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Low-Concentration Atropine Eye Drops for Myopia Progression

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Myopia is a worldwide public health threat with increasing prevalence in most regions over the past decades, especially in East Asia.[1–3] Myopic individuals have excessive eyeball elongation and higher risks of sight-threatening complications that lead to poor vision and even blindness.[4,5]

Eye drops containing atropine, a nonselective muscarinic antagonist, have been used for myopia control for some years.[6] In 2006, the Atropine for the Treatment of Childhood Myopia (ATOM 1) Study by Chua and colleagues provided strong evidence for the therapeutic benefit of high concentration atropine (1%) on myopia control. However, its use was limited due to side effects and a rebound phenomenon following cessation of treatment. In 2012, the ATOM 2 Study evaluated lower concentrations of 0.5%, 0.1%, and 0.01% atropine for myopia control, with 0.01% atropine showing the optimal effect in treatment-to-side effect balance in that study.[7] The results from the ATOM 2 Study shifted the paradigm of myopia control management toward using low-concentration atropine eye drops, which are well tolerated and have less rebound following cessation of treatment. However, the study lacked a placebo group, and there remained unanswered questions regarding long-term efficacy, optimal concentration, and related factors of treatment effect.[7] Subsequently, the Low-concentration Atropine for Myopia Progression (LAMP) Study showed that 0.05%, 0.025%, and 0.01% atropine eye drops reduced myopia progression along a concentration-dependent response, with 0.05% atropine being the most effective, and all concentrations were well tolerated without any adverse effect on the vision-related quality of life over 3 years.[8–11]

As published in this issue of the *Asia-Pacific Journal of Ophthalmology*, Chia et al[12] conducted a randomized, double-masked, placebo-controlled study to compare the efficacy and safety of atropine at 3 different concentrations (0.0025%, 0.005%, and 0.01%) with placebo in children aged 6 to 11 years with mild-to-moderate myopia. Their findings demonstrated that atropine of 0.005% and 0.01% can reduce myopia progression, while the effect for the concentration of 0.0025% of atropine was statistically not significant.[12] This study is the first to demonstrate the efficacy of atropine at concentrations lower than 0.01%. In terms of optimal concentration, studies that have investigated the efficacy of 0.01% atropine have reported a 15% to 34% reduction in myopia progression, with a relative decline of 18% to 46% in axial elongation in Chinese, Japanese, Spanish, and a multiethnic cohort of Australian children. Over 50% reduction in myopia progression and axial elongation was achieved in Indian children who used 0.01% atropine eye drops for 1 year, but there was an unexplained significant difference in corneal curvature between the treatment and control groups. Accordingly, treatment efficacy of the low-concentration 0.01% atropine appears to be different from other studies. There are several possible explanations for the varying efficacy of atropine eye drops in different cohorts. First, treatment efficacy may be influenced by the rate of myopia progression, with slower progression leading to better treatment outcomes. This was demonstrated in a study by Saxena et al,[13] which reported good treatment effects in a

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relatively slow-progressing cohort of Indian children. Similarly, the current study conducted by Chia and colleagues showed a slow myopia progression (-0.55 ± 0.471 D), which may have contributed to the observed treatment efficacy. Second, the age of the study participants may also play a role in the treatment response. LAMP studies have shown that younger children tend to have faster progression and poorer treatment response compared with older children.[9] Younger children may require a higher concentration of atropine to achieve similar efficacy as that observed in older children receiving lower concentrations. Finally, while the current study found that both 0.01% and 0.005% atropine can slow axial elongation, most studies have reported that 0.01% atropine has no effect on the change in axial length, despite its efficacy in reducing spherical equivalent progression. However, it is important to note that axial elongation contributes most to the progression of myopic refractive error and that the antimyopic effects of low-concentration atropine mainly acts on reducing axial elongation, as demonstrated in the LAMP Study.

In conclusion, atropine has emerged as an effective and safe therapy for myopia control in children. Widespread use of low-concentration atropine, especially in East Asia, may help prevent myopia progression in high-risk children. Chia and colleagues' study demonstrated that atropine concentrations <0.01%, such as 0.005% atropine, can reduce myopia progression. The efficacy of low-concentration atropine is influenced by factors such as ethnicity, environment, lifestyle, and age, which mediate myopia progression. For fast-progressing groups and younger children, higher concentrations of atropine, such as 0.05% atropine, may be necessary for myopia control. Conversely, for slow-progressing groups and older children, 0.01% atropine or lower concentrations may confer efficacy.

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