Update on Orthokeratology in Managing Progressive Myopia in Children: Efficacy, Mechanisms, and Concerns

Xintong Li, MD; Ilana B. Friedman, MD; Norman B. Medow, MD; Cheng Zhang, MD

ABSTRACT

Myopia is an important public health issue, and high myopia may lead to severe complications if left untreated. Orthokeratology lenses, worn overnight to reshape the cornea, are one of many recent modalities used to slow down the progression of myopia in children. This treatment has been proven successful, as evidenced by decreased spherical refractive error and axial length relative to the control at interval follow-up ranging from 6 months to 5 years. In this systematic review, the authors collected published controlled studies that analyzed the efficacy of orthokeratology lens wear and calculated longitudinal relative changes in axial length, revealing a weighted average of -45.1% change in axial length at the 2-year follow-up. The exact mechanism by which orthokeratology lenses reduce myopia progression is unknown, but research shows that the corneal reshaping decreases peripheral hyperopic defocus and therefore increases peripheral myopic defocus to likely reduce stimuli for axial elongation and subsequent development of myopia. Use of orthokeratology lenses is generally safe, but cases of associated infectious keratitis may have a higher incidence of virulent organisms such as Pseudomonas, Acanthamoeba, and antibacterial-resistant strains of Staphylococcus, partially due to the required overnight use of these lenses. Orthokeratology is regarded as one of the most effective non-pharmacologic measures to slow progression of myopia in children and, with regular follow-up to ensure safety, continues to be one of the most effective treatments for myopia management around the world. [J Pediatr Ophthalmol Strabismus. 2017;54(3):142-148.]

INTRODUCTION

Myopia, commonly known as near-sightedness, is a spherical refractive error that causes light to focus in front of the retina, resulting in blurry distance vision while preserving clearer near vision. It is due to axial lengthening of the globe or increased refractive power of the eye. Epidemiologic studies of this condition are complicated by age, ethnicity, and the degree of spherical refractive error needed to label an eye as myopic, and its prevalence ranges from 33% in whites to approximately 90% in East Asians. In addition to increasing functional impairment of the patient, myopia increases the risk of subretinal neovascularization, glaucoma, cataract, and retinal detachment. Various modalities to alleviate the symptoms of or to correct existing myopia have been used, ranging from single-vision spectacles, soft or rigid gas permeable contact lenses, atropine, and orthokeratology to refractive surgery. Perhaps the most controversial has been orthokeratology, or corneal reshaping therapy, which is generally prescribed by optometrists and has seen an explosion in use in the past decade. After routine overnight use, the lenses flatten the central cornea while steepening the peripheral cornea so that the eye can see clearly in the daytime without correction. Patients are mainly school-aged children due to the increased rate of myopia progression in this population and use is increasing, especially in East Asian communities secondary to the high prevalence of myopia in these children.
To our knowledge, the overwhelming majority of controlled studies and all of the randomized ones that sought to address the effect of orthokeratology on myopia progression were published within the past 4 years. The last comprehensive review of orthokeratology was published in 2006 by Swarbrick. Using a comprehensive PubMed literature search, we present a focused update into orthokeratology’s effect on myopia progression as measured by various outcomes, potential effect modifiers, proposed mechanisms, and current concerns for the prescription of orthokeratology for myopia.

**DOES ORTHOKERATOLOGY SLOW MYOPIA PROGRESSION?**

Literature in the past decade is prolific with documentation of orthokeratology reducing the rate of progression of myopia, with most studies consisting of only pediatric patients. Although the lenses are generally designed for nighttime use, refraction for patients undergoing orthokeratology may be taken while the lenses are in place. However, the most widely used measure of outcome as a substitute for spherical refractive error taken during manifest refraction was axial length.

