The Myopic Shift in Aphakic Eyes in the Infant Aphakia Treatment Study (IATS) after 10 Years of Follow-up

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Abstract

Objectives: To report the myopic shift in the aphakic eyes of a cohort of children who underwent unilateral cataract surgery during infancy and were then followed longitudinally for 10.5 years.

Methods: One-half of the children enrolled in the Infant Aphakia Treatment Study (IATS) were randomized to aphakia and contact lens correction after unilateral cataract surgery. They then underwent ocular examinations using standardized protocols at prescribed time intervals until age 10.5 years.

Results: Thirty of 57 children randomized to aphakia remained aphakic at age 10.5, having undergone unilateral cataract surgery at a median age of 1.6 (IQR 1.1, 3.1) months. The median refractive error (RE) in the 57 eyes randomized to aphakia immediately after cataract surgery was 19.01 D (IQR: 16.98, 20.49) compared to 10.38 D (IQR: 7.50, 14.00) for the 30 eyes that remained aphakic at age 10.5 years. The mean change in RE in aphakic eyes was −2.11 D/year up to age 1.5 years, −0.68 D/year from 1.5 to 5.0 years and −0.35 D/year from age 5 to 10.5 years. At age 10.5 years, 18 patients continued to wear a contact lens correction (silicone elastomer, n=6; gas permeable, n=6; hydrogel, n=5; and silicone hydrogel, n=1) (median RE, 12.50 D), 9 wore only spectacles (median RE, 4.00 D) and 4 wore no correction (median RE, 11.25 D) to correct their aphakic eye.

Conclusions: The refractive error in aphakic eyes decreased by 44% from infancy to age 10.5 years. About two-thirds of children who remained aphakic at age 10.5 years continued to wear a contact lens.
Aphakia in young children is usually corrected optically with contact lenses or spectacles. Unlike adult eyes that usually have a constant refractive error, the refractive error in the aphakic eyes of young children decreases over time as the eye elongates. This myopic shift has been reported to follow a semi-logarithmic curve from infancy through age 20 years. However, the data used to perform these analyses have been retrospective and included patients who underwent cataract surgery at different ages and in many cases with relatively short follow-ups.

The Infant Aphakia Treatment Study (IATS) is a randomized clinical trial comparing the visual outcome in infants 1–6 months of age who underwent the primary implantation of an intraocular lens (IOL) versus being left aphakic and receiving a contact lens correction following cataract surgery during infancy. These children were followed at regular intervals during the first 5 years of life and then once again at age 10.5 years. We report the myopic shift experienced by children randomized to aphakia from infancy to age 10.5 years.

METHODS

The study design, surgical technique, follow-up schedules, patching and optical correction regimens, and examination methods have been reported previously and are only summarized in this report. 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 Health Insurance Portability and Accountability Act. The off-label research use of the Acrysof SN60AT and MA60AC IOLs (Alcon Laboratories, Fort Worth, Texas) was covered by US Food and Drug Administration investigational device exemption # G020021. The clinical trial is registered in clinicaltrials.gov by Identifier NCT00212134.

Study Design

The main inclusion criteria were a visually significant congenital cataract (≥3 mm central opacity) in one 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 either an IOL placed at the time of the initial surgery with residual hyperopia corrected with spectacles or to be left aphakic and optically corrected with a contact lens. Randomization was stratified according to the age of the infant at surgery (28 – 48 days versus 49 – 210 days.).

Contact Lens Correction

Within 1 week after cataract surgery, patients randomized to aphakia were fitted with either a silicone elastomer (SE) (Silsoft Super Plus; Bausch & Lomb, Rochester, NY) or gas permeable (GP) (X-cel Specialty Contacts, Duluth, GA) contact lens with a +2.00 diopter overcorrection to provide a near-point correction. Contact lenses were supplied at no cost to caregivers.

Patient Follow-up and Measurement of Refractive Error

Refractive errors in the treated and fellow eyes were measured at 1 month, 3 months and then at 3 months intervals after cataract surgery until age 4 years and then at ages 4.25, 4.5, 5.0 and 10.5 years. In young children, refractive errors were measured using retinoscopy.
older children, refractive errors were measured using either retinoscopy or an autorefractor with subjective refinement. Some refractions were performed while the child was wearing a contact lens on their aphakic eye. In these instances, the refraction was converted to the spectacle plane using a vertex distance of 12 mm.

