Answers to Audience Questions - WSPOS Worldwide Webinar 17: Myopia

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WWW 17 Panellists



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1. How do I tell angioid streak from lacquer cracks in ehler danlos associated with pathologic myopia?

PW: Angioid streaks usually emanate from the disc, tend to be straighter, and are brown to reddish in color.

2. What is the earliest age when we can start atropine? & for how long do we use it?

AC: Any age when you have documented progression. Youngest usually 4-year-old. Continue for as long as required.

SR: I start at age 5 or 6 if there is documented progression in the right candidate patient and family. Many families want to do something but are hesitant to use medicine that young. I immediately stress increasing outdoor time with sunscreen to decrease the risk of ultraviolet damage to the skin. I typically advise until 15 or 16 when we taper and sometimes resume if progression off of Atropine.

SWL: The Atom trials had patients from age 6, the LAMP studies had patients from age 4. I have started a few 3-year olds with documented rapid progression. I continue atropine for as long as needed.

3. When do you start atropine eye drops for children? How much progression is required to start it? When do u stop atropine 0.01% eye drops? Do you take age as the criteria or the myopia control?

AC: Depends on discussion with parents. Greater urgency if still young but already has quite high myopia with documented progression with an aim to prevent high myopia whenever possible.

SR: I start at age 5 or 6 if there is documented progression in the right candidate patient and family. This is for simple myopia especially with a family history of pathologic myopia. How much progression is required to start it? SR- > or = 0.75D over 1 year, > or = 0.5D over 6 months. Will consider at lower rate if family history of pathologic myopia or child already moderate to high myope. When do u stop atropine 0.01% eye drops? I typically advise continuing until age 15 or 16 because we often see progression until then. Do you take age as the criteria or the myopia control? I take all factors including the age of the pt., the myopia pattern of progression, family history of myopic progression into account before offering treatment and determining a taper plan.

SWL: It is a decision made together with parents, taking into consideration the patient's age, rate of rapid progression, family history.

4. What are the alternatives if the progression of myopia still doesn't slow down even when you have increased to high dose atropine?

AC: Can consider adding other treatment modalities (e.g. DIMS gls and CL) but accept in some children, even this may not help.

PW: May consider orthokeratology or combination atropine therapy, including increasing time outdoors.

SR: I will add an optical device therapy such as peripheral defocus contact lens. I will also review with the patient and family that they are having adequate outdoor time.

IGM: I would tend to avoid higher dose atropine, but try other alternatives such as myopia control contact lenses such as MiSight, now approved by the US FDA, and myopia control spectacles such as DIMS. An important area for clarification is whether to try 0.01% or 0.05% atropine first.

SWL: I will ensure that lifestyle factors are already optimised (increased outdoor time) and the patient is compliant to drops before advising combination therapy (atropine + optical device)

5. What are the alternatives when the myopia doesn't slow down even when you have increased to high dose atropine? How Long would you monitor with high dose atropine before considering alternatives?

AC: Depends on age, myopia status and degree of progression. Greater urgency if still young but already has quite high myopia with documented progression.

SR: I rarely use high dose atropine beyond 0.5% as I find it not well tolerated in sunny Southern California. However, like any of the atropine dosages, I monitor every 6 months so would offer another approach if there was good compliance.

IGM: as for question 4

SWL : see answer to ques 4

6. How is it used, i.e. frequency of drops for low dose atropine like 0.1%?

AC: Depending on how much of an effect you want. You could go daily if control is important, or 3x per week, if you just need a little nudge.

SWL: To me, 0.01 % is low dose but 0.1% is not that low dose. Frequency is nightly.

7. Do you recommended to preserve the medication at low temperature in the fridge to make it last longer (since in some countries it's hard to get and we need to compound it)?

AC: depends on manufacturers' recommendation.

SR: Refrigeration is one way to preserve and a cool eyedrop may be more or less soothing to a particular child. The manufacturer will advise on this. Some companies are formulating more stable compounds. If it is not commercially available in your country and you get it via a compounding pharmacy, you need to have a good relationship with that pharmacy and know that they are doing quality control on their stock.

