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Corneal Changes in Children after Unilateral Cataract Surgery in the Infant Aphakia Treatment Study

David G. Morrison, MD,[1] Michael J. Lynn, MS,[2] Sharon F. Freedman, MD,[3] Faruk H. Orge, MD,[4] Scott R. Lambert, MD,[5] for the Infant Aphakia Treatment Study Group*

Purpose: We report endothelial cell (EC) characteristics and central corneal thickness (CCT) from the Infant Aphakia Treatment Study (IATS) patients at the 5-year examination.

Design: Randomized, controlled trial of the treatment of unilateral cataract with aphakic contact lens (CL) versus primary intraocular lens (IOL) implant.

Participants: A total of 114 infants with unilateral cataract.

Methods: The EC density, coefficient of variation (CV), and percent hexagonal cells were measured by noncontact specular microscopy. The CCT was measured using contact pachymetry. Fellow eyes served as controls.

Main Outcome Measures: Mean differences between treated and fellow eyes of CL and IOL groups were compared with a paired *t* test. A 1-way analysis of variance model and the Tukey–Kramer multiple comparison procedure were used to assess the effect of a diagnosis of glaucoma or glaucoma suspect.

Results: A total of 105 subjects (52 with CLs, 53 with IOLs) had specular microscopy or corneal thickness data recorded. Mean EC densities were higher in aphakic eyes compared with fellow eyes (3921 vs. 3495 cells/mm^2, $P < 0.0001$). Mean CV was higher (27 vs. 24, $P = 0.0002$) and mean percent hexagonal cells was lower (72% vs. 76%, $P = 0.002$) in aphakic eyes compared with fellow eyes. Mean CCT of aphakic eyes was higher than in controls (637 vs. 563 μm, $P < 0.0001$). There was no difference in EC density in eyes treated with IOLs compared with fellow eyes (3445 and 3487 cells/mm^2, $P = 0.68$). Means for CV (25 vs. 24, $P = 0.07$) and percent hexagonal cells (74 vs. 76%, $P = 0.27$) were also not significantly different. Mean CCT was higher in eyes with IOLs (605 vs. 571 μm, $P < 0.0001$) compared with fellow eyes. Compared with treated eyes without glaucoma or glaucoma suspect, treated eyes with glaucoma had lower EC density (3289 vs. 3783 cells/mm^2, $P = 0.03$) and treated eyes with glaucoma suspect had greater mean corneal thickness (660 vs. 612 μm, $P = 0.0036$).

Conclusions: Cataract extraction during infancy with IOL implantation was not associated with a reduced EC count in treated compared with fellow eyes, although CCT was increased. Extended-wear aphakic CLs may cause corneal polymegathism with increased EC density and CCT. Glaucoma diagnosis was associated with reduced EC counts and increased CCT. *Ophthalmology 2015;■:1–7 © 2015 by the American Academy of Ophthalmology.*

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Cataract surgery is the most commonly performed intraocular surgery in the pediatric population. Although there has been great improvement in the instrumentation, microsurgical techniques, and handling of pediatric eyes, this procedure still seems to be stressful to the intraocular tissues. The corneal monolayer of endothelial cells (ECs) lacks the ability to regenerate[1] and can be reduced by outside stressors, such as physical trauma caused by surgery,[2] intraocular lens (IOL) contact,[3,4] and toxicity of surgical solutions and drugs.[5,6] An increased propensity for postoperative inflammation[7] and glaucoma[8,9] also exists in pediatric eyes. These complications also can be deleterious to the corneal endothelium. Changes in the ECs are believed to affect the corneal thickness. Even if the vision is not altered, increased thickness may cause alteration in the accurate intraocular pressure assessment.[10,11]

The Infant Aphakia Treatment Study (IATS) is a multicenter, randomized clinical trial comparing the use of primary IOL implantation with the correction of aphakia with a contact lens (CL) after cataract surgery performed in infants with a unilateral congenital cataract between 1 and 6 months of age.[12,13] The IATS provides the unique opportunity to objectively examine the EC integrity after pediatric cataract surgery with modern techniques. The purpose of this work is to report the noncontact specular microscopy and corneal thickness results of treated and untreated eyes from the age 5-year follow-up visit.

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Methods

Study Design

The study design, surgical technique, follow-up schedules, optical correction and patching regimens, and examination methods have been reported in detail.[12] The main inclusion criteria were a visually significant congenital cataract (≥3 mm central opacity) in 1 eye, a normal fellow eye, and an age of 28 to <210 days at the time of cataract surgery. Infants were randomly assigned to CL treatment or implantation of an IOL and spectacle overcorrection. Randomization was centrally determined using stratification between 2 age groups (28−48 days and 49−210 days) and study centers, which were grouped into 3 categories on the basis of the surgeon's experience.

The study followed the tenets of the Declaration of Helsinki, was approved by the institutional review boards of the participating institutions, and was in compliance with the Health Insurance Portability and Accountability Act. The off-label research use of the Acrysof SN60AT and MA60AC IOLs (Alcon Laboratories, Fort Worth, TX) was covered by US Food and Drug Administration investigational device exemption #G020021.

