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REVIEW

Current approaches to premyopia

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Abstract

Myopia is a public health problem that is quite common in the world and has an economic burden. For many years, various treatment options have been proposed to control the progression of myopia in children. Recently, the age of myopia onset is gradually decreasing. Due to early onset of myopia increases the risk of developing high myopia, the concept of premyopia has been introduced. The aim of this review is to raise awareness among both ophthalmologists and parents about the concept of premyopia. The importance of identifying and managing premyopia is to prevent sight-threatening complications related to myopia and reduce the economic and healthcare system burdens.

Keywords: Axial length; Low level of hyperopia; Myopia progression; Premyopia.

The prevalence of myopia and high myopia is increasing globally.^[1] Childhood myopia usually develops between the ages of 6 and 12 and is an irreversible progressive disease.^[2,3] Myopia progression stabilizes in most individuals after adolescence. However, the age of myopia onset is of significance. Because the age of myopia onset is a strong predictor of the development of high myopia in adulthood.^[4] In a cohort study involving 443 myopic individuals, the risk of developing high myopia in the future was found to be >50% for those with myopia onset at age 7 or 8.^[5] Due to the vision-threatening complications associated with high myopia, we need to pay attention to the onset of myopia.^[6] The age of myopia onset decreases in the population over time. The mean age of myopia onset was reported as 10.6 years in 2005 and 7.6 years in 2021.^[5,7] Recent studies have shown that children with a low level of hyperopia have a higher

tendency to develop myopia.^[8] For this reason, prevention of the onset of myopia was emphasized, and the concept of premyopia was introduced by the International Myopia Institute. Premyopia can be defined as the refractive state of an eye of <+0.75 diopters (D) and >−0.50 D when ocular accommodation is relaxed.^[9]

The majority of studies on the prevalence of premyopia have been carried out in the Asian population. The prevalence rate of premyopia among primary school students has been reported ranging from 45% to 52% in the Asian population.^[10,11]

All children should undergo a cycloplegic refraction examination at the baseline visit. Because the eye's accommodative mechanism may cause an overestimation of myopia, the difference between cycloplegic and non-cycloplegic refraction is defined as pseudomyopia or accommodative spasm. Accommodation should be relaxed



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with cycloplegic agents to prevent overcorrection.^[12,13] For cycloplegic refraction, two drops of 1% tropicamide or 1% cyclopentolate are applied twice with an interval of 5 min. Cycloplegic measurement should be performed 30–45 min after the first drop is instilled.^[14]

Axial length (AL) measurement should also be recorded at the baseline refraction examination. According to a study conducted, the onset of myopia occurs at approximately the same mean AL in each onset age group. This cutoff point for predicting the onset of myopia has been reported as 24.08 ± 0.67 mm in boys and 23.69 ± 0.69 mm in girls.^[15] In addition, the growth rate of AL before the onset of myopia may be a predictive factor for the onset of myopia. In a study by Mutti et al., it was reported that the mean increase in AL was 0.33 mm in the year before myopia onset, and this slowed to 0.20–0.27 mm in the year after myopia onset. That is, the increase in AL is highest in the year before the onset of myopia.^[16]

Risk Factors

Premyopia has various risk factors including parental myopia,^[17-19] binocular vision dysfunction,^[20,21] time spent outdoors (light exposure),^[22-26] near work (increased digital screen exposure),^[27-34] and gut microbiota profile.^[35,36]

Parental Myopia

Studies have supported the association between parental myopia and the child's risk of developing myopia. A meta-analysis reported that children with two myopic parents have a higher risk of developing myopia than those with one myopic parent.^[17] Zadnik et al. reported that children with two myopic parents have longer AL and less hyperopic refractive error than children with one or no myopic parents.^[18] However, a different opinion can be expressed on this issue. Myopic parents have a higher level of education and more academic demands from their children. That is, environmental and genetic factors may contribute to myopic shift together. In a study conducted on Chinese preschool children, it has been reported that genetic factors play a more substantial role than environmental factors in the development of early-onset myopia.^[19]

