Corneal Epithelium Remodelling After Eye Rubbing Discontinuation in Pediatric Allergic Patients

Alterações Epiteliais da Córnea Após Descontinuação de Coçar os Olhos em Crianças Atópicas

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ABSTRACT

INTRODUCTION: Our purpose was to evaluate the effect of eye rubbing discontinuation on the epithelial thickness profile by spectral-domain AS-OCT (anterior segment optical coherence tomography) in allergic children with no tomographic sign of corneal ectasia.

METHODS: Right-handed boys (average age 11.2 years, 8-12 years) with history of eye rubbing and relatively normal Pentacam (Oculus; Wetzlar, Germany) exams were recruited for the study. Patients were evaluated using AS-OCT (Zeiss Cirrus 5000 HD-OCT, Carl Zeiss Meditec, Dublin, CA, USA) at the baseline and after 8 weeks of treatment. Treatment included education to avoid eye rubbing and preservative free 0.25 mg/mL topical ketotifen. Epithelial thickness (ET) and full corneal thickness (CT) parameters were compared with paired non-parametric Wilcoxon (signed-ranked) test. A *p*-value lower than 0.05 was considered for statistical significance.

RESULTS: Twenty-five boys completed the protocol. No eyes had tomographic criteria for keratoconus (Belin-Ambrosio Deviation Value < 1.22). Minimum epithelial location moved from the inferotemporal to superotemporal octant after treatment. The differences between minimum and maximum epithelial thickness (-2.8 µm vs -5.2 µm; $p<0.01$) and between nasal and temporal octants (N-T) (3.1 µm *vs* 1.4 µm; $p<0.01$) were higher at the baseline. The difference between inferior and superior (I-S) octants (1.1 µm *vs* 2.7 µm; $p<0.01$) was lower at the baseline.

CONCLUSION: AS-OCT analyses reveal epithelial remodeling after allergy treatment and eye rubbing discontinuation, with marked inferotemporal thickening. The importance of educating against eye rubbing and treating allergy should consider its importance on corneal epithelial remodeling. Further studies should include patients with corneal ectatic conditions and to explore other clinical measurements such as biomechanical assessment.

KEYWORDS: Child; Corneal Topography; Epithelium, Corneal; Keratoconus/etiology; Massage; Tomography, Optical Coherence.

RESUMO

INTRODUÇÃO: O nosso objetivo foi fazer a avaliação do efeito de parar de coçar os olhos no perfil epitelial da córnea através de análise com tomografia de coerância ótica do segmento anterior (AS-OCT) em crianças atópicas sem sinais tomográficos de ectasia.

MÉTODOS: Rapazes dextros (idade média 11,2 anos) com hábito de coçar os olhos e tomografia de córnea (Pentacam, Oculus; Wetzlar, Germanh) sem alterações foram incluídos. Foi realizado AS-OCT (Zeiss Cirrus 5000 HD-OCT, Carl Zeiss Meditec, Dublin, CA, USA) na baseline e após 8 semanas de tratamento com cetotifeno tópico sem conservantes (0,25 mg/mL). A espessura epitelial e a espessura total da córnea foram comparadas através de testes não paramétricos emparelhados de Wilcoxon. Um *p*-value inferior a 0,05 foi considerado estatisticamente significativo.

RESULTADOS: Vinte e cinco rapazes completaram o estudo. Nenhum olho apresentou critérios tomográficos de ectasia (Belin-Ambrosio *Deviation Value* < 1,22). A espessura epitelial mínima deslocou-se da região inferotemporal para a região inferotemporal após o tratamento. As diferenças entre a espessura epitelial minima e máxima (-2,8 µm *vs* -5,2 µm; *p*<0,01) e entre as regiões nasal e temporal (N-T) (3,1 µm *vs* 1.4 µm; *p*<0,01) foram superiores na baseline. A diferença entre as regiões inferior e superior (I-S) (1,1 µm *vs* 2,7 µm; *p*<0,01) foi inferior na baseline.

