AMERICAN ACADEMY™
OF OPHTHALMOLOGY

Ophthalmic Technology Assessment

Atropine for the Prevention of Myopia Progression in Children

A Report by the American Academy of Ophthalmology

Stacy L. Pineles, MD,[1] Raymond T. Kraker, MSPH,[2] Deborah K. VanderVeen, MD,[3] Amy K. Hutchinson, MD,[4] Jennifer A. Galvin, MD,[5] Lorri B. Wilson, MD,[6] Scott R. Lambert, MD[7]

Purpose: To review the published literature on the efficacy of topical atropine for the prevention of myopic progression in children.

Methods: Literature searches were last conducted in December 2016 in the PubMed database with no date restrictions, but were limited to studies published in English, and in the Cochrane Library database without any restrictions. The combined searches yielded 98 citations, 23 of which were reviewed in full text. Of these, 17 articles were deemed appropriate for inclusion in this assessment and subsequently were assigned a level of evidence rating by the panel methodologist.

Results: Seventeen level I, II, and III studies were identified. Most of the studies reported less myopic progression in children treated with atropine compared with various control groups. All 8 of the level I and II studies that evaluated primarily myopic progression revealed less myopic progression with atropine (myopic progression ranging from 0.04±0.63 to 0.47±0.91 diopters (D)/year) compared with control participants (myopic progression ranging from 0.38±0.39 to 1.19±2.48 D/year). In studies that evaluated myopic progression after cessation of treatment, a rebound effect was noted. Several studies evaluated the optimal dosage of atropine with regard to myopic progression, rebound after treatment cessation, and minimization of side effects. Lower dosages of atropine (0.5%, 0.1%, and 0.01%) were found to be slightly less effective during treatment periods of 1 to 2 years, but they were associated with less rebound myopic progression (for atropine 0.01%, mean myopic progression after treatment cessation of 0.28±0.33 D/year, compared with atropine 0.5%, 0.87±0.52 D/year), fewer side effects, and similar long-term results for myopic progression after the study period and rebound effect were considered. The most robust and well-designed studies were carried out in Asian populations. Studies involving patients of other ethnic backgrounds failed to provide sufficient evidence of an effect of atropine on myopic progression.

Conclusions: Level I evidence supports the use of atropine to prevent myopic progression. Although there are reports of myopic rebound after treatment is discontinued, this seems to be minimized by using low doses (especially atropine 0.01%). *Ophthalmology 2017;■:1–10 © 2017 by the American Academy of Ophthalmology*

The American Academy of Ophthalmology prepares Ophthalmic Technology Assessments to evaluate new and existing procedures, drugs, and diagnostic and screening tests. The goal of an Ophthalmic Technology Assessment is to review systematically the available research for clinical efficacy, effectiveness, and safety. After review by members of the Ophthalmic Technology Assessment Committee, other Academy committees, relevant subspecialty societies, and legal counsel, assessments are submitted to the Academy's Board of Trustees for consideration as official Academy statements. The purpose of this assessment by the Ophthalmic Technology Assessment Committee Pediatric Ophthalmology/Strabismus Panel is to review the published literature on the efficacy of topical atropine for the prevention of myopic progression in children.

Background

Myopia is a common treatable ocular condition that occurs in up to 50% of the adult population in the United States.[1,2] Although it is less common in children, the prevalence of myopia in the United States is increasing, and between 1971 and 1999, it rose from 25% to 42%.[3] In Asian countries, myopia is more common, and it is increasing in prevalence at an even more rapid rate. Up to 90% of young adults

http://dx.doi.org/10.1016/j.ophtha.2017.05.032
ISSN 0161-6420/17

have myopia in Taiwan, Singapore, and Hong Kong.[4–7] Additionally, myopia seems to be increasing in younger age groups as well, with an increased prevalence from 5.8% in 1983 to 21% in 2000 in 7-year-old children in Taiwan.[6]

The cause and underlying mechanism of myopia progression remain unclear; therefore, its increasing prevalence is not well understood. Several theories have been proposed to explain the recent increase and its earlier onset in children, including a decrease in outdoor activity, an increase in time spent doing near work, and an increase in urbanization.[8,9] Despite these theories and studies showing that increasing outdoor activity and decreasing near work may help to retard myopic progression,[8,9] other treatments have been sought. The prevention of myopia progression has been prioritized largely because the risks of increasing axial myopia include glaucoma, cataract, myopic macular degeneration, and retinal detachment.[10,11]

