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Sensorimotor outcomes by age 5 years after monocular cataract surgery in the Infant Aphakia Treatment Study (IATS)

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Abstract

Purpose—To evaluate sensorimotor outcomes among children in the Infant Aphakia Treatment Study (IATS).

Methods—Secondary outcome analysis was performed in this randomized, multicenter, clinical trial comparing treatment of unilateral aphakia with a primary intraocular lens (IOL) or contact lens (CL) correction. The alignment characteristics and sensory status of children through age 5 years were evaluated.

Results—In the IATS study, 91 of 112 children (81%) developed strabismus through age 5 years. Of 34 infants who were orthotropic at near 12 months after cataract surgery, by age 5 years 14 (41%) were orthotropic at distance, and 15 (44%) were orthotropic at near at age 5 years without strabismus surgery. Eight of 56 children (14%) in the CL group and 13 of 56 (23%) in the IOL group were orthotropic at distance ($P = 0.33$) by 5 years of age and had no history of strabismus

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surgery. Thirteen of 48 (27%) who underwent cataract surgery prior to 49 days of age compared to 8 of 64 (13%) who had surgery after 49 days were orthotropic ($P = 0.085$). Median visual acuity in the operative eye was 0.4 logMAR (20/50) for children with orthotropia or microtropia (<10^{Δ}) versus 1.10 logMAR (20/252) for strabismus ≥10^{Δ} ($P = 0.0001$). Stereopsis was detected in 12 of 21 children (57%) with orthotropia versus 16 of 89 (18%) children with strabismus ($P = 0.0006$).

Conclusions—IOL placement does not reduce the development of strabismus after monocular congenital cataract surgery. Improved ocular alignment by age 5 years correlated strongly with improved visual acuity and stereopsis.

Strabismus is a common finding after unilateral cataract surgery, with reported frequencies varying by population and follow-up time in small retrospective studies.[1-10] Prior reports have suggested that strabismus develops less frequently when an intraocular lens (IOL) is implanted primarily; however, none of these studies randomized IOL implantation.[1,2] The Infant Aphakia Treatment Study (IATS), a multicenter, randomized clinical trial, compared visual outcomes and adverse events in children randomized to either cataract surgery contact lens correction or primarily IOL implantation after unilateral cataract surgery in infants aged 1-6 months. The primary outcome at age 4.5 years was visual acuity. [11] Secondary outcomes included adverse events and additional surgeries.[12] Strabismus developed in a comparable proportion of children in both arms of the study 1 year after cataract surgery.[13] The present study reports the strabismus findings in this cohort of children by age 5 years relative to their sensory status and visual acuity.

Subjects and Methods

The IATS design, surgical treatments, patching and optical regimens, follow-up examination schedule, and evaluation methods have been previously published.[14] Infants with a visually significant congenital cataract (≥3 mm central opacity) in one eye and an age of 28 days to <210 days at the time of cataract surgery were randomized to have either an IOL placed at the time of the initial surgery (with spectacle correction of residual hyperopia) or to be left aphakic (with contact lens correction). The randomization was stratified according to the category of the age of the infant at surgery (28-48 days vs 49-210 days). This study was approved by the institutional review boards at all participating institutions and complied with the Health Insurance Portability and Accountability Act of 1996. 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. Written informed consent was obtained from all guardians or caregivers.

Examination

Ocular alignment at distance and near was assessed at each follow-up examination and immediately prior to strabismus surgery by an IATS-certified investigator through age 5. Strabismus was measured in prism diopters using the simultaneous prism cover test followed by the prism and alternate cover test or Krimsky light reflex testing when fixation was poor. The timing and choice of strabismus surgery was at investigator discretion. Monocular optotype HOTV visual acuity and stereopsis were measured at age 4.5 years by a masked traveling tester.[12] Stereopsis was evaluated by Frisby Stereotest (Richmond Products, Albuquerque, NM), Randot Preschool Stereoacuity test (Stereo Optical, Chicago, IL), and Titmus Fly test (Stereo Optical, Chicago, IL). [15]

Analysis

For reporting all children combined and for analysis of the associations between strabismus and aphakia treatment, visual acuity, stereopsis, age at cataract surgery, adverse events, and additional intraocular surgery, strabismus outcomes at the 5-year examination were used, unless the patient had prior strabismus surgery, in which case the measurements recorded immediately prior to the first strabismus surgery were used. For change in strabismus and the relationship, 5-year examination measurements were used. Children with a combination of horizontal and vertical strabismus were grouped according to the horizontal deviation. Unless otherwise noted, the strabismus result is for the measurement made at distance.

