Clinical Management and Control of Myopia in Children

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Key Points

- Our understanding of the pathogenesis and etiology of myopia continues to evolve, and with it, various interventions that prevent or slow the progression of myopia. These include the use of bifocal spectacles, peripheral defocus spectacles and contact lenses, orthokeratology contact lenses, atropine and environmental interventions.
- With various interventions available for myopia control, understanding the effectiveness, safety profile and cost of each intervention can aid the clinician in making collective decisions with patients and their families on the most appropriate intervention for each child.
- An atropine-based protocol for the treatment of myopia developed based on evidence from studies collected thus far is discussed. This includes assessment of risk factors for myopia progression, factors to consider when starting atropine, monitoring response to atropine treatment and factors to consider before cessation of treatment.
- It is important that there is continued assessment of the long-term effect and value of these treatments in preventing high myopia and its associated complications.

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8.1 Introduction

The understanding of the pathogenesis of myopia and various interventions has evolved over time. The belief of an association between myopia and near work in the 1980s [1–5] led to interventions targeting accommodation such as bifocal glasses [6–8] and topical atropine [9–12]. The discovery of the importance of the peripheral retina [13–15], and how peripheral hyperopic defocus may aggravate eye growth and myopia [16–19] resulted in the exploration of peripheral defocus glasses and contact lenses as potential interventions in the 2000s. Induced peripheral myopic defocus is now thought to be how orthokeratology contact lenses slow myopia [16]. Research has moved on to novel contact lens designs, which also induce peripheral or dual defocus. More recently, it is hoped that with greater understanding of gene and molecular processes involved in eye growth, novel genetic and pharmacological treatments may be developed over time to control myopia.

8.2 Near Activity and Accommodation

8.2.1 Bifocal and Progressive Addition Spectacles

Progressive and bifocal glasses were introduced in the 1990s to try and slow myopia. However, studies with progressive addition lenses (PALs) showed a small and clinically insignificant or no effect on myopia progression [20–23]. One meta-analysis noted small reductions in myopia progression (0.25 D, 95% CI 0.13–0.38; nine trials) and axial length (−0.12 mm, 95% CI −0.18 to −0.05; six trials) [24]. This effect may be greater for children with a higher myopia (<−3.0 D), accommodative lag, or near esophoria [24–28].

In contrast, randomized controlled trials (RCTs) showed that executive bifocal lenses slowed myopia progression by 39% and up to 51% with base-in prisms incorporated [29]. It is possible that the larger near segment made it more likely for children to use the near add during near work, and may also induce more peripheral myopic defocus. However, because of the lack of collaborating evidence, meta-analysis across trials found data to be limited and inconsistent [20].

8.2.2 Atropine

Atropine is a non-specific muscarinic acetylcholine receptor antagonist and was initially thought to work by blocking accommodation. This theory has since been disproved in animal studies [30]. Its exact mechanism is still unknown but it is thought to work through muscarinic or non-muscarinic pathways either in the retina or in the sclera [31, 32]. Atropine has a strong dose-dependent inhibitory effect of myopia progression [30]. The initial high doses of atropine (i.e., 0.5% or 1.0%) slowed myopia progression by more than 70% over 1–2 years [33–36]. However, lower doses (0.1% or less) can also slow myopia by 30–60%, and may be associated with fewer side effects (pupil dilation, glare or blur) [36, 37]. Huang et al. in a review of the data, found that high-dose and low-dose atropine slowed spherical equivalent by 0.68 D

[0.52–0.84] and 0.53 D [0.21–0.85] respectively, and axial length by −0.21 mm [−0.28 to −0.16] and−0.15 mm [−0.25 to −0.05] respectively over 1 year [38].

