Evaluation of the Meibomian Glands Using the Tear Interferometer Wearing Orthokeratology Lenses

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Research Article

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Abstract

Background : To investigate the impact of orthokeratology wear on meibomian glands in Korean pediatric population using the tear interferometer.

Methods : Fifty-three orthokeratology wearers and 79 non-lens wearers were evaluated using the LipiView® II ocular surface interferometer which shows incomplete blink rate, average lipid layer thickness, and meiboscores.

Results : No significant differences in the incomplete blink rate and meiboscores for upper eyelids, but the lipid layer thickness and meiboscores for lower eyelids were significantly higher in the Ortho-K group than in the control group ($p = 0.024$ and 0.007 , respectively). Correlation analysis showed no significant correlation between the duration of orthokeratology wear and the parameters measured by LipiView® ($p > 0.05$ for all). Among subgroups based on average duration of lens wear, the longer duration (≥ 24 months) subgroup showed higher meiboscores of lower eyelids ($p = 0.011$), but no other significant differences.

Conclusions : Ortho-K wearers showed no significant differences in the incomplete blink rate and meiboscores of upper eyelids, but they were associated with increased LLT and higher meiboscores of lower eyelids. Thorough examination and close monitoring of orthokeratology wearers is necessary. Prospective and observational studies are needed to further elucidate the relationship between Orthokeratology and meibomian glands.

Background

Orthokeratology (Ortho-K) is a treatment for myopia that uses reverse geometry gas-permeable contact lenses to reshape the corneal contour temporarily. The lenses are worn overnight for flattening the central cornea and reducing myopia, and their effectiveness has been well documented in previous studies^{1–3}. However, there are concerns about the pathologic changes on ocular surface and meibomian glands (MGs) associated with overnight Ortho-K lens wear⁴.

MGs are modified, holocrine, sebaceous glands that are embedded in the tarsal plate⁵ and they secrete meibum into the tears to prevent excessive evaporation of tear fluid. Meibomian gland dysfunction (MGD) is a chronic, (changes in the glandular secretion⁶ and it has attracted attention as a leading cause of dry eye disease^{7,8}. Contact lens wear is one of the potential causes of alteration in MGs, and may result in MGD⁹. Moreover, contact lens wear can decrease corneal sensitivity^{10,11}, affect the blink frequency¹², and induce an allergic reaction from MGs distortion¹³.

The LipiView II Ocular Surface Interferometer (Tear Science Inc. Morrisville, NC, USA) enables us to measure the average of lipid layer thickness (LLT) quantitatively by assessing tear film interference, visualizing the meibomian gland structure and morphologic changes, and assessing blinking patterns of

individuals^{14,15}. We compared the structure (infrared meibography) and function (LLT) of MGs, and the blinking pattern in Korean pediatric population between those wearing Ortho-K lenses and normal controls. Additionally, we evaluated the correlation between the duration of Ortho-K wear, and the meiboscore, LLT, and incomplete blink rate. The aim of the present study is to investigate the impact of orthokeratology wear on meibomian glands in Korean pediatric population using the tear interferometer.

Methods

Methods

1. Subjects

This study is a retrospective review of clinical records conducted at Yeouido St. Mary's Hospital, Seoul, South Korea. This study adhered to the tenets of the Declaration of Helsinki and approval for retrospective review of clinical records was obtained from the Institutional Review Board (IRB) of the Catholic University of Korea (SC21RISI0001, Seoul, South Korea). Written informed consent obtained from parents/legal guardians for study participation was waived by IRB of the Catholic University of Korea (SC21RISI0001, Seoul, South Korea) because of the retrospective nature of the study.

The study included pediatric population aged 7 to 17 years who visited the Yeouido St. Mary's Hospital between September 2018 and December 2020. Subjects with a history of intraocular or eyelid surgery, ocular infectious (viral or bacterial) or inflammatory diseases, giant papillary conjunctivitis (GPC), as well as those diagnosed with dermatologic diseases including pediatric rosacea or allergic diseases and/or taking medications such as antihistamines, were excluded. Patients who showed any signs or symptoms of dry eye disease (DED) or MGD were also excluded.