**RRG3 Calculations**

The rate of refractive growth was measured using RRG3. RRG3 was calculated by creating a spreadsheet for all patients enrolled in the IATS including: age at surgery, initial refraction, age at initial refraction, final refraction, age at final refraction and IOL power and A-constant for patients in the IOL group. This spreadsheet included a proprietary macro which calculated the RRG3 for each eye. The refractive errors measured closest to the one-month postoperative examination and the age 10.5 year examination were used for the analysis. When refractions were performed for children in the aphakia group wearing a contact lens, the refractive error at a vertex distance of 12 mm was calculated and then added to the over refraction. For children who underwent an IOL exchange, the refraction obtained at the examination immediately prior to IOL exchange was used in the analysis. Three patients in the aphakia group that had incomplete refractive data were not included in the analysis.

**Statistical Analysis**

The purpose of the analyses was to determine and describe the changes in the spherical equivalent refractive error for the eyes of patients with aphakia, including the changes over time from infancy to 10.5 years after randomization, the average rate of change per year, and the average changes stratified by type of correction worn. Previously, we have reported changes between 1 and 18 months of age and 18 months and 5 years of age, for treated eyes of patients who received an IOL. Here we report changes in IATS aphakic eyes for similar age ranges, and include changes between the 5 year visit and the 10.5 year visit. We estimated the paired difference in refractive error between the 1 and 18 month visits, the 18 month and 5 year visits, and the 5 and 10.5 year visits, as well as the rate of change per year for these age ranges.

We previously developed a piecewise longitudinal linear regression model to model the rate of change in refractive error from 1 month of age up to 5 years of age for eyes of IATS patients who received an IOL. In addition to estimating the changes in refractive error as detailed above, we adapted the piecewise longitudinal model, and extended it to include the 10.5 year refractive error data. Details of the model and the estimated rate of change in refractive error between 5 and 10.5 years produced by the model are given in Appendix 1.

The change between 5 and 10.5 years was also stratified by type of correction worn at 10.5 years (contact lens, spectacles or none). The Kruskal-Wallis Test was used to compare median change in refraction between 5 and 10.5 years across the 3 correction groups. A chi-square test was used to compare the likelihood of children wearing contact lenses compared to children not wearing contact lenses at age 10.5 year relative to having private insurance. Contact lens adherence at age 10.5 years between patients still wearing contact lenses at age 10.5 years vs those not wearing contact lenses was evaluated using a two-sample t-test. A significance level of 5% (confidence level 95%) was used in all analyses.
RESULTS

Patients
Between December 2004 and January 2009, 114 infants were enrolled in the Infant Aphakia Treatment Study with 57 randomized to unilateral aphakia. Fifty-three of these children had the refractive error in their aphakic eye measured at age 5 years and 30 at age 10.5 years (Figure 1). The refractive error was not measured in the aphakic eye of 27 patients at age 10.5 years because 24 had undergone secondary IOL implantation prior to this examination, 2 were lost to follow-up and 1 had phthisis bulbi. The median age at cataract surgery for the 30 patients followed longitudinally from infancy to age 10.5 years was 1.6 months (IQR, 1.1, 3.1 months; range, 1.0 – 6.8 months). There were 18 females (60%).

Duration and Completeness of Follow-up
Among the 30 aphakic patients analyzed, the total expected number of follow-up visits was 666, of which 590 were performed; 545 included a measurement of the refractive error for the treated eye.

Change in Refractive Error
Figure 1 shows the distribution of the refractive error in aphakic eyes at each follow up visit, and illustrates the longitudinal myopic shift. The average refractive error at one month after randomization was 18.60 D (95% CI 17.87, 19.33 D), and at 18 months was 15.54 D (95% CI 14.63, 16.45 D), yielding an average rate of change of −2.11 D per year or −0.18 D per month (95% CI −2.63, −1.58 D/year). The average refractive error at 5 years after randomization was 13.17 D (95% CI 12.14, 14.20 D), yielding an average rate of change between 1.5 and 5 years after randomization of −0.68 D per year (95% CI −0.84, −0.53 D/ year). The average refractive error at 10.5 years after randomization was 10.44 D (95% CI 8.29, 12.59 D), yielding an average rate of change between 5 and 10.5 years after randomization of −0.35 D per year (95% CI −0.60, −0.10 D/year). The estimated rate of change between 5 and 10.5 years using the piecewise longitudinal linear model was −0.33 D/year (95% CI = −0.68, 0.02) (Appendix 1). The median rate of refractive growth 3 (RRG3) was −16.52 (IQR, −20.27, −12.09).

