Consensus on progressive myopia management

Myopia Study Group of the Argentine Society of Paediatric Ophthalmology
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Abstract

Purpose: To reach a consensus on the management of progressive school age myopia.
Materials and methods: The Myopia Study Group of the Argentine Society of Pediatric Ophthalmology evaluated the available scientific evidence in August and September 2021 to develop a questionnaire on the diagnosis, follow-up, prevention and treatment of myopia in the ages of progression. In October 2021, the questions were sent electronically to 40 experts in Argentina and the responses were subsequently analyzed, in masked form, considering consensus for each question when 80% of respondents agreed.
Results: Consensus was obtained on the inclusion in the clinical records data of behavioral and environmental history related to near vision tasks and outdoor exposure, controlling the former and encouraging the latter. Consensus was also obtained on the importance of complementary examinations in cases of early onset, high myopia at diagnosis, accelerated progression, signs of fundus atrophy and high astigmatism. There was also consensus on a minimum follow-up of 2 visits per year and the use of pharmacological treatment with atropine 0.01% (or 0.05% for refractory cases or high myopia), which should be discontinued gradually and not before 18 years of age.

Conclusion: As a result of the scientific evidence analyzed by a committee of experts, a consensus was reached on the management of myopia at the age of progression in Argentina, emphasizing that there are multiple tools currently available to establish the diagnosis, optimize follow-up, carry out treatment and take preventive measures, in addition to prescribing glasses.
Keywords: myopia; prevention; treatment; atropine; environment, outdoor exposure.

Introduction

This introduction will cover two topics. Firstly, historical aspects of the management of myopia in childhood will be described. Subsequently the relevance of the topic and the reason why this work has been carried out will be justified, based on the new technological advances that are already available and on the scientific evidence that justifies the need for a therapeutic change; this is mainly aimed to reducing the progression of myopia in childhood and incorporates the environmental and behavioural aspects that may even act as measures to prevent its development.

Historical overview

In the last century, despite the clear observation that there was a progression of myopia in children and young people, Ophthalmology practice could not prove a theory about the genesis of this phenomenon, and could not find a solution to the problem[1]. In many cases, treatments were even tried which, in addition to showing no results, were unfounded. For example, some ophthalmologists at that time tried to stop the development of high myopia by performing subconjunctival placenta transplants on children who showed a rapid progression of myopia[2]. In general the behaviour was always expectant with parents told that the prescribed spectacle was only for this year and that the following year there was an expectation that it would have to be changed to a higher prescription spectacle[1].

The discovery of an experimental model of myopia in monkeys around 1975, and the subsequent extension of this model to chickens and other experimental animals, led to a significant understanding of the pathophysiology of myopia and laid the foundations for further research into the control of progression of myopia[3]. Since then, over the course of the last 45 years, atropine drops (and some ocular hypotensors) have been found to slow the progression of myopia in experimental animals, and in the last decades of the 20th century[4], this research was transferred to the human population in various ways[5-6]. Results of new clinical studies involving accommodative and vergence disorders in the genesis of myopia also began to emerge[7]. In the meantime, the prevalence of myopia was increasing with the new demands of the turn of the century in terms of near vision needs with the beginning of the "digital age"[8].

In 1993, defocus during reading was postulated to be the link between near work and myopia[9], and multifocals and special peripheral defocus lenses began to be tested and have been shown to be effective in recent randomised controlled trials[5, 10-12]. Thus, both contact lenses and peripheral defocus lenses are available now to slow the progression of myopia[10].

In the first 15 years of this century, the ATOM 1 study (Atropine Treatment of Myopia) in 2005, and ATOM 2 in 2015 showed that super diluted atropine also halted the progression of myopia in children[13-14]. Since 2012 this dilution has been introduced into daily practice as a treatment for the progression of myopia in children[15]. In parallel, during the last 15 years and from 2005 onwards, it was possible to demonstrate more rigorously that the lack of outdoor exposure on one hand, and excessive reading or other close-up work on the other, were the main environmental determinants of the exponential growth of myopic prevalence and progression, which can now be slowed down by methodological changes in the educational system and behavioural changes in children with regard to outdoor exposure and near-vision tasks at home[6, 10, 16]. It was also observed that screens with a white background and black letters produced thinning of the cho-

roid (the first sign that the eye is going to grow faster), and so the so-called "dark mode" or a black background with white letters has emerged as a possible treatment, although a randomised study has not yet been carried out on this subject[17-18].

Scientific information about myopia research is reaching the ophthalmic community in a partial and limited manner[19-20]. In many countries it is observed that some professionals choose to initiate treatments for the control of myopic progression while others do not, perhaps due to a lack of knowledge of the new scientifically supported therapeutic options[21]. Precisely because of the above, the present group of authors has asked themselves this question: Can we continue leaving our myopic children subject to the natural progression of their disease?

It has been shown that the onset of myopia before the age of 9 years is a marker of further progression and that these cases are those that can reach amounts of myopia that imply a risk of definitive visual loss in adulthood[22-23]. This is why, according to the International Myopia Institute (IMI), it has been established that eye care practitioners have the obligation to offer preventive treatment, which is also a right that cannot be denied to the patient[8, 24]. This Institute clearly states in its publications the roles of the professionals authorised to apply it and those of the industry that provides the supplies, between which there must be no conflict of interest. Although to date the only therapeutic resource authorised by different regulatory bodies such as the US Food and Drug Administration (FDA) is peripheral defocusing contact lenses, the rest of the treatments are backed by guidelines and consensus of scientific societies, which are justified by weighing the expected risks and benefits when compared to the traditional approach (prescribing lenses and waiting for the natural progression).

