Efficacy of low-concentration atropine (0.01%) eye drops for prevention of axial myopic progression in premyopes

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Purpose: Low-concentration atropine (LCA; 0.01%) is known to reduce the progression of myopia in axial myopes. The purpose of this study was to understand the role of LCA in premyopic children in preventing progression. **Methods:** A randomized case–control study of known premyopes was done between the use of LCA and no intervention. A total of 30 children were included in both groups. **Results:** The mean age in the LCA group was 7.7 ± 2.1 years (5–12 years), and in the control group, it was 7.2 ± 1.9 years (4–12 years). The mean baseline progression per year in the LCA group (before starting the eye drops) was − 0.72 ± 0.3 D, and in the control group, it was − 0.69 ± 0.4 D. At the end of the first year, the mean progression in the LCA group was − 0.31 ± 0.3 D versus − 0.76 ± 0.4 D, and the axial length increase was 0.12 ± 0.1 mm in the LCA group and 0.21 ± 0.2 mm in the control group. At the end of the second year, the mean progression compared with the baseline in the LCA group was − 0.6 ± 0.3 D versus − 1.75 ± 0.4 D, and the axial length showed an increase from baseline in the LCA group by 0.21 ± 0.2 mm, and in the control group, the increase was 0.48 ± 0.2 mm in 2 years. **Conclusion:** Low-concentration eye drops (0.01%) work in preventing the progression of axial myopia in premyopic children.

Key words: Axial myopia, children, low-concentration atropine, premyopia

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Low-concentration atropine (LCA; 0.01%) has become the cornerstone for the treatment of myopic progression.[1-7] Holden *et al*.[8] have projected that myopia may affect 50% of the world population by 2050. An important group comprises the premyopes where the usefulness of this drug has not been studied well.[9,10] Few reports from India by Jethani and Dave[11] and Saxena *et al*.[12] do suggest that LCA is efficacious in preventing the progression of myopia in Indian children.[11,12]

We present our experience of using LCA (0.01%) eye drops in preventing the progression in premyopes.

Methods

A randomized case–control study was done between the premyopes who started using LCA and those who were not advised any intervention. A premyope was defined as a child who had a change in glass power of more than 0.5 D per year on the myopic side at least for the past 2 years and the spherical equivalent was less than +1.00 D.[9,10] All children between 4 and 12 years of age were included in the study. Children with ocular pathology (e.g., amblyopia, strabismus), previous history of an allergy to atropine, systemic ill health (e.g., cardiac or respiratory illness), or history of any eye surgery were excluded. Children with a history of prematurity, parental history of high/pathological myopia were not included. Children with cylindrical power <1.5 D were included in the study. Children within keratometry readings of +40.0 D to +48.0 D were included in the study with normal topography (normal Keratoconus prediction Index; Visionix 120, Luneau Technology, USA). Written informed consent was obtained from the parents or guardians, and verbal assent was obtained from the children. Participants were randomized to receive 0.01% atropine (myatro eye drops, Entod Pharma) once nightly in both eyes or no intervention at an allocation ratio of 1:1. The randomization was done by a computer-generated random list. After assessment at the time of recruitment (baseline), the children were reassessed 2 weeks after starting atropine (baseline 2) and then at 6, 12, 18, and 24 months. At each visit, the distance best-corrected visual acuity logarithm of the minimum angle of resolution was assessed using a computerized chart (Unisys, USA). Near visual acuity was assessed using best-corrected distance spectacle correction with a reduced Snellen's reading chart placed at 40 cm under well-lit conditions.

An RAF (Royal Air Force) ruler was used to measure the near point of accommodation (NPA) and accommodative amplitude with the child wearing the best-corrected distance spectacle correction. The pupil size was measured for mesopic and photopic conditions using Visionix 120 (Luneau Technology, USA). In both cases, at least five pupil size readings (with a range of 0.5 mm) were recorded and averaged. Cycloplegic autorefraction was determined 40 minutes after three drops

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of homatropine 2% (Homacid, Entod Pharma, India) were administered 10 minutes apart using a URK-800 (Unicos, Daejeon, Republic of Korea). Dynamic retinoscopy was done to assess whether complete cycloplegia has been achieved. A total of five readings, 0.25 or less than that apart from each other, were obtained and averaged. Only a spherical component was taken. Axial length was measured using a contact A scan (Accutome, Keeler, USA). A total of five readings, with a maximum–minimum deviation of 0.05 mm or less, were taken and averaged. Parents who were advised to use drops were asked to keep a log of drops being instilled. The compliance level of each subject was classified according to the mean number of frequency of using atropine per week as reported by the participants over the first 24 months. Subjects with less than 75% compliance rate (5.25 days/week) were removed from the study. The primary end point was myopia progression over 2 years. The baseline was taken after 14 days of starting, and myopic progression was calculated from this reading.