CONCLUSÃO: A análise do epitélio da córnea atráves de OCT do segmento anterior revelou um espessamento inferotemporal após tratamento antialérgico e consequente descontinuação do ato de coçar os olhos. Estes resultados parecem ilustrar o dano deste ato repetido sobre a córnea e salientam a importância de educação da população acerca dos riscos associados ao mesmo.

PALAVRAS-CHAVE: Córnea; Criança; Epitélio de Córnea; Massagem; Queratocone; Tomografia de Coerência Óptica; Topografia da Córnea.

INTRODUCTION

Keratoconus is the most common corneal ectasia worldwide.[1] It is characterized by focal corneal steepening and thinning. Patients usually present with decreased visual acuity due to irregular astigmatism. Its onset usually occurs in early adolescence, and its progression goes until the fourth decade.

KC results from genetic and environmental interactions. There are identified risk factors for its development, such as family history, eye rubbing, allergy, and asthma.[1-5] Family history of KC has been identified as the strongest risk factor and some genetic alterations have been already identified.[1] However, according to some authors, eye rubbing is considered the most important risk factor for KC development with an odds ratio between 3.35 and 10.31.[1,3,4]

Repeated mechanical trauma due to eye rubbing has been intensely associated with KC development and progression. Gatinel described eye rubbing as a sine qua noncondition for KC development.[5] As such, eye rubbing became a major concern in ophthalmology. In 2015, the Global Consensus on Keratoconus and Ectatic Diseases recognized 'not rubbing the eyes' as one of the most important measures in KC.[6] Ambrosio created a public awareness campaign called Violet June to educate the population about the risks associated with eye rubbing.[7]

Corneal epithelial thickness analyses have raising interest in many ocular diseases such as KC. Reinstein *et al* described that epithelial thinning at the apical conic area with surrounding thickening (doughnut pattern) is an important manifestation in the earliest stages and improved sensitivity and specificity in conjunction with tomography.[8–10] Epithelial thickness changes may be the first morphological alterations detected in keratoconus and KC could be accurately detected based only on epithelial thickness analysis from its early stages.[8,11,12] Anterior segment optical coherence tomography (AS-OCT) provides high-resolution images of the cornea and enables reliable and reproducible epithelial thickness measurement.[13–15]

Our group previously demonstrated inferotemporal epithelial thinning in eye rubbers, which was more pronounced in the dominant-hand side. This study aimed to evaluate allergy treatment and eye rubbing discontinuation on the epithelial thickness profile in the same population.

METHODS

This single-center prospective study included atopic boys between 8 and 12 years of age with eye rubbing history (with the knuckle). Boys with history of corneal pathology, previous ocular surgery or trauma, contact lens wearing, corrected distance visual acuity (CDVA) < 0.1 logMAR, and manifest refractive cylinder of more than 2.00 diopters (D) were excluded. Irregular topography and tomographic parameters using Scheimpflug (Pentacam HR, Oculus Wetzlar, Germany), such as Belin-Ambrosio Deviation Value > 1.22, and positive family history of keratoconus, were exclusion criteria. Boys who had a history of treatment with

artificial tears or anti-histaminic eyedrops over the past six months were also excluded. The study was conducted by the principles of the Declaration of Helsinki, the parents given their written informed consent and approval was obtained from the institutional Research Committee of Hospital Garcia de Orta (Almada, Portugal).

Ophthalmological evaluation included CDVA presented in logMAR, spherical equivalent (SE) from the refraction of the correcting glasses, intraocular pressure (IOP) measured with Goldmann tonometer, biomicroscopy of the anterior segment, and fundoscopy.

Corneal epithelial thickness (ET) and full corneal thickness (CT) were automatically measured by anterior segment spectral-domain Zeiss Cirrus 5000 (Carl Zeiss Meditec, Dublin, CA, USA). The pachymetry map includes eight radial scans (1024 axial scans each) repeated five times. The children were positioned on the headrest, looking to the fixation light so that the scan was centered on the pupil center. Two scans were obtained for each eye by the same examiner with a minute break, and average values were registered.