Binocular Vision Dysfunction

Binocular vision dysfunction may be another predictive factor for myopia. The combination of esophoria and accommodative lag has a higher risk of developing myopia in low hyperopia children aged 6–7 years.^[20] Another form of strabismus associated with myopia is intermittent

exotropia. A study reported that 50% of children with intermittent exotropia become myopic by the age of 10.^[21]

Time Spent Outdoors and Light Exposure

Studies investigating the relationship between time spent outdoors and myopia have been conducted.^[22,23] A meta-analysis by Xiong et al. reported that increased outdoor time was effective in preventing the onset of myopia, but was not effective in slowing the progression of myopia in myopic children.^[23]

Both the light wavelength and the light intensity can affect myopia. Outdoor light illumination is approximately 10–1,000 times higher than indoor illumination.^[24] Wu et al. reported that longer duration of exposure to moderate light intensities such as 1,000 lux or more 3,000 lux or more outdoors also may have a myopia prevention effect.^[25] In addition, recent studies reported that short-wavelength blue light inhibited the development of myopia, whereas long-wavelength red light accelerated the progression of myopia.^[26]

Near Work and Increased Digital Screen Exposure

The exposure to near work may have an impact on myopia progression. Previous studies reported that prolonged screen time was associated with higher myopia prevalence in children.^[27] On the contrary, some authors have revealed that the association between near work and myopia seems to be greater in adults than in children.^[28] However, it is not clear which kind of near work stimulates eye growth. According to a study, reading black text from a white screen or tablet may stimulate myopia, or white text on a black screen may inhibit myopia.^[29]

As it is known, the world has experienced the COVID-19 pandemic in recent years. During home quarantine, children experienced increased screen exposure due to online learning and reduced outdoor activity. Therefore, myopia progression accelerated.^[30] Aslan and Şahinoğlu-Keşkek reported that annual myopia progression due to home education during the COVID-19 pandemic was significantly higher compared to other years.^[31] In a study by Ma et al., it was reported that there was an association between increased time of digital screen device use for online learning during home confinement and rapid progression of myopia. The authors concluded that myopia progression was slower in students using projectors and television than in students using mobile phones and tablets.^[32]

Increased screen exposure may also cause ocular surface problems. In a study conducted on this subject by Öztürk and Özen it was reported that the overuse of smartphones, tablets, and computers during the pandemic might increase

the tendency toward dry eye and myopia.^[33] Moreover, myopia progression may vary depending on the refractive error type in the pre-COVID-19 period. Myopic refractions tend to progress more rapidly than other refractive errors such as hyperopia.^[34]

Gut Microbiota Profile

There are studies in the literature reporting a relationship between the gut microbiota profiles of individuals and myopia.^[35,36] Omar et al. reported that myopic individuals have more bacteria associated with the regulation of dopaminergic signalling and GABA production compared to non-myopic individuals.^[36] Therefore, it is thought that the gut microbiota may play a crucial role in the onset and progression of myopia. Studies on this subject are still limited in number but may contribute to developing new treatment methods for myopia control in the future.

Management of Premyopia

Several interventions such as low-dose atropine,^[37-43] myopia control spectacles,^[44,45] and repeated low-level red-light therapy^[46-49] have been proposed to prevent the onset of myopia.

Low-Dose Atropine

Previous studies have reported that low-concentrations atropine (0.01% and 0.05%) are effective and safe in slowing the progression of myopia.^[37,38] Although the mechanism of action of atropine is not fully understood, more emphasis is placed on the non-accommodative mechanism. Atropine causes scleral thickening and reduced elasticity, preventing AL increase.^[39]

Atropine eye drops were introduced to prevent myopic shift in premyopic children.^[40-43] Recent studies in East Asia have shown that 0.01% atropine eye drops effectively prevented myopic shift, axial elongation, and the onset of myopia in premyopic schoolchildren.^[40,41] In these studies, it was found that 0.01% atropine slowed myopia progression by approximately 50% compared to the control group.^[40,41] However, Yam et al. reported that among children aged 4–9 years without myopia, the use of 0.05% atropine eye drops compared with placebo resulted in a significantly lower incidence of myopia, while there was no significant difference between 0.01% atropine and placebo.^[42] Side effects of atropine therapy, such as photophobia and blurred near vision, were similar in premyopic and myopic children and tended to decrease over time.^[43] The evidence for the effectiveness of atropine eye drops is mostly derived from studies conducted in East