The percentage of children with strabismus was compared among groups using the Fisher exact test. The median visual acuity was compared between groups of children with and without strabismus using the Wilcoxon rank-sum test. All statistical tests were 2-sided. No adjustment was made for multiple testing. A *P* value of <0.05 was deemed statistically significant.

Results

A total of 114 children were enrolled in the IATS, with 57 randomized to each treatment group. One IOL patient was lost to follow-up at 18 months of age; the remaining 113 children were examined at age 5 years. Strabismus measurements could not be made for 1 contact lens (CL) patient with phthisis bulbi. We report strabismus results for the remaining 112 children. Of these, strabismus measurements from the age 5 examination are included for the 67 (60%) followed to that point without strabismus surgery; measurements made at the time of the first strabismus surgery are included for the 45 (40%) who had undergone strabismus surgery before 5 years of age. The median time to strabismus surgery after enrollment was 18.3 months (interquartile range, 9.7-30.6 months; range, 2.8-53.8 months).

Strabismus Outcomes

Of the 112 children, 91 (81%) had strabismus when measured at distance (Table 1). Esotropia was present in 56 children (50%), with angles ranging from 2^{Δ} to 70^{Δ}. Exotropia was present in 30 children (27%), with angles ranging from 3^{Δ} to 50^{Δ}. Nineteen children (17%) had an intermittent or constant hyperdeviation ranging from 2^{Δ} to 20^{Δ}, of which 14 were in the setting of a horizontal deviation. A phoria was documented in 2 children (2%), and intermittent deviations were detected in 17 (15%). A microtropia (1^{Δ}-9^{Δ}) was present at distance and near in only 7 of 109 (7%) children. At age 5 years, inferior oblique overaction was present in 15 of 109 (14%) children. Of 109 children, an A- or V-pattern strabismus was present in 7 (7%) and 5 (5%) children, respectively at age 5 years. Of the 112 children, 93 (83%) had the same set of deviations at distance and near (Table 2).

Aphakia Treatment and Age at Cataract Surgery

There was no significant difference between the aphakia treatment groups with respect to the occurrence of strabismus. By age 5 years, 8 of 56 children (14%) in the CL group and 13 (23%) in the IOL group were orthotropic at distance ($P = 0.33$), without a history of strabismus surgery. When microtropia ($<10^{\Delta}$) was included with orthotropia, these straighter eyes accounted for 16 of 53 (30%) in the CL group compared to 17 of 50 (34%) in the IOL group ($P = 0.83$). A similar proportion of children in each treatment group had strabismus surgery (CL, 21/56 [38%]; IOL, 24/56 [43%]; $P = 0.70$). Orthotropia was found in 13 of 48 children (27%) who underwent cataract surgery prior to 49 days of age versus 8 of 64 (13%) who underwent surgery after 49 days ($P = 0.085$). Orthotropia and microtropia were found in 20 of 44 of the younger cohort (45%) at cataract surgery versus 13 of 59 (22%) of the older ($P = 0.018$).

Adverse Events and Additional Intraocular Surgery

The occurrence of adverse events and additional intraocular surgeries in the IATS children up to age 5 years has been previously reported.[12] Among the children with one or more adverse event, 60 of 76 (79%) had strabismus compared with 31 of 36 (86%) in the children without an adverse event ($P = 0.44$). For children with one or more additional intraocular surgical procedures, 44 of 51 (86%) had strabismus compared with 47 of 61 (77%) for children without surgery ($P = 0.23$).

Changes in Strabismus

Of 34 infants who were orthotropic at near 12 months after cataract surgery, 14 (41%) were orthotropic at distance and 15 (44%) were orthotropic at near at age 5 years without strabismus surgery.[13] Of the 28 of 114 infants (25%) that had strabismus at enrollment, 1 was lost to follow-up. Of the remaining 27, 3 (11%) were orthotropic at age 5 years without strabismus surgery.