The software algorithm measures epithelial thickness as the distance between the middle of the first (tear film) and second (anterior surface of the Bowman layer) hyperreflective lines on the B-scan. CT was measured as the distance between the air-tear and cornea-aqueous interfaces.

Data was exported and processed with Cirrus HD-OCT review software (version 10.0) which provides average automated ET of four concentric ring-shaped zones centered on the center of the cornea (central (CET): 0-2 mm, paracentral: 2-5 mm, and mid-peripheral: 5-7 mm). ET and CT were also presented for specific octants of the cornea: superior (S), inferior (I), temporal (T), nasal (N), superonasal (SN), superotemporal (ST), inferotemporal (IT), and inferonasal (IN) within the paracentral and midperipheral zones. The differences between corresponding corneal octants were calculated.

Only the right eyes data were included in statistical analysis. Boys were advised to stop rubbing the eyes and were treated with preservative free 0.25 mg/mL topical ketotifen twice daily for 8 weeks. After treatment, parents were asked about compliance and only the boys who fulfilled the treatment and whose parents ensured they considerably stopped rubbing the eyes were considered for the second evaluation.

Quantitative variables are presented as mean and standard deviation. Continuous variables were checked to meet the normality conditions of the Shapiro-Wilk test. The Wilcoxon test was preformed to compare ET and CT at baseline and after treatment. Correlations were tested using Spearman's correlation coefficient. Statistical significance was set at $p<0.05$ (two-sided). IBM® SPSS® Statistics v23.0 was used.

RESULTS

This study included 30 right-handed atopic boys with an eye rubbing history. Five were excluded because do not stop rubbing their eyes. As such, twenty-five (83.3%) were considered for analysis. The mean age was 11.2 ± 2.1 years (8 – 12 years).

The mean CDVA was 0.006 ± 0.018 logMAR (0 to 0.091 logMAR), the mean SE was -0.44 ± 1.1 D (-2.00 to +2.00 D) and the mean IOP was 13.2 ± 2.1 mmHg (11 to 16 mmHg), with no differences between baseline and after treatment (p=0.89). All eyes had an unremarkable ophthalmological evaluation regarding slit-lamp microscopy, fundoscopy, and no tomographic criteria for corneal ectasia.

The epithelial thickness profiles at baseline and after treatment are presented in Fig.s 1 and 2, respectively. The differences between evaluations are shown in Table 1. There was no statistically significant difference for average

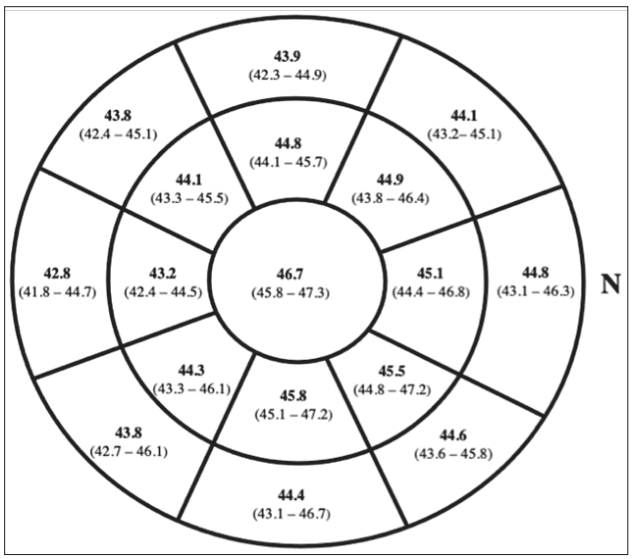

Figure 1. Epithelial thickness (mean, range; μm) mapping at the baseline. N: Nasal.

