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Complications, adverse events and additional intraocular surgery one year after cataract surgery in the Infant Aphakia Treatment Study

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Abstract

Purpose—To compare rates and severity of complications between infants undergoing cataract surgery with and without intraocular lens (IOL) implant.

Design—Prospective randomized clinical trial.

Participants—The Infant Aphakia Treatment Study (IATS) is a randomized, multi-center (12) clinical trial comparing treatment of aphakia with a primary IOL or contact lens in 114 infants with unilateral congenital cataract.

Intervention—Infants underwent cataract surgery with or without placement of IOL.

Main Outcome Measures—The rate, character and severity of intraoperative complications (IC), adverse events (AE) and additional intraocular surgeries (AIS) during the first post operative year in the two groups were analyzed.

Results—There were more patients with ICs (28% vs. 11%, p=.031), AEs (77% vs 25%, p< . 0001) and AIS (63% vs 12%, p< .0001) in the IOL group than the contact lens group. Iris prolapse was the most common intraoperative complication. The most common adverse event was visual axis opacification and the most common additional intraocular reoperation was a clearing of visual axis opacification.

Conclusion—The rates of intra operative complications, adverse events and additional intraocular surgeries one year postoperatively were numerically higher in the IOL group, but their functional impact does not clearly favor either treatment group.

The advisability of implanting an intraocular lens (IOL) at the time of cataract surgery in infants, as opposed to leaving the child aphakic with the potential for secondary IOL implantation later in childhood, is controversial. The potential advantages of IOL implantation at the time of cataract extraction must be weighed against the possible disadvantages.(1–6) Among the potential disadvantages are the rate and severity of intra and postoperative complications with the two treatment options. The Infant Aphakia Treatment Study (IATS) is a multi-center, randomized, clinical trial sponsored by the National Eye

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*(Appendix 1, available at http://aaojournal.org)

No conflicting relationship exists for any author.

Institute. (7, 8) The study was designed to compare the use of immediate IOL implantation to the correction of aphakia with a contact lens after cataract surgery performed in infants with a unilateral congenital cataract between 1 and 6 months of age. Visual results 12 months after surgery have been previously reported (8). This paper reports the details of one group of secondary outcomes- intraoperative complications, postoperative adverse events and need for additional intraocular surgeries occuring in the first 12 months following surgery. All of these measures were tracked prospectively per the study protocol.

Methods

The study design, surgical techniques, follow up schedule and patient characteristics at baseline have been reported in detail previously and are only summarized here. (7) This study was approved by the Institutional Review Boards of all 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.

Study Design

The main inclusion criteria were 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. Infants with a unilateral cataract due to persistent fetal vasculature (PFV) were allowed in the study as long as the PFV was not associated with visible stretching of the ciliary processes or involvement of the retina or optic nerve. The other main exclusion criteria were an acquired cataract, a corneal diameter <9 mm, and prematurity (<36 gestational weeks). Patients were randomized to have either an IOL placed at the time of the initial surgery or to be left aphakic.

Follow-up examinations were performed by an IATS certified investigator at one day, one week, one month, and 3 months after cataract surgery. Subsequent follow-up examinations were obtained at 3 month (± 2 weeks) intervals. The investigator performed a standard clinical exam, checking the appropriateness of the optical correction and monitoring for adverse events. All of the patients underwent an examination-under-anesthesia at approximately one year of age.

Complications were divided into intra operative complications (IC), adverse events (AE) occurring in the first postoperative year and conditions necessitating additional intraocular surgery (AIS) in the first year.

Surgical Technique

Infants randomized to the contact lens (CL) group underwent a lensectomy and anterior vitrectomy. Infants randomized to the IOL group had the lens contents aspirated followed by the implantation of an AcrySof SN60AT 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 based on the Holladay 1 formula targeting an 8 D undercorrection for infants 4–6 weeks of age and a 6 D undercorrection for infants older than 6 weeks. Following IOL placement, a posterior capsulectomy and an anterior vitrectomy were performed through the pars plana/plicata. When either a pre-existing opening was present or a rent developed intraoperatively in the posterior capsule and in some eyes with mild PFV, the posterior capsulectomy and anterior vitrectomy were performed through the anterior incision prior to IOL implantation.

