AMERICAN ACADEMY™
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Myopic Shift 5 Years after Intraocular Lens Implantation in the Infant Aphakia Treatment Study

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Purpose: To report the myopic shift at 5 years of age after cataract surgery with intraocular lens (IOL) implantation for infants enrolled in the Infant Aphakia Treatment Study (IATS).

Methods: Refractions were performed at 1 month and every 3 months postoperatively until age 4 years and then at ages 4.25, 4.5, and 5 years. The change in refraction over time was estimated by linear mixed model analysis.

Results: Intraocular lens implantation was completed in 56 eyes; 43 were analyzed (median age, 2.4 months; range, 1.0−6.8 months). Exclusions included 11 patients with glaucoma, 1 patient with Stickler syndrome, and 1 patient with an IOL exchange at 8 months postoperatively. The mean rate of change in a myopic direction from 1 month after cataract surgery to age 1.5 years was 0.35 diopters (D)/month (95% confidence interval [CI], 0.29−0.40 D/month); after age 1.5 years, the mean rate of change in a myopic direction was 0.97 D/year (95% CI, 0.66−1.28 D/year). The mean refractive change was 8.97 D (95% CI, 7.25−10.68 D) at age 5 years for children 1 month of age at surgery and 7.22 D (95% CI, 5.54−8.91 D) for children 6 months of age at surgery. The mean refractive error at age 5 years was −2.53 D (95% CI, −4.05 to −1.02).

Conclusions: After IOL implantation during infancy, the rate of myopic shift occurs most rapidly during the first 1.5 years of life. Myopic shift varies substantially among patients. If the goal is emmetropia at age 5 years, then the immediate postoperative hypermetropic targets should be +10.5 D at 4 to 6 weeks and +8.50 D from 7 weeks to 6 months. However, even using these targets, it is likely that many children will require additional refractive correction given the high variability of refractive outcomes. *Ophthalmology 2017;■:1−6 © 2017 by the American Academy of Ophthalmology*

Supplemental material is available at www.aaojournal.org.

The human eye usually experiences 3 to 4 mm of axial elongation during the first year of life.[1−3] Concurrently, the cornea and crystalline lens flatten, resulting in a relatively stable refractive error. The myopic shift induced by axial elongation after infantile cataract surgery cannot be fully offset by corneal flattening resulting in overall myopic shift. In aphakic eyes, the myopic shift can be corrected easily as needed by reducing the power of corrective contact lenses or spectacles.[4,5] Likewise, small myopic shifts can be corrected with contact lenses or spectacles in pseudophakic eyes. However, large myopic shifts may necessitate an intraocular lens (IOL) exchange.[6] In children with unilateral pseudophakia, a large myopic shift may contribute to the development of significant anisometropia, amblyopia, and impaired binocularity, particularly when the IOL is implanted at an early age. Although there is no agreement regarding the optimal magnitude of immediate postoperative hypermetropia, most clinicians undercorrect infants after cataract surgery and IOL implantation in anticipation of this myopic shift.[7−11]

Although small case series have reported a mean myopic shift ranging from 5 to 7 diopters (D) after IOL implantation during infancy, these studies were retrospective with variable lengths of follow-up.[12−15] The Infant Aphakia Treatment Study (IATS) is a randomized clinical trial comparing the visual outcome in infants 1 to 6 months of age who underwent primary implantation of an IOL versus being left aphakic and receiving a contact lens correction after cataract surgery in infancy.[16,17] We report the myopic shift experienced by children randomized to IOL correction in the IATS from the time of cataract surgery to age 5 years.

Methods

The study design, surgical technique, follow-up schedules, patching and optical correction regimens, and examination methods have been reported in detail and are only summarized in this report.[18] The study followed the tenets of the Declaration of Helsinki and was approved by the institutional review boards of the participating institutions and was in compliance with the

http://dx.doi.org/10.1016/j.ophtha.2016.12.040
ISSN 0161-6420/17

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.

Study Design

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 days to <210 days at the time of cataract surgery. Patients were randomized to have an IOL placed at the time of the initial surgery with spectacle correction of residual hyperopia or to be left aphakic and optically corrected with a contact lens. The randomization was stratified according to the category of the age of the infant at surgery (28−48 days vs. 49−210 days.).

Surgical Technique for Intraocular Lens Implantation

Infants randomized to the IOL group had their lens aspirated followed by the implantation of an AcrySof SN60AT (Alcon Laboratories) IOL into the capsular bag. In the event that both haptics could not be implanted into the capsular bag, an AcrySof MA60AC IOL was implanted into the ciliary sulcus. The IOL power was calculated on the basis of the Holladay 1 formula targeting an 8 D undercorrection (postoperative hypermetropia) for infants aged <48 days and a 6 D undercorrection for infants aged 48 to 210 days. After IOL placement, a posterior capsulectomy and an anterior vitrectomy were performed through the pars plana/plicata.