Any child having an adverse effect of the LCA eye drops was advised to stop the drops and was removed from the study. One child developed an allergic reaction to the drops at the end of the first week and was replaced by another patient in the study. Children who were advised to start LCA eye drops but did not start were also removed from the study. These children were observed over a period of 2 years. Both the groups underwent similar investigations on follow-ups, including visual acuity, axial length measurement, pupil size, NPA, and fusional amplitudes.

Results

A total of 30 children were included in the LCA group of premyopes, and 30 children were there in the control group. To avoid any further bias, one eye was randomly chosen from a computer-based chart for the sake of statistical analysis. The mean age of the LCA group was 7.7 ± 2.1 years (5–12 years), and in the control group, it was 7.2 ± 1.9 years (4–12 years). The patients were age-matched.

Only the spherical component of each child was taken into consideration for the purpose of statistical analysis. The mean average keratometry at baseline in the LCA group was 43.87 ± 1.7 D, and in the control group, it was 44.06 ± 2.1 D. A Student *t*-test found the *P* value to be not significant. The mean baseline progression per year in the LCA group (before starting the eye drops) was − 0.72 ± 0.3 D, and in the control group, it was − 0.69 ± 0.4 D. The mean baseline axial length was 20.8 ± 0.6 mm in the LCA group and 21.0 ± 0.5 mm in the control group. The *P* value was not significant between the control group and the LCA group preatropine.

At the end of the first year, the mean progression in the LCA group was − 0.31 ± 0.3 D versus − 0.76 ± 0.4 D, and the axial length increase was 0.12 ± 0.1 mm in the LCA group; in the control group, the increase was 0.21 ± 0.2 mm. At the end of the second year, the mean progression compared with the baseline in the LCA group was − 0.6 ± 0.3 D versus − 1.75 ± 0.4 D, and the axial length showed an increase from baseline in the LCA group by 0.21 ± 0.2 mm; and in the control group, the increase was 0.48 ± 0.2 mm in 2 years. The *P* value was significant and was less than 0.05 between the two groups at the end of the first and second years.

The change in myopic progression in preatropine and postatropine at the end of 1 year and 2 years was significant. The *P* value was less than 0.05 on doing a paired *t*-test. The comparison between the atropine and control groups also showed a statistically significant difference in the myopic progression.

The mean pupil size increased in the LCA group by 0.8 ± 0.3 mm, whereas in the control group, the pupil size increased by 0.12 ± 0.3 mm at the end of 1 month. The *P* value was less than 0.05 and was statistically significant, although clinically there was no complaint about photophobia or light intolerance by any child. The NPA receded by 2.6 ± 1.4 D in the LCA group, whereas in the control group, it remained unchanged.

Statistical analysis

A Student *t*-test was performed to compare the preatropine and postatropine progression of myopia. A Student *t*-test was also performed to compare the progression of myopia and progression of axial length in the atropine group and the control group. A *P* value of less than 0.05 was considered to be significant.

Discussion

The use of LCA (0.01%) eye drops to prevent the progression of myopia in school-going children is gradually becoming the treatment of choice due to increasing evidence about low adverse effects and therefore better compliance.[1-4,11-14] Premyopic children are defined as either emmetropes or myopes of less than −1.0 D spherical equivalent.[9,10] The child may have a history of progression toward the myopic side with a progression of more than 0.5 D in a year. The effect of LCA eye drops in these children is little known. Looking at the future, it is prudent to treat this group at the earliest. Fang *et al*.[10] used LCA (0.025%) eye drops in premyopic children and compared it with the control group. He found that these drops significantly reduced the progression of myopia in the group of children who used these drops.

Although the actual mechanism of action is still not clear as to how LCA prevents the progression of axial myopia in children, the role of dopamine has been studied extensively.[15-18] Some studies have suggested that altered levels of dopamine in the eye may result in myopic progression both clinically and experimentally.

Because premyopes are a very important group, we believe that they should be protected against the progression at an early stage. Few characteristics of premyopes such as reduction in the physiological hyperopia and a more positive near retinoscopy have been suggested.[9] We suggest that the axial length should be taken up as an important parameter whenever such children are examined and when there is a suspicion of premyopia.[19]

In our study, we did have the data to compare the preatropine period with the atropine period along with the comparison with the control group. The axial length also did not rise significantly in the atropine group. The myopic change in the spherical component was also significantly halted in the atropine group compared with the control group where no intervention was used. The change was comparable with the study by Fang *et al*.[10] The changes in the past 2 years when

compared with the previous years also showed a significant reduction in progression of myopia compared with the control group, which increased at a similar speed.

A limitation of our study is the small sample size. Although the study had randomization, larger sample size would be able to give more clinical evidence to protect this susceptible group from the progression of myopia.

Conclusion

LCA (0.01%) eye drops are an effective therapy for the control of the progression of axial myopia in premyopic children susceptible to myopic progression. More studies with a larger sample size are needed to use it in premyopic children.

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Conflicts of interest

There are no conflicts of interest.

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