Washout data from the Atropine Treatment of Myopia (ATOM) studies, however, showed that there was a myopic rebound if atropine was stopped suddenly, especially at higher doses and in younger children [39, 40]. Up to 12% of children may exhibit a poor response (i.e., progress >1.0 D over 1 year) even on high-dose atropine. A poorer response was associated with younger children, a higher degree of myopia at baseline and myopic parents [41]. Similarly, in the ATOM2 study, 9.3%, 6.4%, and 4.3% of children in the 0.01%, 0.1%, and 0.5% group, respectively, progressed by 1.5 D or more in the first 2 years of treatment [42].

More recently, in the Low-Concentration Atropine for Myopia Progression (LAMP) study involving children aged 4–12 years, those treated with 0.01%, 0.02%, and 0.05% atropine showed a reduction of SE progression of 27%, 43%, and 67%, and axial length growth of 12%, 29%, and 51%, respectively [37]. Overall, the effect on spherical equivalent was larger than that of axial length.

8.3 Peripheral Defocus

From animal studies, it is known that eyeball growth (i.e., hyperopia or myopia) could be induced by using positive and negative lenses, respectively [43, 44]. These studies also showed that peripheral refraction could influence eye growth, independent of central vision. Excessive near work could induce hyperopic defocus in the peripheral retina and promote eye growth [25, 45–48]. The increased prolate growth of the myopic eyeball and use of spherical glasses correcting for central vision may aggravate this effect [46, 49–52]. Based on this theory, optical interventions that induce a myopic defocus in the periphery should slow myopia.

8.3.1 Peripheral Myopic Defocus Glasses

In 2010, Sankaridurg et al. published their results of three novel spectacle lenses. All lenses had a central clear aperture with varying amounts of plus defocus in the periphery. Unfortunately, there was no significant effect on myopic progression with all three designs compared to single vision lenses (SVLs). In a subgroup of younger children with parental myopia, however, the prototype where the central aperture extended into the horizontal and inferior meridians with a peripheral power of +1.9 D did result in less myopia progression [53]. However, in a recent RCT conducted in Japanese children involving this design, no difference in myopia reduction was found [54].

8.3.2 Bifocal or Dual-Focus Contact Lenses

Bifocal contact lens designs often include a central distance focus, and peripheral rings with near add, creating a peripheral myopic defocus. Studies exploring the effect of these bifocal soft contact lenses indicate slowing of myopia progression by

30–38% and axial length by 31–51% over a period of 24 months [55–57]. Different studies suggest that efficacy may improve with increase in wear time, in children with faster rates of progression [58], near esophoria [59], and with designs possessing a higher hyperopic power in the mid-periphery (up to 6 D) [60]. With the myriad of lens designs possible, the challenge now is to develop the most effective design with the least compromise to visual quality, comfort, and safety [61].

8.3.3 Orthokeratology

Orthokeratology (Ortho-k) lenses optically correct myopia by flattening the central cornea, resulting in a relative peripheral myopic defocus [62, 63]. Individual studies and meta-analyses have shown a 40–60% reduction in the rate of myopia progression with ortho-k lenses compared with controls using SVL spectacles [64–69]. In a meta-analysis by Sun et al., the combined results showed a mean AL reduction of 0.27 mm (95% CI: 0.22, 0.32) after 2 years, corresponding to a 45% reduction in myopic progression [69]. Younger children (aged 7–8 years) with faster myopic progression (>1.0 D/year) might benefit more [66], and benefits were noted even in partially corrected children with high myopia [68]. However, studies show that the efficacy may decrease over time, especially after 4–5 years [70–72], and a potential "rebound" after discontinuation, especially in children under 14 years [73]. There is also a potential non-response rate of 7–12% [74, 75]. The risk of infective keratitis remains [76–81]; a recent systemic review suggested an infection rate similar to overnight wear of soft contact lenses, which is estimated at 13.9 per 10,000 [82, 83].

