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Methods to treat myopia progression in pediatric patients

Michael J. Wan, MD, FRCSC

Background

Myopia is an enormous, and growing, public health issue across the globe. The prevalence of myopia has doubled in just the past 50 years and it is estimated that approximately half of the world's population (4.8 billion people) will be affected by 2050.[1,2] The increase has been especially pronounced in individuals of East Asian descent, where 80-90% of young adults are now myopic.[3] Myopia is now the most common cause of visual impairment and the second most common cause of blindness worldwide.[4]

While often considered a "correctable" cause of vision loss, people with myopia have an increased lifetime risk of complications, such as macular degeneration and retinal detachment, which can cause long-term visual impairment or even blindness.[5] Although all levels of myopia are associated with an increased risk of complications, the risk is substantially greater in people with high myopia (defined by the World Health Organization as a refractive error of ≤-5 diopters).[6] In addition to a large burden of visual impairment, myopia also has a significant global economic cost, estimated to be $250 billion per year in lost productivity, which is almost certain to rise.[7]

With these factors in mind, preventing the progression of myopia is a global public health priority. The purpose of this article is to review the currently available methods to treat myopia progression in children.

Treatment

Atropine

The use of topical atropine to treat myopia progression is supported by an impressive number of high-quality studies. The first randomized, placebo-controlled, double masked clinical trial (RCT), Atropine in the Treatment of Childhood Myopia Study (ATOM1), was published in 2006.[8] ATOM1 results demonstrated that daily 1% topical atropine reduced the progression of myopia in children aged 6-12 years old (both refractive error and axial length) compared to placebo over 2 years of treatment. However, eyes treated with 1% atropine suffered significant visual side effects related to cycloplegia and mydriasis, and there was a significant rebound effect after the atropine was stopped.[9]

The follow-up RCT (aptly named ATOM2) compared 3 lower doses of atropine – 0.5%, 0.1%, and 0.01% - over 2 years.[10] The main outcome measure of myopic progression was comparable between the different doses, but the 0.01% atropine dose was the best tolerated. In phase 2 of the ATOM2 trial, treatment was stopped for 12 months, and a rebound effect was again noted. The severity of the rebound was directly related to the concentration of atropine, such that the 0.01% atropine had the most sustained effect on minimizing myopic progression.[11] In phase 3 of the study, all children with myopic progression were treated with 0.01% atropine for 2 additional years

and a convincing reduction in myopic progression was achieved.[12]

Since the publication of the ATOM trials, there have been additional studies on the optimal use of topical atropine. The Low-Concentration Atropine for Myopia Progression (LAMP) study compared even lower doses of atropine – 0.05%, 0.025%, and 0.01% - and found that 0.05% atropine was approximately twice as effective as 0.01% at reducing myopic progression over 2 years with no additional side effects.[13,14] However, longer-term results and the risk of rebound have yet to be published from the LAMP study. There are also ongoing clinical trials in North America and Europe aimed at addressing generalizability concerns in light of both the ATOM and LAMP studies having been conducted exclusively in children of East Asian descent. While the optimal treatment regimen for atropine may change with time, the cumulative evidence strongly supports the use of daily atropine (0.01% or 0.05%) to reduce progression in myopic children.

Orthokeratology (Ortho-k)

In addition to low-dose atropine, there are several non-pharmacologic treatments which have strong evidence of reducing myopic progression in children. Orthokeratology (Ortho-k) is one of the most well studied of these. Ortho-k involves the use of specially designed, rigid contact lenses which are worn overnight to flatten the central cornea. The cornea remains flattened for a period of time when the lenses are removed, allowing myopic children to achieve acceptable visual acuity without correction during the day. Ortho-k can correct refractive errors of approximately -5 diopters, but may induce optical aberrations and daytime vision can fluctuate.[15] Several systematic reviews and meta-analyses have concluded that ortho-k does reduce axial length elongation compared to control subjects.[16-19] However, the long-term effect and potential for myopic rebound with ortho-k have yet to be elucidated. The risk of complications is low when ortho-k lenses are used properly, but there are several reports of severe complications such as infectious keratitis.[20] Therefore, ortho-k is an effective management option for myopic control, and the only modality that improves daytime vision without correction, but it does require nightly application of specially designed contact lenses and has a small risk of serious adverse effects.