PS: Store in a cool, dark place as light can reduce the stability of the compound

SWL: check with manufacturer

8. (a) Is preservative free atropine formulation available in India? (b) What would you call normal axial length growth as per age, and what would you call progression of myopia? (c) Were lifestyle changes advised to these subjects at the beginning of atropine, in the studies? Would that be a confounding factor? (d) What is the reliable method of measuring axial length?

AC: (a) you need check with your distributor, (b) AL in myopia children is never 'normal', but try to keep it down to <0.2mm/year, or target more if AL already very long, (c) always, (d) anything you use to measure biometry. PW: (d) non-contact biometry is suggested.

PS: Oculus has developed a new instrument called MYOPIA MASTER which combines autorefraction and non-contact biometer in one. We (BHVI) have developed nomograms for axial length initially for Asian eyes based on a data set of approximately 20000 eyes

SWL: b)) 0.3 mm and more is considered progression, d) I use biometry

9. Can atropine 0.01% be given safely in anisometropia?

AC: Yes

SR: Yes

SWL: of course

10. How many years atropine 0.01% eye drops can be given continuously in children?

AC: as long as required.

SR: I am not aware of a study that answers that particular question. However, many physicians have used this treatment in practice for years. My longest patient has been on Atropine for 8 years with no side effects.

SWL: as long as needed.

11. What do mean by taper? Decrease the dose or use it less frequently?

AC: Both. Although avoid big changes, esp. with higher doses.

SR: I taper by using less frequently. However, if the patient is on a higher dose then it makes sense to taper by both routes – dosage and less frequency just like a steroid taper.

SWL: both dosage and frequency

12. Using atropine 0.01% if the axial elongation occurs in spite of control of spherical equivalent, does it have protective effect against retinal changes in high myopia?

AC: Target both.

SR: This is a great question and really gets to how little we definitively know about mechanism of action. If the SE is controlled the AL usually follows suit but not always. We will have to wait decades for this data to be realized as this generation of low dose Atropine treated patients age.

IGM: The results of Yam et al. suggest that reduction in changes in AL parallel those in SER. We need more detailed studies

SWL: Ideally should have both effects in spherical equivalent and Axial length

13. Are we expecting an increase in myopia due to Covid generation spending more screen and indoor time?

PW: It is noted in some clinical case, but still not large-scale study confirmed. 2 references as followings:

Will COVID-19 pandemic-associated lockdown increase myopia in Indian children? Sumitha M, Sanjay S, Kemmanu V, Bhanumathi MR, Shetty R. Indian J Ophthalmol. 2020 Jul;68(7):1496

SR: I do not know but I agree with Ian Morgan's statement that the decreased outdoor time may be a factor if this occurs.

IGM: Preliminary results from China suggest there are no major effects, but Chinese children spend little time outdoors. Larger effects may be seen where the changes in behaviour have been more extreme.

Digital Screen Time During COVID-19 Pandemic: Risk for a Further Myopia Boom? Wai Wong C, Tsai A, Jonas JB, Ohno-Matsui K, Chen J, Ang M, Wei Ting DS. Am J Ophthalmol. 2020 Jul 29:S0002-9394(20)30392-5. doi: 10.1016/j.ajo.2020.07.034. Online ahead of print.

SWL: I have seen some clinical cases suggestive of this

14. My girl is now on combination of atropine 0.01% and MiSight myopic control contact lenses. In future when I try to withdraw the atropine slowly, will the rebound worse than isolated use of atropine alone?

AC: No. should be ok, just watch what happens and titrate as necessary.

SR: I do not think so if you continue the CLs but tapering is IMPORTANT just like amblyopia treatment. These studies will likely be done in the near future.

PS: Since your child is on a lower dose of atropine, evidence indicates that rebound if any is likely to be minimal. As said, it does not appear that there is rebound with contact lenses but there are further studies underway.

IGM: Progression rates generally decline towards in zero in older children. It is not clear if delaying withdrawal will lead to less rebound

SWL: I don't think so

15. Contact lenses help! Which ones do you advise?

AC: each have pro and cons. Daily disposable mfCL likely safer overnight Oks.

SR: I prefer daily wear.