The control group comprised of subjects who visited the clinic for the prescription of Ortho-K and they did not have a history of lens wear, irrespective of whether they wore glasses. Subjects in the Ortho-K group had been using the lenses for at least 4 months. The final cohort comprised 79 patients of control group and fifty-three patients of Ortho-K group. Right eye of each patients were used in the analysis.

2. Lenses

We prescribed rigid gas-permeable contact lenses with a reverse geometry design (Lucid LK; Lucid Korea, Seoul, South Korea) to all subjects and checked the lens-fitting according to the manufacturer's guidelines. All patients wore the lenses for at least seven continuous hours while sleeping and immediately removed the lenses on awakening. The treatment policy at our lens clinic is that we neither prescribed the lens to the candidate subjects nor discontinued its use in the Ortho-K group participants with symptoms of DED or MGD¹⁶⁻¹⁹. Thorough ophthalmic examination were performed at any time of visits.

3. Data collection

Information of the LipiView II Ocular Surface Interferometer (Tear Science Inc. Morrisville, NC, USA) was used for the evaluation of the lipid layer thickness (μm), and the percentage of incomplete blinks (incomplete blink rate).

Both the upper and lower eyelids were everted and MGs were observed using a noncontact meibography system. Partial or complete loss was scored according to the meiboscores for the upper and lower eyelids from the LipiView images as follows²⁰: 0, no gland dropout; 1, dropout with less than 25% of the loss; 2, dropout with 26% to 50% loss; 3, dropout with 51% to 75% loss; and 4, dropout with more than 75% loss.

4. Statistical Analysis

We used propensity score (PS) weighting to compare between the variables^{21,22}. We assessed the PS between the control and Ortho-K groups, using ordinal logistic regression based on the baseline covariates, including age, BCVA, axial length, and astigmatism. In addition, we used the inverse probability technique (IPTW) to balance the baseline covariates among the two groups during time-to-event analyses using stabilized weights calculated from the PS²³. Comparisons of demographic characteristics (age, gender, BCVA, axial length, and astigmatism) and parameters measured by the LipiView (incomplete blink rate, average lipid layer thickness, and meiboscores of lower and upper eyelids) between the two groups were analyzed using paired t-tests. Pearson's correlation analysis was used to determine the relationship of parameters measured by the LipiView with the duration of Ortho-K lens wear. A p-value of <0.05 was considered statistically significant.

Results

1. Demographic characteristics

In total, 79 eyes were enrolled in the control group and fifty-three eyes in the Ortho-K group (Fig. 1). The mean age of patients in the control and Ortho-K groups was 9.94 ± 1.94 and 9.97 ± 2.05 years, respectively. Detailed demographic characteristics of patients in both groups are presented in Table 1 and Supplementary Table S1.

2. Comparison analysis of meibomian glands

Table 2 and supplementary Table S2 presents the values for the parameters measured by the LipiView for both groups. There were no significant differences in the incomplete blink rate and meiboscores of upper eyelids between the two groups. However, the LLT and meiboscores of lower eyelids were significantly higher in the Ortho-K group than in the control group (p-value = 0.024 and 0.007, respectively).

3. Correlation analysis

The average duration of lens wear in the Ortho-K group was 24 months, with a minimum of 4 months and a maximum of 48 months. The findings of correlation analyses are shown in Table 3 and Figure 2; there

was no significant association of the duration of Ortho-K lens wear with the incomplete blink rate (Fig. 2a: $R^2 = 0.009$; $p=0.499$), average lipid layer thickness (Fig. 2b: $R^2 = 0.04$; $p=0.150$), and meiboscores for the upper and lower eyelids ($p > 0.05$). We subsequently divided the patients in the Ortho-K group according to the average duration of lens wear: long (≥ 24 months) and short (< 24 months). The detailed demographic characteristics of patients in both the groups are summarized in Table 4. Table 5 showed significantly higher lower-eyelid meiboscores in the longer duration subgroup ($p=0.011$), but other parameters did not show significant differences between the longer duration ($n=26$) and shorter duration ($n=27$) groups.

