The safety of orthokeratology contact lens wear in slowing the axial elongation of the eye in children

Jacinto Santodomingo-Rubido,[1] Sin-Wan Cheung,[2] César Villa-Collar[3] and the ROMIO/MCOS/TO-SEE Groups

E-mail: j.santodomingo@menicon.com

Financial disclosure: JS-R is a full-time employee of Menicon Co. Ltd

1. Global R&D, Menicon Co., Ltd, Nagoya, Japan ; 2. School of Optometry, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong, China ; 3. Optics & Optometry Department, Faculty of Health Sciences, Universidad Europea, Madrid, Spain

Purpose

Although many studies have documented the efficacy of orthokeratology in slowing myopia progression, fewer studies have assessed the safety of this modality of contact lens wear. As orthokeratology contact lenses are commonly used for slowing myopia progression, it is important that eye care practitioners are better informed about the safety issues that might be encountered when orthokeratology lenses are prescribed for slowing myopia progression to myopic children. This study pooled safety data from three prospective clinical trials to assess differences in incidence rates of adverse events and slitlamp findings between myopic children wearing orthokeratology lenses and distance, single-vision spectacles over a 2-year period.[1-3]

Methods

- Safety data from three prospective studies, which evaluated the use of orthokeratology for slowing myopia progression in children in comparison to a parallel control group of single-vision spectacle lens wearers over a 2-year period, were pooled together for analysis. The primary and secondary safety endpoints are the comparisons of adverse events and slit-lamp findings grades ≥ 2 between orthokeratology and control groups, respectively.

Classification Symptomatology	Serious Symptomatic	Significant Commonly symptomatic	Non-significant Asymptomatic
Description	An adverse event that produces or has the potential to produce significant visual impairment and might warrant permanent discontinuation from lens wear	An adverse event of sufficient clinical concern to warrant clinical intervention and perhaps temporal discontinuation from lens wear	An adverse event which is of no immediate clinical concern and does not warrant discontinuation from lens wear
Condition	Presumed Microbial keratitis /infectious corneal ulcer Permanent decrease of ≥ 2 lines of BCVA Central or paracentral corneal opacity Corneal warpage Epithelial wrinkling Hypopyon Penetration of Bowman's membrane neovascularization within the central 6 mm of the cornea Persistent epithelial defect Corneal abrasion requiring medical intervention Uveitis Endophthalmitis Hyphaema Iritis	Peripheral non-infectious corneal ulcers/scars Symptomatic corneal infiltrative events Corneal scarring Corneal abrasion requiring no medical intervention Corneal staining ≥ grade 3 Corneal neovascularization ≥ grade 2 Any temporary loss of ≥ 2 lines of BCVA (for ≥ 2 weeks) Any event which necessitates temporary lens discontinuation ≥ 2 weeks	Asymptomatic corneal infiltrative events Deep stromal opacities Localized allergic reaction Corneal white lines Corneal epithelial iron lines Corneal staining ≥ grade 2 Disorders of the eyelids and lashes (e.g., blepharitis, meibomitis, hordeolum) Conjunctivitis

Table 1. Adverse events classification. BSCVA, best-corrected visual acuity.

- Subjects who discontinued the study were further classified as adverse and non-adverse dropouts. Adverse dropout refers to subjects who did not complete the study because of an adverse event. All adverse events, whether they occurred in subjects who completed or discontinued the study, were recorded and classified into serious, significant or non-significant according to Table 1 using previously reported methodology, which is based largely upon ISO11980:2012: Contact Lens and Lens Care Products – Guidance for Clinical Investigations.
- Recurrences of the same adverse event(s) in the same or fellow eye at any of the subsequent study visits were classified as separate events; bilateral events of the same condition were counted as independent events. Patient-years of lens wear was calculated for each individual subject from the time of dispensing to the time of discontinuation or completion of the 2-year visit. No discounting was performed for temporary discontinuation of lens wear during the trials. The crude incidence of adverse events was calculated per 100 patient years of lens wear (i.e., [total number of events/number of patient-years of wear]*100), and the 95% confidence intervals were calculated.

Results

Collectively, the three studies enrolled 125 orthokeratology and 118 control subjects. Of these, 101 (81%) and 88 (75%) orthokeratology and control subjects completed the 2-year follow-up period, respectively. As such, 24 and 30 subjects from each group discontinued the study. The overall pooled retention rate was 77.8%. No significant differences were found between groups in the number subjects that discontinued or completed vs. the total number of subjects collectively enrolled in the three studies (both p>0.05). No significant differences were found between groups in any of the baseline demographics (Table 2).

	Orthokeratology N=101	Control N=88	Statistical significance (p-value)
Age (years)	9.12 ± 1.36	9.16 ± 1.43	0.973
Male/female ratio	51/50	43/45	0.823
Ethnicity ratio (HK/WE)	72/29	64/24	0.826
MSE (D)	-2.70 ± 1.20	-2.55 ± 1.06	0.723
Axial length (mm)	24.43 ± 0.79	24.29 ± 0.92	0.256

Table 2. Baseline demographics of subjects who completed the 2-year follow-up period. N, number of subjects; MSE, mean spherical refractive error; D, dioptres; HK, Hong Kong Chinese; WE, White European. Variables are expressed as mean ± standard deviation.