PS: MiSight and MYLO contact lenses are FDA approved and CE marked lenses. If they are not available, a multifocal contact lens (preferably centre distance, +2.00D add power and if not a centre near lens) is the starting lens of choice. It is preferable to use the lens on a daily wear, preferably daily disposable basis. If daily wear, please choose a more frequently option (not more than fortnightly replacement)

16. Any advice / algorithm for explaining therapy alternatives to parents in a comprehensible or user-friendly fashion?

AC: just provide info of each treatment – effectiveness, tolerance, safety and costs, and tailor to each child's needs.

SR: If I get them in early, I am looking at dual therapy (increased outdoor time +?) and usually the parents self-select for pharmacology or CLs. If they come in older and/or they already have significant myopia, I advocate a 3-pronged approach of low dose atropine, CL and increased outdoor time. As far as verbiage I tell them the best thing they can do is get their kid involved in an outdoor sport. We talk about not limiting their reading time but using the 20-20-20 rule. All Tx options are reviewed emphasizing safety issues. There is no shortcut to this education process that I have found. However, Padmaja's infographics from BHVI are powerful and easily understood.

PS: You may want to check out BHVI myopia calculator at <u>www.bhvi.org</u> or simply google BHVI myopia calculator. It is simply a tool to explain the risk of normal progression and what might happen with one of the many myopia control options.

SWL: I actually go through a PowerPoint with the different options

17. What are your thoughts about using atropine 2x/week? what is the logic for using it daily given the long half-life of atropine?

AC: can use 2x per week if effective.

SR: Logic is an interesting term when we still do not even know the mechanism for sure. If you tell them 2x/week, it will likely happen less. I advise daily use expecting that they will use it between 3-6x/week. It is scary to actually check your child's toothbrush to see how often it is dry right after they go to sleep. Even in the most well-intentioned families, life is busy.

SWL: I only use 2 x a week for atropine 1% when tailing down. For ultra-low dose, I think nightly is needed.

18. Any role of starting atropine in pseudophakic children with myopic shift in amblyopia?

AC: can consider if progressing rapidly.

SR: I am unaware of any scientific evidence for that.

SWL: No studies on this but can do consider if parents willing to try

19. Is there really any data that shows that atropine Rx prevents progression into Pathologic Myopia?

AC: since we have not followed these children into their 40s and 50s, it is hard to be certain, but it is inferred that keeping myopia low will help reduce risk.

SR: We need decades to show that. Given us another 10-20 years.

IGM: All the evidence links the development of PM to high myopia, so it is a reasonable guess that less high myopia will lead to less PM. But we do need the evidence

SWL: It is logical to think so since atropine reduce progression to high myopia

20. I have hyper myopia since birth, now I am 35yrs old with RP, I wish to know the chances of myopia for my 6-yearold. Also precautions for her?

AC: make sure good environment – more outdoor – to delay onset, and monitor.

SR: While myopia is very common in RP, there is no scientifically proven benefit of low dose Atropine for myopia associated with inherited retinal disorders.

SWL: increase out door time and start atropine early if she becomes myopic

21. For atropine for myopia any use for premature but NOT ROP previous patients?

AC: can consider if progressing on a case- to-case basis, but understand it may respond differently.

SR: We do not have the studies to show efficacy in prematurity or ROP.

SWL: I have used for cases with rapid progression

22. Is there a role for atropine in non-glaucoma psuedophakic patients showing Myopic shift?

AC: can consider if progressing on a case- to-case basis, but understand it may respond differently.

SR: No scientific evidence on this.

SWL : no study on this

23. Anyone with experience on effectiveness of atropine to high myopia post-laser Tx of ROP?

AC: no

SR: I think there are many physicians using this on an occasional pt. We have no scientific studies for now.

SWL: no study in this

24. Will the use of digital book projected onto TV (i.e. increased reading distance) reduce myopia progression?

AC: no evidence

PW: If use the diopter-hour as the risk factor, it might have some help.

SR: I do not know.

PS: Maybe as close reading distances have been found to be associated with myopia;

IGM: No evidence, but seems plausible. Needs to be properly tested as an intervention

SWL: No study but if asked to choose between the 2, I would think increased reading distance is better

25. Any thoughts on any of these strategies for former premature patients many of whom have high myopia? Also, would anyone consider any of these treatments more in post Laser ROP patients etc?

AC: can consider if progressing on a case- to-case basis, but understand it may respond differently.