Consequently, it is understandable that, nowadays, consultation for the prescription of myopia lenses has become more complex as there is a need to discuss with the myopic patient's family what combination of treatments for progression control might be useful in each particular case. This combines a series of new recommendations about lifestyle, outdoor exposure, time-effective study guidelines to reduce the number of hours of near vision, the possibility of using a pharmacological treatment for myopia (atropine drops in a specific dilution), and perhaps whether the use of glasses or peripheral defocusing contact lenses would be necessary[11-12].

While these practices are slowly spreading in the ophthalmological community and the whole society, researchers on the subject have a dual role to play[19-20]. In addition to training ophthalmologists, and paediatricians who are responsible for the health of these children, researchers in the field have the dual role of informing the educational community about the environmental mechanisms that can be put in place. In this way, a consensus of specialists in this field becomes necessary in order to define in each particular case the necessary action to be taken. We hope that this consensus will be a healthy guide for ophthalmology in general and for ophthalmopediatrics in particular.

Therefore, the aim of the present work was to develop a consensus that could formulate the scientific evidence and show practical concepts about the set of diagnostic, preventive and therapeutic approaches that a group of experts consider necessary in individuals at risk of suffering or already suffering from axial myopia, with the possibility of progression towards irreversible lesions that may decrease visual function in adulthood.

Methodology

In order to reach a consensus on the management of progressive myopia, the current Myopia Study Group of the Argentine Society of Pediatric Ophthalmology designed a study based on a list of questions elaborated by its members, taking into account the recommendations issued by the World Health Organization[25], the Task Force on Myopia of the American Academy of Ophthalmology[26-27] the International Society of Paediatric Ophthalmology and Strabismus[28], the Consensus of the European Society of Ophthalmology[29], the White Papers of the

International Myopia Institute[5, 8, 10, 24, 30] and by the recently published Indian Consensus[31]. In addition to the above recommendations, the questions were developed to answer concerns that have arisen after clinical practice and analysis of scientific evidence from systematic reviews, meta-analyses and randomised controlled studies.

This Myopia Study Group recommended to a panel of experts the timely reading of the aforementioned consensus and papers during the months of August and September 2021. The questions were aimed to investigate aspects related to establishing the diagnosis of myopia, how to follow it up and how to treat it, always with school-age myopia in mind. A total of 50 questions were generated and submitted via an online electronic form (Google Forms) in October 2021. Forty-seven experts were proposed by the members, and invited to participate, including not only ophthalmopediatricians but also experienced general ophthalmologists from different areas, such as Refraction & Contact Lenses, Refractive Surgery, Glaucoma and Retinal Disease. In total, 40 ophthalmologists agreed to participate in the study and answered the questions. Ophthalmologists practising in different provinces of Argentina with different regional realities worked on this project. The invited experts worked during a period of 15 days on the answers while being masked as to who their peers were in answering the questions.

The questions could be answered optionally in all cases. Therefore, for the analysis of the answers, the number of experts who answered was taken into account and the percentages of answers were calculated over the total number of experts involved. The number of experts who answered each question is also reported. The questions were developed between March and August 2021 by members of the Myopia Study Group and reviewed by an independent ophthalmologist involved in basic and clinical research and previous consensus (Rodrigo Torres).

For the assessment of consensus, it was established that if 80% or more of the answers were in answered in one direction, there was agreement. In the event of a lack of consensus on a question, the percentages of responses obtained were then shown and the question was left open, with a text explaining the reasons for the controversy, which could perhaps be resolved over time with further research in that particular area. The methodology used to reach this consensus has been designed in such a way that after a few years, in the light of new reports and clinical experiences, a new consensus or an update of the present one can be reached.

Results

The following is a presentation of the issues addressed in the different questions and the resulting information. Due to the modality of the present consensus, which used an extensive questionnaire as a tool, the analysis and discussion of the answers obtained will be carried out in this "Results" section. The questions were grouped into 5 themes, to make them easier to read, as follows: A) Diagnosis and follow-up, B) Pharmacological treatment, C) Environmental and behavioural measures, D) Special optical devices (lenses with defocusing, orthokeratology) and E) Communication. At the end of the last point, a synopsis has been drawn up presenting the recommendations generated by this Argentine Myopia Study Group.

A. Diagnosis and monitoring

1. Refraction

When asked about the choice of using cyclopentolate or tropicamide for refraction under cycloplegia in myopic patients, 67.5% opted to use the former. Actually, it is interesting that there was no definition in this case, as there are a couple of randomised trials that have shown equal effectiveness in producing cycloplegia in myopes (not so in hyperopes where cyclopentolate could be more effective)[32-33]. Thus, although there was a tendency to use cyclopentolate, there was no consensus on this question.

2. Accommodation

Would you measure the amplitude of accommodation and the accommodation/convergence

ratio in myopic patients to be treated with atropine? Here 59% chose to measure it. Again, there is no consensus, possibly because accommodation disturbances with super diluted atropine are very rare and disappear with use. On the other hand, accommodation-convergence disturbances are not useful for predicting the onset of myopia either, as they occur after the onset of myopia and not before it[7].

3. Pupillometry

Would you measure pupillometry in these patients?

Here 57.9% answered that they would measure the pupil. Again, the lack of consensus is possibly associated with the fact that super diluted atropine drops hardly alter pupillary diameter and visual acuity.34

4. Medical history and lifestyle history: outdoor exposure and visual activity

Here 95% of the experts said they would include data on outdoor exposure and near work in their patients' medical records. Indeed, the consensus reached reflects the strong evidence for these risk factors in myopia and its progression[10, 30].

5. Complementaryexaminations: general aspects

Do you consider it is necessary to request complementary examinations in the initial visit of a myopic patient under 10 years of age?

It is interesting to note that only 60.5% answered "yes", and no consensus was reached, possibly because in the initial consultation there are several issues to be dealt with and generally, as can be seen from the following questions, it is possible that the specialists would ask for examinations in subsequent visits according to the evolution of the patient.

6. Complementary studies: OCT

Do you consider it is necessary in the initial diagnosis and/or follow-up of a child or young person with myopia to carry out a macular OCT study?