Type of Correction:
At age 10.5 years, 18 patients were still wearing a contact lens correction on their aphakic eye (silicone elastomer (n=6; gas permeable (BXO2) n=6; hydrogel (Omafilcon A or Hioxifilcon D) n=5; and silicone hydrogel (Comfilcon A) n=1). Nine patients were only wearing spectacles and 4 were not wearing any optical correction for their aphakic eye. The median refractive error was 12.50 D (IQR: 9.88, 14.00 D) for the children continuing to wear a contact lens correction, 11.25 D (5.94, 16.50) for the children wearing no correction and 4.00 D (IQR: 3.06, 9.06) for the children only wearing spectacles (Table 1). The median change in refractive error per year between ages 5 and 10.5 years was similar for these 3 groups (p=0.61) (Table 2). The children who continued to wear contact lenses at age 10.5 years were more likely to have private insurance than the children who were wearing spectacles or no correction (83% vs 54%; p=0.034). The likelihood of a child continuing to
wear contact lenses at age 10.5 years was similar whether they had originally worn GP vs SE lenses (29% vs 14%; p=0.20). Children who wore a contact lens a higher percentage of their waking hours at age 5 years were more likely to be wearing a contact lens at age 10.5 years compared to children not wearing a contact lens at age 10.5 years (86% vs 62%; p=0.0496).

Discussion

We report marked variability in the myopic shift in aphakic eyes in our series, but on average the rate of the myopic shift was about one-third of a diopter per year from ages 5 to 10.5 years. At age 10.5 years, only 18 of the original 57 patients randomized to aphakia were still wearing a contact lens on their aphakic eye. The types of contact lenses used to correct their aphakia was nearly equally divided between SE, GP and hydrogel lenses.

The myopic shift we report in eyes randomized to aphakia in the IATS mirrors those reported by others. Moore\(^2\) followed 14 children with unilateral aphakia longitudinally for 3 years. He reported the rate of the myopic shift in these eyes decreased from \(-0.43\) D/month for the first 6 months of life to \(-0.19\) D/month after age 2 years. McClatchey and Parks\(^1\) reported the myopic shift in 156 aphakic eyes of children who underwent cataract surgery at a mean age of 8 months and had a median follow-up of 8.8 years. They noted the average myopic shift followed a logarithmic curve and only age at surgery correlated with the rate of the myopic shift. Superstein et al\(^4\) reported the myopic shift in 233 aphakic eyes who underwent cataract surgery at a median age of 0.8 years and were followed for a median of 3.8 years. They noted that the rate of refractive growth for these aphakic eyes was logarithmic with a rate of refractive growth (RRG) of \(-8.0\) D. McClatchey et al\(^11\) evaluated the myopic shift in 106 aphakic eyes in children who underwent cataract surgery when 3 months to 10 years of age and who were followed for at least 3 years. They reported a rate of refractive growth in these eyes of \(-5.7\) D. A revised RRG3 formula was subsequently created to account for the growth of the eye in utero and to calculate the aphakic refraction at the crystalline lens plane rather than the spectacle plane. Whitmer et al\(^8\) calculated the RRG3 as \(-16\) D in 70 aphakic eyes of children who underwent cataract surgery at age 10 years or younger and were followed at least 3.6 years. We report a mean RRG3 of \(-16.52\) in our cohort which is similar to the RRG3 we reported in 54 of the 57 IATS aphakic eyes at age 5 years (\(-18\) D).\(^9\) We have previously reported the RRG3 did not differ between eyes randomized to aphakia who underwent cataract surgery between 4–6 weeks vs. \(>6\) weeks of age. However, there was a higher mean RRG3 for aphakic eyes with visual acuity worse than 20/100 compared to aphakic eyes with vision better than 20/100.\(^9\)