Specular Microscopy and Endothelial Cell Assessment

The IATS protocol specified that noncontact specular microscopy should be performed on both eyes of each patient at the age 5-year follow-up visit. The Konan specular microscope model SP4000 (Konan Medical Inc., Hyogo, Japan) was the preferred instrument. Three images of the corneal endothelium of both the treated and fellow eyes were to be taken and captured as bitmap files and saved to a CD. If bitmap files could not be saved, then the images were printed. The CD or pictures were sent to the Data Coordinating Center (DCC) in the Department of Biostatistics and Bioinformatics at Emory University and delivered to the Specular Microscopy Reading Center in the Department of Ophthalmology at Emory University. Non-bitmap files and paper prints were converted to bitmap format before analysis. The images were analyzed using all contiguous cells in the image field with discernible cell borders with a center-to-center algorithm in the Konan KSS 300 software (V2.20), which produced the corneal EC density (cells/mm^2), coefficient of variation (CV) of cell area, and hexagonality (% of cells with 6 sides). On an ongoing basis, as batches of images were processed, Excel (Microsoft Corp., Redmond, WA) spreadsheets containing for each image the patient identification, eye indicator, image number, number of cells counted, corneal EC density, CV of cell area, and hexagonality were e−mailed to the DCC. At the DCC, the spreadsheets were compiled into a single SAS dataset (SAS Inc., Cary, NC). For each eye, the data for the 3 measures were combined across the images by calculating a weighted average with the number of cells counted in an image as the weights, creating a single value for corneal endothelia cell density, CV of cell area, and hexagonality for each eye.

Corneal Thickness

Corneal thickness of the treated and fellow eyes was measured only at the age 5-year examination using the Pachmate (DGH Technology, Inc., Exton, PA). The pachymeter was calibrated before taking measurements using the Calibration Verification Box (CalBox; DGH Technology, Inc.) provided with the instrument. The operational mode was to set for "Continuous Average," with the Standard Deviation and Bilateral Modes enabled and the Number of Measurements set at 25. The Pachmate does not have an activation switch, but automatically takes and averages 25 measurements when the probe tip is properly applanated onto the cornea. After the instillation of topical anesthetic drops, a measurement was made by touching the probe tip to the center of the cornea. Three separate measurements were recorded on the case report form and averaged to produce a single value for analysis.

Statistical Methods

Specular microscopy and corneal thickness measurement were performed only at the age 5-year examinations and were not done before cataract surgery. The means of the outcome factors evaluated in this article (EC measures [cell density, CV of cell area, and hexagonality] and corneal thickness at age 5 years) were compared between the treated and fellow eyes using a paired t test separately for the treatment groups. The means for the outcome factors of the treated eyes were compared between the 2 treatment groups using an independent groups t test. The same method was used to evaluate the effect of the type of CL worn. The relationships of age at surgery and the outcome factors for the treated eyes were evaluated using an independent groups t test to compare the means between the age strata and using the correlation coefficient to assess the association with age at surgery in continuous form. The effect of additional intraocular surgery during follow-up was evaluated along with treatment using a 2-way analysis of variance model with interaction. The P values were based on the type III sums of squares calculated in SAS Proc GLM (SAS Institute Inc.), and the least squares mean and 95% confidence interval were determined for each treatment/surgery group. The means for the outcome factors in the treated eyes combining the patients with CL and IOL were compared among the 3 glaucoma diagnosis groups (glaucoma, glaucoma suspect, neither) using a 1-way analysis of variance model and the Tukey−Kramer multiple comparison procedure. All reported P values are 2-sided. A P value <0.05 was considered statistically significant. All analyses were done with SAS 9.3 (SAS Inc.).

Results

Patients

There were 114 patients enrolled in the IATS, with 57 randomized to each treatment group. One patient in the IOL group was lost to follow-up, and the remaining 113 patients had an age 5-year examination. Of the 113 patients, 80 (71%) had digitizable specular microscopy images of both eyes, 8 (7%) had images of only the treated eye, 8 (7%) had images of only the fellow eye, and 17 (15%) had no images of either eye. Of the 17 patients without images for either eye, 9 were in the CL group and 8 were in the IOL group. Although the protocol called for 3 images to be taken of each eye, the lack of patient cooperation and other factors often resulted in fewer images per eye: Of the 88 treated eyes, 49 (56%) had 1 image, 8 (9%) had 2 images, 30 (34%) had 3 images, and 1 (1%) had 4 images. Of the 113 patients examined at age 5 years, 94 (83%) had corneal thickness measured in both eye, 3 (3%) had only the treated eye measured, 3 (3%) had only the fellow eye measured, and 13 (12%) had neither eye measured. Of the 13 eyes without corneal thickness measurements, 8 were in the CL group and 5 were in the IOL group. Of the 113 patients examined at age 5 years, 105 had specular microscopy or corneal thickness data for the treated or the fellow eye. Of the 8 patients examined at age 5 years without any specular microscopy or corneal thickness measurements, 5 were in the CL group and 3 were in the IOL group.

For the 105 patients with specular microscopy or corneal thickness data (CL = 52, IOL = 53), the median age at cataract