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Optical densitometric measurements of the cornea and lens in children with allergic rhinoconjunctivitis

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Background: Our aim was to investigate the impact of allergic rhinoconjunctivitis on corneal and lenticular optical densitometry, pachymetry and anterior chamber depth in children.
Methods: Fifty-four patients who had allergic rhinoconjunctivitis (study group) and 54 age-matched healthy children (control group) were recruited in this cross-sectional and comparative study. Corneal and lenticular optical densitometry, pachymetry, corneal volume and anterior chamber depth measurements were taken with the Scheimpflug imaging system.
Results: The lens density and anterior chamber depth were similar between the groups ($p > 0.05$), while corneal density and thickness were significantly higher in the study group ($p < 0.05$). Although the corneal volume was higher in children with allergic rhinoconjunctivitis, the difference was not statistically significant ($p = 0.07$).
Conclusions: The cornea is affected in allergic rhinoconjunctivitis in respect to optical density and thickness, while the anterior chamber and lens are not influenced.

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Allergic rhinoconjunctivitis (ARC) is a common disorder in children, characterised by nasal and ocular congestion, discharge and itching.[1] Allergic rhinoconjunctivitis has seasonal/intermittent and perennial/persistent forms. It has a predilection for male gender[2] and is induced by immunoglobulin E (IgE) and T-cell mediated inflammation of the nasal and ocular surface membranes caused by exposure to airborne allergens.[3] Allergic rhinoconjunctivitis is not a significant health problem but it is related to important morbidity, including annoying physical symptoms, decreased quality of life and economic burden.[4–6]

General complaints such as fatigue and cough may be seen in ARC,[1] while children with the condition have twice the likelihood of a history of asthma, eczema and chronic sinusitis compared to healthy children.[1,7] The ocular findings of ARC are conjunctivitis, chemosis and darkening of the lower eyelids due to vasodilation and congestion.[6,8] Allergic rhinoconjunctivitis is usually self-limited without severe ocular surface damage.[8] In severe cases of ocular allergies, the cornea is affected.[9] Allergy is also independently associated with cataract formation;[10] however, it is not clear whether ARC affects the cornea, anterior chamber or lens.

Severe forms of allergic conjunctivitis, such as vernal conjunctivitis, induce several corneal stromal alterations, including inflammatory cells in the anterior stroma, increased tortuosity of stromal nerves and increased activity of keratocytes.[11] Of course, ARC does not cause harm to the cornea as does vernal conjunctivitis but it is important to establish the level of corneal stromal changes in ARC, as it is a common public health problem worldwide. Moreover, seasonal allergic conjunctivitis, which is a subtype of ARC, is associated with advanced pre-ocular tear film instability that in turn affects the ocular surface.[12] Perennial ARC may also affect the corneal surface by forming punctate epithelial erosions and corneal epithelial defects.[13] It is reasonable to expect corneal stromal changes, such as haze and oedema in association with tear film and corneal epithelial disturbances that exist in allergic rhinoconjunctivitis. We also wondered if ARC could cause structural alterations in the anterior segment.

We performed the Scheimpflug anterior segment imaging (Pentacam HR) to examine ocular structures in ARC. This involves densitometric measurements of the cornea and topographic measurements of the anterior segment. Pentacam HR optic densitometry of the cornea and lens provides objective measurements of corneal haze and lens opacities.[14,15] In the present study, our aim was to investigate the impact of ARC on corneal and lenticular density, corneal thickness and anterior chamber depth. We hypothesised that the inflammatory processes generated by allergic conjunctivitis, eye rubbing due to itchiness in ARC and the medications used for relief may affect the these ocular parameters. To the best of our knowledge, this is the first study related to measurements of corneal volume, density of the lens and anterior chamber depth in children with ARC.

METHODS

In this cross-sectional, comparative and observational study, 54 patients who had ARC (study group: 37 males) and 54 healthy children (control group: 30 males) were recruited. This study was conducted in accordance with the ethics standards of the

Declaration of Helsinki and was approved by the Institutional Ethics Committee.

Study population

The subjects were within the same age range (seven to 14 years) in both groups. Only one eye of each participant was selected randomly for statistical analysis. There were 26 right and 28 left eyes in the study group and 31 right eyes and 23 left eyes in the control group. The diagnosis of ARC was sent to the paediatric allergy division and then the patients were returned to our ophthalmology clinic. Although ARC remains a clinical diagnosis, allergen testing was also performed for the diagnosis. Seasonal and perennial ARC cases were considered eligible for the study. The previous medical history of the patients also helped us to confirm the diagnosis.