In response to this question, which had three options, 66.7% answered that they would only ask for it in the case of a school-age patient with myopia of more than 6 dioptres. Only 7.7% considered it necessary to order macular OCT in all cases.

7. Complementary studies: topography

Here 80% of the experts thought that it is only necessary to order a topography (or more complex examination such as a Pentacam or Galilei) in a myopic patient when the keratometry is suspicious, and 17.5% thought it would be advisable to order it in all cases. Interestingly, the consensus favours a moderate approach as the burden of many exams makes treatment more complex, possibly decreasing adherence and increasing costs for the whole healthcare system.

8. Complementary studies: pachymetry

Do you think it is necessary to ask for pachymetry in simple myopia in children with no other alteration than refraction?

Answers were close to a consensus, as 77.5% of the experts answered that they would not ask for pachymetry in these cases.

9. Complementary studies: optical biometry

Too questions were asked about optical biometry in these cases.

Do you consider it is necessary to ask for optical biometry (Lenstar, IOLMaster or Aladdin) at the initial visit of a myope?

Answered "yes" by 45% of respondents (no consensus).

Do you consider it is necessary to perform optical biometry in the follow-up of your myopic patients to see how the eye is growing?

Then 80% of the respondents answered "yes". This makes it clear that the expert panel believes that optical biometry is useful in monitoring progression. This topic is interesting and controversial in the sense that the gold standard for progression is refraction under cycloplegia, which should remain stable and unchanged in cases of successful treatment. But it is noteworthy that the biometry changes in all cases, a little more (0.20 mm) per year in myopes that progress and a little less (0.10 mm per year) in myopes that do not progress. This is why this topic was the subject of a review paper to which we refer to[35].

10. Astigmatism: complementary studies and changes in treatment

What amount of astigmatism would you consider to ask for complementary diagnostic tests or changes in the treatment?

Here 77.5% would suggest complementary diagnostics in case of astigmatism that change with follow-up, probably because this leads to think about corneal changes that are not common in school-age myopia. Only 22.5% of the experts stated that they would ask for complementary examinations in cases of astigmatism greater than two dioptres or even those same experts answered that they would do so for oblique astigmatism greater than two dioptres, which could also indicate corneal alterations such as keratoconus.

11. Keratometry

In which cases do you think it is necessary to have keratometry data?

Here again there was almost a consensus with 70% of respondents acknowledging that they would perform keratometry in all cases, and not only when there was high astigmatism.

12. Myopia: age of onset

Here 92.5% of the experts considered it is necessary to include in a special category the group of children with myopia beginning before the age of 6 years old- sometimes with a family history of high myopia. In this respect all the evidence shows that age of onset is a marker for the risk of high myopia and that this group deserves more timely interventions on habits and treatment options[10, 22].

13. Physiological farsightedness

Do you consider a special category for those children under 8 years of age who are not physiologically farsighted and who "de-hypermetropise" rapidly with follow-up under cycloplegia?

Here again there was consensus with 87.2% answering "yes". These children under 8 years of age usually have good visual acuity at the periodic check-up. If the technique of fogging with +1.00 sphere is used systematically after dynamic retinoscopy to assess accommodation, it is very easy to make a presumptive diagnosis of a child who is not physiologically hyperopic; when +1.00 D spheres are placed bilaterally looking at distance charts, the emmetropic child notices that his vision becomes blurred, unlike a normal hyperopic child who usually tolerates fogging with +1.00 D perfectly well. Cycloplegia then confirms the assumption.

14. Frequency of controls when there is a presumptive diagnosis of high risk of developing myopia

With regard to check-ups following a presumed diagnosis of high risk of developing myopia ("pre-myopic": child who does not have the expected age-appropriate hyperopic reserve...), how often would you suggest check-ups?

Here 82.1% suggested checking these children twice a year. The consensus seems to us to be adequate, since times shorter than 6 months do not usually show changes, and a longer times could lose the opportunity of a treatment with super diluted atropine drops. It is known that refractive change is faster at the beginning of myopia[36-37].

15. Frequency of monitoring in children treated with super diluted atropine

Two questions were asked about *How often do you suggest monitoring of children treated with super diluted atropine after the first three months of tolerance testing.*

One concerned children under twelve years of age and the other concerned children over twelve years of age. The options were: once, twice or three times a year in both cases. It is interesting to note that almost none of the experts suggested checking once a year as was the custom for myopic children. In both cases more than 90% suggested checking between 2 and 4 times a year. For minors, 61.5% suggested twice a year and 39.5% four times a year. For those over 12 years old, 76.9% suggested twice a year and 12.8% four times a year. These significant differences in criteria probably have to do with the known fact that myopia progresses more slowly as children get older[38], and that there is also no "burst" of myopia with puberty, a concept that is falling into disuse[38]. In addition, it is known that children who start late are the least at risk, and so it is possible to relax screening as they get older.

16. Myopia and genetic studies

In case of a myopic patient under 10 years of age with myopia greater than six dioptres in both eyes (in our environment with a low prevalence of high myopia), would you suggest a genetic examination to rule out syndromic myopia? A patient with these characteristics obliges the ophthalmologist, more than others, to carry out an exhaustive ophthalmological examination to confirm that the myopia is axial and not corneal or crystalline in nature. The findings of this examination could justify a request for inter-consultations, among others with genetics, a behaviour that 37.5% of the experts would adopt.

17. Myopia progression

Do you consider it is necessary in all cases to wait 6 months to a year without treatment to see if there is progression, or is the evolution of previous prescriptions from other professionals and the visual history referred to by the patient enough to evaluate if there is progression and make treatment decisions?