Controlled studies in pediatric patients generally agree that, with at least 6 months of extended use, orthokeratology reduces the rate of myopia progression as quantified by increased axial length and/or spherical refractive error over the orthokeratology lens (Table 1). The results of a series of meta-analyses on the effect of orthokeratology on myopic progression arrived at a similar conclusion, using a subset of the studies presented here. In a randomized study published in 2013, Charm and Cho became the first group to assay the effect of partial-reduction orthokeratology in high myopes with spherical refractive error greater than -5.75 diopters (D) and daytime spectacle correction for the remaining spherical refractive error, finding a 63% reduction in axial length increase in the orthokeratology group versus the control group. The largest cohort so far with an appropriate control group was studied by Zhu et al. in 2014, with 65 patients in the orthokeratology group consisting of all myopes with a spherical refractive error of more than -0.50 D. Axial length elongation was found to be 49%, 59%, and 46% slower in the low (-3.00 D < spherical refractive error < -0.50 D), moderate (-6.00 D < spherical refractive error ≤ -3.00 D), and high (spherical refractive error ≤ -6.00 D) myope subgroups, respectively, when compared to control subgroups. Interestingly, axial length slowing was more marked in the first year of follow-up than in the second year, and the investigators also found that axial elongation was significantly associated with the patient’s age at baseline.

In 2015, Swarbrick et al. published a prospective, randomized crossover study of East Asian children living in Australia that allowed each patient to serve as his or her own control, with 6 months of orthokeratology lens wear in one randomly selected eye, followed by a 2-week period of no lens wear and then 6 months of lens wear in the contralateral eye. During both periods of orthokeratology lens wear, axial length decreased significantly in the eye under study, whereas the control eye had no increase in axial length. This study, in addition to other recent prospective, randomized trials, lends strong credence to the slowing of myopic progression in patients with myopia using orthokeratology.

In 2013, Smith published a visual collating longitudinal axial length and age data from all of the orthokeratology trials published to date; Figure 1 shows a continuation of this figure that includes six more studies from Table 1 (excluding Downie and Lowe’s trial because the authors used spherical refractive error instead of axial length to quantify myopia progression) for a total of 13 studies. The weighted average in Figure 1A of the studies included is -45.1% change in axial growth, which is up from Smith’s value of -41.7%. This may be due to a combination of improved lens design and the efficacy of randomized, controlled trials in extricating orthokeratology’s effect on myopia progression from confounding variables such as age and baseline spherical refractive error.

**MECHANISM**

Other factors that have been associated with a reduced rate of axial elongation in patients using orthokeratology may provide clues to the mechanism by which these lenses slow myopia progression. Currently, the predominant hypothesis appears to be that orthokeratology decreases peripheral hyperopic defocus and thus increases peripheral myopic defocus to reduce stimuli for axial elongation. Larger pupils were associated with more marked slowing in one study, and the authors hypothesized that this is due to more rays falling onto the peripheral retina,
thereby increasing the effect of the orthokeratology-induced peripheral myopia.

19 Symmetry of baseline vertical corneal topography was found to be independently associated with myopic eyes that underwent orthokeratology and did not have spherical refractive error progression, 20 and a recent study found that refractive changes after orthokeratology discontinuation were due to corneal changes instead of axial elongation.

21 However, in accordance with previous documentation that orthokeratology works by reversing peripheral hyperopic and central myopic defocus to reduce stimuli for axial growth, studies also show that peripheral corneal power change predicts axial elongation and myopic progression in children undergoing orthokeratology therapy. 22,23 A recent corneal topographical study showed that orthokeratology flattens the central 40 degrees of visual field and reduces greater tangential and sagittal power within 25 to 35 degrees of the central cornea. 24 Taken together, these studies show that orthokeratology's long-term effect on myopia is mostly due to the peripheral corneal changes it induces.