Peripheral myopic defocus lenses (contact lenses and glasses)

Another non-pharmacologic intervention for myopic progression is the use of peripheral defocus lenses. The proof-of-concept for the use of peripheral defocus lenses came from animal studies demonstrating that artificially focusing light in front of the retina (i.e. myopic defocus) could inhibit growth of the eye.[21] To harness this effect, contact lenses were designed with a central zone to correct distance refractive error combined with peripheral zones of additional plus power to create myopic defocus.[22,23] These soft contact lenses have been shown to be effective in reducing myopic progression in high-quality RCTs.[24] Furthermore, follow-up studies have reported no evidence of myopic rebound after discontinuation.[25] In addition, vision-related quality-of-life measures have been shown to be similar (and may even be superior) in children wearing the contact lenses compared to those wearing spectacles.[26] However, like all contact lenses, peripheral defocus lenses require proper care and have a small risk of keratitis.

For children who cannot manage the daily use and care of contact lenses, peripheral defocus spectacles will soon be an option. Recent RCTs have shown that peripheral defocus spectacles also effectively slow myopic progression for at least 3 years compared to single vision glasses.[23,27] Peripheral defocus spectacles present an attractive option as a non-pharmacologic intervention with no risk of microbial keratitis. However, the advanced design means that these spectacles are likely to be significantly more costly than single vision glasses.

Environmental Factors

The dramatic increase in myopia in just a single generation strongly suggests that environmental factors play a significant role. A large prospective study from the Netherlands found that the risk of childhood myopia was almost equally related to genetic and environmental factors.[28] Another epidemiological study compared age- and ethnicity-matched children (to minimize the effect of genetics) in Singapore and Sydney and found that the prevalence of myopia was almost 10 times higher in Singaporean children.[29] This has led to a concerted effort to identify which environmental factors are most influential and, as such, potential targets for behavioral modification. To date, outdoor activity time has been found to be the most powerful environmental factor contributing to childhood myopia.[29,30] A recent meta-analysis looking at five studies with over 3,000 children aged 6 to 12 years concluded that, in children who spent more time spent outdoors, there were fewer de novo cases of myopia and less myopic progression.[31] Some studies have also identified near work as a risk factor for myopia,[30] but others have not.[29] Therefore, the evidence to date indicates that environmental factors do play a role in the development of myopia and that more outdoor time is strongly associated with decreased risk.

Comparison of Treatments

Having several effective treatments for myopia progression is critical in ensuring optimal patient outcomes.

TREATMENT	PROS	CONS
Topical atropine (0.01% or 0.05%)	Strong evidence Minimal side effects No risk of infectious keratitis	Needs to be compounded Does not replace refractive correction
Ortho-k	Able to see well uncorrected during the day Parents can perform all aspects of lens care	Requires specially designed lenses Small risk of infectious keratitis Cannot correct high myopia Daytime vision can fluctuate
Peripheral defocus lenses	Able to correct high myopia Option of contact lenses or glasses	Small risk of infectious keratitis with contact lenses Higher cost than single vision glasses or contact lenses
Environmental factor	Very cost-effective May augment other treatments	Uncertainty about the effect of some factors (e.g. near work)

Table 1. Pros and cons of currently available methods to treat myopia progression in children; courtesy of Michael Wan, MD

Unfortunately, the optimal treatment for a given patient is often uncertain as there are few studies directly comparing various interventions.[32] A meta-analysis[33] and a Cochrane Review [34] synthesized the available evidence in order to indirectly compare treatments and both concluded that the most effective intervention for myopia control in pediatric patients was pharmacologic (i.e. atropine) followed by specially designed contact lenses (i.e. ortho-k and peripheral defocus lenses).

The "best" treatment also depends on individual patient preferences. Parents and children may prefer the strong scientific evidence supporting the use of atropine, the correction-free vision provided by ortho-k, the soft contact lenses of peripheral defocus lenses, or the convenience of peripheral defocus spectacles. Combining treatments, such as topical atropine and ortho-k, may provide synergistic effects but these combined treatment approaches have yet to be studied. Finally, it is always a good idea to encourage children to spend time outdoors, an intervention with important benefits and minimal cost **(Table 1**).

Who to Treat and How to Monitor?

