

Phakic Intraocular Lens Implantation for Treatment of Anisometropia and Amblyopia in Children: 5-year Follow-up

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ABSTRACT

PURPOSE: To evaluate the safety and efficacy during 5-year follow-up of phakic intraocular lens (PIOL) implantation to correct high anisometropia in amblyopic children who were non-compliant with traditional medical treatment including spectacles or contact lenses.

METHODS: Retrospective study of 10 eyes of 10 children with high anisometropia who underwent PIOL implantation (9 with an iris-supported IOL and 1 with a posterior chamber IOL). Patient age at the time of implantation ranged from 2 to 15 years. Mean preoperative spherical equivalent refraction was -10.14 ± 6.96 diopters (D) (range: $+8.00$ to -18.00 D). Mean logMAR corrected distance visual acuity (CDVA) was 0.84 ± 0.52 . Postoperative data at 6, 24, and 60 months were evaluated.

RESULTS: Corrected distance visual acuity improved in all children. At 24 months, logMAR CDVA was 0.39 ± 0.35 and at 5 years was 0.36 ± 0.38 (range for both: 0.1 to 1.0) ($P=.01$). Improvement of more than three logMAR lines of CDVA was achieved in all children except for one (one line improvement) who was implanted with a posterior chamber PIOL. No loss of CDVA was detected in any patient. Five years after surgery, endothelial cell count was >2000 cells/mm² in eight (80%) patients; for the remaining two patients, one reported frequent eye rubbing and the other suffered ocular trauma.

CONCLUSIONS: Phakic IOL implantation in children with anisometropic amblyopia showed a positive long-term impact on visual acuity. [*J Refract Surg.* 2011;27(7):494-501.]

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mblyopia refers to a decrease in best-corrected visual acuity in an eye with no evident organic cause.¹ It is one of the most common causes of visual loss in childhood and is characterized by reduced spatial vision in the presence of strabismus, refractive error, or form deprivation during the visually sensitive developmental period. Anisometropia is a difference in refractive error between the two eyes of an individual, which leads to a projection of unequal images on the fovea (aniseikonia) and causes unilateral blur. If moderate to high anisometropia is left untreated, the image of the eye providing the blurred image to the brain is suppressed and leads to the development of amblyopia. Amblyopia is directly related to the magnitude of anisometropia.¹ A variety of treatments for anisometropic amblyopia have been described, such as patching, refractive correction with spectacles or contact lenses, atropine penalization, and some techniques of refractive surgery.²⁻⁴

Pediatric refractive surgery was developed with the aim of finding a solution for those cases of amblyopia where compliance is poor and/or conventional treatments are ineffective, such as high anisometropia and poor compliance due to social circumstances or neurobehavioral disorders. Indeed, the first studies of pediatric refractive surgery were of children with neurobehavioral disorders for whom spectacles or contact lenses were not a viable option.^{5,6}

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Two types of pediatric refractive surgery can be distinguished⁷: intraocular refractive surgery with intraocular lens (IOL) implantation and corneal refractive surgery (photorefractive keratectomy and LASIK). In select cases, these types of surgery eliminate or reduce anisometropic ametropia, allowing the correction of high myopia and astigmatism. Intraocular pediatric refractive surgery began with IOL implantation in children with congenital or traumatic cataract. Such children initially were left aphakic and were treated subsequently with contact lens wear or epikeratophakia.⁸ Different models of phakic IOLs (PIOLs) implanted in children have been reported in the literature.^{2,9-15} In most of these cases, surgical refractive treatment was used to reverse anisometropic ametropia associated with amblyopia, which had failed with previous conventional treatments, and laser refractive surgery was not possible mainly due to corneal thickness limitations.^{2,10,12-15}

A controversy regarding the use of PIOLs in children is the potential development of complications over time (short- and long-term complications),⁷ such as cataract formation, PIOL dislocation, or endothelial cell count loss. However, the prevalence of these complications reported in the peer-reviewed literature is low.^{2,9-15} To date, the maximum follow-up reported in such cases is 48 months.

In the current study, a series of 10 children implanted with different PIOL models and with 60-month postoperative follow-up is reported with the aim of analyzing the visual changes achieved and the potential corneal and intraocular complications. All children presented with severe anisometropic ametropia and secondary amblyopia that could not be reversed with spectacle or contact lens correction and occlusion therapy.