In another study, axial elongation was significantly correlated with changes in higher-order aberrations, spherical-like aberration, total power change, and central myopic defocus in children undergoing orthokeratology treatment. 25,26 However, in accordance with previous documentation that orthokeratology flattens the central 40 degrees of visual field and induces greater tangential and sagittal power within 25 to 35 degrees of the central cornea, 24 these studies also show that peripheral corneal power change predicts axial elongation and myopic progression in children. 25,26

Older age was also found to be correlated with slower axial growth in eyes with orthokeratology lenses. 20 This may be due to more marked development of the eye in younger versus older patients. 23 This may be due to more marked development of the eye in younger versus older patients. 23

20 Partial-reduction orthokeratology lenses only using lowest target lens that gave maximum myopic correction.

21 Toric orthokeratology lenses used.

**TABLE 1**

<table>
<thead>
<tr>
<th>Authors</th>
<th>Publication Year</th>
<th>Study Origin</th>
<th>Age (y)</th>
<th>Sphere (D)</th>
<th>Cylinder (D)</th>
<th>No.</th>
<th>Follow-up Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cho et al. 20</td>
<td>2005</td>
<td>Hong Kong</td>
<td>7 to 12</td>
<td>-0.25 to -4.00</td>
<td>&lt; 2.00</td>
<td>35</td>
<td>2 years</td>
</tr>
<tr>
<td>Walline et al. 50</td>
<td>2009</td>
<td>United States (patients 15% Asian)</td>
<td>8 to 11</td>
<td>-0.75 to -4.00</td>
<td>&lt; 1.00</td>
<td>28</td>
<td>2 years</td>
</tr>
<tr>
<td>Ōkita et al. 50</td>
<td>2011</td>
<td>Japan</td>
<td>8 to 16</td>
<td>-0.50 to -10.00</td>
<td>≤ 1.50</td>
<td>45</td>
<td>2 years</td>
</tr>
<tr>
<td>Cho &amp; Cheung 50</td>
<td>2012</td>
<td>Hong Kong</td>
<td>6 to 10</td>
<td>-0.50 to -4.00</td>
<td>≤ 1.25</td>
<td>37</td>
<td>2 years</td>
</tr>
<tr>
<td>Hirao et al. 15</td>
<td>2012</td>
<td>Japan</td>
<td>8 to 12</td>
<td>-0.50 to -4.00</td>
<td>≤ 1.50</td>
<td>22</td>
<td>2 years</td>
</tr>
<tr>
<td>Santodomingo-Rubido et al. 52</td>
<td>2012</td>
<td>Spain</td>
<td>6 to 12</td>
<td>-0.75 to -4.00</td>
<td>≤ 1.00</td>
<td>31</td>
<td>2 years</td>
</tr>
<tr>
<td>Charm &amp; Cho 72</td>
<td>2013</td>
<td>Hong Kong</td>
<td>8 to 11</td>
<td>Atleast -5.75</td>
<td>Any</td>
<td>12</td>
<td>2 years</td>
</tr>
<tr>
<td>Chen et al. 52</td>
<td>2013</td>
<td>Hong Kong</td>
<td>6 to 12</td>
<td>-0.50 to -5.00</td>
<td>≤ 1.25</td>
<td>37</td>
<td>2 years</td>
</tr>
<tr>
<td>Cheung &amp; Cho 50</td>
<td>2013</td>
<td>Hong Kong</td>
<td>7 to 10</td>
<td>-0.75 to -4.00</td>
<td>≤ 1.50</td>
<td>22</td>
<td>2 years</td>
</tr>
<tr>
<td>Downie &amp; Lowe 50</td>
<td>2013</td>
<td>Australia (patients 54% Asian)</td>
<td>5 to 16</td>
<td>-0.50 to -7.00</td>
<td>&lt; 2.00</td>
<td>26</td>
<td>2 to 8 years</td>
</tr>
<tr>
<td>Zhu et al. 53</td>
<td>2014</td>
<td>China</td>
<td>7 to 14</td>
<td>More than -0.50</td>
<td>≤ 1.50</td>
<td>65</td>
<td>2 years</td>
</tr>
<tr>
<td>Swarbrick et al. 48</td>
<td>2015</td>
<td>Australia (patients 100% East Asian)</td>
<td>11 to 17</td>
<td>-1.00 to -4.00</td>
<td>≤ 1.50</td>
<td>26</td>
<td>6 months, then crossover for 6 more months</td>
</tr>
<tr>
<td>Pauné et al. 53</td>
<td>2015</td>
<td>Spain</td>
<td>9 to 16</td>
<td>-0.75 to -7.00</td>
<td>&lt; -1.25</td>
<td>18</td>
<td>2 years</td>
</tr>
</tbody>
</table>