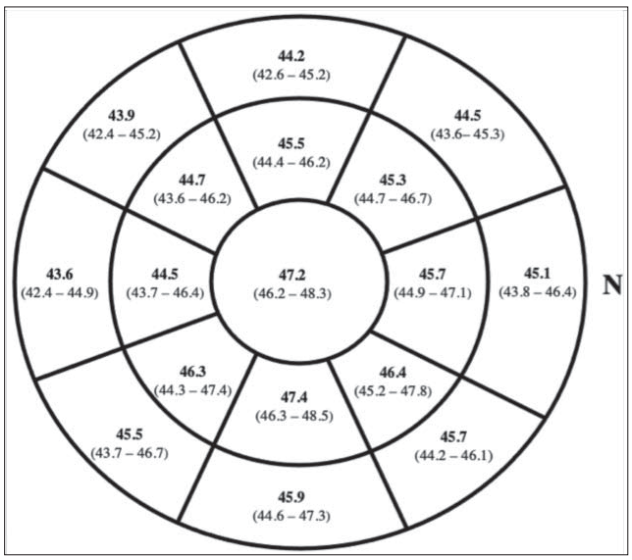

Figure 2. Epithelial thickness (mean, range; μm) mapping after treatment. N: Nasal.

Table 1. Corneal epithelial thickness comparison (mean ± standard deviation, range; µm) between baseline and after treatment.

	Baseline	After treatment	Mean difference	*p*-value
Central				
Mean	46.7 ± 1.1 (45.8 – 47.3)	47.2 ± 0.8 (46.2 – 48.3)	0.5	0.51
Minimum	42.3 ± 3.1 (38.9 – 42.3)	44.5 ± 2.2 (41.4 – 45.1)	2.2	**0.01**
Maximum	49.3 ± 3.5 (47.5 – 52.6)	49.9 ± 3.1 (48.3 – 54.1)	0.6	0.51
Paracentral				
Mean	45.8 ± 2.1 (44.1 – 47.3)	46.6 ± 1.6 (45.2 – 48.6)	0.8	0.33
Minimum	41.3 ± 1.7 (39.2 – 43.1)	43.1 ± 1.5 (42.4 – 43.8)	1.6	**0.03**
Maximum	48.5 ± 1.5 (46.5 – 48.7)	48.6 ± 1.3 (46.2 – 49.8)	0.1	0.89
Superior	44.8 ± 1.2 (44.1 – 45.7)	45.5 ± 1.1 (44.4 – 46.2)	0.7	0.33
Superotemporal	44.1 ± 1.4 (43.3 – 45.4)	44.7 ± 1.5 (42.4 – 46.2)	0.6	0.42
Temporal	43.2 ± 1.1 (42.4 – 44.5)	44.5 ± 1.4 (43.7 – 46.4)	1.3	0.15
Inferotemporal	44.3 ± 1.5 (39.2 – 46.1)	46.3 ± 1.2 (44.3 – 47.4)	2.0	**0.02**
Inferior	45.8 ± 1.3 (45.1 – 47.2)	47.4 ± 1.4 (46.3 – 49.8)	1.6	**0.03**
Inferonasal	45.5 ± 1.6 (44.8 – 48.7)	46.4 ± 1.2 (45.2 – 47.8)	0.9	0.33
Nasal	45.1 ± 1.5 (44.4 – 46.8)	45.7 ± 1.1 (45.2 – 47.8)	0.6	0.51
Superonasal	44.9 ± 1.6 (43.8 – 46.4)	45.3 ± 1.1 (44.7 – 46.7)	0.4	0.66
Midperipheral				
Mean	43.8 ± 1.8 (41.1 – 45.1)	45.1 ± 1.3 (43.9 – 46.7)	1.3	0.15
Minimum	40.6 ± 2.5 (37.6 – 42.3)	42.3 ± 2.3 (39.4 – 44.7)	1.7	**0.03**
Maximum	47.8 ± 2.4 (45.5 – 48.3)	48.8 ± 2.4 (47.4 – 50.1)	1.0	0.13
Superior	43.9 ± 1.6 (42.3 – 44.9)	44.2 ± 1.2 (42.6 – 45.2)	0.3	0.72
Superotemporal	43.8 ± 1.7 (42.4 – 45.1)	43.9 ± 1.4 (39.4 – 45.2)	0.1	0.89
Temporal	42.8 ± 1.5 (41.8 – 44.7)	43.6 ± 1.1 (42.4 – 44.9)	0.8	0.33
Inferotemporal	43.8 ± 1.4 (37.6 – 46.1)	45.5 ± 1.3 (43.7 – 46.7)	1.7	**0.03**
Inferior	44.4 ± 2.1 (43.1 – 46.7)	45.9 ± 1.3 (44.6 – 50.1)	1.5	**0.04**
Inferonasal	44.6 ± 1.3 (43.6 – 48.3)	45.7 ± 1.6 (44.2 – 46.1)	1.1	0.09
Nasal	44.8 ± 1.6 (43.1 – 46.3)	45.1 ± 1.6 (43.8 – 46.4)	0.3	0.71
Superonasal	44.1 ± 1.7 (43.2 – 45.1)	44.5 ± 1.2 (43.6 – 45.3)	0.4	0.66