Visual Acuity and Stereopsis

There was a significant relationship between visual acuity at age 4.5 years and orthotropia at distance by age 5 years (Table 3). Median visual acuity in the operative eye was 0.30 logMAR (20/50) for children with orthotropia and 1.10 logMAR (20/252) for nonorthotropic children ($P = 0.0001$). The proportion of children 20/200 or worse was 19% among orthotropic children and 56% among nonorthotropic children ($P = 0.0005$). These results did not change when children with a microtropia ($<10^{\Delta}$) were grouped with the orthotropia children: Median visual acuity was 0.4 logMAR (20/50) for children with orthotropia or microtropia $<10^{\Delta}$ and 1.10 logMAR (20/252) for strabismus $\geq 10^{\Delta}$ ($P = 0.0001$). Stereopsis was detected at age 4.5 years by one or more of the three tests in 12 of 21 (57%) children with orthotropia at near by age 5 years versus 16 of 89 (18%) of those with strabismus ($P = 0.0006$). When orthotropia was grouped with microtropias $<10^{\Delta}$, 24% (8/33) of this cohort children showed measurable stereopsis on Frisby stereoacuity testing compared to 7% (7/75) with strabismus of $\geq 10^{\Delta}$ ($P = 0.02$). Among the 21 children with orthotropia at near by age 5 years, the mean near point of convergence was 5.5 ± 3.6 cm (standard deviation; range, 1–14 cm) for the 11 patients with this measurement was made.

Discussion

In the IATS, a similar percentage of patients developed strabismus by age 5 years after unilateral cataract surgery coupled with contact lens or primary IOL implantation (86% vs 77%, $P = 0.33$). These rates are consistent with previous reports of strabismus in the setting of unilateral congenital cataracts.[1-10] Some reports have suggested that IOL insertion lowers the frequency of strabismus. Lambert and colleagues[1] described rates of strabismus of 75% using IOLs and 92% using contact lenses in a small series of infants after unilateral cataract surgery. Autrata and colleagues[2] reported a lower percentage of patients with strabismus after IOL implantation compared to CL correction (55% vs 83%). We did not find a statistically significant difference in the frequency or characteristics strabismus based on aphakia management. Strabismus was not more common in children who experience an adverse event or who underwent additional intraocular surgeries.

Esotropia was the most common type of strabismus in both treatment groups and outnumbered exotropia 2:1. This is consistent with other reports of strabismus following cataract surgery in infancy.[1,3,5,16,17] Exotropia has been reported as more common when older children develop cataracts.[9, 18] Horizontal deviations were typically poorly controlled and present at distance and near. Small-angle vertical deviations (17%) were typically found in the setting of concomitant horizontal deviation. Inferior oblique overaction, dissociated vertical deviation, and pattern strabismus were rare in our cohort. Despite meaningful periods of reported patching and fixating with a non-accommodating, pseudophakia eye in early childhood, the near point of convergence was normal in the orthotropic children.[19]

There was a trend for orthotropia to occur more commonly in children who underwent cataract surgery before age 49 days although this difference did not reach statistical significance. In addition, if strabismus had developed prior to cataract surgery, it was uncommon for those children to later become orthotropic. Removing a cataract at an earlier age and before the development of strabismus may facilitate binocularity and the maintenance of orthotropia.[4,7,17,20-23] The longitudinal development of strabismus in the first year after cataract surgery was previously described for this cohort.[11] With 4 years of additional follow-up, we found that >40% of children orthotropic at 12 months after cataract surgery were still orthotropic at age 5 years. Although many factors may contribute to the detection and development of strabismus, our results suggest that the sensorimotor findings are not stable 1 year after cataract surgery.

We previously reported a trend for better grating acuity at one year after cataract surgery in the treated eye in children without strabismus.[11] By age 5 years, children without strabismus more commonly had better visual acuity and stereopsis than those with strabismus. Orthotropia was found in 10 of 19 (53%) children with vision better than 20/40 in the operative eye compared to only 4 of 54 (7%) children with vision 20/200 or worse. It is not known whether better visual acuity in the treated eye is protective for the development of strabismus or whether better ocular alignment improves amblyopia treatment after cataract surgery.