In response to this question, 60.5% thought that the previous history was sufficient and 39.5% thought that it was always necessary to wait. The lack of consensus may be related to the fact that it is difficult to know for sure whether the refractive examinations prior to the current consultation of a progressing myope were conducted with the correct cycloplegia. Before starting a long treatment of several years, the position of "always wait to evaluate if there is progression" seems to be correct, as it would be undesirable to treat a child who is not progressing. However, given the lack of consensus, the most advisable thing to do would be to talk to each family consulting a patient with an apparent progression followed in another clinic, and if needed so, to consult the specialist who has followed the patient up to that point in order to reach a particular agreement in each case.

This lack of consensus could possibly also be related to the different disease awareness of parents towards their children's myopia. Some keep neatly all prescriptions from different professionals and are attentive to the progression of their children's myopia, while others are inattentive to this problem. In the latter cases, if the parent is emmetropic, a test can be done with them and they can be fitted with a frame for distance vision with a +4.00 (for example) in both eyes, telling them "this is how your child will see without glasses if their myopia progresses". For parents with strong early onset myopia, it is completely different as they are usually well aware of the problem their myopia poses and are the first to seek treatment for their child's progression.

18. Myopia progression

Up to what age do you think myopia can progress?

Here only 25 of the 40 experts defined a probable age which turned out to be on average 25 years for the age of stabilisation. This is very interesting as the published papers on the matter suggest ages around 15-18 years and as this is an under-explored area[39] as the arrest of progression is very gradual and there is no defined cut-off point that allows us to say that at such a moment it has stopped. We believe that the average age of myopia cessation given by this panel of experts is very appropriate and conservative, especially in the case of young people going to university, in whom it is common for myopia to stop only after completing their studies.

19. Complementary studies: colour retinography

Do you think it is necessary to order colour retinal imaging to follow the changes around the papilla in children who progress to high myopia?

Observation and documentation of the fundus with colour imaging would be useful if there were a biomarker at the time of onset that could predict progression. In this line, Jonas *et al*. have shown that the presence of diffuse peri-papillary atrophy in childhood could be an indicator of progression to more severe changes in adulthood[10]. Until this is confirmed, colour retinal imaging is useful in severe cases to communicate prognosis and help make therapeutic decisions. Still, only 60% of the experts answered that they would ask for it in cases of high myopia, thus not reaching an agreement on what would be most appropriate.

B. Therapeutic attitude and use of atropine

20. Myopia: therapeutic approach

When faced with a first-time patient, under 3 years of age, with myopia of more than -8.00 D in both eyes, symmetrical, and without corneal, crystalline or retinal pathology, do you give him/her glasses and study him/her to see if he/she progresses before giving any other treatment?

Again, there was consensus on this question, with 85% answering "yes". To our knowledge, only one paper[40], unique in its kind, shows a follow-up of cases of such patients with congenital myopia showing that a large proportion do not progress.

21. Bilateral and symmetrical simple myopic astigmatism: therapeutic attitude

Faced with a school-age patient who consults for asthenopia with a simple myopic astigmatism, bilateral, symmetrical, with the rule, of up to 3-4 dioptres, with keratometrys that do not reach 47 D, with no family history of myopia, what would the medical approach be?

Following in line with the previous section, here there was a great consensus as 89.7% answered that they "believe that they are dealing with a child with simple myopic astigmatism who will live with this without changes until adulthood and then prescribe glasses and control annually evaluating refraction and risk factors"[22].

22. Atropine: timing of indication

Would you consider not waiting to treat with diluted atropine, if you are dealing with a patient with early onset, with a family history of high myopia and with an already moderate spherical equivalent value at baseline?

Here 33.3% answered that "it is necessary to wait" and 66.7% answered that they would "start treatment". Here the lack of consensus takes us back to question 17 with the difference that in this case the child is already starting with high values and has no previous history with other professionals. The fact that consensus has not been reached here makes it necessary to discuss the pros and cons with the family in order to reach a particular agreement in each case. However, it should be noted that there is a modern tendency to treat even the pre-myopic, so a child with these characteristics may deserve to be treated from the onset.

23. Intraocular pressure and treatment with atropine

Do you think it is necessary to measure intraocular pressure in patients undergoing treatment?

Here 71.8% answered "yes" to this question. We believe that this seems to be the most appropriate option, since in the case of children with borderline ocular pressure associated with myopia, hypotensive drops could be added to the treatment[41].

Theoretically, the lower the eye pressure, the more difficult it is for the eye to elongate, as happens in congenital glaucoma. Furthermore, animal experiments suggest that some ocular hypotensors may be acting at the level of the message from the retina to the sclera that produces elongation, and not necessarily by lowering the intraocular pressure[42].

24. Atropine: dilution to be used

With the most accepted dilution of atropine being 0.01%, would you in any case change the dilution to 0.05%? Here 67.5% of the 40 experts answered the option that they would switch to 0.05% if there is progression with 0.01%. Only 5% of the respondents would use it for the treatment of children under 12 years of age, as suggested by one of the other options. We believe that nearly a consensus was reached in this question as case reports at local congresses (before the pandemic) showed very good effectiveness of atropine at 0.01% in our setting where children spent a lot of time outdoors[43-44]. We hope to ask this question again in a new consensus in due course, hoping for new guidelines in this regard, and always bearing in mind that the Latin and European populations spend more time outdoors than the Asian population (multicentre study in Spain)[45].

25. Atropine: duration of treatment

Having chosen a particular dilution of atropine, do you consider it is necessary to stop at two years to see if it has stopped?

Here 62.2% of respondents felt that super diluted atropine should not be stopped after two years to see if progression had stopped. Here the lack of consensus has to do with the fact that the ATOM study, the first randomised study of atropine, after two years of treatment performed a six-month discontinuation test and found that progression resumed more markedly in cases treated with 1% atropine dilution[46]. Many ophthalmologists (the other 37.8%) may still want to know if myopia has stopped in their patients, perhaps just to avoid treating them with drops for many years. Here the interests and autonomy of the patients have to be considered, giving the correct information of the parents about the pros and cons of both positions. Surely in time there will be other, more moderate positions. There are several of them. For example, tapering is highly advisable, as tapering to five days and then to three days per week after a couple of years of stability has shown good effectiveness with sufficient adherence as seen in oral presentations in our country. Other alternatives include tapering associated with reinforcing outdoor exposure. And even tapering associated with the use of peripheral plus add spectacles or contact lenses could be an option when they are available in our environment. In this respect, the following question becomes important.