OD: Right eye; OS: Left eye; S: Superior; ST: Superotemporal; T: Temporal; IT: Inferotemporal; I: Inferior; IN: Inferonasal; N: Nasal; SN: Superonasal.

central epithelial thickness (46.7 ± 1.1 µm *vs* 47.2 ± 0.8 µm, *p*=0.51). Minimum central epithelial thickness was lower at the baseline (42.3 ± 3.1 µm *vs* 44.5 ± 2.2 µm, *p*=0.01). The paracentral minimum (41.3 ± 1.7 µm *vs* 43.1 ± 1.5 µm, *p*=0.03), inferotemporal (44.3 ± 1.5 µm *vs* 46.3 ± 1.2 µm, *p*=0.02) and inferior (45.8 ± 1.3 µm *vs* 47.4 ± 1.4 µm, *p*=0.03) epithelial thicknesses were lower at the baseline. The midperipheral minimum (40.6 ± 2.5 µm *vs* 42.3 ± 2.3 µm, *p*=0.03), inferotemporal (43.8 ± 1.4 µm *vs* 45.5 ± 1.3 µm, *p*=0.03) and inferior (44.4 ± 2.1 µm vs 45.9 ± 1.3 µm, p=0.04) epithelial thicknesses were also lower at the baseline.

At the baseline, minimum epithelial thickness was reg-

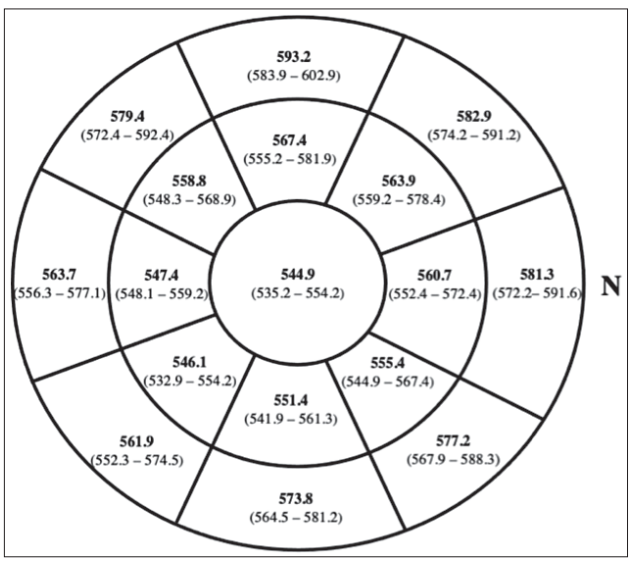

Figure 3. Corneal full thickness (mean, range; µm) at the baseline.

N: Nasal.