8.4 Time Spent Outdoors

While initial strategies were targeted at minimizing near work, it became apparent that increasing time spent outdoors could be more important [84, 85]. In the Sydney Myopia Study, exposure to more than 2 h of outdoor activity per day decreased the odds of myopia and countered the effects of near work [86]. Interventions involving increasing time outdoors appeared to reduce the onset of myopia and also its progression in myopic children [87, 88]. A meta-analysis has suggested a 2% reduced odds of myopia per additional hour of time spent outdoors per week [89]. Another meta-analysis showed that time outdoors protected children against incident myopia with a risk ratio (RR) of 0.536–0.574 in clinical trials and longitudinal cohort studies, and an odds ratio of 0.964 in cross-sectional studies, but had less effect in slowing progression in children who were already myopic [90].

8.4.1 Environmental Interventions

Based on new evidence, the advice has shifted from spending at least 2 h/day outdoors in addition to avoiding excessive near work. This has changed health and school messaging in many East Asian countries [88].

8.4.2 Higher Light Intensities and Dopamine

Potential reasons why time outdoors may be protective include higher light intensities [91, 92], differences in chromatic composition [93–95], the reduction in dioptric accommodative focus and psychometric influences encountered outdoors [96]. Higher light intensities increase retina dopamine production, which is believed to retard axial length elongation [97]. In animal studies, higher light levels greatly retarded form-deprivation myopia [91, 92, 98], a reaction which is abolished by dopamine antagonists [97]. The role of chromaticity (red and blue) and ultraviolet (UV) light is still uncertain [99–102], while that of higher vitamin D levels has been debunked [103, 104].

8.5 Inheritance and Genetics of Myopia

Epidemiology studies suggest that the risk of myopia is doubled if children had one myopic parent, and 3–5 times if they had two [105], with a possible additive effect with subsequent generations [106]. In addition, monozygous twins have a 75–90% chance of having a similar refraction compared to 30% in dizygous twins [107–109].

From pedigree analysis, multiple inheritance patterns (i.e., autosomal dominant, autosomal recessive, and X-linked) have been identified. Genome-wide sequencing analyses have identified more than 20 myopia and high myopia loci and over 130 potential genes (MYP1-3, 5–19) in different populations [107, 110]. These loci have been linked to neuronal signaling, retinoic acid synthesis, ion transport, channel activity, and membrane potential [110], which may influence ocular development, differentiation, and growth [111]. It is hoped that by understanding the genetics of myopia, it may be possible to predict who may develop high myopia or complications of myopia early, how people may respond to various interventions, and uncover novel interventions.

8.6 Application to Clinical Practice

In deciding on treatment regimes, questions on which children would benefit most from treatment in terms of age, baseline myopia, rate of progression, and family history remain. In addition, the appropriate duration of treatment and the best time to start, stop, and restart treatment need to be further studied. With the various interventions available for myopia control, decisions need to be made in conjunction with patients and their families on the most appropriate one, taking into consideration the effectiveness, safety profile, and cost of the each intervention (Table 8.1).

The following is an atropine-based protocol which has been developed, based on evidence collected thus far (Table 8.2 and Fig. 8.1). On presentation, the risk of the child developing myopia and its potential complications are assessed. Low-risk children may be older children (aged >11 years), those with little or no myopia progression in the last 1 year, and relatively low myopia. High-risk children may be those who have a strong family history of high myopia or myopic complications, are younger (<9 years), and with documented rapid progression of myopia over the last year. Parental and child

Table 8.1 Summary of interventions for myopia control efficacy, safety, and accessibility