SR: as above. In addition, if you use a CL in a high myope you lose the protective effect of blockage of blunt trauma to these RD prone eyes from polycarbonate eyeglasses.

SWL: no study on this but can consider if progressing rapidly. Parents need to be informed that the response may be different from the usual childhood myopia

26. Any comment on effect of DIMS lenses?

AC: initial study looks promising.

SR: Seems promising.

PS: The lens is marketed by HOYA and available in certain countries. There has been a single study that has reported on the efficacy of DIMS lens.

IGM: There is considerable interest from industry. Rumours of new products in this area soon.

SWL: early days

27. Can Atropine be used in the morning instead of bedtime, will it be more effective?

AC: Yes. Can use in morning. No good evidence more effective in morning as no good study.

SR: I find most families prefer evening when they have more time but ultimately like patching whatever the family is best able to do consistently is my preference.

SWL: I have always used evening dose as per trials and parents prefer evening dose (mornings are usually tricky)

28. How do you tear apart time outdoors versus scholarizaton as risk factors?

AC: need balance both so children have time to go outdoors.

SR: Every family needs to make their own decisions but explaining the importance of time outdoors will often motivate a family to budget that time into their child's schedule. Sometimes the 2 goals can be achieved simultaneously.

PS: Education (or near based activities) and time outdoors are interlinked to an extent; there are currently large- scale studies that are addressing considering these and trying to understand behaviour with the use of objective data collection with wearables. Additionally, there may be additional factors involved in time outdoors and/or near work-such as for example, does intensity of light when being outdoors matters?

IGM: You need to measure both as accurately as possible, and look for natural experiments where one or the other changes.

29. Do you notice a higher prevalence of myopia in the children population in these pandemic days with online classes?

PW: It is noted in some clinical case, but still not large-scale study confirmed. 2 references as followings:
Will COVID-19 pandemic-associated lockdown increase myopia in Indian children?
Sumitha M, Sanjay S, Kemmanu V, Bhanumathi MR, Shetty R.
Indian J Ophthalmol. 2020 Jul;68(7):1496
Digital Screen Time During COVID-19 Pandemic: Risk for a Further Myopia Boom?
Wai Wong C, Tsai A, Jonas JB, Ohno-Matsui K, Chen J, Ang M, Wei Ting DS.
Am J Ophthalmol. 2020 Jul 29:S0002-9394(20)30392-5. doi: 10.1016/j.ajo.2020.07.034. Online ahead of print.

SR: No, but I suspect if there is an increase in myopia progression many may be undercorrected as their lives are not utilizing their distance vision as much and their typical eye exams may not be happening for many reasons.

SWL: I have seen some clinical cases.

30. Due to COVID 19 prevalence, being the schools shut & kids spending lot of time on electronic gadgets, I started seeing many kids with increase in myopia. how about all of you? share your experiences?

PW: It is noted in some clinical case, but still not large-scale study confirmed. 2 references as followings:
Will COVID-19 pandemic-associated lockdown increase myopia in Indian children?
Sumitha M, Sanjay S, Kemmanu V, Bhanumathi MR, Shetty R.
Indian J Ophthalmol. 2020 Jul;68(7):1496
Digital Screen Time During COVID-19 Pandemic: Risk for a Further Myopia Boom?
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Am J Ophthalmol. 2020 Jul 29:S0002-9394(20)30392-5. doi: 10.1016/j.ajo.2020.07.034. Online ahead of print.

SR: I have not had the same experience but agree with Ian Morgan's comments (made during the webinar) about potential for lack of outdoor time.

PS: We are monitoring this data but it may require few more months to read the data and compare with trends from before COVID or previous years

31. What is the atropine regimen daily? thrice a week?

AC: Depends on dose. Higher doses could be used less frequently.

SR: Daily for my practice

SWL: nightly

32. Is it worth to start atropine even after age of 14 year of age?

AC: Can try is documented progression, esp. if already quite high.

SR: Yes, if you have a pattern of progression.

SWL: yes, if still progressing

33. Most of the children are not satisfied due to blurring; what is the alternate method?

PW: May consider lower dose, orthokeratology or CL.

SR: If you are referring to Atropine then skip the pharmacologic route and go to one of the Cl options plus outdoor time.

