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Open Access Journal of Ophthalmology
ISSN: 2578-465X

Myopia Progression: Recent Advances in Diagnosis and Management

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Review Article
Volume 8 Issue 2
Received Date: July 12, 2023
Published Date: October 02, 2023
DOI: 10.23880/oajo-16000287

Abstract

Importantly, environmental factors, it has now become a world-wide epidemic. By the year 2050, the global prevalence is estimated to reach 4.8 billion. Progressive myopia causes gross Loss of vision and is both a personal and public health burden. Various Pharmacological, Optical myopia is the most prevalent refractive error globally. Due to various genetic and more and environmental measures are present in our armamentarium at present to prevent Myopic progression. In view of the epidemic, progressive and vision-depriving nature of the Condition, it becomes imperative to understand its diagnosis and management. This review aims to give a comprehensive overview of the current available modalities of management of progressive myopia.

Keywords: Myopia; Progressive Myopia; Atropine; Sunlight; Vitamin D; Multifocal; Orthokeratology; Myopia Calculator

Introduction

Myopia is the most widespread refractive error. It is defined as the refractive error in which rays of light entering the eye parallel to the optic axis are brought to a focus in front of the retina when ocular accommodation is relaxed [1]. Its global prevalence is on the rise, especially in East and Southeast Asia [2]. By the year 2050, the global prevalence is estimated to reach 4.8 billion with around 938 million expected to have high myopia by then [3]. High myopia is defined as spherical equivalent refractive error of the eye </= - 6D when ocular accommodation is relaxed, while pathological myopia is defined as excessive axial length elongation associated with myopia leading to the structural changes in the posterior segment of the eye and hence the loss of best corrected visual acuity [1]. It is of concern to us since pathological myopia can lead to adverse consequences such as myopic maculopathy, retinal breaks, retinal detachment, choroid neo-vascularization, glaucoma and posterior staphyloma. They also have an adverse impact on quality of life, Affects school performance, have psychological implications and even causes economic implications for public health [4]. Owing to these factors, there has been a global concern, active research and a number of measures being attempted in order to identify it at an early stage, prevent and control myopia progression. This article provides an overview of recent advances made in terms of myopia diagnosis, risk factors and its treatment.

Why the Epidemic?

The sudden increase in prevalence could be attributed to various reasons. Myopia and its progression are multi-factorial and can be attributed to various reasons such as Genetic factors, environmental factors, ethnicity and even age of onset. The Consortium for Refractive Error and Myopia (CREAM) study, which was the largest genome-based study on myopia concluded that there are 24 genomic variations which were associated with 10-fold increase in myopia prevalence [5-7]. Parental history of myopia is

associated with increased risk of axial length elongation and myopic progression [8,9]. Various environmental factors have been implicated including increased time spent doing near work, less time spent outdoors, increased durations and amount of education. A multitude of studies have concluded that the environmental factors play a larger role than genetic factors [6,7]. Many studies have implicated the rise in use of digital devices as a reason for the sudden surge in the prevalence of the condition [10,11]. But few other studies have found conflicting results regarding the same [12]. Whether the increased time spent indoors as a result of device usage is the causative factor, is yet to be determined.

Interventions for Control of Myopia

In view of its increasing prevalence and vision-threatening consequences, it becomes vital to take measures to prevent its incidence and progression. Currently available measures for controlling the progression- can be grouped under environmental measures, pharmacological measures, optical and surgical measures.

Environmental Measures

Spending More Time Outdoors

Studies have conclusively proven that spending more time outdoors has been shown to be beneficial for myopia control [13-16]. While it is proved that outdoor time is protective, the exact mechanism of this remains unclear. Jun Zhang ei al.elaborated on the potential mechanisms as to why outdoor time is protective [16]. These include the release of retinal dopamine which prevents axial length elongation, the spectral composition and colour of light (daylight being predominantly blue light which is supposed to stimulate hyperopic refractive error and inhibit myopia) and by ultraviolet trigger of Vitamin D synthesis. Though many studies proved that outdoor time prevents onset of myopia, the evidence regarding its role on progression is unclear [15].

Role of Vitamin D

Various studies have shown that serum levels of Vitamin D are lower in myopes, when compared to non-myopes. [17,18]. Low levels of 25-hydroxy vitamin D has been independently identified to be associated with longer axial length and as a risk factor for myopia, which was independent of outdoor exposure time [17,19]. A study by Russo, et al. [20] did not find any association between Vitamin D metabolism, its serum levels and myopia.