Discussion

The prevalence of myopia in adolescents is increasing worldwide²⁴ and Ortho-K is currently accepted for one of the major interventions for myopia correction in pediatric population which is regarded a safe and effective approach by several studies^{25,26}. So far, many studies have been conducted to investigate the effects of contact lens (CL) wear on MGs structure and function. Arita et al.²⁷ found that CL wear is associated with a decrease in the number of functional MGs while Machalinska et al. and Pucker et al.²⁸⁻³¹ made a conclusion that CL wear does not appear to influence MGs. Alghamdi et al.³² found alterations to MGs morphology and function but it occurred during the first 2 years of CL wear. Depending on inclusion and exclusion criteria, there are some controversies in the conclusion between the studies. And there have been little research related to the overnight wear of reverse geometry contact lens under 18 age so far.

In the current study, the LLT was 67.98 nm in the control group and 76.7 nm in the Ortho-K group; although these values are in the normal range for LLT, they are higher than the average value reported by Zhao et al.³³. It is interesting that average LLT was significantly higher in the Ortho-K group than in the control group even with the decrease in the numbers of MGs of the lower eyelids. It might be the result of true hypersecretion of the meibomian glands, or damming back of secretions in the presence of mild obstruction.⁶ Also, there has been reported a trend that the lipid secretion scores of MGs after wearing Ortho-K were higher than those of the baseline in teenagers with myopia³⁴. Meanwhile, inflammatory mediators may promote subclinical inflammatory changes of MGs and lead to qualitative changes in the composition of meibum³⁵, and contact lens wear is one of the risk factors for ocular surface inflammation³⁶. Mathers and Billborough³⁷ showed thickened meibum and MGs dropout in contact lens associated GPC patients supporting the potential involvement of inflammatory mediators in the pathogenesis of MGD. There were no subjects showing GPC in the study, but long-term follow up studies should be conducted to explore and evaluate the qualitative change of meibum secretion and the presence of GPC, thus suggesting MGs inflammation. Additionally, compensatory mechanism could also be applied in the present study. Previous study suggested that obstruction of the lower eyelid orifice might result in increased lipid secretion in the upper eyelid for the maintenance of homeostasis³⁸.

Contact lens wear may induce mild obstruction of MGs orifice as a result of the aggregation of desquamated epithelial cells at the orifices the glands^{9,39}.

According to Arita et al.²⁷, the meiboscores for contact lens wearers were significantly higher for the upper eyelid; it suggests that the upper eyelid may experience contact lens-mediated irritation of MGs. However, we found higher lower-eyelid meiboscores in Ortho-K group than in control group which is consistent with a previous study showing MGs distortion on the distal aspect of the lower eyelids⁴. One possibility is that these patients may have had subclinical allergic conjunctivitis and distorted MGs before lens wear, with Ortho-K treatment merely aggravating the pre-existing condition and causing further distortion or structural abnormalities in MGs. Wu et al.⁴⁰ found MGs loss occurring in both children and adolescents using a noncontact infrared meibography system even though there were no abnormality of ocular surface parameters. These findings suggest MGs dropout may exist without any history of DED or MGD in pediatric subjects. In addition, Gupta et al.⁴¹ reported relatively high levels of atrophic changes in MGs as a normal variation in the pediatric population. Zhao et al.³³ found only 16 children had no MGs deficiency among the 266 asymptomatic children. Wang et al.⁴² reported an average meiboscore of 0.61 for the control group. Although correlation analysis of pre-IPTW showed no significant association between the duration of Ortho-K wear and lower eyelids meiboscores (Table 3), the meiboscores of lower eyelids showed higher values in the long duration of Ortho-K wear subgroup than short duration after applying IPTW method (Table 5). Future studies should focus on prospective and observational designs to assess the changes and the correlations between the LLT and meiboscores in pediatric population.