IGM: Or DIMS spectacles, if available

SWL: ultra-low dose atropine should not blur the near vision

34. Do any of you dilute the 1% atropine with artificial tears?

AC: no. luckily don't need to resort to that as may be hard to provide consistent dose.

SR: no

SWL: NO

35. When reducing Atropine 0.01, is it better to lower the dose or using alternate days?

AC: since there is often no lower dose, often just reduce frequency.

SR: Alternate days.

SWL: atropine 0.01 is already the lowest dose

36. How frequently should Atropine be compounded?

AC: depends on your compounding company.

SR: Depends on its stability. Each compounding pharmacy should be doing quality control checks.

37. When do you think we will see a contact lens that releases atropine? A combination of contact lens myopia control with atropine myopia control?

AC: you can combine it now. A combined product may be possible in the future.

SR: I hope soon but for now both treatments can be used simultaneously!

38. Would any of the panel recommend use of atropine in adults with new onset myopia showing progression?

AC: no evidence

SR: I am not sure this is the same disease. Would need to ensure there are no other ocular diseases occurring.

PS: Adult wearers are likely to be in situations where they are more likely to observe and more affected by visual compromise (for example, driving, outdoors, in working situations). Additionally, data indicates that age is related to progression and therefore an adult onset myope may show lower progression than in children. Consideration of these factors would be important in choosing the appropriate strategy for an adult myope.

IGM: if in older adults developing cataract, it is probably not going to be effective

SWL: different disease, atropine wont work and will probably blur the near vision too much for an adult

39. Audrey, do you start atropine right away? for example a 5-year-old with a minus 1.5 or do we wait for progression first?

AC: Depends on what parents decide on after discussion. You could wait 6m and see (I often suggest this in young children with low myopia), but if parents are worried (they have high myopia themselves, or there is an older sibling already on atropine) you could start.

SR: I need documented progression to offer treatment. There are NO treatments without side effects. This can be a reading from another office and then mine to show progression.

40. The discussion has centered on myopia progression. But what are the data for reducing the risk of myopic complications - if the studies show that atropine does not retard the axial length changes?

AC: atropine does reduce AL – just need to find the right dose for each child. Since we have not followed these children into their 40s and 50s, it is hard to be certain, but it is inferred that keeping myopia low will help reduce risk.

IGM: My reading of the literature is that atropine does slow axial elongation. Whether less high myopia will lead to less pathological myopia is not clear, but it seems likely.

SR: Great point! We need another decade or two to show that. With the rates rising the way they are projected not sure if we have time from a public health standpoint to not try these treatments.

SWL: atropine does reduce axial length elongation (in tandem with reducing spherical equivalent)

41. What about prophylactic use in kids of parents with high myopia?

AC: work in progress.

SR: possibly with the right education of the family and some baseline readings separated in time.

IGM: myopic control contact lenses and particularly spectacles might be a better bet.

SWL: I have had a few cases where parents requested for atropine in premyopes. These are families where the parents have pathological myopia and the older siblings have done well with atropine to retard myopia progression

42. Anybody tried combining low dose atropine with PAL? Do you get better control of myopia?

AC: There is no RCT so no evidence.

SR: 'Anybody tried combining low dose atropine with PAL' yes in a few pts. 'Do you get better control of myopia?' Not in my experience

SWL: no evidence

43. Does myopia start after 36 yrs. due to long screen times?

AC: usually not.

PW: There is study shows adult acquired myopia in microsopists. Therefore, it might occur.

SR: It is more likely that mild-moderate myopia becomes symptomatic rather than started at 36.

44. Has anyone ever used diluted Atropine for Down's syndrome patients?

AC: can consider if there is documented progression.

SR: no

SWL : no

45. I am 35yrs old with RP and high on myopia at-12, can Atropine help me?

AC: usually not.

SR: unfortunately, there is no scientific evidence to show that would be helpful for you.

SWL: No

46. Is there evidence that 0.025 is better than 0.01 or 0.05?

AC: 0.025% may be better than 0.01% if respond to 0.01% is suboptimal. It may be better than 0.05% in terms of having less side effects.

SR: The LAMP study has had very interesting findings but the follow up is still ongoing so the dataset is limited in timepoints. Give it a few more years.