Adverse events

Time (months)	Orthokeratology	Control
0 to ≤ 1	1 Corneal abrasion 2 Corneal staining	-
>1 to ≤ 3	2 Papillary conjunctivitis	-
> 3 to ≤ 6	1 Peripheral non-infectious CU*ʒ	1 Recurrent ocular inflammation ʒ
> 6 to ≤ 12	3 Corneal abrasion 1 Corneal abrasion* 2 Blepharitis 2 Bacterial conjunctivitis 1 Hordeolum	
> 12 to ≤ 18	1 Conjunctival staining 1 Corneal abrasion 1 Corneal neovascularization* 1 Hordeolum*ʒ 1 Papillary conjunctivitis* 1 Dimple veiling	-
> 18 to 24	1 Symptomatic CIE 3 Rhinitisʒʒ 2 Conjunctival hyperemiaʒʒ 1 Chalazionʒʒ	-
Total	28 (6 significant*)	1 (1 significant*)

Table 3. Type and timeline of adverse events for both subjects who completed and discontinued the study. , female; , male; CU, corneal ulcer; CIE, corneal infiltrative event; *significant adverse events; ʒrequired temporary contact lens wear discontinuation (≥ 2 weeks); ʒʒrequired permanent contact lens wear discontinuation (i.e., adverse dropout).

Of the 24 orthokeratology and 30 control subjects that discontinued the study, 19 and 29 were non-adverse dropouts, respectively thus leaving 5 and 1 adverse dropouts, respectively. Nineteen orthokeratology subjects experienced 28 adverse events, of which 6 were significant, whereas just one adverse event was found in the control group; this difference was statistically significant (p<0.001) (Table 3). Most adverse events found in the orthokeratology group were corneal in nature, primarily corneal abrasion/staining, accounting for around 40% of all and device-related adverse events. Of the 28 adverse events, only 18 (3 significant) are likely to be contact lens-related, leading to incidence rates of total and device-related adverse events per 100 patient years of lens wear (95% confidence intervals) of 13.1 (9.2–18.2) and 8.4 (5.4–10.7), respectively (Table 4).

Type of adverse event	All events: N = 28 (6 significant)	Likely to be CL-related: N = 18 (4 significant)
Serious	0.0 (0.0 – 1.8)	0.0 (0.0 – 1.8)
Significant	2.8 (1.3 – 6.0)	1.9 (0.7 – 4.7)
Non-significant	10.3 (6.9 – 15.1)	6.5 (3.9 – 7.2)
Total	13.1 (9.2 – 18.2)	8.4 (5.4 – 10.7)

Table 4. Crude incidence rates of adverse events per 100 patient years of lens wear (95% confidence intervals) found with orthokeratology lens wear for all events and for those likely to be contact lens (CL)-related.

Slit-lamp findings

	Orthokeratology (N=1000)	Control (N=204)	Statistical significance (p-value)
	n (%)	n (%)	
Corneal staining extent ≥ Grade 2	0 (0.0)ª	0 (0.0)	P=1.000
Corneal staining depth ≥ Grade 2	2 (0.2)ª	0 (0.0)	P=0.566
Limbal Injection ≥ Grade 2	0 (0.0)	0 (0.0)	P=1.000
Bulbar conjunctival injection ≥ Grade 2	2 (0.2)	2 (1.0)	P=0.079
Palpebral conjunctival injection ≥ Grade 2	15 (1.5)	9 (4.4)	P=0.008
Palpebral conjunctival papillae ≥ Grade 2	112 (11.2)	12 (5.8)	P=0.037
Palpebral conjunctival follicles ≥ Grade 2	21 (2.1)	4 (2.0)	P=0.901
All ≥ Grade	152 (15.2)	27 (13.2)	P=0.534

A greater number of grade ≥ 2 of palpebral conjunctival injection was found in the control group in comparison with the orthokeratology group (p=0.008), whereas a greater number of grade ≥ 2 of palpebral conjunctival papillae was found in the orthokeratology group in comparison with the control group (p=0.037). However, no significant differences were found between groups in the total number of silt-lamps findings with grades ≥ 2 (p=0. 534) (Table 5).

Table 5. Number of slit-lamp findings (n) found across all study visits (N) in both the orthokeratology and control groups. % = (n/N)*(100).

Discussion/Conclusions

This study informs eye care practitioners as to safety issues that might be encountered when orthokeratology lenses are prescribed for slowing myopia progression to myopic children. More specifically, around 20% of orthokeratology lens wearers are likely to discontinue lens wear primarily because of lens fitting issues, principally under-response to treatment and poor lens centration. Between 10 and 20% of eyes wearing these lenses are likely to experience adverse events over one year of lens wear, with this figure going below 10% when considering device-related adverse events alone. Most importantly, most adverse events were non-significant and resolve successfully with no cases of any loss of best-corrected visual acuity. No significant differences were found between groups in the total number of slit-lamp finding, and those with grade ≥ 2 were relatively rare affecting 15% and 13% of the orthokeratology and control groups, respectively. These results support overnight orthokeratology as a relatively safe option for myopia management in children.

References

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