This study has several limitations. The retrospective and cross-sectional study design did not provide an explanation for the causal relationship between the use of Ortho-K lens and the changes in MGs morphology and function. The number of subjects was small, and the observation period was relatively short (maximum 48 weeks). A long-term follow-up is required to explore the reversibility of the changes and the differences between the control group and the Ortho-K group. A more detailed analysis according to wearing period is also needed and future studies should focus on a larger sample size. Failure to account for the longitudinal variations of measurements in same subjects can be accredited to the parameters being evaluated once, so prospective studies should analyze the changes over time to strengthen the research. Also, we used subjective and objective ocular surface parameters and tear dynamics including Schirmer test I, tear break-up time, and Oxford scale with 'Pass / Fail grading' for Ortho-K fitting, and detailed values of these parameters were not recorded. Moreover, another limitation was that the children with dry eye may display fewer symptom scores than adults⁴³, and a recent study reported that when applying the Ocular Surface Disease Index to children, there was lower repeatability and it needed more assistance than adults⁴⁴. Consequently, new symptom questionnaires and diagnostic criteria that specifically reflect the characteristics of pediatric patients and are easy for them to understand, should be developed. Use of the LipiView device could facilitate data collection for children with low compliance.

Although the quality of the meibum was not evaluated in this study, further study should examine it with the values of meiboscores to evaluate the mechanical effect of orthokeratology lenses in MGs. The LipiView device was used to assess the “normal” subjects who visited the clinic for the prescription of Ortho-K lenses. This might have introduced a selection bias. Considering the relatively young age of the subjects, they might have shown poor co-operation, thus resulting in an unnatural blinking pattern. The use of infrared video recordings collected by the Keratograph 5M (Oculus, Wetzlar, Germany) might facilitate observing a more natural blinking pattern⁴⁵. Furthermore, the video recordings⁴⁶ could allow the rapid and noninvasive observation of MGs, thus revealing a more detailed relationship between the incomplete blinking rate and Ortho-K lens wear. Future studies should thoroughly examine the detailed location and pattern of findings in meibography with the simultaneous use of multiple recording systems. Lastly, a corneal and external eye specialist graded the images to minimize bias. However, intra-grader and inter-grader variability should be taken into consideration.

Conclusion

In conclusion, Ortho-K wearers showed no significant differences in the incomplete blink rate and meiboscores of upper eyelids, but they were associated with increased LLT and higher meiboscores of lower eyelids. Future prospective and observational studies are needed to evaluate the relationship between Ortho-K wear and the changes in MGs morphology and function, including ocular surface parameters and tear dynamics. Also, thorough examination of the ocular surface and MGs is warranted before prescribing Ortho-K because there were MGs dropout without any history of DED or MGD. Regular follow-up assessment and close monitoring of MGs are also needed to evaluate the changes in the ocular surface in Ortho-K wearers.

Abbreviations

CL : Contact Lens

DED : Dry Eye Disease

GPC : Giant papillary Conjunctivitis

IPTW : Inverse Probability Technique

LLT : Lipid Layer Thickness

MGD : Meibomian Gland Dysfunction

MGs : Meibomian Glands

Ortho-K : Orthokeratology

PS : Propensity Score

Declarations

- Ethics approval and consent to participate

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- Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

- Competing interests

There are no conflicts of interest to declare.

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- Authors' contributions

J.Y.L: Data collection, data analysis, draft of manuscript. G.D.H: Data collection. M.J.H, H.S.K: Critical revision of manuscript. K.D.H : Data validity and statistical analysis and K.S.N : Research design, data analysis, and critical revision of manuscript.