Optical Correction and Patching Regimen

For patients randomized to the IOL group, spectacles were prescribed before the 1-month postoperative visit or at any later visit providing that 1 of the following conditions existed in the treated eye: hyperopia >1.0 D, myopia >3.0 D, or astigmatism >1.5 D. The overall aim was to overcorrect the refractive error by 2.0 D to achieve a near point focus. The prescribed optical correction was to be worn at all times while the patient was awake.

Starting the second postoperative week, parents were instructed to have their child wear an adhesive occlusive patch over the eye that did not undergo surgery for 1 hour per day per each month of age until age 8 months. Thereafter, patching was prescribed for all waking hours every other day or for one half of the patient's waking hours every day.

Definition of Glaucoma

Glaucoma was defined as IOP >21 mmHg with 1 or more of the following anatomic changes: (1) corneal enlargement; (2) asymmetrical progressive myopic shift coupled with enlargement of the corneal diameter or axial length; (3) increased optic nerve cupping defined as an increase of ≥0.2 in the cup-to-disc ratio; or (4) use of a surgical procedure for IOP control. A patient was designated a glaucoma suspect if (1) there were 2 consecutive IOP measurements >21 mmHg on different dates after topical corticosteroids had been discontinued without any of the anatomic changes listed or (2) glaucoma medications were used to control IOP without any of the anatomic changes listed.

Patient Follow-up and Measurement of Refractive Error

Refractive error was measured using retinoscopy at follow-up clinical examinations by an IATS-certified investigator postoperatively at 1 month and 3 months and then at 3-month (±2 weeks) intervals until age 4 years (±2 weeks) and then at ages 4.25, 4.5, and 5 years (±2 weeks). Refractive error also was measured at an examination under anesthesia using cycloplegic retinoscopy 2 to 4 weeks before a grating acuity assessment performed at age 1 year (±2 months).

Statistical Analysis

The purpose of the analyses was to determine the rate of change in spherical equivalent refractive error for the treated eyes of patients with an IOL implanted and whether selected baseline characteristics affected the rate of change. For the longitudinal analyses, the time factor used in the modeling was the age of the patient. Thus, the statistical models related the refractive error to the patient's age at the time the refractive error was measured. Patient age was used rather than the time since cataract surgery because the physiologic changes that would influence changes in refractive error were thought to be more associated with the age of the patient rather than the time since surgery. However, patients in IATS underwent surgery at ages ranging from 1 to <7 months, and we explored whether the rate of change in refractive error was related to the age at which the cataract surgery was performed.

Individual patient profiles relating refractive error to patient age were plotted to visualize the relationship between refractive error and age and to check for possible errors in data measurement, recording, or entry. To explore the potential functional relationship between refractive error and age, a locally weighted scatterplot smoother (Loess) curve[19] was fit with the fraction of points used set to 0.5 and the number of additional iterations for determining weights in the weighted regression step set to 2.

The refractive error was related to age in years at the follow-up visit using a linear mixed effects model.[20] The model was fit using Proc Mixed in SAS 9.3 (SAS Institute Inc, Cary, NC) with an unstructured covariance matrix and using the restricted maximum likelihood estimation method. On the basis of examination of the Loess curve described, the following piecewise linear mixed effects model with a knot at 1.5 years of age was fit:

$$(\text{Refractive Error})_{ij} = \beta_1 + \beta_2\,\text{Age}_{ij} + \beta_3\,(\text{Age}_{ij}-1.5)^{+} + b_{1i} + b_{2i}\,\text{Age}_{ij} + b_{3i}\,(\text{Age}_{ij}-1.5)^{+} + \varepsilon_{ij}$$

- i refers to the i^{th} patient
- j refers to the j^{th} follow-up data point for the patient
- $(\text{Refractive Error})_{ij}$ refers to the refractive error of the ith patient at the jth follow-up data point
- Age_{ij} refers to the age of the i^{th} patient at the j^{th} follow-up data point
- β_1, β_2, β_3 are fixed effects
- b_{1i}, b_{2i}, b_{3i} are random effects
- ε_{ij} is random error
- $(\text{Age}_{ij}-1.5)^{+} = 0$, if $\text{Age}_{ij} \le 1.5$ and $\text{Age}_{ij}-1.5$, if $\text{Age}_{ij} > 1.5$

For this model, the fixed effects, β_1, β_2, β_3, have the following interpretations: β_1 = intercept; β_2 = rate of change (D/year) in refractive error up until age 1.5 years; $\beta_2 + \beta_3$ = rate of change (D/year) in refractive error after age 1.5 years up to age 5 years (the "Results" section shows the rationale for choosing age 1.5 years).

To evaluate whether certain baseline characteristics (the age at surgery, axial length, average central keratometric power, and power of the IOL implanted) had an effect on the rate of change in refractive error, main effect and interaction terms were added to this model separately for each of these characteristics. A statistically significant coefficient for the interaction of the characteristic with the term Age_{ij} or with the term $(\text{Age}_{ij}\text{-}1.5)^{+}$ would indicate that the characteristic had an effect on the change in refractive error before or after age 1.5 years, respectively. Further details regarding this model are presented in the Supplemental materials