Definitions for intraoperative complications

These included unexpected difficulty or events occurring during the course of the surgery:

Iris prolapse- extrusion of the iris through the operative wound during surgery

Hyphema- intraoperative bleeding that necessitated intraocular cautery or washout

Iris damage- permanent structural change to the iris occurring during surgery

Retained cortex- Cortical material remaining in the eye following cataract surgery

Corneal clouding- loss of corneal clarity occuring during the surgical procedure

Iris sphincterotomy- intentional permanent enlargement of the pupil

Lens fragment in vitreous- known loss of lens fragment into vitreous that was not retrieved

Ruptured posterior capsule- inadvertent rupture of the posterior capsule during the procedure

Definitions for Adverse Events

Glaucoma- was defined as IOP >21 mmHg with one or more of the following anatomical changes: 1) corneal enlargement, 2) asymmetrical progressive myopic shift coupled with enlargement of the corneal diameter and/or axial length, 3) increased optic nerve cupping defined as an increase of ≥ 0.2 in the cup-to-disc ratio, or 4) the use of a surgical procedure for IOP control.

Glaucoma suspect- A patient was designated a glaucoma suspect if there was either: 1) two consecutive IOP measurements above 21 mmHg on different dates after topical corticosteroids had been discontinued without any of the anatomical changes listed above; or 2) glaucoma medications were used to control IOP without any of the anatomical changes listed above.

[Although the raw numbers for patients diagnosed with glaucoma and ocular hypertension are reported here, an in depth analysis of this important topic will be the subject of a separate report.]

Pupillary membrane-fibrous tissue extending across the pupil.

Lens reproliferation into the visual axis- lens material regrowth extending into the pupillary space and interfering with vision.

Strabismus- Children who had strabismus surgery were not classified as “orthotropic” even if they were later orthotropic on motility testing.

Other adverse events that were encountered but do not require definition included the following:

corectopia, vitreous hemorrhage, retinal hemorrhage, hyphema, retained cortex, retinal detachment, endophthalmitis, phthisis bulbi, keratitis, corneal abrasion, corneal opacity, corneal edema lasting >30 days, capsular phimosis and wound leak/dehiscence.

Definition for additional intraocular surgery

Additional intraocular surgery was defined as any return to the operating room for an intraocular surgery during the first postoperative year due to an adverse event or complication.

Statistical Methods

Percentages were compared between groups using Fisher's exact test. The median visual acuity in logMAR (logarithm of the Minimal Angle of Resolution) units was compared between patients with and without additional surgery to clear the visual axis using the Wilcoxon rank-sum test. The effect of age was evaluated by categorizing patients into younger (≤48 days) and older (≥49 days) age groups. Patients were stratified into these groups for randomization and the degree of undercorrection for the IOL power calculation was determined according to these categories. Given the large differences in the occurrence of intraoperative complications, adverse events, and additional surgery between the IOL and CL groups, the analyses comparing age groups were done for the treatment groups separately. The significance level was 0.05.

Results

Intraoperative complications

There were more patients with intraoperative complications reported in the IOL group-16 (21%)- than the CL group - 6 (11%), p= .031]. There were a total of 22 intraoperative complications in 16 IOL patients. Of these, iris prolapse was the most common (12), followed by iris damage (3) and hyphema (2). There was one occurrence each of retained cortex, corneal clouding, iris sphincterotomy, lens fragment in vitreous and inadvertent rupture of the posterior capsule.

More specifically in the IOL group:

Iris prolapse- 9 of the 12 incidents of iris prolapse were associated with no known adverse sequelae. Iris prolapse usually occurred following enlargement of the superior wound prior to IOL placement or during IOL implantation. The other three are detailed under iris damage.