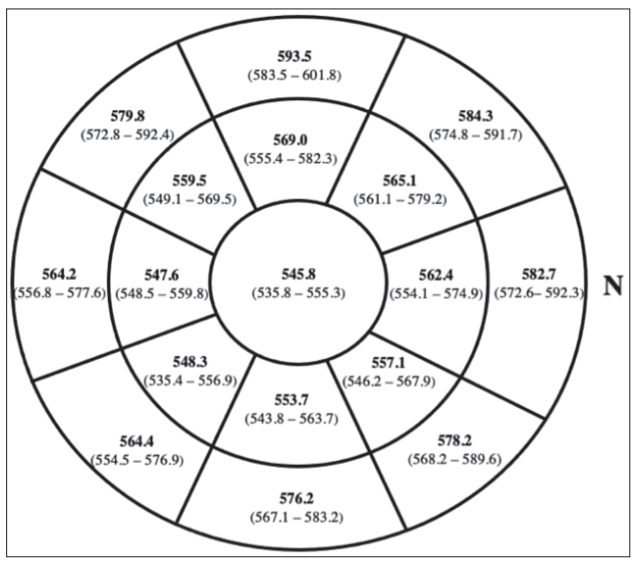

Figure 4. Corneal full thickness (mean, range; µm) after treatment.

N: Nasal.

Table 2. Full corneal thickness (mean ± standard deviation, reange; µm) comparison between baseline and after treatment.

	Baseline	After treatment	Mean difference	*p*-value
Central (OD / OS)				
Mean	544.9 ± 21.2	545.8 ± 20.4	0.9	0.42
Minimum	532.5 ± 28.1	533.5 ± 27.7	1.0	0.42
Maximum	561.1 ± 26.5	561.3 ± 24.2	0.2	0.89
Paracentral (OD / OS)				
Mean	649.3 ± 27.2	651.0 ± 26.7	1.7	0.21
Minimum	542.3 ± 28.3	544.2 ± 26.9	2.1	0.12
Maximum	584.6 ± 29.1	583.4 ± 27.1	1.2	0.42
S	567.4 ± 21.3	569.0 ± 21.5	1.6	0.21
ST	558.8 ± 23.1	559.5 ± 22.1	0.7	0.51
T	547.4 ± 26.5	547.6 ± 23.3	0.2	0.89
IT	546.1 ± 26.7	548.3 ± 26.8	2.2	**0.03**
I	551.4 ± 24.3	553.7 ± 25.1	2.6	**0.02**
IN	555.4 ± 24.4	557.1 ± 23.8	1.7	0.21
N	560.7± 22.6	562.4 ± 23.4	1.7	0.21
SN	563.9 ± 24.6	565.1 ± 22.1	1.2	0.42
Midperipheral (OD / OS)				
Mean	584.3 ± 29.9	586.1 ± 26.2	1.8	0.21
Minimum	559.2 ± 28.1	560.9 ± 26.3	1.7	0.21
Maximum	603.2 ± 28.7	604.4 ± 26.1	1.2	0.42
S	593.2 ± 23.3	593.5 ± 23.7	0.3	0.89
ST	579.4 ± 24.2	579.8 ± 25.2	0.4	0.72
T	563.7 ± 26.2	564.2 ± 25.2	0.5	0.66
IT	561.9 ± 27.9	564.4 ± 29.1	2.5	**0.02**
I	573.8 ± 28.2	576.2 ± 27.1	2.4	**0.02**
IN	577.2 ± 24.2	578.2 ± 23.8	1.0	0.51
N	581.3 ± 24.1	582.7 ± 24.4	1.4	0.33
SN	582.9 ± 24.3	582.7 ± 24.1	0.2	0.89

OD: Right eye; OS: Left eye; S: Superior; ST: Superotemporal; T: Temporal; IT: Inferotemporal; I: Inferior; IN: Inferonasal; N: Nasal; SN: Superonasal.

istered in inferotemporal octant (39.2 µm), and maximum epithelial thickness was registered in the inferonasal area (48.7 µm). After treatment, minimum epithelial thickness was registered in superotemporal octant (42.4 µm), and maximum epithelial thickness was registered in the inferior area (49.). The difference between the minimum and maximum epithelial thicknesses (min-max) was -2.8 µm at the baseline and -5.2 µm after treatment ($p<0.01$)