Despite anecdotal reports of good stereopsis outcomes, most children do not develop stereopsis after unilateral congenital cataract surgery.[4,7,20-22] Hartmann and colleagues[15] reported gross stereopsis using one or more of three stereopsis tests in 25.5% of children enrolled in the IATS at age 4.5 years. Based on our data, 12 of 28 (43%) of the IATS children with stereopsis at age 4.5 years were orthotropic at age 5 years. Detectable stereopsis is more than three times more likely (18 vs 57%) in children with orthotropia at near by age 5 years versus those with strabismus ($P = 0.0006$). In Hartmann's report, the highest levels of measured stereopsis was 170 arcsec using Frisby stereoacuity testing. When orthotropia was grouped with microtropias $<10^{\Delta}$, 24% of IATS children showed measurable stereopsis on Frisby stereoacuity testing compared to 7% with strabismus of $\geq 10^{\Delta}$.

The largest limitation in this study is the inherent challenges of subgroup analysis within the IATS. In addition, there were no protocols to direct investigators regarding the indications for strabismus surgery.

In conclusion, at age 5 years, IOL implantation does not appear to influence the rate of strabismus development. Better visual acuity in the operated eye and higher levels of stereopsis were associated with lower rates of strabismus.

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References

1. Lambert SR, Lynn M, Drews-Botsch C, et al. A comparison of grating visual acuity, strabismus, and reoperation outcomes among infants with aphakia and pseudophakia after unilateral cataract surgery during the first six months of life. J AAPOS. 2001; 5:70–75. [PubMed: 11304812]
2. Autrata R, Rehurek J, Vodickova K. Visual results after primary intraocular lens implantation or contract lens correction for aphakia in the first year of age. Ophthalmologica. 2005; 219:72–9. [PubMed: 15802930]
3. Spanou N, Alexopoulos L, Manta G, et al. Strabismus in pediatric lens disorders. J Pediatr Ophthalmol Strabismus. 2011; 48:163–6. [PubMed: 21608524]
4. Wright KW, Matsumoto E, Edelman PM. Binocular fusion and stereopsis associated with early surgery for monocular congenital cataracts. Arch Ophthalmol. 1992; 110:1607–9. [PubMed: 1444921]
5. Cheng KP, Hiles DA, Biglan AW, Pettapiece MC. Visual results after early surgical treatment of unilateral congenital cataract. Ophthalmology. 1991; 98:903–10. [PubMed: 1866144]
6. Hosal BM, Biglan AW, Elhan AH. High levels of binocular function are achievable after removal of monocular cataracts in infants before 8 years of age. Ophthalmology. 2000; 107:1647–55. [PubMed: 10964822]
7. Brown SM, Archer SA, Del Monte MA. Stereopsis and binocular vision after surgery for unilateral infantile cataract. J AAPOS. 1999; 3:109–13. [PubMed: 10221805]
8. Watts P, Abdolell M, Levin AV. Complications in infants undergoing surgery for congenital cataract in the first 12 weeks of life: is early surgery better? J AAPOS. 2003; 7:81–5. [PubMed: 12736618]
9. Hiles DA, Sheridan SJ. Strabismus associated with infantile cataracts. Int Ophthalmol Clin. 1977; 17:193–202. [PubMed: 924731]
10. Awner S, Buckley EG, DeVaro JM, Seaber JH. Unilateral pseudophakia in children under 4 years. J Pediatr Ophthalmol Strabismus. 1996; 33:230–36. [PubMed: 8827558]

11. Lambert SR, Lynn MJ, Hartmann EE, et al. Infant Aphakia Treatment Study Group. Comparison of contact lens and intraocular lens correction of monocular aphakia during infancy: a randomized clinical trial of HOTV optotype acuity at age 4.5 years and clinical findings at age 5 years. JAMA Ophthalmol. 2014; 132:676–82. [PubMed: 24604348]

12. Plager DA, Lynn MJ, Buckley EG, Wilson ME, Lambert SR. Infant Aphakia Treatment Study Group. Complications in the first 5 years following cataract surgery in infants with and without intraocular lens implantation in the Infant Aphakia Treatment Study. Am J Ophthalmol. 2014; 158:892–8. [PubMed: 25077835]

13. Bothun ED, Cleveland J, Lynn MJ, et al. Infant Aphakic Treatment Study. One-year strabismus outcomes in the Infant Aphakia Treatment Study. Ophthalmology. 2013; 120:1227–31. [PubMed: 23419803]

14. Infant Aphakia Treatment Study Group. The Infant Aphakia Treatment Study: design and clinical measures at enrollment. Arch Ophthalmol. 2010; 128:21–7. [PubMed: 20065212]

