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***Acanthamoeba* Keratitis in Minors with Orthokeratology (OK) Lens Use: A Case Series**

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Abstract

Objectives: Myopia progression is a significant public health issue. Methods to halt myopia progression in minors continue to gain momentum. Orthokeratology, with market penetrance estimates approximating 1%, is a corneal reshaping therapy and potential myopia progression treatment. Our objective was to explore whether orthokeratology may increase the frequency of *Acanthamoeba* keratitis in minors compared to other lens modalities.

Methods: Individuals <18 years diagnosed with *Acanthamoeba* keratitis (AK) at the University of Illinois at Chicago (UIC) Cornea Service between January 1st, 2003 and December 31st, 2016 were retrospectively reviewed. Subjects were grouped by lens modality (soft; rigid gas permeable, RGP; orthokeratology) and all cases with orthokeratology lens use were reviewed. Primary outcome was history of orthokeratology lens use in minors diagnosed with AK.

Results: Forty-seven contact lens users <18 years were diagnosed with AK. Mean age was 15.0 (range 12–17), 26 (55%) were female, and 4 (8.5%) had bilateral disease. Lens modality included 6 (13%) with orthokeratology, 39 (83%) with soft contact lenses, 0 with non-orthokeratology RGP (0%), and 2 (4%) unknown.

Conclusions: The proportion of orthokeratology cases among AK minors (13%) in our case series exceeds the expected proportion of orthokeratology cases expected based on orthokeratology market penetrance (1%). Results from this case series suggest a potential increased risk of AK in orthokeratology users compared to other lens modalities. In the context of the current myopia epidemic and concerns for halting myopia progression in minors, caution should be exercised when selecting appropriate treatment options to minimize the risk of AK.

Keywords

Orthokeratology; *Acanthamoeba* keratitis; minors

Myopia progression is a significant public health issue, with considerable clinical and research interest dedicated to prevention methods.¹ According to the National Health and

Nutrition Examination Survey, myopia prevalence increased by 66.4% from 1971–72 to 1999–2004 in individuals aged 12–54 years, and currently affects one in three individuals in this age group.² Among others, pathologic myopia complications include cataract, choroidal neovascularization, glaucoma, macular hole, and retinal detachment.³

Current theory in myopia progression is that peripheral hyperopic retinal defocus causes axial elongation, consequently increasing myopia.⁴ Hypotheses for halting myopia progression suggest optical changes as the most likely mechanism of action, with orthokeratology lenses or other similar optical prescriptions inducing peripheral myopic defocus to halt axial elongation.^{4–6} Orthokeratology is one potential treatment option in the prevention of myopia progression, in which a flat-fitting rigid gas permeable lens is worn overnight, transiently reducing corneal power.⁷ Histologic feline studies demonstrate central epithelial thinning and mid-peripheral thickening with increased wear time, corresponding to the zone of treatment.⁸

Orthokeratology has been identified as a possible risk factor for *Acanthamoeba* keratitis (AK).^{9,10} With the increasing use of orthokeratology to halt myopia progression in minors, it is worthwhile to further investigate whether benefits outweigh risks of use. Previous reports have suggested a high suspicion for *Acanthamoeba* keratitis in orthokeratology lens users,¹¹ with AK identified as the causative agent in one third of microbial keratitis cases among orthokeratology lens users.¹² Here, we aimed to assess the proportion of orthokeratology lens use among AK in minors with contact lens use at a tertiary care facility. Our objective was to explore the frequency of orthokeratology lens use compared to other lens modalities in confirmed AK cases.

