 2 years. However, when atropine was stopped, there was an increase in myopia, with rebound being greater in the children previously on higher doses. This resulted in myopia progression being significantly lower in children previously assigned to the 0.01% group at 36 months compared with that in the 0.1% and 0.5% groups. Younger children and those with greater myopic progression in year 1 were more likely to require re-treatment. By the end of 5 years, myopia progression remained lowest in the 0.01% group. It was estimated that, overall, atropine 0.01% slowed myopia progression by at least 50%.

The efficacy of lower dose atropine is corroborated by Taiwanese cohort studies. However, there may be children who are poor responders to atropine. Atropine 0.01% caused minimal pupil dilation (on average 0.8 mm), minor loss of accommodation (2-3 D), and no near vision problems (children on atropine 0.01% did not need progressive additional lenses). Nevertheless, in more recent studies examining the rate of axial elongation, 0.01% atropine had minimal benefit[93,94].

In the Low-Concentration Atropine for Myopia Progression (LAMP) study involving 438 children from Hong Kong aged 4 to 12 years, treated with Atropine 0.01%, 0.025%, and 0.05%, there was a reduction of spherical equivalent (SE) progression by 27%, 43%, and 67%, and a slowing of axial length growth of 12%, 29%, and 51%, respectively after a year[95]. Of interest, the effect on spherical equivalent refraction was larger than that on axial length. The second-year efficacy of 0.05% atropine eye drops and 0.025% atropine eye drops remained similar ($p>0.1$) and improved slightly in the 0.01% atropine group ($p=0.04$)[96]. In the LAMP-II Study, the efficacy of 0.05% atropine eye drops was double that of the 0.01% eye drops and therefore the 0.05% was considered to be the optimal concentration. In the third year, children in each group were randomized at a 1:1 ratio to continued treatment and washout subgroups[97]. During the third year, continued atropine treatment achieved a better effect across all concentrations compared with the washout regimen. 0.05% atropine remained the optimal concentration over 3 years in Chinese children. The differences in rebound effects were clinically small across all 3 studied atropine concentrations. Stopping treatment at an older age and lower concentration were associated with a smaller rebound[98].

A recent Network Meta-Analysis involving 30 pairwise comparisons from 16 randomised controlled trials (3272 participants) ranked the 1%, 0.5%, and 0.05% atropine concentrations as the 3 most beneficial for myopia control, as assessed for both primary outcomes: 1% atropine (mean differences compared with control): refraction, 0.81; axial length elongation (AXL), -0.35; 0.5% atropine: refraction, 0.70: AXL, -0.23; 0.05% atropine: refraction, 0.62; AXL, -0.21[99]. In terms of myopia control as assessed by relative risk (RR) for overall myopia progression, 0.05% was ranked as the most beneficial concentration (RR, 0.39). The risk for adverse effects tended to rise as the atropine concentration was increased, although this tendency was not evident for distance BCVA.

A report from the American Academy of Ophthalmology concluded that the use of atropine to prevent myopic progression is supported by level I evidence[100]. In general, there is a dose-related response in atropine for myopia control[101,102]. Low-dose atropine (0.01%-0.1%) has efficacy of 30-60% in myopia control. 20-30% children started on low dose atropine may benefit from higher concentration, especially younger children with family history of high myopia. High-dose atropine (0.5%-1%) is more efficacious at 60-80%. 10% may still respond poorly. Children on higher dose atropine may require photochromatic glasses with or without a reading add. Lower doses are also associated with less rebound effect when stopped, whereas children on high-dose atropine require a slow taper and should not be stopped suddenly. Patients may also need different doses at different times of their lives.

Conclusions

There is sufficient evidence to warrant the adoption of myopia prevention and control measures in clinical practice in children with progressive myopia of childhood. Although there remain gaps in knowledge about mechanism of action and long-term outcomes, the benefits outweigh the risks if they are appropriately managed. However, the efficacy of such interventions especially pharmacological, is unclear in cases of pathological myopia due to connective tissue disorders, retinal dystrophies, vitreoretinopathies, retinopathy of prematurity associated myopia, and in myopia seen in children with pseudophakia.

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