The ARC related medication history of the patients included only anti-histaminic drugs (olopatadine or ketotifen). The exclusion criteria were any history of ocular surgery, any systemic disorders and any ocular diseases except for ARC. Patients who had corneal or lenticular abnormalities detected by slitlamp biomicroscopy, contact lens users and participants with blepharitis were excluded. None of the participants were detected with keratoconus or sub-clinical keratoconus. None of the patients in the study group had active disease or symptoms at the time of the ocular examinations. Patients who had ever used steroids by any route of administration (ocular, nasal or systemic) were also excluded. Vernal conjunctivitis cases were excluded, as corneal involvement is common and topical steroids play an important role in the treatment. Participants who had refractive error higher than 3.00 D were excluded. All of the eyes had at least 6/6 visual acuity using the Snellen chart. All participants underwent an ophthalmic examination, including visual acuity assessment, biomicroscopy, air-puff tonometer, indirect retinoscopy and the Pentacam HR (Oculus, Wetzlar, Germany) measurements. Central corneal thickness (CCT), corneal volume (CV), anterior chamber depth (ACD), corneal density (CD) and lens density (LD) were taken with the Pentacam HR.

Cornea and lens optical densitometry measurement techniques

Pentacam HR densitometry is a quantitative measurement of optical density in cornea and lens that is represented in grayscale units. The densitometric values range from zero to 100, indicating increased opacity with increasing value. The examinations were performed by one researcher (GP). Several measurements were taken to ensure one good-quality Scheimpflug image. The images of 90 to 270 degrees were assessed for all the subjects. The corneal densitometric measurements were performed on the central 6.0 mm cornea by areal selection of the stroma. The techniques for the measurement of the density of the lens were as follows: vertical linear, horizontal linear and areal. To provide better visualisation of the lens, the lenticular densitometric examinations were taken following pupillary dilation with tropicamide drops. Figure 1 shows the areal corneal and lenticular densitometric measurement screen of the Pentacam HR. A 1.5 mm vertical line and a 3.0 mm horizontal line at the centre of the lens nucleus were drawn for linear measurements of the density of the lens. For areal measurements, a 1.5 mm (vertical) by 3.0 mm (horizontal) rectangle was drawn. The length and areal size selection for measurements of the density of the cornea and lens were done to maintain standardisation. The Pentacam HR automatically calculated the corneal, linear and areal lens densities.

Statistical analysis

The SPSS 17.0 software for Windows (SPSS Inc, Chicago, Illinois, USA) was used to analyse the outcomes. Values of 'p' lower than 0.05 were accepted as statistically significant. Quantitative variables were reported as mean and standard deviation. Independent samples t-test was used for comparison of the studied parameters between the study and control groups. Pearson correlation analysis was performed to detect correlations between cornea and areal lenticular densitometric measurements

RESULTS

Fifty-four eyes of 54 paediatric patients with ARC and 54 eyes of 54 age-matched healthy participants were examined and compared. Some of the demographical and clinical properties of the subjects are shown in Table 1. The corneal volume and anterior chamber depth were similar between the groups, while the mean central corneal thickness was significantly thicker in the study group. The mean visual acuity was 1.0 in decimal units in both groups ($p = 1.00$).

Table 2 shows the mean corneal and lens densitometric measurements of the subjects. The densities of the lenses were similar in both groups for all the techniques. The mean corneal density was markedly higher in the study group when compared with the control group. There were moderate positive correlations between areal lens density and corneal density both in the study group ($r = 0.38$, $p = 0.01$) and control group ($r = 0.32$, $p = 0.02$).

There were no statistically significant correlations between central corneal thickness and corneal density ($r = -0.18$, $p = 0.06$), as well as for corneal density and corneal volume ($r = -0.18$, $p = 0.06$), when all the participants were analysed but the correlation became stronger when only ARC cases were analysed ($r = -0.28$, $p = 0.05$). There was no association between anterior chamber depth and areal density of the lens for both the study and control groups ($p > 0.05$). As should be expected, there was a positive correlation between age and areal density of the lens ($r = 0.43$, $p < 0.001$). Figure 2 shows the box plot graphics of central corneal thickness, corneal volume and anterior chamber depth for the ARC and control groups.

DISCUSSION

Our results show that corneal densitometric and pachymetric values are increased, whereas the density of the lens and anterior chamber depth remain unchanged in children with ARC compared to healthy controls. As increased corneal optic density means increased corneal haze, we suggest that detailed corneal examination should not be underestimated in ARC. Since it is a chronic disease that has an inflammatory component, children with ARC may be at risk of ocular surface disorders.