26. Atropine: Long-term treatment

Do you think it is better to talk about long treatments or to propose annual renewable contracts? (there were three options in this respect).

Approximately half of the respondents proposed to talk about long treatments, a quarter of the respondents proposed to talk about annual renewable treatments and finally a quarter of the experts thought that one or the other attitude was optional depending on the anxiety of the family group. This is because when faced with a proposal for long-term treatment, parents who are overwhelmed and overburdened by the task of raising their children are often not inclined to think in the long term. Thus, we find the lack of consensus on this response interesting and it leads us to think that there is still a lot of research to be done in the area of adherence to these treatments.

27. Atropine: age range for indication

Although the randomised studies enrolled children aged 6-12 years, do you think atropine can be used in children younger than that age with progressive myopia?

In this dilemma there was no consensus as only 56.4% considered that super diluted atropine could be used in children under 6 years of age. The recent LAMP (Low-concentration Atropine for Myopia Progression) study was done in children aged 4 to 12 years, so this would show that a wider age range of ages can be included[47-48]. It is indeed difficult in clinical practice not to intervene with a patient aged 4 or 5 years who has a family history of high myopia and begins to show progression at such an early age. Given the lack of consensus, we believe that in each individual case the family can be offered the alternative of starting treatment, which could last many years, or waiting for spontaneous progression until the second visit. In this way, by discussing the pros and cons, it can be said that there is no definite scientific position, and an informed agreement with the family should be sought.

28. Atropine: diluted product aspects

How long do you estimate that the dilution of atropine in a generic prescription eye drops remains stable and effective in the bottle?

Here 56.4% of respondents estimated that it could last one month, 15.4% two months and another 15.4% up to three months. In summary, it is apparent that the 0.01% concentration of atropine is not stable despite the fact that there is no published evidence of its long-term stability. From the results of this consensus it does not seem advisable to use it for more than three months, and it may be safer to renew the bottle once a month.

29. Atropine in university students

Do you think it is necessary or important to sometimes initiate dilute atropine treatment in university students with myopia starting after the age of 18 years?

Here only 29 of the experts answered the question, being tied for yes or no (37% and 35% respectively). This is an unexplored area in Asia

as most of the incidence appears there before 18 years of age. In our environment with low prevalence or incidence[49-51] a proportion of myopes start with their myopia after 18 years of age at university or tertiary studies with high demand in near vision[52]. These young people develop myopia of 4-5 dioptres, so it would be interesting to carry out prospective scientific studies with diluted atropine in this age group and in this case it would be difficult to develop those studies in Asia where 95% of young people are already myopic at 18 years of age[48-49].

30. Atropine: criteria for treatment discontinuation

In treated patients who should be stopped on atropine, what schedule and criteria do you mostly use for discontinuing it?

Here 36 experts gave responses with 28 (70%) answering "Tapering, moving to 5 times per week for a few months and then to 3 times per week" and 11 (25%) saying "I am guided by risk factors and age to assess possible rebound on stopping". Interestingly, only two specialists marked the option "I would stop using atropine and switch to peripheral defocus lenses" and it is possible that in a few years, when these special lenses become available, if they are cost-effective, this may be a more popular choice among specialists, as spectacle lenses lacks the potential undesirable effects of a daily drop for many years.

31. Procurement of diluted atropine (generic drug preparation)

Do you have problems getting your patients a supply of diluted atropine eye drops from pharmacies in your area?

Here 72.5% said that they had no problem in getting the generic prescription of the eye drop. At the moment we do not have any commercial preparation of diluted atropine eye drops. The preparation of atropine 0.01% from a commercial 1% eye drop is an alternative to the preparation of the formula of this eye drop from the active ingredient and the necessary excipients. Diluted atropine has been shown to be stable for up to 30 days when the preparations are kept refrigerated (3-8°C) and meet sterility requirements[53]. Although when diluting the commercial eye drops, the concentration of the preservatives may be below the effective concentration, storage of the eye drops in the refrigerator may be sufficient to maintain their sterility for 30 days.

32. Diluted atropine: method of administration

In order to improve adherence, do you think it is advisable to suggest placing the diluted atropine drop at night when brushing the teeth, another habit to prevent disease?

This is a recommended practice to achieve compliance, although each family can make adjustments to achieve the same goal. Here 95% of the 40 respondents approved this recommendation that could improve adherence.

33. Diluted atropine and contraindications

Do you know of any contraindications to the use of diluted atropine drops in children? (note those known or leave blank).

Allergy to atropine, allergic dermatitis, Down's syndrome, heart disease, asthma, general ocular and systemic diseases, syndromic myopia, treatment with sulphonamides, growth hormone or topiramate, collagen diseases and congenital glaucoma were noted. And it was also noted that there was a need to have the agreement of the paediatrician if he/she is influential, communicating with him/her about this treatment.

34. Astigmatism: atropine treatment

Is there a limit to the amount of astigmatism for including children in atropine treatment in the ophthalmopediatric practice?

There was no consensus on this question as 48.6% answered that there is a limit and 32.4% that there is no limit. This lack of consensus may have to do with several factors. One of them is that some specialists are guided by the fact that the clinical trials of the various treatments do not include children with high astigmatism, but they do not take into account that the experience of these trials does not rule out that they can be effective in these cases. On the other hand, high astigmatisms could evolve into keratoconus, the progression of myopia then being caused by cor-

neal change. It is true that some patients with keratoconus also have axial myopia and that many highly myopic patients have astigmatism of more than two dioptres without having keratoconus. Because of the complexity and variety of these problems, it is understandable that there is still no consensus and more research is needed.