Thus, regarding environmental modifications, one can conclude that less time indoors, with more time spent outdoors is protective against the onset of myopia. The role of Vitamin D in myopia prevention remains inconclusive.

Pharmacological Measures

A number of pharmacological measures have been tried in controlling myopia progression. Some of them include: Atropine, Pirenzepine, 7-Methylxanthine and drugs used to lower intra-ocular pressure like tombolo and latanoprost.

Atropine

The most widely studied and used drug for myopia progression is atropine. It is a selective muscarinic receptor antagonist. Its mechanism of action has been reported to be regulation of extracellular matrix synthesis in scleral fibroblast cells, thereby thickening the sclera and making it less elastic [1]. This is supposed to prevent axial length elongation and slow down myopia progression [21]. Atropine appears to have a dose dependent inhibitory effect on myopia progression. The main side-effects of atropine are mydriasis, photophobia, reduced accommodation and blur for near. These are likely related to the actions on ciliary muscle and iris sphincter.

Various concentrations of atropine have been studied including 1%, 0.5%, 0.05%, 0.025% and 0.01%. Landmark studies on atropine use for myopia include ATOM (Atropine in the Treatment of Myopia) 1 and 2 and LAMP (Low concentration Atropine for Myopia Progression 1 and 2) studies. ATOM 1 was a randomized double-blinded placebo-controlled trial where 400 children received atropine 1% eye drops in one eye and placebo in the other. After a 2 year follow-up period, 77% showed reduction in myopia in treated group [22]. Though it was effective; the rebound phenomenon after drug stoppage was very high. Then came ATOM 2 study [23]. which compared the lower concentrations of 0.5%, 0.1% and 0.01% atropine eyedrops in 400 children. The mean myopia progression over 2-year treatment was −0.30 (0.60) D in 0.5% group, −0.38 (0.60) D in 0.1% group, and −0.49 (0.63) D in 0.01% group while the axial elongation was 0.27 (0.25) mm, 0.28 (0.28) mm, and 0.41 (0.32) mm in the 0.5%, 0.1%, and 0.01% atropine groups, respectively. Compared to the first year, the children on 0.01% atropine had relatively slower progression in the second year. Rebound phenomenon and side effects was seen to be much more in 0.5% and 0.1% group in comparison to 0.01%, ATOM2 study concluded that 0.01% atropine was a better option [23]. Low concentration atropine for myopia progression (LAMP) study was a double-blinded, placebo-controlled, randomized controlled trial where 0.05%, 0.025% and 0.01% atropine eyedrops were compared. After 1 year, the mean spherical equivalent change was 67%, 43% and 27% slowing, respectively. Meanwhile, the mean axial

length slowing was 51%, 29% and 12% respectively. LAMP phase 2 concluded that efficacy of 0.05% was observed to be twice that of 0.01% and that it was the most optimal concentration of atropine eyedrops for myopia control [24]. A study by our group have concluded that Atropine 0.01% is effective in controlling the progression in Indian children.[25]

Thus, it can be concluded that atropine is a relatively safe, well-tolerated and effective drug for myopia progression. While the higher doses are more efficacious, they tend to cause adverse effects and higher rebound phenomenon, while lower concentrations are better tolerated and has lesser rebound phenomenon.

Optical Measures

Different measures were tried in the past, showing minimal to no benefit. These include under-correction of myopia, using pin-hole glasses and bi-focal glasses. The COMET (Correction OF Myopia Evaluation Trial) group studied the effectiveness of progressive addition lenses (PALs) in comparison to single vision lenses and concluded that PALs slowed the progression of myopia [25,26]. The overall results of the study were statistically significant but clinically these are not used routinely. The currently used optical measures to treat myopia progression can be classified into spectacles and contact lenses.

Spectacles

Some of the latest spectacles being used for myopia control are:

Defocus-Incorporated Multi-segment spectacle lenses (DIMS)

These lenses have a central optical zone of 9mm diameter that corrects the refractive error and multiple (396) segments of 1.03mm diameter of myopic de-focus (+3.50 D) surrounding the central zone. The central zone provides clear vision while the segments introduce myopic defocus in the retina, thereby producing images in front of the retina and inducing blur in the periphery. Lam ei al.did a 3 year double-masked randomized control trial to compare the effect of DIMS and control group and found that myopia control was better with DIMS group and also noted that these lenses were more effective in those with baseline hyperopic relative peripheral refraction than myopic [27].