The corneal full-thickness profiles at baseline and after treatment are presented in Fig.s 3 and 4, respectively. The differences between evaluations are shown in Table 2. There was no statistically significant difference for central corneal thickness (544.9 ± 21.2 µm *vs* 545.8 ± 20.4 µm, $p=0.42$). At the baseline, paracentral CT were lower in inferotemporal (546.1 ± 26.7 µm *vs* 548.3 ± 26.8 µm, $p=0.03$) and inferior (551.4 ± 24.3 µm *vs* 553.7 ± 25.1 µm, $p=0.02$) octants. Midperipheral CT was lower in inferotemporal (561.9 ± 27.9 µm *vs* 564.4 ± 29.1 µm, $p=0.02$) and inferior (573.8 ± 28.2 µm *vs* 576.2 ± 27.1 µm, $p=0.02$) octants, at the baseline. Unlike these areas, there were no statistically significant differences for epithelial thickness in the other octants. Finally, the study did not find any correlations between ET and age ($p=0.89$) and between ET and SE ($p=0.66$).

DISCUSSION

The present study shows the corneal remodeling epithelial thickness after stopping to rub the eyes. Epithelium restores its normal distribution due to inferotemporal thickening.

Eye rubbing has been strongly associated with keratoconus development and progression. It leads to progressive distortion and disorganization of the corneal collagen fibers, impairing corneal biomechanics.[5] Additionally, eye rubbing increases the level of tear-film pro-inflammatory factors (matrix metalloproteinases, interleukin 6, and tumor necrosis factor-alpha), which proved to be relevant in the pathogenesis of KC.[16] As such, children who frequently rub their eyes have been considered to have a higher risk of developing KC.[17–19]

Epithelial thickness analysis could be relevant in many ocular disorders, and epithelial changes may be the first morphological alterations to be detected in keratoconus. VHF digital ultrasound scanning was firstly used by Reinstein to evaluate epithelial thickness profiles and is considered the gold standard for epithelial thickness analysis. Anterior segment optical coherence tomography (AS-OCT) provides high-resolution images of the corneal epithelium with no need of contact or anesthesia and has been placed as an alternative to VHF in clinical practice. AS-OCT has a reproducibility of 0.93 and repeatability of 0.8.[15,20–22] However, AS-OCT measurements include the tear film, which can vary between 2 and 7 µm, and epithelial thickness are expected to be thicker on OCT.[23–25,26]

Analyzing epithelial thickness in tomographically normal corneas could better demonstrate the corneal damage associated with eye rubbing. The cut-off of 1.22 for BAD-D

raises the specificity to select corneas with no ectasia, even fruste forms.[27,28] Moreover, children between 8 and 12 years have less probability of having stromal damage due to less cumulative stress. Additionally, we included children who preferably rub the eyes with the knuckle as we believe it may better reflect the impact of eye rubbing in cornea, according to Hafezi *et al*, who have demonstrated that rubbing with knuckle (proximal interphalangeal joint) applies more force on the eyelids than rubbing with a fingernail or with the fingertip.[29]

Corneal epithelial thickness pattern in healthy children was elucidated in our previous paper.[30] Later, we have demonstrated that inferotemporal area is the most prone to eye rubbing damage, precisely where the majority of keratoconus are found. Additionally, there was a positive influence of hand dominance with lower epithelial thickness reported in hand-dominant side.[31] As such, we only included right eyes of right-handed children, which more intensely reflect the damage. Comparing with normal age-match children, eye rubbers had lower epithelial thickness in inferior (45.8 ± 1.3 µm *vs* 47.7 ± 1.1 µm), temporal (43.2 ± 1.1 µm *vs* 45.9 ± 1.1 µm) and inferotemporal (43.3 ± 1.5 µm *vs* 46.8 ± 1.2 µm) octants. Moreover, eye rubbers epithelial thickness pattern differed from the normative one due to inferior and temporal thinning. The paracentral thinnest point was lower (39.2 µm *vs* 42.9 µm) and moved from its normal location in superotemporal to inferotemporal octant. The difference between the minimum and maximum epithelial thickness were lower in eye rubbers (-2.8 µm *vs* -7.2 µm) due to global thinning in inferior areas, where the epithelium is usually thicker. Inferotemporal thinning was reflected in lower I-S (1.1 µm *vs* 3.3 µm) and higher N-T (3.1 µm *vs* 0.7 µm) comparing with age match-controls. The IN-ST (1.5 µm *vs* 2.1 µm) and IT-SN (-0.1 µm *vs* 0.6 µm) differences were not significantly different than normative database.