	Effectiveness	Safety	Accessibility
Time outdoors	Decrease onset of myopia by 30%; and progression of myopia by 18% [87, 88]	Safe. Requires sun protection of eyes and skin	Available to all. Limited by social factors (academic expectations), weather, and seasonal variations
Executive bifocal spectacles	Decrease myopia progression by 39%; 51% with base-in prisms incorporated [29]	Safe although may result in some visual distortion	Moderately expensive Readily available in most spectacle shops
PAL spectacles	Decrease myopia progression 0–20% [24]		
Peripheral myopic defocus spectacles	No significant difference from SVL [53, 54]		
Bifocal or dual focus soft contact lenses	Decrease myopia progression 30–38% over 24 months [57] Better effect with near esophoria [59]	Possible risk of infective keratitis, contact lens intolerance No data on discontinuation and rebound effect	Moderately expensive although likely readily available in most spectacle shops
Orthokeratology contact lenses	40–50% reduction in myopia progression over 1–2 years Effect may wane over time Rebound noted if stopped suddenly [69, 70]	Risk of infective keratitis similar to overnight soft CL wear: 13.9 per 10,000 [83] Ocular surface problems, corneal staining [82]	Can be expensive Require clinical expertise to ensure proper fit
Atropine	Dose-related response for myopia control with 70–80% reduction with high dose (0.5–1%) [33–36] and 30–60% with low dose (0.01–0.05%) [36, 37] Rebound noted if stopped suddenly (esp. in younger children and at higher doses) [39, 40]	Glare and near blur with higher doses Allergy 1–4% Systemic effects rare Effect on spherical equivalent greater than axial length	Can be cost-effective if manufactured in bulk Lower doses not readily available in all communities

sentiments are also assessed (e.g., overall anxiety, willingness to administer eye drops every day, possibly till the child is in his/her mid-teens). Various options are discussed, ensuring that parents have realistic expectations of the outcome. The possibility of a poor response and need for a higher dose of atropine or alternative treatments are also carefully explained. Options would then include starting atropine or waiting another 6–12 months to monitor the natural progression of refraction.

In this protocol, children are first started on a lower dose of atropine with a plan to increase the dose as necessary. However, an alternative would be to start initially

Table 8.2 An atropine-based protocol for myopia treatment

A. Starting atropine – Assess child's risk of myopia – High risk: family history of high myopia or myopic complications, younger age, documented rapid progression of myopia, poor life-style profile (outdoor–near work) – Assess parents' and children's risk aversion to treatment, willingness to continue on treatment till at least teenage years – Age 4–13 years of age with documented progression of myopia of at least >0.5 D in the last year
B1: Not keen on treatment: monitor over next 6–12 months B2: Keen on treatment: commence atropine 0.01% daily for at least 2 years
C. Follow-up on treatment – Review child every 6 months – Monitor for compliance and side effects : near blur, glare, and allergy – Cycloplegic refraction and axial length measurements at least once per year
D1: Good or acceptable response to treatment (<0.5 D/year) Age <12 years old: consider continuing dose or slowly taper if no myopia progression noted in the past year Age >12 years old: consider taper of medication if no/little progression noted in the past year D2: Poor response to treatment (>0.5 D/year) – Particularly in younger children (<9 years), with strong family history, with baseline high myopia and rapid progression prior to starting atropine – Consider an increased dose (e.g., atropine 0.01% 2× per day, 0.1% daily or 1.0% 2–3× per week) – Consider tinted glasses with near add if required – Once stabilization of myopia is achieved, continue at that dose, and taper frequency of drops as child reaches teenage years D3: Poor response despite maximum atropine dose – Consider stopping and changing or adding different treatment options
E. Long-term follow-up – Continue to monitor child for at least 1 year after stopping treatment

on a higher dose, with an aim to taper medication over time. Once medication is started, progression (refraction and/or axial length) is monitored every 6 months, with an initial aim to continue children on medication (i.e., atropine 0.01% daily) for at least 2 years. Children may respond to treatment in three ways: well (with little or no progression); adequately (with acceptable amount of progression, e.g., <0.5 D/year); or poorly (>0.5 D/year).