Methods:

This study was approved by the Institutional Review Board at the University of Illinois at Chicago (UIC). Data abstraction was performed on all patients under the age of 18 who were seen in the Cornea Service at UIC Department of Ophthalmology and Visual Sciences between January 1st, 2003 and December 31st, 2016. Cases were identified using ICD-9 (136.21, 370.0, 370.8, 371.82), ICD-10 (B60.13, H16.0, H18.82) and CPT (92286) codes, and further chart review was performed to identify all individuals who received a clinical diagnosis of AK. Diagnosis of AK was consistent with previous analyses and defined as having one or more of the following: a positive *Acanthamoeba* culture, keratoplasty specimens with AK pathology identified, trophozoites or cysts through smears when specimens were stained with Diff-Quick stain, trophozoites or cysts on confocal microscopy, or definitive clinical presentation (epitheliitis, epitheliitis with radial neuritis, anterior stromal disease, deep stromal disease, or ring infiltrate)¹³ that resolved with anti-*Acanthamoeba* treatment.^{14,15} Basic descriptive analyses were performed using Microsoft Excel (2016) on all identified minors diagnosed with AK who used contact lenses.

Results:

Forty-seven minors under the age of 18 years with contact lens use were diagnosed with AK at UIC. Of these, 26 (55%) were female and 21 (45%) were male, with an age range from 12

to 17 years (mean, 15.0). More than half of all AK cases were white (n=30, 64%), with the balance a mixture of race/ethnicity including Hispanic (n=5, 11%), Asian (n=4, 9%), African American (n=1, 2%), other (n=5, 11%), and unknown or unavailable (n=2, 4%). Four patients had bilateral disease (8.5%). Among minors diagnosed with AK, type of lens use included soft contact lens (n=39, 83%), orthokeratology (n=6, 13%), and unknown lens modality (n=2, 4%). None of the minors diagnosed with AK used traditional rigid gas permeable (RGP) lenses.

Among AK minors with orthokeratology lens use, the mean age (15.0) and gender distribution (66% female) were similar to AK minors with use of other lens types (15.0; 55% female). In contrast, half of AK minors with orthokeratology lens use were of Asian descent (n=3, 50%), and the balance either white (n=1), other (n=1), or unavailable (n=1), as compared to AK minors with use of other lens types who were 70.7% white (n=29), followed by Hispanic (n=5), Asian (n=1), Black (n=1) or other (n=5).

Discussion:

Results identified 13% of all contact lens-related AK cases in minors associated with orthokeratology lens use. None occurred in rigid gas permeable lens use alone. While the actual marketplace penetration of orthokeratology among minors compared to other modalities is unknown, most sources suggest it was far less than 13% between 2003–2016.¹² This suggests our findings represent an increased risk of AK with orthokeratology lens use compared to other lens modalities. For comparison, we can use previous literature to support orthokeratology market trends, which likely approximate 1% of the general contact lens-wearing population.

Specifically, among international contact lens prescribers, rigid lenses consist of 10.8% of lenses, of which only 11.5% are orthokeratology,¹⁶ suggesting orthokeratology represents only 1.2% of international lens fits (10.8% * 11.5% = 1.2%). More recently in the US, rigid lenses comprise 9.4% of lenses, of which 4.5% were orthokeratology,¹⁷ suggesting orthokeratology represents only 0.4% of U.S. lens fits. Although these market trends are not specific to minors and may reflect artificial estimates, we believe our findings remain valuable given that 6 of 47 AK cases in minors used orthokeratology lenses *at a single tertiary care referral center*.

Microbial keratitis, including AK, has been previously reported in minors with a history of overnight orthokeratology lens use.⁹ Although previous reports have identified *Acanthamoeba* as the etiology agent in one third of microbial keratitis cases with orthokeratology lens use,¹² none have investigated the proportion of orthokeratology lens users within a series of AK minors with contact lens use. Some authors suggest AK risk may be similar to other lens modalities.¹⁸ A case-control study of patients of all ages diagnosed with AK and a history of rigid gas permeable lens wear identified orthokeratology lens use in approximately a quarter of cases.¹⁰ Histologic primate research suggests a mechanical barrier compromise to the corneal epithelium through damaged intercellular junctions during long-term orthokeratology lens wear.¹⁹ Perhaps structural changes to the cornea with orthokeratology lens use may increase the risk of microbial keratitis.