PATIENTS AND METHODS

PATIENTS

This retrospective, interventional, consecutive case series comprised 10 children followed from early childhood in the specialized pediatric unit of the Visum/ Instituto Oftalmológico de Alicante, Spain. A retrospective analysis of the clinical histories of all children with the diagnosis of anisometropic amblyopia who underwent PIOL implantation in our clinic was performed. All patients fulfilled the following inclusion criteria: refractive amblyopia, anisometropia, and unsuccessful conventional amblyopia therapy using various combinations of spectacles, contact lenses, and occlusion therapy (contact lens intolerance, spectacle intolerance, patching therapy failure). The initial amblyopia treatment was performed by re-

fractive correction and patching (occlusion) therapy for 4 to 6 hours per day and was maintained as long as possible. Exclusion criteria for this retrospective analysis were patients with anisometropic amblyopia and PIOL implantation older than 16 years.

Mean age of the eight boys and two girls included in the study was 8 years (range: 2 to 15 years). All cases presented with anisometropic ametropia associated with severe amblyopia (difference in logMAR visual acuity among eyes of five lines or more). In addition, three cases presented with strabismus (two cases of exotropia and one of esotropia). Preoperatively, mean spherical equivalent cycloplegic refraction (cyclopentolate 1%) was -9.50 diopters (D) (range: $+8.00$ to -18.00 D). Preoperative logMAR corrected distance visual acuity (CDVA) ranged from counting fingers to 1.0.

EXAMINATION PROTOCOL

Pre- and postoperative clinical evaluation of all eyes included slit-lamp examination, intraocular pressure (IOP), uncorrected distance visual acuity (UDVA), CDVA, cycloplegic refraction, cover test, ocular motility evaluation, corneal topography using the Corneal Analysis System (CAS; EyeSys Vision Inc, Houston, Texas), biometry (IOLMaster; Carl Zeiss Meditec, Jena, Germany), and endothelial cell count using the Non-com ROBO-CA specular microscope (Konan Medical Inc, Hyogo, Japan) or the Topcon SP-3000P (Topcon Corp, Tokyo, Japan). The Snellen or Pigassou visual acuity chart was used to determine preoperative visual acuity in eight children (5 years or older); two 2-year-old children were evaluated by preferential looking charts. Retinoscopy was used in all cases for objective preoperative refraction; subjective refraction was determined in the older patients. Refraction was always performed under cycloplegia. All examinations were performed by the pediatric and strabismus clinic consultant (C.L.) with the protocol described above.

All data were recorded in a model database including the most relevant variables for evaluating the efficacy and safety of the treatment: UDVA, refraction, CDVA, endothelial changes, IOP, and complications. We evaluated the data at 6, 24, and 60 months after PIOL implantation as all patients presented for follow-up at these time intervals. In all cases, PIOL implantation was performed because corneal refractive surgery was not possible due to corneal thickness limitations (myopic cases) or excimer laser limitations (hyperopic cases).

Prior to surgery, all patients and their parents/guardians were informed about the procedure as well as its risks and benefits and provided written informed

consent. The targeted postoperative refraction was emmetropia or a certain residual power for the purpose of isometropia with the other eye. In addition, patients and parents were informed about this retrospective analysis and signed informed consent was obtained in accordance with the Declaration of Helsinki.

SURGICAL PROCEDURE

Nine eyes were implanted with an anterior chamber, iris-fixated PIOL (Artisan; Ophtec, Groningen, The Netherlands) and one with a posterior chamber PIOL (PRL; CIBA Vision AG, Embrach, Switzerland). The iris-supported PIOL was the preferred option in these patients to avoid the potential risk of complications with the angle-supported and posterior chamber PIOLs (eg, hypertension, cataract) in the immature child eye. A posterior chamber PIOL was required in one patient due to the special anatomical features of the iris. The power of the IOL was calculated by the manufacturer according to the refraction, keratometry, and anterior chamber depth as well as the postoperative refractive target. No PIOL implantation was performed in any patient with anterior chamber depth <3.0 mm.

All surgeries were performed by the same experienced surgeon (J.L.A.). No intraoperative complications occurred in any patient. The surgical procedure differed depending on the type of PIOL implanted.