Corneal densitometry could provide an objective assessment of corneal transparency and haze.[16–19] Otri and colleagues[17] found that the mean optical densitometric value of normal corneas was 12.3 ± 2.4 in adults, which was similar to our measurements. There was no difference in corneal density between the central zone and the surrounding 6.0 mm annulus but higher values were found at the peripheral 6 to 12 mm zones.[16] Thus, we measured the density of the central 6.0 mm annulus of cornea for standardisation. The higher corneal density in ARC indicates increased haze and decreased corneal transparency but its clinical impact seems not to be very significant in relation to visual acuity.

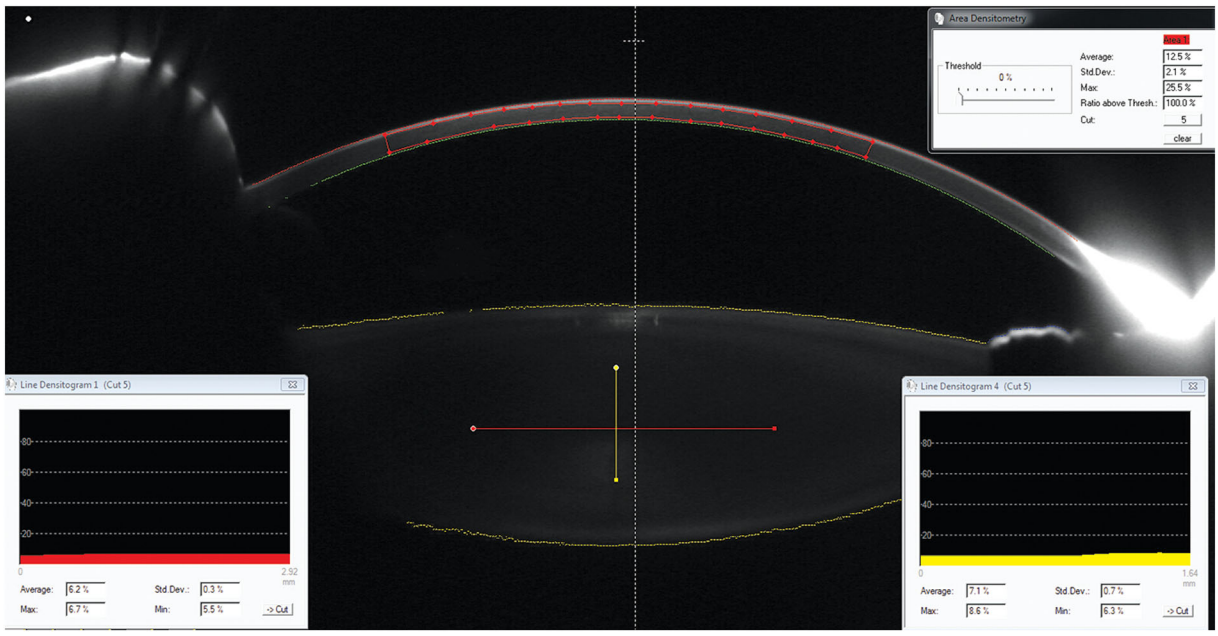

Figure 1. Linear (horizontal and vertical) lens densitometric and areal corneal densitometric measurement screen of Pentacam HR

	Study group	Control group	p
Age (years)	10.4 ± 2.3	10.5 ± 2.3	0.80
CCT (μm)	569.6 ± 32.6	555.0 ± 34.0	0.03
CV (mm^3)	62.8 ± 3.6	61.5 ± 4.0	0.07
ACD (mm)	3.22 ± 0.18	3.16 ± 0.27	0.17

CCT: central corneal thickness, C: corneal volume, ACD: anterior chamber depth

Table 1. Some of the demographic and clinical parameters of the participants

	Study group	Control group	p
LD-horizontal	6.6 ± 0.3	6.5 ± 0.2	0.15
LD-vertical	7.0 ± 0.4	6.9 ± 0.4	0.13
LD-areal	6.4 ± 0.4	6.3 ± 0.3	0.39
CD	12.8 ± 0.9	12.2 ± 0.9	0.002

LD: lens density, CD: corneal density

Table 2. Optic densitometric values for the lens and cornea of the participants in greyscale units

Evaluation and grading of lens opacity is difficult in children, because their lenses seem clear when examined by slitlamp biomicroscopy, but Pentacam HR could provide objective and quantitative data about the lens even in children. It was demonstrated that the intra observer and inter observer repeatability of Pentacam Scheimpflug densitometric measurements of the lenses were high in eyes without cataracts.[20] The present study showed that ARC does not affect the density of the lens nucleus and this result may be interpreted as the disease does not have a cataractogenic impact.

We also compared the measurements of central corneal thickness, corneal volume and anterior chamber depth. The mean corneal volume and anterior chamber depth were similar in both groups, while central corneal thickness was significantly higher in children with ARC. Although ARC is not associated with severe ocular damage, it could change the corneal morphology due to eye rubbing, conjunctival inflammation or preocular tear film instability. Tanaka and colleagues[21] reported that inflammation of the conjunctiva may play a role in the formation of corneal damage in ocular allergies.