Children were re-evaluated after eight weeks of treatment according to the average time for resolution of rigid gas-permeable contact-lens corneal warpage.[32] Corneal epithelial mapping recovered its normal pattern due to inferotemporal thickening. The paracentral central thinnest point was thicker than baseline evaluation (39.2 µm *vs* 42.4 µm) and returned to its normal position, in superotemporal octant. The min-max became more physiological (-2.8 µm *vs* -5.2 µm, $p<0.01$), as the I-S (1.1 µm *vs* 2.7 µm, $p<0.01$) and N-T (3.1 µm *vs* 1.4 µm, $p<0.01$).

Corneal full-thickness profile followed epithelial thickness changes. Inferior and inferotemporal areas thickened after the treatment. Despite acknowledging that compensatory epithelial changes occur in response to stromal irregularities, we believe these results only reflect epithelial damage and may represent the very early stage of KC pathogenesis, with no actual stromal damage.[12,33–37]

Limitations of our study are the small sample and the fact that we only included boys. However, we prefer not to include girls due to known gender-based ET variations, which could bias our results. Moreover, we recognize that it is extremely difficult to stop rubbing the eyes and we cannot ensure that every child stopped. Additionally, eye rubbing stop also decreases the levels of pro-inflammatory cytokines, which, in turn, softens the epithelial damage and could alter epithelial thickness profile. At last, we recognize device-related limitations. Cirrus OCT tends measuring epithelial thickness 5-6 µm thinner than the other devices due to the refractive index used for the measurements. Rather than considering the absolute thickness values as accurate, the main findings of this study are related to the change in epithelial thickness due to eye rubbing, so these differences can be translated to apply to epithelial measurements with other devices.

Despite this, we believe our results demonstrate the effect of eye rubbing in the corneal epithelium and support the theories regarding the negative impact of rubbing. Moreover, our results could help elucidate the pathogenesis of keratoconus and highlight the importance of children's children's education to not rub the eyes.

CONCLUSION

Anterior segment optical coherence tomography analyses reveal epithelial remodeling associated with eye rubbing in tomographically normal corneas. Corneal epithelium recovers its normal distribution after stopping to rub the eyes due to inferotemporal epithelium thickening. Our results demonstrate the dangers of eye rubbing and highlight the importance of educating patients not to rub their eyes. Further work is needed to elucidate the effect of eye rubbing in the corneal epithelium in keratoconus cases.

RESPONSABILIDADES ÉTICAS

Conflitos de Interesse: Dr Renato Ambrósio Jr é consultor de: Oculus, Alcon, Zeiss, Essilor, Genom, Mediphacos. Os restantes autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

Fontes de Financiamento: Não existiram fontes externas de financiamento para a realização deste artigo.

Confidencialidade dos Dados: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.

Proteção de Pessoas e Animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pelos responsáveis da Comissão de Investigação Clínica e Ética e de acordo com a Declaração de Helsínquia revista em 2013 e da Associação Médica Mundial.

Proveniência e Revisão por Pares: Não comissionado; revisão externa por pares.

ETHICAL DISCLOSURES

Conflicts of Interest: Dr Renato Ambrósio Jr is a consultant for Oculus, Alcon, Zeiss, Essilor, Genom, Mediphacos.

The remaining authors have no financial or proprietary interest in the materials presented herein.

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