35. Sun filter or photochromatic lenses in atropine patients

Do you suggest the use of photochromatic lenses or sun filters?

Here opinions were divided into three main groups: 41.0% said that they do not suggest them, 30.8% that they do suggest them and 23.1% said that they suggest them in some cases. It is noteworthy here that the visual symptom most commonly associated with atropine treatment is photophobia, affecting 75% of patients, which significantly improves after wearing photochromatic glasses, as these general visual symptoms improve in 63% of patients[34]. Furthermore, there was no significant difference in monocular contrast sensitivity between patients wearing glasses with achromatic trial lenses and photochromatic glasses[54]. Many studies in this regard are done on Asian population with darker irises and exposed to much less sunlight intensity, which would indicate, perhaps, that in our latitudes they are more necessary. Perhaps they are also necessary for dilutions of 0.05%, for example.

C. Environment and Behaviour

36. Environment, behavioural patterns and myopia

With regard to environmental issues, which one(s) do you recommend for clinical practice?

Here 97.5% recommend outdoor exposure and 90.0% recommend limiting near vision work. In this sense, it is understood that the experts reached a broad consensus in this regard, as there is sufficient evidence to recommend both changes in habits if the anamnesis reveals that the myopic or pre-myopic child falls within the parameters of limited outdoor activities and a lot of nearwork with books, tablets and mobile phones. On the other hand, 57.5% recommend attention to nutritional factors and 45.0% suggested at least 8 hours of sleep. In both cases, no consensus was reached because, although research is being carried out on both the possible influence of antioxidants[55] and insulin on ocular growth[56] and on the involvement of circadian rhythms in eye growth[57], the evidence in humans is still inconclusive.

37. Myopia and near vision tasks

What would be your methodology to optimise myopia control when performing near vision tasks?

In total 32 (80.0%) experts suggest limiting the use of electronic devices, 33 (82.5%) to avoid using the mobile phone in bed to go to sleep, 14 (35.0%) suggest more spoken studying habits instead of reading so much, 15 (37.5%) suggest using apps to control device use, 15 (37.5%) suggest collaborating in household chores as an extra peer, and finally 33 (82.5%) suggest the 20x20x20 Guide recommended by many (every 20 minutes look for 20 seconds 20 feet away).

38. Environment and outdoor exposure time

How much outdoor time do you recommend? (write down your suggested hours per day).

The average of the 40 experts was 2.5 hours of outdoor time per day. This is probably because a meta-analysis on the subject recommends two hours per day[58]. In our environment before the pandemic, children spent an average of 4 hours outdoors, with large inter-individual variations[43]. Eighty-five per cent of schooling in our country is half-day public schooling of 4 hours (National Institute of Statistics and Census data). It is possible that the family and social structure of fathers, mothers, grandmothers, uncles, aunts and employees in our country allows the favourable implementation of these two and a half hours outdoors every day, taking into account the frequent existence of parks, sports centres and clubs in all the cities of our extended country.

39. Environment and type of exposure

What type of outdoor exposure do you recommend?

Here 80.0% choose the park and 85.0% choose outdoor sports. Also 72.5% suggested going to clubs and 65.0% staying in the patio, balcony or

terrace. It is worth remembering that outdoor sports are not more effective in prevention than the staying in the park. Here 27.5% suggest going to the window side even when indoors. The next question was "What type of indoor ambient lighting would you recommend". Here opinions were split between LED lighting (51.4%) and incandescent lighting (48.6%). Animal studies are still ongoing as to which spectral composition of light stops the progression of experimental myopia[59]. Incandescent lighting has more frequencies in the yellow spectrum and LED lighting has more frequencies in the blue, (as this was shown by the physicist who created the emitting diode), as do screens which also have more blue light, which could be protective for myopia[59]. We therefore understand that there is no consensus as research in this area is still in progress[60-61].

40. Blue light and myopia

There is in animal research on the effects of blue light to stop the progression of myopia and a controlled trial is underway subjecting myopic children to blue violet light to see if it stops the progression with promising results[62]*. Would you recommend putting blue light filters in glasses for myopic children?*

Following on from the previous section, in this case there was a consensus that 85.0% do not recommend the blue filter for myopic children. Blue light has been shown to produce apoptosis in cell cultures of mouse retinal cells, so it was suggested to use blue light filters that do not cut off the light needed to set the biological clock. In the light of the new evidence, perhaps this consensus could be used to suggest that such filters should be used in adults and hyperopic children, given that there seems to be no experience of when to start preventing the oxidation of tissues that occurs with age[63].

41. Interior lighting

Would you indicate more power for interior lighting?

Here 70.3% answered yes, approaching consensus. In that sense there are not many publications that support the evidence. A study in Israel found that kindergarten children in that country have less hyperopic reserve when they grow up in less well-lit environments[62-63]. These children remain in such environments for two years about 8 hours a day for 6 days a week for 11 months of the year. This is the first time that an effect of ambient lighting on refraction has been shown in children who do not yet read. Research in this area is very promising[64-65].

42. Digital reading in dark mode (black background and white letters)

Would you recommend reading on black background and white letters in digital reading formats?

Here only 12.8% refused this recommendation. The rest were divided into 66.7% recommending it and 20.5% recommending it when the patient is well disposed to change. Although the evidence from research is scarce and certainly recent, with less than 4 years of development, the approach on screens is interesting[17-18, 66]. The approach on the screens is so simple that there is here a consensus to apply this recommendation.

43. Early-onset myopia: behavioural recommendations

Would you start recommending behavioural changes (on open air and less near vision) in a preventive or protective way against myopia in these early onset myopic patients? Still on the subject of prevention with simple measures, 100% of the 40 experts answered this question "yes". The unanimity in this case confirms the importance of an approach whose only cost is the time spent by parents and grandparents to take their children outdoors. This may be the only barrier, as was seen to be the case when government campaigns were started in Singapore and parents did not have the time to take their children outdoors because of their working schedules[28, 67-68].