IGM: We need more evidence as to what is the best does to use

SWL : the LAMP study's preliminary results suggest that.

47. When do u conclude that atropine 0.01% is not effective? 6 months or 1 year?

AC: In ATOM2, it looked like effect in 2nd year was better than 1st. However, you could go by progression at any time, and increase it if there is still significant increase either at 6m or 1 yr.

SR: I use 6 months although the ATOM studies showed that it might take longer.

SWL : I use a year

48. What is your experience with ortho K and infiltrative events? Is there a significant safety concern?

SR: I have seen corneal ulcers, edema and even scarring in patients who did not have good CL hygiene and/or follow up with their eyecare practitioners.

PS: Overnight wear of any contact lenses carries a risk and there have been some reports of infiltrates with Orthokeratology – good education on lens care and solutions is important to keep the risk of any possible events low.

SWL : although the overall reported prevalence of infective keratitis may not seem that high (7.7 cases per 10,000 patients), the infiltrates are often more central than peripheral and the keratitis tend to be quite severe, resulting in significant vision loss

49. Has anyone ever seen strabismus (ET) associated with the beginning of the atropine treatment?

AC: I usually do a cover test on every visit, and have not noted this.

SR: no, however that would concern me for an underlying phoria/tropia with an accommodative component. I would stop the treatment and re-check the sensorimotor exam after a 1-month washout period.

SWL: I check the alignment before and after atropine and have not noticed any E(T)

50. Does any RCT in myopia control include IOP data? Wouldn't it be interesting to have an understanding of how aqueous drainage works in this progressive myopia patients?

AC: Response does not appear to be influenced by IOP (unpublished data).

PW: 2 studies show atropine eye drop would not increase the IOP of children.

Wu TE, Yang CC, Chen HS. Does atropine use increase intraocular pressure in myopic children? Optom Vis Sci. 2012;89(2):E161-E167.

Lee CY, Sun CC, Lin YF, Lin KK. Effects of topical atropine on intraocular pressure and myopia progression: a prospective comparative study. BMC Ophthalmol. 2016;16:114.

SR: I am sure the glaucoma specialists agree with you.

51. What are the alternatives when the myopia doesn't slow down even when you have increased to high dose atropine? How Long would you monitor with high dose atropine before considering alternatives?

AC: you could try other myopia treatments depends on likely tolerance, availability and affordability. Depends age, progression and likelihood of high myopia.

SR- WRT 'What are the alternatives when the myopia doesn't slow down even when you have increased to high dose atropine? 'add an optical device such as one of the CLs discussed. WRT 'How Long would you monitor with high dose atropine before considering alternatives?' 6 months

IGM: Because of the evidence on high dose atropine and rebound effects, I would suggests looking at other alternatives

SWL: I will monitor for a year

52. One speaker noted that while atropine does slow myopia progression it may NOT slow axial elongation. If that is true then does atropine reduce the risks of myopic degeneration over time ? If not then maybe it is not as useful as we think?

SR: This is a great question. Studies have shown both a more symmetric as well as asymmetric response to Atropine in some subjects. This highlights how much more we need to learn about mechanism of action. We need another decade or two to have scientific evidence that slowing myopic refractive and often AL changes will lower the numbers of pathologic myopia sequelae. Given the current rate of this disease process, it does not make sense to me to wait for the tidal wave to hit us but rather treat with methods that we have access to which in theory should decrease the sequelae.

IGM: I don't think that there is any real doubt that atropine reduces axial elongation, and that this is the basis of the reductions in myopic progression. There are several lines of evidence.

The first comes from animal studies that have consistently shown that atropine does reduce axial elongation, so much so that in many such studies, axial length and axial elongation tends to be measured rather than refraction.

The second comes from the evidence on what changes during human refractive development. From about the age of 2, the cornea stabilises, and plays little role in refractive development. The two factors that continue to change are axial length and lens power. Axial elongation leads to myopic shifts in refraction, but the impact of these changes is minimised by reductions in lens power, which lead to hyperopic shifts in refraction. It is unfortunate that we cannot directly measure lens power, although it can be estimated if appropriate measurements of ocular biometry and refraction are made. There is currently no evidence that atropine affects lens power, which leaves us logically with the hypothesis that atropine reduces axial elongation and hence myopic shifts in refraction.