The type of contact lenses worn by patients in the IATS at age 10.5 years differed from what we have previously reported in this same cohort of patients at younger ages. At age 12 months, 74% of the aphakic patients in the IATS were wearing SE contact lenses, 21% were wearing GP contact lenses and 5% alternated between wearing both types of contact lenses. By age 5 years, the percentage of patients wearing silicone elastomer lenses had decreased to 46%.\(^13\) At age 10.5 years, the percentage of patients wearing SE contact lenses had further decreased to one-third. At this age the percentage of patients wearing GP lenses had increased to one-third and one-third of patients were wearing hydrogel or silicone-
hydrogel contact lenses. Presumably, more patients were wearing hydrogel contact lenses at age 10.5 years because these lenses are not available in the high powers needed to optically correct aphakia in young children, but they are available in the powers needed to optically correct aphakia in older children. The decreased use of SE lenses at age 10.5 years may have been due to the higher cost of these lenses and the higher incidence of deposits on these lenses in older children which may have offset the convenience of being able to wear them on an extended-wear basis.\textsuperscript{14,15} The increased use of GP contact lenses between the ages of 5 to 10.5 years may have been due to their lower cost, superior optics or their lower risk of associated adverse events.\textsuperscript{16}

Nine patients were only wearing spectacles to correct their aphakic eye at age 10.5 years. Their median refractive error was only 4.0 D compared to 12.5 D for the aphakic eyes still being corrected with a contact lens correction. We have previously reported better visual acuity in the aphakic eyes of children in the IATS who continued to wear a contact lens correction at age 10.5 years compared to children who corrected their aphakia with spectacles only.\textsuperscript{17} Weakley et al have also greater rate of refractive growth in eyes with unilateral aphakia with poor visual acuity.\textsuperscript{18}

The weakness of our study is that 27 of the 57 patients randomized to aphakia in the IATS either underwent secondary IOL implantation or were lost to follow-up before the 10.5 years examination. The strength of the study is that refractive errors were obtained longitudinally over 10 years used established protocols for 30 children.

In conclusion, children with unilateral aphakia continue to have a myopic shift in their aphakic eyes between ages 5 and 10.5 years albeit the rate of the shift is reduced compared to the shift at younger ages.

**Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

**Acknowledgments**

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**References**


Figure 1.
Box plots showing the distribution of refractive error in aphakic eyes at scheduled follow up examinations. The typical age at follow up, and the number of patients evaluated at each age is shown on the horizontal axis.
Table 1:
10.5 year Refractive Error (D) in Aphakic Eyes by Type of Correction Worn at 10.5 Years

<table>
<thead>
<tr>
<th>Correction</th>
<th>N Obs</th>
<th>N</th>
<th>Mean</th>
<th>Std Dev</th>
<th>Lower 95% CI for Mean</th>
<th>Upper 95% CI for Mean</th>
<th>Median</th>
<th>25th Percentile</th>
<th>75th Percentile</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
</table>
Table 2:
Rate of Change (per year) in Refractive Error (D) in Aphakic Eyes Between 5 and 10.5 Years By Type of Correction Worn at 10.5 Years

<table>
<thead>
<tr>
<th>Correction</th>
<th>Mean (Std. Dev.)</th>
<th>95% CI for Mean</th>
<th>Median</th>
<th>25th Percentile</th>
<th>75th Percentile</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contact Lens (n=18)</td>
<td>−0.35 (0.73)</td>
<td>−0.71, 0.01</td>
<td>−0.31</td>
<td>−0.52</td>
<td>−0.07</td>
<td>−2.84</td>
<td>0.95</td>
</tr>
<tr>
<td>None (n=4)</td>
<td>−0.10 (0.55)</td>
<td>−0.98, 0.78</td>
<td>−0.21</td>
<td>−0.46</td>
<td>0.26</td>
<td>−0.65</td>
<td>0.66</td>
</tr>
<tr>
<td>Only Spectacles (n=8)*</td>
<td>−0.47 (0.66)</td>
<td>−1.02, 0.09</td>
<td>−0.68</td>
<td>−0.95</td>
<td>0.22</td>
<td>−1.32</td>
<td>0.42</td>
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</table>

* Data were unavailable for one subject.