Iris damage occurred in three patients. One required McCannell suture repair of an iris defect caused by the vitrector, one was a superior cyclodialysis that occurred during placement of the superior haptic of the IOL and the third was a minor defect induced by iris prolapse that occurred during replacement of the IOL following posterior capsule rupture.

Hyphemas occurred in two patients- one was secondary to the cyclodialysis reported above and the second was secondary to iris prolapse during lens positioning. Both were cleared prior to conclusion of the surgery.

Other one time complications included:

Retained cortex- did not cause any postoperative issues.

Cornea clouding- transient and not significant.

Iris shincterotomy- was done purposefully in one eye to achieve adequate pupillary dilation.

Lens fragment in vitreous- necessitated a pars plana approach to remove it at the time of original surgery.

Ruptured posterior capsule- occurred during injection of foldable one piece IOL. This IOL was then removed from the compromised capsular bag and replaced with a three piece IOL in the sulcus.

In the contact lens group, six patients experienced eight intraoperative complications- three with hyphema, two iris prolopse, and one each iris damage, retained cortex and corneal clouding.

More specifically in the contact lens group:

Hyphema- three patients had blood in the eye during the procedure- two from the scleral wound and one from the iris. All 3 were controlled and there was no residual blood in the anterior segment at the end of the procedures.

Iris prolapse- there were 2 instances of minor iris prolapse following removal of the vitrectomy hand piece. The iris was easily reposited.

Iris damage- one patient had minor damage to the iris associated with a small hyphema.

A small amount of *retained cortex* at the edges of the posterior capsulotomy was noted in one eye and another eye had transient *corneal clouding* during the procedure. Neither had any lasting effect.

Adverse events

In the first post operative year, there were more patients with adverse events in the IOL group- 44 (77%) than the CL group- 14 (25%), $p < .0001$. Total adverse events were 75 in the IOL group and 22 in the CL group.

52 (of the 75, 69%) adverse events in the IOL group were related to the visual axis- 24 lens reproliferation, 17 pupillary membranes and 11 corectopia.- vs. only 2 such events in the CL group. The number of non-visual axis related adverse events between the two groups was similar- 23 in the IOL group and 20 in the CL group.

Severe complications associated with permanent visual loss- retinal detachment, endophthalmitis and phthisis- were confined to the CL group. There were two retinal detachments, one of which was associated with endophthalmitis and the other resulted in phthisis bulbi.

There was one case of contact lens associated bacterial keratitis that resulted in a visually insignificant corneal opacity and one corneal abrasion in a contact lens patient.

Glaucoma was diagnosed more often in the IOL group than the CL group- 7 vs 3- though this did not reach statistical significance. There were two additional patients in each group labeled as glaucoma suspects.

Additional intraocular surgeries

More patients underwent additional intraocular surgeries in the first twelve months after cataract surgery in the IOL group (36) than the CL group (7), $p < .0001$. The total number of surgeries in the IOL group (43) was also significantly higher than the CL group (11).

Looked at another way, only 13 % of CL patients required additional intraocular surgery in the first 12 months while 63% of the IOL group required an additional surgery.

The majority of additional surgeries in both groups were necessary to clear visual axis opacities- 34 of the 43 in the IOL group and 6 of 11 in the CL group.

4 pts in the IOL group underwent surgery for glaucoma versus 1 patient in the CL group.

There were 2 retinal detachment surgeries in the CL group.

There was 1 case each of wound dehiscence repair, IOL exchange, iridectomy/iridotomy, scleral patch graft and lysis of vitreous wick in the IOL group and one case each of iridectomy/iridotomy and laser for treatment of lattice degeneration in the CL group.

The visual acuity of the children in the IOL group who required additional intraocular surgery for visual axis opacification was compared to the IOL patients who did not require such surgery. At one year of age, the median logMAR acuity of patients with additional intraocular surgery (.88, n=34) is not statistically different from that of patients without additional intraocular surgery(.97, n=27), p= .97.