A limitation of this case series is the small sample size limiting inferential statistics; however, published reports of AK in minors using orthokeratology are insufficient, suggesting this lower level of evidence may be appropriate. Moreover, as AK is a rare disease and orthokeratology lens is an uncommon exposure, epidemiologic study designs are limited. To this point and to the best of our knowledge, this cases series including 47 cases of AK in minors is the largest-ever case series of AK in minors, and the only one to assess the proportion of orthokeratology lens use within.

Our findings are important when taken in the context of an international concern regarding myopia progression,^{1,2} and the frequency with which orthokeratology is recommended in minors to halt myopia progression. Avoiding overnight lens use, a well-known risk factor for microbial keratitis,²⁰ is likely prudent when considering the millions of minors on an international scale who may undergo treatment to halt myopia progression, even if the reduction in risk is small. One possible alternative lens option for prevention of myopia progression is a daily disposable soft multifocal lens with similar optical profiles as orthokeratology, such as those under investigation in the NIH/NEI-funded Bifocal Lenses in Nearsighted Kids (BLINK) study.²¹ Though younger age is a risk factor for non-compliance,^{22,23} reduction of risk with daily disposables has been suggested due to the reduced care requirements of this lens type.²⁴ Daily disposable contact lens use is associated with a low risk of microbial keratitis;²⁴ however, no study has specifically focused on the risk of AK in minors wearing daily disposable lenses, and further studies to assess the incidence of AK in minors are necessary.

In conclusion, we report 6 cases of AK in minors with orthokeratology lens use, representing 13% of all AK cases in minors with contact lens use at our tertiary care referral center. To be clear, the proportion of AK cases in orthokeratology patients exceeds the expected proportion of AK cases based on orthokeratology market penetrance alone. In the context of a myopia epidemic and concerns regarding halting myopia progression, caution should be exercised when selecting appropriate treatment options to minimize microbial risk in minors. A future well-designed case-control study may further assist in evaluating the relationship between AK and different contact lens modalities.

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Table 1:

Orthokeratology vs. non-orthokeratology demographic distribution

	Total	Non-OK	OK
Mean age	15	15	15
Race	n (%)	n (%)	n (%)
White	30 (63.8)	29 (70.7)	1 (16.6)
Black	1 (2.1)	1 (2.4)	0 (0)
Hispanic	5 (10.6)	5 (12.2)	0 (0)
Asian	4 (8.5)	1 (2.4)	3 (50)
Other/Unavailable	7 (14.8)	5 (12.2)	2 (33.3)
Gender			
Male	21 (44.7)	19 (46.3)	2 (33.3)
Female	26 (55.3)	22 (53.6)	4 (66.6)
Solution			
Clearcare	4	3	1
Renu	3	3	0
Opti-free	4	4	0
AMO Complete	4	4	0
Generic	2	2	0
Multiple	3	3	0
Other	1	1	0
City water	2	1	1
Unknown	24	20	4

Table 2:Orthokeratology cases with confirmed *Acanthamoeba* keratitis

N	Year ¹	Age ²	Gender	Race	Eye ³	Onset ⁴	Solution	Confocal ⁵	Culture
1	2004	17	F	White	OD	2	Unknown	(+)	(+)
2	2009	16	M	Asian	OS	5	Unknown	(+)	(+)
3	2014	15	F	Other	OD	9	ClearCare	.	(+)
4	2016	14	F	Unavailable	OD	3	Unknown	(+)	(-)
5	2016	16	F	Asian	OU	25	Tap water	.	(+)
6	2016	12	M	Asian	OS	3	Unknown	.	(-)

¹Year at presentation;²Age at presentation;³Eye affected;⁴Time since onset of symptoms (weeks) prior to presentation at UIC;⁵Confocal microscopy