Eye rubbing is frequently seen in patients with allergic conjunctivitis.[22] Eye rubbing and ocular allergy are important risk factors for keratoconus.[22] McMonnies[23] reported that eye rubbing-related corneal trauma is associated with both the development and progression of keratoconus. Balasubramanian, Pye and Willcox[24] reported that the increase in protease activity and inflammatory mediators in tears after eye rubbing may contribute to the progression of keratoconus.[24] Moreover, the biomechanical properties of the cornea (that is, corneal hysteresis and corneal resistance factor) are significantly altered after eye rubbing.[25] In our study, we did not detect keratoconus in the participants, which may be because of their young ages.

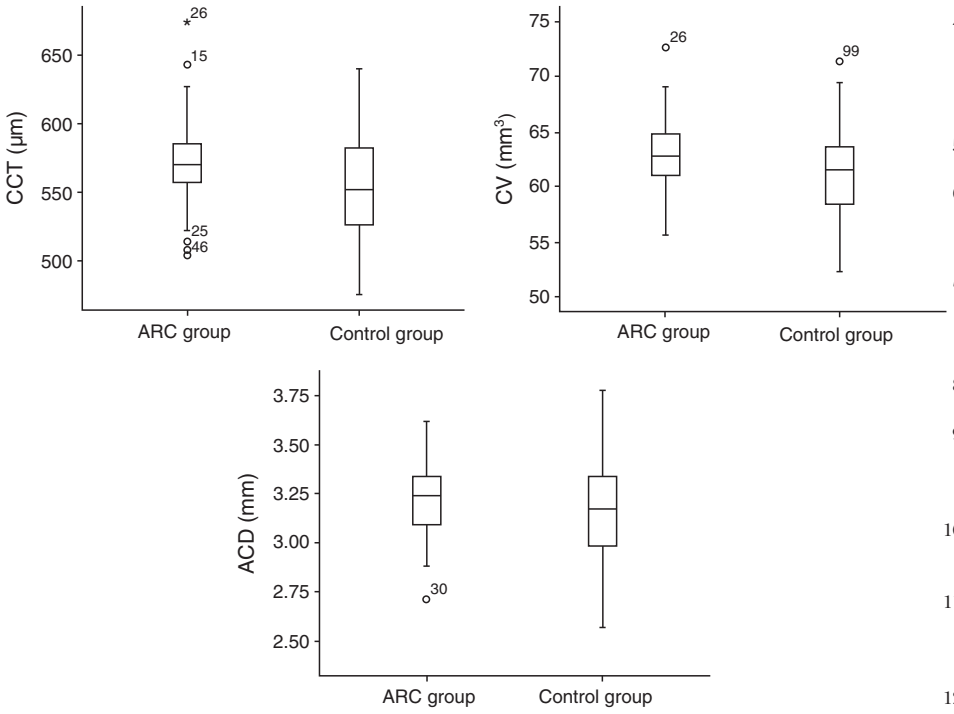

Figure 2. Box-plot graphics of central corneal thickness (CCT), corneal volume (CV) and anterior chamber depth (ACD) for the arc (allergic rhinoconjunctivitis) and control groups

Since we found that areal lens density was associated with age in children aged between seven and 14 years, it should be suggested that the Scheimpflug densitometric measurements have high sensitivity in detecting the transparency of the lens. This outcome may indicate that lens opacities should occur much earlier in life. We also found that the depth of the anterior chamber is not associated with lens density. It was reported that anterior chamber depth is associated with a thicker lens.[26]

Our study has several limitations. First, there is the inability to perform the measurements on the active status of ARC. In fact, it was our preference not to perform the examinations in eyes with discharge and congestion, as this condition might create imaging artefacts. Another limitation is the lack of corneal confocal microscopy that might support our findings. We believe that contrast sensitivity measurements in patients with ARC may be a valuable option in seeking clinical significance.

The clinical significance of the present study is that the severity and grade of ARC may be assessed by corneal densitometry, as haze reflects the inflammation. Also, we should speculate that topical allergy drops (olopatadine and ketotifen) do not have cataractogenic impact. It would be beneficial to examine the cornea carefully in ARC cases, since it is usually underestimated in routine clinical practice.

In conclusion, the measurements of corneal optical density and thickness are increased in children with ARC compared to healthy controls. Additionally, we found that ARC does not have a significant risk of early cataract development. More severe ocular allergic diseases, such as vernal and atopic keratoconjunctivitis should be investigated in further studies by anterior segment optical densitometry.

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