Before moving to consider the two sets of human data, those from the ATOM studies, and from Yam et al., it is worth making a few points about appropriate analysis. What we should really be looking for are correlations between changes in axial length and changes in refraction, and in particular for correlations in percentage reductions in the two measures. In view of some of the arguments used in the literature, it is also worth noting that absolute measures of axial length show considerable inter-individual variability. Just looking at emmetropes, there are clear gender differences, with males having longer axial lengths. And within each gender, there are differences in axial length related to body stature, which add further variability. As a result, without careful analysis, this variability in axial length, when there is little variability in refraction, may make it harder to see statistically significant differences in axial length, even when there are statistically significant differences in refraction.

I will turn now to the study by Yam et al. which deserves more attention than it generally receives. Importantly, it suggests that 0.05% atropine may give a better balance between efficacy and side-effects in a Chinese population. This is consistent with a number of anecdotal reports of only slight effects of 0.01% atropine, which are leading to active exploration of slightly higher doses. Watch this space.

It is important to note "in a Chinese population," because we know that cycloplegia is harder to achieve in patients with dark irises. Thus, I would have a starting expectation that lower doses might be more effective in populations of European ancestry, and be less effective in populations of African, South Asian (particularly those from southern India), Melanesian and Polynesian ancestry, and indigenous Australians.

Finally, to Yam et al., I have extracted the relevant data from the paper, which is shown below.

	3) 0.0	3) 0.05%		2) 0.025%		1) 0.01%		0) Placebo	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Spherical equivalent (D)									
Change at 4 mos	-0.03	0.40	-0.20	0.32	-0.26	0.35	-0.34	0.31	
Change at 8 mos	-0.14	0.51	-0.37	0.38	-0.43	0.56	-0.61	0.52	
Change at 12 mos	-0.27	0.61	-0.46	0.45	-0.59	0.61	-0.81	0.53	
Axial length (mm)									
Change at 4 mos	0.06	0.20	0.12	0.11	0.13	0.16	0.16	0.13	
Change at 8 mos	0.15	0.28	0.22	0.25	0.26	0.20	0.30	0.17	
Change at 12 mos	0.20	0.25	0.29	0.20	0.36	0.29	0.41	0.22	

From this data, it is clear that greater reductions in both axial length and SE are seen with 0.05% than with 0.01%. Somewhat greater side effects are also observed, so the question of the best balance needs further work. But in general, where the aim is prevention of high myopia, I would tend to err in favour of greater efficacy, with minimisation of side-effects.

The percentage reduction in changes in SE caused by 0.05% atropine is 66.6%. That in axial elongation is 51.2%. Plotting all the 12 month data shows a pretty convincing parallel between percentage reduction in changes in SE and AL, with difference doses of atropine. The percentage reduction of changes in SE is always higher than those in AL, which is hard to explain, but the picture is still very clear dose-dependent effects of atropine on both axial elongation and myopic shifts in SE..



Because of an absence of a control group in the ATOM 2 study, we cannot perform the same analysis of percentage reductions relative to a control, but we can plot the absolute changes in SE and AL. I have chosen to plot the changes at 24 months, because these are not complicated by rebound effects, which I believe should bias clinical practice towards ceasing drug treatment at older ages, when progression, and potentially rebound, is lower.



Essentially, the same picture is seen. If it were possible to refer these changes to a control group, then the percentage reduction in change would be higher at higher doses, and again there is reasonable parallel between changes in AL and SE. Not perfect, but pretty good, given the complexity of the protocols.

I do not know why the idea that atropine does not produce reductions in axial length has become so wide-spread, given the available evidence. I think the available evidence on low dose atropine (0.01% or 0.05%) tells us that, if used systematically, atropine for myopia control can reduce progression by at least 50% and perhaps as much as 60-70%, and should prevent myopes with onset of myopia in the preschool or early school years from progressing to high myopia, thus virtually eliminating the major load of environmentally induced high myopia that is so obvious in East and Southeast Asia. Whether this will result in less pathological myopia is not certain, but highly likely from the way in which pathology varies with myopic refractive error, and we simply cannot afford to delay action until the evidence on links to pathology is in.

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