44. Myopia and nutritional aspects

When are the dietary recommendations applicable to these patients?

In this case, opinions were divided, with 48.6% saying that these recommendations were appropriate in all cases and 45.9% considering that the evidence was not sufficient to recommend them[29]. Some 10.8% suggested applying them only in cases

of high myopia. Although the message from the retina to the sclera that modulates eye growth is especially sensitive to defocus and illumination (optical environmental factors) it is possible to argue that systemic factors could influence this message involving insulin, glucagon and nitric oxide[69]. It is true that there is a blood-retinal barrier and that the somatic circadian clock based on melatonin secretion is independent of the retinal biological clock based on other similar hormones[70]. But it has been shown that the eyes of Japanese children on a Westernised diet including dairy products (which have insulin-like growth factor) have longer eyes than Japanese children on a diet of fish, cereals, legumes and vegetables without dairy products[71]. Although the eyes of the latter children were longer, they did not have more myopia, probably because the lens may to some extent compensate for the accelerated growth of the human eye[71]. The only systemic drug approved to halt the progression of myopia with moderate results in this regard is methyl-xanthine available in Denmark[72]. This experience alone suggests that research into nutritional factors may be promising in this area, as nutrition is a very important factor in the development of many different chronic diseases in our culture and childhood is the best time to suggest healthy habits.

45. Blood tests and myopia

Do you suggest blood tests for any or all of these parameters in cases of myopia in children?

Here 82.1% of the experts answered that they do not do blood tests for myopic children. It is possible that the consensus found here is due to several factors among which taking care of the child from unnecessary tests is perhaps the priority. It is true that vitamin D1 dosing (recommended by 23.1% of the experts) is a marker of outdoor exposure in patients who are not supplemented[73]. But perhaps here careful and respectful anamnesis can succeed in assessing outdoor exposure without the need for blood dosing.

46. Nutritional supplements and myopia

Would you give myopic schoolchildren the following supplements? (You can indicate one, several or none).

Here only 14 out of 40 surveyed experts (35.0%) would use supplements, mainly Omega 3 fatty acids (27.5%) and vitamin C (22.5%). Here again as in the previous question the remaining 65.0% do not attach importance to this practice, perhaps because of the lack of evidence to date and so there is no consensus on supplementation for myopic patients.

D. Special medical (optical) devices

47. Spectacles or contact lenses with peripheral defocusing

If available in your environment, would you recommend glasses or contact lenses with peripheral defocusing?

Here 87.5% believe they would recommend this option. The consensus in this regard leads us to believe that since these devices have shown some effectiveness in slowing the progression of myopia in several randomised trials, and that the theory as to why they work in this way has been well established in line with animal experimentation[74-76], it would be interesting to replace the prescription of usual spectacles with a prescription of defocus lenses[4]. In addition, it would be interesting to replace the prescription of single vision lenses in adolescents with the new peripheral defocus spectacles and contact lenses. In that sense, it is necessary to develop such lenses on an industrial level at the lowest possible cost, as this would result in a decrease of the burden of myopia for the population.

48. Spectacles or contact lenses with peripheral defocusing and atropine

Concerning these lenses from the previous question, would you recommend them as the only treatment or in combination with pharmacological treatment?

Here 75% scored with the option "My decision would depend on risk factors, costs and patient's willingness" and 20% on "I would recommend them in combination with pharmacological treatment". Signals for axial growth are possibly hyperopic defocus, black-white contrast and ambient illumination with its light spectrum. If we can compensate for the hyperopic blur, the

progression can be slowed down. In Bifocal & Atropine in Myopia (BAM), the synergy of optical and pharmacological treatments was investigated and it was concluded that the response is better than if they were used separately[77]. Both achieve choroidal thickening, but the response was faster including special lenses than with atropine alone. Applying the special glasses as the only treatment is an option when there are contraindications to atropine, refusal of pharmacological treatment and/or perhaps to quit topical treatment in young children who would have to be treated for many years.

49. Contact lenses with peripheral defocusing and orthokeratology

From what age would you suggest using peripherally defocused contact lenses when they become available in our environment?

There is sufficient evidence that contact lens wear is safe from the age of 10 years. The most frequent complications are seen in adolescence. This question was answered by only 24 experts who on average rightly said that they would recommend them from the age of 10.

Since orthokeratology stops the progression of myopia, do you usually prescribe this therapeutic alternative?

Here 92.3% do not recommend orthokeratology in our country.

E. Communication

50. Myopia and communication: patients and the family unit

Do you provide written or e-mailed information to the family of your myopic patients?

The affirmative answer of 70.0% supports the need to document the information given verbally. To this end, the Argentine Council of Ophthalmology (CAO) has published an "informed consent" written by Dr. Roberto Borrone[78]. And there are a number of information leaflets for family members and adolescent patients that are very appropriate to implement at the first consultation.