A total of 38 patients required intervention for clearing of a pupil related visual axis opacity including lens reproliferation into visual axis, pupillary membrane, visually significant corectopia, retained cortex, capsular phimosis or excess deposits on IOL. 34 of the 38 were in the IOL group (IOL: 60% vs. CL: 7%. ($p < .0001$). 36 of the 38 procedures to clear the visual axis were intraocular; 2 were YAG laser capsulotomies.

More detail regarding the adverse events that led to additional intraocular surgeries is in Table 1.

Effect of Age

In the CL group, the occurrence of intraoperative complications, adverse events, and additional surgery was higher for younger patients but the difference did not approach statistical significance except for a visual axis opacity adverse event (younger: 12%, older: 0%, $p = 0.079$) (Table 2). In the IOL group, the occurrence of events was markedly higher for the younger patients and was statistically significant for any adverse event (younger: 92%, older: 66%, $p = 0.026$) and for the specific adverse event of visual axis opacification (younger: 84%, older: 50%, $p = 0.011$).

Discussion

The decision on whether to implant an IOL in an infant eye at the time of surgery for congenital cataract, as with any surgery, requires balancing the expected benefit of the surgery against the risks associated with the procedure. One of the potential benefits of placing an IOL at the time of infant cataract surgery and the primary outcome measure of the IATS is the visual acuity. At one year, the acuity in the two groups has not been different (8). This measure will be reassessed in all study patients at age 4.5 years. Among the secondary outcome measures of the study are some of the risks of this procedure-intraoperative complications, adverse events and the need for additional intraocular surgeries. At first glance the number of these secondary measures occurring in the first 12 months post operatively appear to strongly favor not placing a primary IOL in the infant eye. However, closer inspection makes this conclusion less compelling.

Twelve of the 22 intraoperative complications listed for IOL patients were iris prolapse. In nine of these, the iris was easily reposited with no long-term sequelae. One of the listed “complications” in the IOL group was a sphincterotomy. This was an intentional enlargement of a very small poorly dilating pupil. The number of patients experiencing other intraoperative complications in the two groups was not statistically different- -4 in the CL group and 7 in the IOL group.

The number of adverse events during the first year was also significantly higher in the IOL group than the CL group, but the difference in the two groups largely relates to the higher rate of pupil and visual axis related adverse events in the IOL group. There were 52 such

AE's in the IOL group vs. 2 in the CL group. The total of all other reported AEs in the two groups was essentially identical- 23 in the IOL group vs 20 in the CL group.

The high incidence of lens reproliferation into the visual axis and pupillary membrane formation after IOL implantation was expected based on previous reports.(9,10) This is thought to arise because the IOL in the capsular bag prevents the anterior and posterior capsule leaflets from fusing together thereby not sequestering the proliferating lens epithelial cells. Although a similar proliferation of cells across the visual axis can occur in an aphakic infant, these cells are usually sequestered behind the iris in the donut shaped residual lens capsule remnants forming a so called Sommerring ring. With time, some of these residual rings grow so large that they narrow the anterior chamber angle from posterior pressure on the iris.

It is the large difference in visual axis related AEs between the two groups that resulted in a similarly large difference in additional intraocular surgeries in the first postoperative year. Thirty-six patients in the IOL group underwent 49 additional intraocular surgeries vs 7 patients undergoing 10 additional intraocular surgeries in the CL group. Thirty-four patients in the IOL group underwent surgery for clearing the visual axis versus only 6 in the CL group.

Additional intraocular surgeries for reasons other than VAO were rare in both groups- 9 in the IOL group vs 5 in the CL group. Four of the surgeries in the IOL group were for glaucoma.