A 2011 Cochrane database review[12] evaluated the published evidence for various treatments aimed at slowing the progression of myopia in children. The treatment methods included eyeglasses that undercorrect, multifocal eyeglasses, novel lens eyeglasses, various contact lens therapies such as bifocal or multifocal contact lenses or orthokeratology, topical timolol, and topical antimuscarinic agents, including pirenzepine and atropine. The conclusion of the Cochrane review was that antimuscarinic agents are "the most likely effective treatment to slow myopia progression."[12] The most commonly used and studied antimuscarinic agent for slowing myopic progression is atropine. Although there is much interest in its use, how atropine exerts antimyopia effects is not well understood. Atropine initially was used on the premise that accommodation was the causative factor in myopia progression, and therefore, cycloplegia may retard myopic advancement. However, because atropine prevents myopic progression even in animals that have striated ciliary muscles and because nonpharmacologic mechanisms for decreasing accommodation (i.e., bifocals) do not seem to retard myopic progression, researchers have shifted away from hypotheses of accommodation as the primary factor in progression.[13,14] Current theories about the primary factor include a local retinal effect that may retard myopia progression or a potential biochemical change brought about by binding muscarinic receptors,[14] which have been shown to be present in the sclera of certain animals.[15] Two newer theories suggest that pupillary dilation may result in increased ultraviolet A exposure, which may limit axial elongation,[16] or that myopia may be associated with increased chronic inflammation in the eye, which may be downregulated by atropine.[17] Given the broad interest in preventing myopia and numerous more recent studies evaluating atropine, we set out to review the current evidence for the use of atropine to retard the progression of myopia.

Questions for Assessment

The purpose of this assessment is to address the following questions: (1) Does topical atropine prevent the progression of myopia in children? and (2) Does this effect vary with atropine dosage?

Description of Evidence

Literature searches were conducted last in December 2016 in the PubMed database with no date restrictions, but were limited to studies published in English, and in the Cochrane Library database without any restrictions. The following terms were used, along with publication and language filters:

(*Myopia*[mh] OR *myop** OR *shortsight** OR *nearsight**) AND (*Eyeglasses*[mh] OR *spectacle** OR *glasses* OR *contact lens** OR *atropine*[mh] OR *atropine sulfate* OR *usp* OR *atropa belladonna* OR *atropen* OR *tropic acid*) AND (*Refractive errors*[mh] OR *Refraction, Ocular*[mh] OR *Accommodation, Ocular*[mh] OR *Visual Acuity*[mh] OR *accommodat** OR *acuity* OR *progress** OR *slow** OR *retard** OR *function** OR *delay**) AND (*Infant*[MeSH] OR *Infant** OR *infancy* OR *Newborn** OR *Baby** OR *Babies* OR *Neonat** OR *Preterm** OR *Prematur** OR *Postmatur** OR *Child*[MeSH] OR *Child** OR *Schoolchild** OR *School age** OR *Preschool** OR *Kid* OR *kids* OR *Toddler** OR Adolescent[MeSH] OR *Adoles** OR *Teen** OR *Boy* OR *boys* OR *Girl** OR *Minors*[MeSH] OR *Minors** OR *Puberty*[MeSH] OR *Pubert** OR *Pubescen** OR *Prepubescen** OR *Pediatrics*[MeSH] OR *Paediatric** OR *Schools*[MeSH] OR *Nursery school** OR *Kindergar** OR *Primary school** OR *Secondary school** OR *Elementary school** OR *High school** OR *Highschool**).

The combined searches yielded 98 citations, and the panel reviewed 23 articles in full text. Of these, 17 articles were deemed appropriate for inclusion in this assessment (including 4 articles that are not clinical trials) and subsequently were assigned a level of evidence rating by the panel methodologist (R.T.K.). The 75 articles that were not reviewed consisted of editorials, review articles, and research that was not directly related to this assessment. The rating scale was based on that developed by the Oxford Centre for Evidence-Based Medicine.[18] A level I rating was assigned to well-designed and well-conducted randomized clinical trials; a level II rating was assigned to well-designed case-control and cohort studies and lower-quality randomized studies; and a level III rating was assigned to case series, case reports, and lower-quality cohort and case-control studies. Six studies met level I criteria and 6 studies met level II criteria. In addition, 6 studies that met level III criteria were included because of their impact on the use of atropine for the prevention of myopia, particularly in non-Asians.

Published Results

The treatment evaluated for this assessment involves the administration of atropine ophthalmic solution of varying concentrations in children with myopia in an attempt to prevent myopia