D = diopters

*No. column reflects the number of patients in the orthokeratology group in each study. A separate control group of patients who wore single-vision spectacles was used in each study except for that of Walline et al., 50 in which soft contact lenses were used, and that of Swarbrick et al., 48 in which orthokeratology lenses were prescribed for one eye and rigid gas permeable daytime contact lenses for the contralateral eye.

b Partial-reduction orthokeratology lenses only using lowest target lens that gave maximum myopic correction.

c Toric orthokeratology lenses used.
younger patients or adaptation of the visual system to the shifts in retinal focus induced by orthokeratology that has led to reports of lesser reduction of axial elongation in the second year of treatment. Higher baseline myopia before orthokeratology use has been associated with slower axial elongation versus control in some studies, and in a linear regression analysis of three studies, but not in another recent study. Further investigation is needed to clarify this potential correlation.

SAFETY CONCERNS

In 2008, the American Academy of Ophthalmology issued an official statement on the safety of orthokeratology, recommending a wide margin of safety for patients undergoing this therapy due to case reports of vision-threatening complications, such as infectious keratitis and milder complications of corneal erosions and iritis. Since then, case reports and series have been published that noted a high incidence of *Pseudomonas* and *Acanthamoeba* species and other gram-negative organisms including *Serratia* from corneal isolates of infectious keratitis cases associated with orthokeratology use.

In 2016, researchers from the United States published results from a multistate case-control retrospective study of 37 cases of *Acanthamoeba* keratitis, finding that 24% of cases were found in orthokeratology lens wearers and that orthokeratology was a significant risk factor for the development of *Acanthamoeba* keratitis. A prospective study published the month prior by a group in Hong Kong found significant increases in the prevalence of a resistance gene, *qac*, in staphylococcal isolates from the conjunctiva after 6 months of orthokeratology lens wear (**Staphylococcus aureus**: 4.4% to 15.4%, coagulase-negative *Staphylococcus*: 6.7% to 25%) with significant increases in the minimum inhibitory and bacteriocidal concentrations for these post-orthokeratology strains.
Overall, orthokeratology is estimated to be implicated in approximately 19.1% to 38.8% of cases of infectious keratitis in recent years; however, a prospective study on the true incidence of infectious keratitis and other serious complications over a period of a few years remains to be completed.

A 2016 systematic review of the safety of orthokeratology, using both English- and Chinese-language articles, found that lens binding, or adherence of the contact lens to the cornea, was another complication of orthokeratology lens wear and was significantly associated with central corneal staining. Lens material may play a role in reducing the rate of hypoxia-related complications; a prospective study also published this year on 126 participants of all ages fitted for a high-Dk/t (144) orthokeratology lens with high oxygen permeability revealed no cases of serious complications, such as infectious keratitis or lens binding, at 6-month follow-up.

Although associated with a low incidence of adverse events, overnight lens wear has an uncertain safety profile that necessitates regular ophthalmological follow-up for patients receiving orthokeratology therapy for early detection and treatment of any serious complications that may arise.