There is clearly a large need for additional intraocular surgery in the first postoperative year if an IOL is placed primarily in an infant as opposed to leaving the child aphakic. This difference is almost exclusively due to development of VAO. However, this difference needs to be put into perspective, both long and short- term. The surgery to remove the reproliferated lens epithelial cells is straightforward- requiring a pars plana entry or limbal incision for aspiration of the opacity with a vitreous cutting instrument. Separate infusion into the anterior chamber is sufficient so that no additional sclerotomies are necessary. In the short term, it is somewhat comforting to know that the additional intraocular surgeries have not themselves been associated with additional complications.

A previous report from the IATS noted that the visual acuity in the IOL and CL groups are not statistically different (8) documenting that the higher rates of IC, AE and AIS in the IOL group reported here are not associated with a poorer visual outcome. However, it is instructive to analyze further whether the visual acuity among the IOL patients who required additional intraocular surgery for visual axis opacity is poorer than the IOL patients that did not require additional intraocular surgery. At one year, there is not a statistical difference between the two groups.

This apparently higher rate of additional intraocular surgery in the IOL group must also be put in a long term perspective. The two groups are not equivalent at the one year mark- one group is pseudophakic, the other is aphakic. In order to make the two groups equal, all of the CL group will need to undergo an additional intraocular surgery to place a secondary IOL. It is likely that the majority of the aphakic group will choose this option at some point in the next decade or so. If those additional intraocular surgeries (up to 57) are eventually counted, the ultimate number of additional intraocular surgeries in the two groups may become higher in the CL group than the original IOL group. This assumes that there will not be a significant number of IOL related additional intraocular surgeries in that group over that same time span, an assumption that is likely valid based on previously published intermediate and long term studies of IOLs in children.

The effect of IOL placement on the potential development of pseudophakic glaucoma remains controversial and there has been suggestion that placing an IOL in a child's eye may decrease the incidence of glaucoma in comparison to leaving the child aphakic (11–13). However, most of such reports had a selection bias and included few if any infants. In the present study, ten infants have been diagnosed with glaucoma in the first year of follow-up following cataract surgery. Seven of the 10 are pseudophakic, though this difference is not statistically significant. A more detailed examination of glaucoma in the IATS study will be the topic of a separate publication.

In conclusion, at one year postoperatively, there have been more intraoperative complications, adverse events and need for additional intraocular surgeries in the IOL group compared to the contact lens group. These differences between the two groups have not been associated with a worse visual outcome to date. There is reason to believe that, over the long term, the number of additional intraocular surgeries between the two groups will become more even.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Number of Patients with Selected Adverse Events and with Surgery for that Event

Adverse Event	CL (57 patients)		IOL (57 patients)	
	# with Event	# with Surgery	# with Event	# with Surgery
Lens reproliferation into visual axis	1	1	24	23
Pupillary membrane	0		17	17
Corectopia	1	0	11	8
Glaucoma	3	1	7	4
Retinal detachment	2	2	0	
Wound dehisence	0		1	1
IOL exchange	0		1	1
Vitreous wick	0		1	1
Lattice Degeneration*	1	1	0	

*Not considered related to cataract surgery.

IOL- intra ocular lens

CL- contact lens

Note: Numbers do not represent unique patients, i.e., one patient could be in more than one category.

Table 2

Percent of Patients with Intraoperative Complications, Adverse Events, and Additional Surgery According to Treatment and Age

	CL			IOL		
	≤48 days(n = 25)	**≥49 days(n = 32)**	**p- value**	**≤48 days(n = 25)**	**≥49 days(n = 32)**	**p- value**
Intraoperative Complication	4 (16%)	2 (6%)	0.39	10 (40%)	6 (19%)	0.14
Any Adverse Event	7 (28%)	7 (22%)	0.76	23 (92%)	21 (66%)	0.026
Visual Axis Opacity AE	3 (12%)	0 (0%)	0.079	21 (84%)	16 (50%)	0.011
Any Additional Surgery	4 (16%)	3 (9%)	0.69	19 (76%)	17(53%)	0.10
Visual Axis Opacity Surgery	3 (12%)	3 (9%)	0.99	17 (68%)	17 (53%)	0.29

CL- contact lens

IOL- intraocular lens

AE- adverse event