Asian populations. Since there are only a few studies on the use of atropine in premyopic children, important issues such as the optimal dosage, treatment duration, rebound effects, and ethnic differences remain unclear.^[43]

Myopia Control Spectacles

According to the theory of peripheral hyperopia, the peripheral retina is relatively more hyperopic than the fovea in emmetropic eyes. Therefore, the image in the periphery is focused behind the retina and is blurred. This condition disrupts the dopamine balance in peripheral cells and causes the AL of the globe to increase to clarify the image.^[16] In light of this information, new designs of spectacle lenses (Defocus Incorporated Multiple Segments-D.I.M.S. and Highly Aspherical Lenslet Target-H.A.L.T. designs) were developed to prevent myopia progression. While the focus zone at the center of the lens provides clear vision, the defocus zone at the periphery controls myopia. In a study involving 108 premyopic Chinese children, it was reported that spectacle lenses with H.A.L.T. significantly reduced AL elongation at the end of the 12-month follow-up period.^[44] However, there are very few studies in the literature on this topic, and the results regarding long-term effects and rebound after cessation remain uncertain.^[45]

Repeated Low-Level Red-Light

Recent studies reported that repeated low-level red-light therapy causes increased choroidal thickness, improved blood flow, and stabilization of axial elongation.^[46] Therefore, it may be thought that repeated low-level red light may prevent structural changes such as choroidal thinning and hypoxia seen in myopia. Currently, repeated low-level red-light therapy applied by a device emitting 650 nm visible red light has been proposed to prevent myopia shift. In a study carried out in premyopic Chinese children, it was reported that the repeated low-level red-light therapy significantly reduced the myopic shift in terms of AL and spherical equivalence refraction compared with the control group.^[47] Liu et al. reported that repeated low-level red-light therapy is more effective in children with myopia than in those with premyopia.^[48] However, the safety of repeated low-level red-light therapy is controversial. Prior studies reported that reversible decline in visual function and discontinuity of the foveal ellipsoid and interdigitation zones due to the repeated low-level red-light therapy.^[49] Temporary afterimage is the most common ocular symptom following treatment. Participants with afterimage duration exceeding 6 min may be more sensitive to the light stimulus, and phototoxicity may occur.

Conclusion

Premyopia is a current concept that has been frequently the subject of studies lately. The importance of premyopia diagnosis is the prediction of high myopia with vision-threatening complications. At the baseline visit of the premyopic child, accommodation should be relaxed with cycloplegic agents to prevent overcorrection. In addition, AL should be recorded during visits, and children with AL measurements (24.08 ± 0.67 mm in boys and 23.69 ± 0.69 mm in girls) that are a precursor to the onset of myopia should be followed closely. Myopic shift can be prevented before myopia develops. The first step for this is to inform the family. If parents are informed about premyopia and risk factors, their support will also be provided. Parents should be informed about precautions such as good lighting during close work, reduced screen time, and increased time spent outdoors. In addition, it has been emphasized that the use of projectors and televisions is less harmful in terms of myopia progression compared to the use of tablets and phones. It should also be explained that dry eye symptoms may occur due to increased screen exposure.

Studies have supported premyopia management methods such as low-dose atropine, myopia control spectacles, and repeated low-level red-light therapy. The safety of repeated low-level red-light therapy remains controversial, as clinicians have concerns about the risk of phototoxicity. Currently, low-dose atropine and myopia control spectacles are more widely accepted treatment methods. Atropine eye drops appear to be effective in reducing myopia progression and are considered cost-effective. However, there are limitations regarding side effects, rebound after cessation, and the challenge of convincing families to use a pharmacological agent on their children. Although the new myopia control spectacles are effective and safe, their high cost is a significant disadvantage. Moreover, there is insufficient evidence regarding the long-term effectiveness of these treatment methods. Therefore, further randomized controlled studies are needed to gain a better understanding of myopia progression.

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