Existing atropine studies on the management of myopia in pediatric patients have been restricted to children who are already myopic and at least 4 years old. In contact lens studies, the age cut-off has been 8 years old and inclusion criteria have similarly included only those subjects with pre-existing myopia.[34] However, these age cut-offs are chosen specifically for clinical trials and may not reflect clinical practice. It is reasonable (and possibly beneficial) to start treatment in younger children if myopia develops early. It may also be useful to treat high-risk children prior to the development of myopia (the ongoing ATOM3 trial is treating high-risk children with atropine to see if myopia prevention is possible).[35]

Once treatment has been initiated, regular monitoring of refractive error and axial length is crucial. It is also important to monitor for any complications, such as photophobia with atropine use or keratitis from contact lens use. Most existing clinical trials have a treatment duration and/or evaluation timepoint at 2 years, but the optimal treatment duration is unknown. It is reasonable to treat for longer periods of time (many centers continue treatment into late adolescence) or restart treatment if myopic rebound is detected.[36]

Summary

Myopia in children is a significant and increasing worldwide public health issue. There are several evidence-based methods available to treat myopia progression. Topical atropine has the strongest evidence of efficacy; ortho-k provides correction-free vision during the day; and peripheral defocus lenses provide the option of soft contact lenses or spectacles. The optimal method in any given situation must consider the likelihood of success based on the evidence available to the clinician as well as the preferences of the patient. Initiating treatment early and monitoring closely for effect and tolerance can help to minimize the economic burden and vision-threatening complications of myopia in our pediatric patient population.

References

1. Dolgin E. The myopia boom. Nature. 2015;519(7543):276-278.

2. Holden BA, Fricke TR, Wilson DA, et al. Global Prevalence of Myopia and High Myopia and Temporal Trends from 2000 through 2050. Ophthalmology. 2016;123(5):1036-1042.

3. Morgan IG, French AN, Ashby RS, et al. The epidemics of myopia: Aetiology and prevention. Prog Retin Eye Res. 2018;62:134-149.

4. Bourne RR, Stevens GA, White RA, et al. Causes of vision loss worldwide, 1990-2010: a systematic analysis. Lancet Glob Health. 2013;1(6):e339-349.

5. Ikuno Y. Overview of the Complications of High Myopia. Retina. 2017;37(12):2347-2351.

6. Haarman AEG, Enthoven CA, Tideman JWL, Tedja MS, Verhoeven VJM, Klaver CCW. The Complications of Myopia: A Review and Meta-Analysis. Investigative ophthalmology & visual science. 2020;61(4):49.

7. Naidoo KS, Fricke TR, Frick KD, et al. Potential Lost Productivity Resulting from the Global Burden of Myopia: Systematic Review, Meta-analysis, and Modeling. Ophthalmology. 2019;126(3):338-346.

8. Chua WH, Balakrishnan V, Chan YH, et al. Atropine for the treatment of childhood myopia. Ophthalmology. 2006;113(12):2285-2291.

9. Tong L, Huang XL, Koh AL, Zhang X, Tan DT, Chua WH. Atropine for the treatment of childhood myopia: effect on myopia progression after cessation of atropine. Ophthalmology. 2009;116(3):572-579.

10. Chia A, Chua WH, Cheung YB, et al. Atropine for the treatment of childhood myopia: safety and efficacy of 0.5%, 0.1%, and 0.01% doses (Atropine for the Treatment of Myopia 2). Ophthalmology. 2012;119(2):347-354.

11. Chia A, Chua WH, Wen L, Fong A, Goon YY, Tan D. Atropine for the treatment of childhood myopia: changes after stopping atropine 0.01%, 0.1% and 0.5%. American journal of ophthalmology. 2014;157(2):451-457 e451.

12. Chia A, Lu QS, Tan D. Five-Year Clinical Trial on Atropine for the Treatment of Myopia 2: Myopia Control with Atropine 0.01% Eyedrops. Ophthalmology. 2016;123(2):391-399.

13. Li FF, Kam KW, Zhang Y, et al. Differential Effects on Ocular Biometrics by 0.05%, 0.025%, and 0.01% Atropine: Low-Concentration Atropine for Myopia Progression Study. Ophthalmology. 2020;127(12):1603-1611.

14. Yam JC, Li FF, Zhang X, et al. Two-Year Clinical Trial of the Low-Concentration Atropine for Myopia Progression (LAMP) Study: Phase 2 Report. Ophthalmology. 2020;127(7):910-919.

15. Swarbrick HA. Orthokeratology review and update. Clin Exp Optom. 2006;89(3):124-143.

16. Hiraoka T. Myopia Control With Orthokeratology: A Review. Eye Contact Lens. 2022;48(3):100-104.

17. Lipson MJ, Brooks MM, Koffler BH. The Role of Orthokeratology in Myopia Control: A Review. Eye Contact Lens. 2018;44(4):224-230.