If a good response is obtained, the next question is how long treatment should continue for and when treatment should be stopped. From the ATOM 2 study, we know that stopping atropine 0.01% between 8 and 10 years resulted in a 60% risk of a rebound effect, compared to 30% at age 10–12 years and 8% after the age of 12 years. In addition, children who did not demonstrate rebound tended to show little or no myopic progression within the last year [67]. This suggests that in children younger than 12 years who showed no progression in the past year, atropine 0.01% may be slowly tapered (e.g., by reducing drop frequency by 1–2 days/week each year). However, if children are older than 12 years, then the frequency of eye drops could be tapered more quickly (e.g., by 1–2 days/week every 6 months). Using this regime, most children will be off medication by about 14–15 years of age.

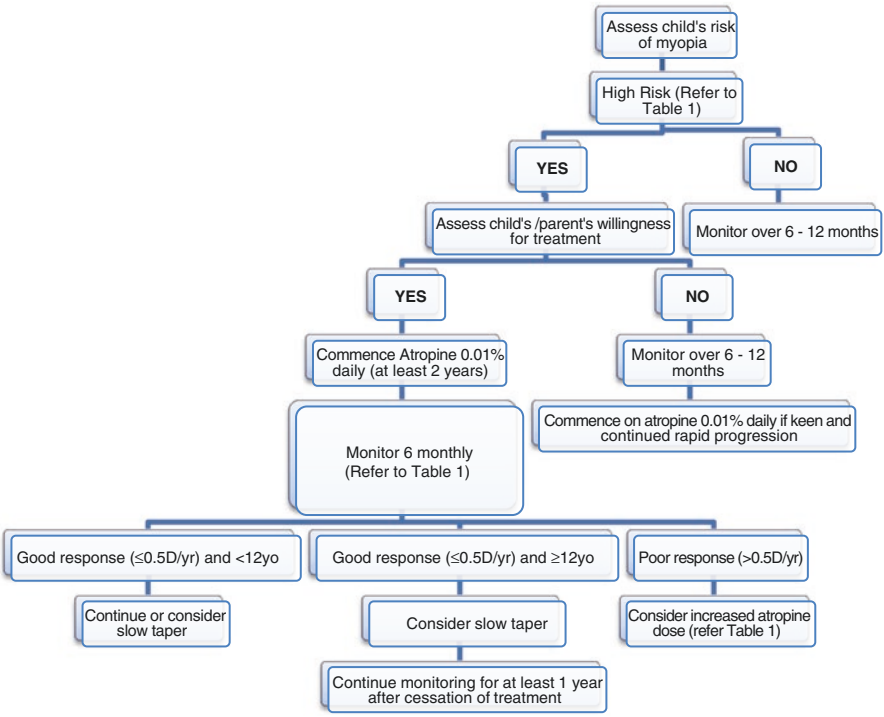

Fig. 8.1 Flow chart of atropine-based protocol for myopia treatment.

In children who progress on low-dose atropine, the frequency of application or dose could be increased (e.g., using atropine 0.01% twice a day; or using a higher concentration, e.g., 0.1% or 1%). Note that while using higher concentrations, a daily dose may not be necessary and children may require tinted glasses with near add to cope with any glare or near blur. Once an adequate control of myopia is achieved, medication can be continued till the child reaches teenage years and then tapered as required. There are some children (10%), however, who may progress rapidly even on higher doses of atropine [68]. If this occurs, then the possibility of stopping treatment or trying other treatment modalities should be discussed. Even after stopping treatment, it may be necessary to monitor children for a further 6–12 months to ensure that there is no further rebound.

Since our knowledge of how children respond to atropine and other interventions continues to increase over time, any protocol developed needs to be evaluated regularly, taking full advantage of our knowledge and accessibility to different treatment options.

8.7 Conclusion

Our management of myopia continues to evolve over time with a better understanding of the pathogenesis of myopia and its interventions. The challenge is to identify which individuals to treat, when to start treatment and which

interventions one should use. There are differences in efficacy, safety, and cost which need to be balanced. More work is required to determine how to combine or time treatments to optimize outcome, and when treatments can be safely stopped. It is also important that there is continued assessment of the long-term effect and value of these treatments in preventing high myopia and its associated complications.

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