Highly Aspheric Lenslet Target lenses (HAL) lenses

These lenses have a constellation of 11 aspheric lenses let rings around a central 9mm clear zone.These rings deviate rays of light continuously in a nonlinear manner that creates a three-dimensional quantity of light in front of the retina, which we call volume of myopic defocus (VoMD). Stellest lenses by essilor is an example of HAL lenses. In a double-masked randomized clinical trial by Bao et al, 157 children were randomised into HAL lenses, slightly aspheric lenses and single vision lenses. For children who wore HAL at least 12 hours every day, the mean change in SER (spherical equivalent refraction) was slowed by 0.99 D and increase in axial length slowed by 0.41mm in comparison to single vision lenses [28].

Contact Lenses

Multifocal Contact Lenses

These contact lenses have a centre-distance design and include lenses with concentric rings as distinct zones of relative plus power, creating a peripheral myopic defocus. These lenses usually have relative plus power toward the lens periphery- incorporated as a gradual increase towards periphery(progressive design) or in distinct zones (concentric ring design) (Example: Misight contact lenses-Coopervision). Studies have showed these lenses to slow down the myopia progression by around 30-38% and axial length elongation by 30-51% over a 2 year period [29,30].

Orthokeratology

These are specially designed rigid gas permeable contact lenses worn 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 -1.75astigmatism) seems to be achieved by central corneal epithelial thinning, midperipheral epithelial, and stromal thickening. It induces a myopic shift in all meridians in the periphery. A number of studies have shown that there is significant decrease in axial length elongation in ortho-K wearers when compared to spectacle users [30,31]. Many authors have reported a rebound effect after treatment is discontinued [32,33]. The most serious concern with Ortho-K usage is microbial keratitis. The incidence of this complication in children has been reported to be 13.9 per 10,000 patient years [34].

Surgical Measures

Various surgical measures have been tried in order to control the progression of myopia and they include**:**

Posterior Scleral Reinforcement

Sclera is remodeled to cause direct mechanical reinforcement of eyeball [35].

Injection Based Scleral Strengthening

Chemical agents are injected under tenon's capsule to stabilize the collagen matrix of sclera [36].

Collagen Cross-Linking

Collagen cross-linking using riboflavin has been tried on animal models and has shown some success [37].

Due to the invasive nature and lack of controlled trials with supportive evidence, these methods are currently not popular.

Recent Advances in Diagnosis

In lieu of its epidemic nature, progression and dreaded complications, more headway is being made in identifying the individuals who are at risk at an early stage. A number of devices have been introduced for the same.

There are devices available such as Topcon's MYAH, which offers corneal topography, pupillometry and axial length measurements along with dry eye evaluation, which claims to make identifying and managing myopic patients easier.

Brien Holden Vision institute has developed an online calculator, wherein we input basic patient characteristics, current prescription and baseline details, and it gives an estimate of progression expected. It also helps to visualize how different strategies could control progression for the given patient. Yang, et al. reported that the extent of myopia progression over 1–2 years corrected with single-vision spectacles was accurately predicted by the Brien Holden Vision Institute Myopia Calculator in 32%–38% of 7–13-year-old Hong Kong children [38].

Combination Therapy

To increase the efficacy of the interventions, combination of more than one modality of treatment has been tried. Most pediatric ophthalmologists use a combination of two or three modalities for treatment [39]. Atropine forms the mainstay in most of the combination therapies. A study done combining the pharmacological (i.e Atropine 0.01%) and environmental intervention have proved the effectiveness of combination therapies in controlling the progression [40]. Current evidence shows that combined atropine and Ortho-K treatment is more effective for axial length elongation than Ortho-K alone [41-43]. Another modality of combination therapy has been tried using combination of atropine eye drops and multifocal spectacles, and this too has shown an additive benefit when compared to either intervention alone [44,45]. Jones, et al. in their Bifocals and Atropine in Myopia (BAM) study, have studied the effect of adding 0.01% atropine eye drops in combination with soft multifocal contact lenses (+2.50D). The combination did not prove more effective than Soft multifocal contact lenses, when used alone [46]. Thus in conclusion, one can state that though combination modalities have shown some benefit, no definitive conclusions can be drawn till further evidence is available regarding the specific guidelines for the same.

Conclusion

This review brings out the various treatment modalities available for controlling myopia progression. There are so many unanswered questions here:

- Which is the appropriate age to start these control measures?
- How many years to continue the measures?
- When to switch over to combination therapies?
- What will happen once we stop the intervention?
- Long term side effects of the pharmacological agents used?

Future research should aim to answer these questions and come up with the consensus for myopia control measures.

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