18. Sun Y, Xu F, Zhang T, et al. Orthokeratology to control myopia progression: a meta-analysis. PloS one. 2015;10(4):e0124535.

19. Si JK, Tang K, Bi HS, Guo DD, Guo JG, Wang XR. Orthokeratology for myopia control: a meta-analysis. Optometry and vision science : official publication of the American Academy of Optometry. 2015;92(3):252-257.

20. Kam KW, Yung W, Li GKH, Chen LJ, Young AL. Infectious keratitis and orthokeratology lens use: a systematic review. Infection. 2017;45(6):727-735.

21. Wallman J, Winawer J. Homeostasis of eye growth and the question of myopia. Neuron. 2004;43(4):447-468.

22. Ruiz-Pomeda A, Perez-Sanchez B, Valls I, Prieto-Garrido FL, Gutierrez-Ortega R, Villa-Collar C. MiSight Assessment Study Spain (MASS). A 2-year randomized clinical trial. Graefe's archive for clinical and experimental ophthalmology = Albrecht von Graefes Archiv fur klinische und experimentelle Ophthalmologie. 2018;256(5):1011-1021.

23. Lam CSY, Tang WC, Tse DY, et al. Defocus Incorporated Multiple Segments (DIMS) spectacle lenses slow myopia progression: a 2-year randomised clinical trial. The British journal of ophthalmology. 2020;104(3):363-368.

24. Li SM, Kang MT, Wu SS, et al. Studies using concentric ring bifocal and peripheral add multifocal contact lenses to slow myopia progression in school-aged children: a meta-analysis. Ophthalmic Physiol Opt. 2017;37(1):51-59.

25. Ruiz-Pomeda A, Prieto-Garrido FL, Hernandez Verdejo JL, Villa-Collar C. Rebound Effect in the Misight Assessment Study Spain (Mass). Curr Eye Res. 2021;46(8):1223-1226.

26. Pomeda AR, Perez-Sanchez B, Canadas Suarez MDP, Prieto Garrido FL, Gutierrez-Ortega R, Villa-Collar C. MiSight Assessment Study Spain: A Comparison of Vision-Related Quality-of-Life Measures Between MiSight Contact Lenses and Single-Vision Spectacles. Eye Contact Lens. 2018;44 Suppl 2:S99-S104.

27. Lam CS, Tang WC, Lee PH, et al. Myopia control effect of defocus incorporated multiple segments (DIMS) spectacle lens in Chinese children: results of a 3-year follow-up study. The British journal of ophthalmology. 2021.

28. Enthoven CA, Tideman JWL, Polling JR, et al. Interaction between lifestyle and genetic susceptibility in myopia: the Generation R study. Eur J Epidemiol. 2019;34(8):777-784.

29. Rose KA, Morgan IG, Smith W, Burlutsky G, Mitchell P, Saw SM. Myopia, lifestyle, and schooling in students of Chinese ethnicity in Singapore and Sydney. Archives of ophthalmology. 2008;126(4):527-530.

30. Enthoven CA, Tideman JWL, Polling JR, Yang-Huang J, Raat H, Klaver CCW. The impact of computer use on myopia development in childhood: The Generation R study. Prev Med. 2020;132:105988.

31. Cao K, Wan Y, Yusufu M, Wang N. Significance of Outdoor Time for Myopia Prevention: A Systematic Review and Meta-Analysis Based on Randomized Controlled Trials. Ophthalmic Res. 2020;63(2):97-105.

32. Lyu Y, Ji N, Fu AC, et al. Comparison of Administration of 0.02% Atropine and Orthokeratology for Myopia Control. Eye Contact Lens. 2021;47(2):81-85.

33. Huang J, Wen D, Wang Q, et al. Efficacy Comparison of 16 Interventions for Myopia Control in Children: A Network Meta-analysis. Ophthalmology. 2016;123(4):697-708.

34. Walline JJ, Lindsley KB, Vedula SS, et al. Interventions to slow progression of myopia in children. The Cochrane database of systematic reviews. 2020;1:CD004916.

35. Chen YX, Liao CM, Tan Z, He MG. Who needs myopia control? International journal of ophthalmology. 2021;14(9):1297-1301.

36. Wu PC, Chuang MN, Choi J, et al. Update in myopia and treatment strategy of atropine use in myopia control. Eye. 2019;33(1):3-13.