Synopsis

Main recommendations on the management of progressive myopia

DIAGNOSIS AND FOLLOW-UP: clinical history, visits, complementary studies, diagnosis	The medical records should contain information on environmental and behavioural aspects, because of their potential association with the development of myopia. Although most ophthalmologists use cyclopentolate to paralyse accommodation, no consensus has been reached and the use of tropicamide + phenylephrine for an adequate refractive diagnosis is accepted in our environment as a valid option. It is always advisable to include the keratometric study in the records. Regarding other complementary studies, more sophisticated studies such as the following: axial length —macular OCT/choroidal thickness—, pupillometry, retinography, topography, pachymetry and accommodation study among others, receive consensus to request them in cases of: early myopic debut —high myopia at diagnosis— accelerated progression-signs of atrophy in the fundus examination and suspicious astigmatism, among other causes. With regard to complementary examination, there is consensus that highly sophisticated examinations should not be requested initially or as a matter of routine. There is consensus to ask for them if necessary throughout the evolution and follow-up. A minimum of two visits per year for myopia at the age of progression and even more frequently for pre-myopia, early-onset myopia or rapidly progressive myopia is the consensus recommendation. Myopia greater than 8 dioptres (D) before the age of 6 will be considered syndromic or congenital and will receive conventional refractive treatment in addition to environmental and behavioural visual guidelines. It is correct to initiate some form of treatment (pharmacological or refractive) in low myopia that starts before the age of 6, paying special attention to accommodative status and setting early guidelines on reading habits and outdoor time.
MANAGEMENT OF MIOPIA WITH ASTIGMATISM	Simple myopic astigmatism should not be considered as myopia with the possibility of progression. Astigmatism with high keratometric values or those that change in a non-physiological way during the evolution of myopia (possible keratoconus) are considered as astigmatism that need to be examined.
ASPECTS OF ENVIRONMENT AND CONDUCT RELATED WITH MYOPIA	The following environmental and behavioural factors are considered high risk for myopia progression: • Excessive and sustained time on near vision tasks • Low outdoor exposure time The following actions are recommended by consensus: • Eradicate digital devices and the habit of reading in bed at night. • Decrease or limit, prolonged work on near vision tasks. • Indicate the practice of the 20x20x20 methodology (20 minutes of reading + 20 seconds of relaxation of accommodation, fixing the eyes at a distance greater than 20 feet, which is equivalent to about 6 meters). • Spending at least 2.5 hours outdoors (in parks, patios, balconies, terraces) • Suggest the use of "dark mode" (dark background and white letters) of digital devices. With regard to ambient lighting, there is no consensus on the benefits of blue light and therefore the use of blue light filters for the glasses of children with myopia is discouraged. Greater intensity of artificial light is recommended in the rooms of the house for reading purposes.

TREATMENT WITH ATROPINE	By consensus, it is advisable not to start treatment with diluted atropine at the first consultation, except in cases where the previous history of myopia with other professionals is verifiable and highly reliable. The recommended dilution of atropine remains 0.01% from the startpoint, although dilutions such as 0.05% could be applied in refractory cases or high myopia. On the estimated time for discontinuation of atropine treatment, consensus was found that it should not be before the age of 18 years, when stabilisation may be starting (around 25 years). There is a consensus that treatment should be discontinued gradually to reduce the rebound effect.
MEDICAL DEVICES: spectacles and contact lenses with peripheral defocusing	The use of refractive treatments with peripheral defocusing, both in contact lenses and spectacles, and/or the use of orthokeratology, when approved by the health authorities in the region and available in the area or city of care, is recommended by consensus.

Final considerations of the consensus on the management of myopia

The main concepts emerging from this consensus are grouped below.

a. Diagnosis and monitoring

There was a consensus of more than 80% of responses in one direction in the case of requesting corneal topography for high keratometric measurements, and also in believing it necessary to measure axial length with laser biometry during the follow-up of children under treatment. There is agreement that myopic children of 6 years of age at onset with a family history of myopia require special follow-up. And that if a 3 year old child appears with -8.00 dioptres in both eyes the specialist prefers to prescribe the appropriate correction and to study them for a while to see if it is progressive. It was also agreed that those who are less hyperopic for their age should be included in a special group to be followed closely.

Therefore, requesting complementary examinations is justified in high astigmatism, in the follow-up of progression and in the search for syndromic associations in those of younger age and higher spherical equivalent at onset. It is generally noted that the early onset and/or less hyperopic population for their age should receive special attention.

b. Environment and behavioural aspects

Regarding prevention and risk factors, all experts recommended healthy habits, adopting the international guidelines for the use of digital devices, recommending going out to parks, practising sports and staying outdoors, always prioritising outdoor activities. It is not considered relevant to recommend blue light filters in the prescription of lenses for myopic patients. Most do not do blood dosages of vitamin D or other possible factors theoretically related to the progression of myopia. The importance of healthy habits gets the highest proportion of adherence.

c. Treatment

Regarding treatment and follow-up, it is suggested that pre-myopic patients should be checked frequently, myopic patients every six months and contact lenses should be recommended after the age of 10-12 years, with the new peripheral defocus designs, as there is insufficient adherence to the use of orthokeratology in our particular environment despite its known effectiveness. The concept of pre-myopia is clarified, as published in 2021 by Jong *et al.*[79] which is the child with a refractive state between +0.75 D and -0.50 D at a given age, which in combination with a series of risk factors, will make the eye care practitioner consider that this patient may develop myopia in the future and justify taking preventive measures

such as those discussed in this consensus. In other words, and perhaps more simply, a subject has pre-myopia when he-she does not have the physiological hyperopia expected for his or her age.

Questions that do not yet have a consensus are topics for further research and consensus-based therapeutic options with well-informed patients. It is to be hoped that diluted atropine will become a specific formulation accessible in all countries of the world. But the current "off-label" use does not imply any legal medical problem as it is commonly used in medicine and is fully authorised by regulatory norms, as well as having the scientific backing of evidence-based consensus such as the present one. We also hope that these questions will help the community and organisations involved in vision care to broaden the horizons of fruitful myopia research.

Conclusions

A doctor's attitude towards patients with progressive myopia should not be limited to prescribing glasses. Advances in science and technology have brought new tools of great utility, both to establish a timely diagnosis, optimise follow-up appointments, and to carry out more effective treatments, which are not only aimed to optical correction, but mainly to slowing down its progression. Likewise, although these are subjects that have been studied for a long time, pandemic-related confinement and the intensification of the digital tools have re-evaluated the relevance of environment and behavioural activities in relation to the development and progression of myopia. We hope that further advances will let us continue to improve, something we wish to evaluate in a future second version of this consensus.

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