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Tables

Table 1. Demographic characteristics without (Control group) and with (Ortho-K group) orthokeratology treatment in Korean children

	Control group (n = 79)	Ortho-K group (n = 53)	p-value
Age (years)	9.92 ± 1.94	9.97 ± 2.05	0.899
Gender, female (%)	70.26	66.47	0.644
BCVA (logMAR)	0.06 ± 0.1	0.07 ± 0.07	0.897
Axial length (mm)	24.78 ± 1.01	24.67 ± 0.8	0.502
Astigmatism (diopter)	1.42 ± 0.88	1.39 ± 0.71	0.841

Ortho-K, Orthokeratology; BCVA, distance best-corrected visual acuity; logMAR, logarithm of the minimum angle of resolution

Table 2. Parameters measured by the LipiView® II ocular surface interferometer without (Control group) and with (Ortho-K group) orthokeratology treatment in Korean children

	Control group (n = 79)	Ortho-K group (n=53)	p-value
Incomplete blink rate (%)	55.81 ± 31.47	53.54 ± 36.37	0.702
Average lipid layer thickness (μm)	67.98 ± 21.46	76.7 ± 21.93	0.024*
Meiboscores, lower eyelids (0–3)	0.82 ± 0.62	1.15 ± 0.74	0.007*
Meiboscores, upper eyelids (0–3)	0.45 ± 0.6	0.62 ± 0.63	0.116

* Statistically significant

Ortho-K, Orthokeratology;

Table 3. Correlation of the duration of orthokeratology (Ortho-K) lens wear with the incomplete blink rate, lipid layer thickness, and meiboscores in Korean children

	Pearson's correlation	p-value
Incomplete blink rate (%)	0.0949	0.499
Average lipid layer thickness (μm)	0.2004	0.150
Meiboscores, lower eyelids (0–3)	0.1685	0.228
Meiboscores, upper eyelids (0–3)	-0.2131	0.126

Table 4. Demographic characteristics according to the duration of orthokeratology (Ortho-K) lens wear in Korean children

	Short duration [#] (n = 27)	Long duration [#] (n = 26)	p-value
Age (years)	12.05 ± 3.51	11.15 ± 1.93	0.249
Gender, female (%)	82.33	84.81	0.805
BCVA (logMAR)	0.06 ± 0.07	0.06 ± 0.05	0.979
Axial length (mm)	25.09 ± 0.92	24.98 ± 0.67	0.593
Astigmatism (diopter)	1.34 ± 0.61	1.35 ± 0.82	0.964

: Short duration(<24 months)/ Long duration(≥24 months)

Ortho-K, Orthokeratology; BCVA, distance best-corrected visual acuity; logMAR, logarithm of the minimum angle of resolution

Table 5. Incomplete blink rate, lipid layer thickness, and meiboscores according to the duration of orthokeratology (Ortho-K) lens wear in Korean children

	Short duration (n = 27)	Long duration (n = 26)	p-value
Incomplete blink rate (%)	57.44 ± 41.99	54.26 ± 32.24	0.755
Average lipid layer thickness (μm)	79 ± 26.09	83.54 ± 19.19	0.468
Meiboscores, lower eyelids (0–3)	0.81 ± 0.78	1.38 ± 0.79	0.011*
Meiboscores, upper eyelids (0–3)	0.7 ± 0.71	0.55 ± 0.69	0.437

Figures

Figure 1

Representative cases involving children examined by the LipiView® ocular surface interferometer without (candidate group) and with orthokeratology lens wear (Ortho-K group) (a) Images for a 14-year old girl from the control group. The average lipid layer thicknesses in the right and left eyes of the girl were 92 and 97 nm, respectively. In addition, she did not show any signs of MGs loss in the upper and lower eyelids. (b) Images for a 10-year old boy from the Ortho-K group. He showed average lipid layer thicknesses of 59 and 55 nm in the right and left eyes, respectively, with corresponding incomplete blinking rates of 100% and 25%. A 25% MGs loss was noted in the distal portion of the upper and lower eyelids.

Figure 2

Association of the duration of orthokeratology lens wear with the rate of incomplete blinking (a) and average lipid layer thickness (b) in children. No significant associations are observed.

Supplementary Files

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- [SupplementarytableS1.docx](#)
- [SupplementarytableS2.docx](#)