**COMPARISON WITH OTHER THERAPIES**

To date, few trials directly compare outcomes of myopic eyes that underwent orthokeratology with alternative methods to potentially slow myopia progression. The largest such study, published by Lin et al. in 2014, retrospectively compared 104 patients aged 7 to 17 years who were prescribed orthokeratology and 105 controls who used 0.125% atropine every night for 3 years. The authors found that the orthokeratology group showed significantly lower rates of annual increase in myopia (0.28 D vs 0.34 D, \(P = 0.001\)) and axial length (0.28 mm vs 0.37 mm, \(P < 0.001\)) when compared to the atropine group.

Recently, groups have extensively reviewed other methods to control myopia progression and concluded that contact lenses that induce myopic defocus, including orthokeratology, result in a more clinically significant and well-documented slowing of myopia progression than executive bifocal spectacles, progressive addition lenses, or pharmacologic measures (ie, atropine or pirenzepine). Also, undercorrection of myopia may even increase the rate of progression. Outdoor activity has also been studied as a non-optical therapy that may lead to slowing of myopia progression, although the mechanism behind this correlation remains unclear.

Aller then illustrated a hypothetical family of five daughters and the outcome of myopia using different efficacies of therapy to slow myopia progression. The author designated efficacies as myopia control (MC) 33 (33% effective for slowing down progression of myopia) for progressive addition lenses and bifocal spectacles, MC50 for orthokeratology and bifocal or multifocal soft contact lenses, and MC80 for simultaneous vision bifocal contact lenses in patients with near esotropia fixation deviations. These were based on the maximal effective concentration terminology to measure drug response and average values in the published literature.

A Cochrane review published in 2011 compared various methods to decrease myopia progression in children, including undercorrection, rigid gas permeable contact lenses, multifocal spectacles, and anti-muscarinic medications. The authors concluded that, at year 1, patients who received pirenzepine gel, cyclopentolate drops, or atropine drops had significantly less sphere than placebo (respective mean differences of 0.31, 0.34, and 0.80).

Generally, past reviews concur that orthokeratology efficacy is better than other non-pharmacologic measures, but 1% atropine has still been shown to achieve the highest efficacy in slowing myopia progression. However, the side effect profile of anti-muscarinics, which includes hypersensitivity reactions, dry mouth, blurry vision, and light sensitivity, may lower patient compliance.

Despite the general consensus that orthokeratology is effective in reducing the rate of myopia progression, a 2011 survey of ophthalmologists in Korea revealed that less than one-fourth recommended orthokeratology to pediatric patients with myopia, and that the most-prescribed therapy was prescription of spectacles to the full cycloplegic refraction. Although there is a small risk of vision-threatening complications, with proper hygiene and care, the option of orthokeratology may be offered to school-aged children with myopia, especially those with high myopia. This method could slow progression of myopia and reduce the chance of complications related to high and pathological myopia.

The mechanism of the myopia-slowing effect of orthokeratology is still unclear, although various associations and hypotheses have been studied. Future research may be tailored toward controlled, ran-
domized trials directly comparing orthokeratology to other forms of therapy that have been shown to slow myopia progression, such as bifocal spectacles, progressive addition lenses, and simultaneous defocus lenses, with more studies comparing its efficacy to that of atropine and possibly pirenzipine. The cost of orthokeratology lenses in the United States is approximately $1,500 to $2,500 for the initial fitting fee and 1-year care. Thereafter, there are annual visit fees and occasional lens change fees. In the United States, most orthokeratology lenses are fit by optometrists (> 95%) working either in their own practice or in conjunction with an ophthalmologist. Most optometrists favor orthokeratology, whereas ophthalmologists are either unaware of it or generally opposed to it. The market penetration of orthokeratology in the United States is relatively small and is followed mostly by ethnic groups that have a large penetration of orthokeratology such as those of Chinese, Taiwanese, or Singaporean descent. Determining the incidence of vision-threatening complications in orthokeratology patients would allow the parents, optometrist, and ophthalmologist to accurately weigh risks and benefits before coming to an informed decision on whether to proceed with orthokeratology therapy.

REFERENCES