15. Hartman EE, Stout AU, Lynn MJ, Yen KG, Kruger SJ, Lambert SR. Infant Aphakia Treatment Study. Stereopsis Results at 4.5 Years of Age in the Infant Aphakia Treatment Study. Am J Ophthalmol. 2015; 159:64–70. [PubMed: 25261241]

16. Parks MM, Hiles DA. Management of infantile cataracts. Am J Ophthalmol. 1967; 63:10–19. [PubMed: 6018201]

17. France TD, Frank JW. The association of strabismus and aphakia in infants. J Pediatr Ophthalmol Strabismus. 1984; 21:223–6. [PubMed: 6334154]

18. Weisberg OL, Sprunger DT, Plager DA, Neely DE, Sondhi N. Strabismus in Pediatric Pseudophakia. Ophthalmology. 2005; 112:1626–8.

19. Drews-Botsch CD, Celano M, Kruger S, Hartmann EE. Infant Aphakia Treatment Study. Adherence to occlusion therapy in the first six months of follow-up and visual acuity among participants in the Infant Aphakia Treatment Study. Invest Ophthalmol Vis Sci. 2012; 53:3368–75. [PubMed: 22491410]

20. Gregg FM, Parks MM. Stereopsis after congenital monocular cataract extraction. Am J Ophthalmol. 1992; 114:314–17. [PubMed: 1524121]

21. Birch EE, Swanson WH, Stager DR, Woody M, Everett M. Outcome after very early treatment of dense congenital unilateral cataract. Invest Ophthalmol Vis Sci. 1993:343687–99.

22. Brown SM, Archer S, Del Monte MA. Stereopsis and binocular vision after surgery for unilateral infantile cataract. J AAPOS. 1999; 3:109–13. [PubMed: 10221805]

23. Fawcett SL, Wang Y, Birch EE. The critical period for susceptibility of human stereopsis. Invest Ophthalmol Vis Sci. 2005; 46:521–5. [PubMed: 15671277]

Table 1

Ocular alignment by 5 years of age

Deviation	**n (%)**[a]			**Frequency n (%)**[b]		**Mean ± SD (range), PD, n**[c]
Orthophoria	21 (19)					
		Total no.	Phoria	Intermittent	Constant	
Esotropia	56 (50)[d]	55	0	5 (10)	50 (90)	21.7 ± 14.1 (2-70), 49
Exotropia	30 (27)[e]	30	2 (7)	10 (33)	18 (60)	25.8 ± 13.7 (3-50) 29
Pure hypertropia	5 (4)	4	0	2 (50)	2 (50)	13.0 ± 7.7 (2-20), 4

PD, prism diopter; *SD*, standard deviation.

[a]Percent based on total number of patients (112).

[b]Percent based on number of patients with frequency data for each deviation (“Total no”).

[c]Percent based on number of 56 patients with the specified deviation.

[d]Nine of the 56 patients with esotropia also exhibited hypertropia.

[e]5 of the 30 patients with exotropia also exhibited hypertropia.

Table 2

Ocular alignment at distance versus near by age 5 years

Deviation	No. patients with deviation (%)	
	Distance	**Near**
Orthophoria	21 (19)	21 (19)
Esotropia	47 (42)	53 (47)
Exotropia	25 (22)	25 (22)
Hypertropia	5 (4)	4 (4)
Esotropia with hypertropia	9 (8)	6 (5)
Exotropia with hyperopia	5 (4)	3 (3)
Total	112	112

Table 3

Orthophoria relative to visual acuity by age 5 years

Visual acuity	Orthophoria at distance		*P* value
	Yes (n = 21)	No (n = 90)	
Median logMAR, median (IQR)	0.30 (0.20-0.70)	1.10 (0.40-1.92)	0.0001[a]
Snellen categories, no. (%)			0.0005[b]
20/20 to <20/40	10 (48)	9 (10)	
20/40 to <20/80	5 (24)	22 (24)	
20/80 to <20/200	2 (10)	9 (10)	
20/200 or worse	4 (19)	50 (56)	

IQR, interquartile range.

[a] Wilcoxon rank sum test comparing medians of the two groups.

[b] Fisher exact test comparing percentages of patients in the VA categories between the two groups.