ARTISAN PIOL IMPLANTATION TECHNIQUE

A frown scleral tunnel incision (6.5 mm) was performed. A paracentesis was made at 3 o'clock and 9 o'clock. The anterior chamber was filled with a sodium hyaluronate high density viscoelastic. The Artisan PIOL was implanted through the incision and rotated and positioned in the horizontal meridian. Phakic IOL enclavation was done by the double-clamp technique using specific microincision forceps. Once the PIOL was positioned, the viscoelastic was removed, a small peripheral iridectomy was performed, and the scleral incision was sutured with a 3-bite running nylon 10/0 suture. The sutures were not removed. The 6.0-mm optical zone Artisan PIOL was intended to be used in all patients (largest optical zone to avoid photic phenomena). However, there were two patients in which the 5.0-mm model was implanted due to the limitation in the optical zone according to the required PIOL power.

PRL PIOL IMPLANTATION TECHNIQUE

A clear corneal incision (3.0 mm) was created and the anterior chamber was filled with viscoelastic (Healon; Abbott Medical Optics, Abbott Park, Illinois). The PIOL was loaded into the cartridge and injected

intraocularly, placing it within the posterior chamber by an iris manipulator. One milliliter of miocchol chloride (CIBAVision, Claremont, California) was injected into the anterior chamber, and a small peripheral iridectomy was performed. The viscoelastic material was removed. No corneal sutures were required.

POSTOPERATIVE PROTOCOL

A cycloplegic agent (cyclopentolate 1%) was prescribed to be applied twice a day for the first 5 days after surgery as well as dexamethasone 0.1% drops (Maxidex; Alcon Laboratories Inc, Ft Worth, Texas) during the first 15 days. Patching occlusion therapy was prescribed for all patients after the first postoperative month, once the residual refraction was corrected by means of appropriate spectacles. The initial patching protocol was occlusion of 4 to 6 hours per day and was modified according to the outcomes.

STATISTICAL ANALYSIS

Data were collected in Excel (Microsoft Corp, Redmond, Washington) and exported to SPSS for Windows (version 15.0; SPSS Inc, Chicago, Illinois) for data analysis. The analyzed data were CDVA, cycloplegic refraction, endothelial cell count, keratometry, and complications. Differences between pre- and postoperative outcomes were analyzed using the paired Student *t* test or Wilcoxon test depending on whether the samples followed a normal distribution. A *P* value <.05 was considered statistically significant. All variables were described as mean±standard deviation (range).

For an accurate statistical analysis of the visual acuity outcomes, decimal values were transformed to the logMAR scale, calculating the minus logarithm of the decimal visual acuity.¹⁶ However, safety and efficacy indices were calculated with visual acuity decimal values according to the standard definition of these indices.¹⁷ The efficacy index was calculated as the ratio of postoperative uncorrected visual acuity to preoperative corrected visual acuity, and the safety index was calculated as the ratio of the postoperative corrected visual acuity to the preoperative corrected visual acuity.

It should be noted that when reviewing the outcomes of the statistical analysis, the sample size was small and the power of statistical tests was limited.

RESULTS

Mean patient age was 8 years, ranging from 2 to 15 years. In all patients, occlusion therapy was applied after surgery. Strabismus surgery was necessary in three

TABLE 1

Visual and Refractive Outcomes of 10 Eyes of 10 Children Implanted With Phakic Intraocular Lens for Treatment of Anisometropic Amblyopia

Patient (Age [y])	Sphere (D)		Cylinder (D)		LogMAR CDVA	
	Preop	5 Years Postop	Preop	5 Years Postop	Preop	5 Years Postop
1* (7)	-10.75	-2.00	2.25	3.50	0.40	0.40
2* (8)	-9.50	-2.50	2.00	3.50	1.00	0.40
3* (2)	-18.00	-0.50	0.00	1.00	2.00	1.00
4 (15)	-11.00	-1.25	2.00	1.00	1.30	1.00
5 (12)	-9.00	-1.50	1.00	0.75	0.22	0.10
6 (5)	+8.00	+2.75	0.00	1.75	1.00	0.10
7 (2)	-12.00	-1.50	0.00	2.00	0.80	0.10
8 (8)	-16.00	0.00	0.00	0.00	0.70	0.22
9 (6)	-8.00	-3.00	3.00	3.00	0.50	0.10
10 (15)	-10.00	0.00	0.00	3.00	0.50	0.22

CDVA = corrected distance visual acuity
 *Patients with associated strabismus.

TABLE 2

Statistical Analysis of Visual Outcomes of 10 Eyes of 10 Children Implanted With Phakic Intraocular Lens for Treatment of Anisometropic Amblyopia

	Mean ± Standard Deviation (Range)		Change in CDVA Over Time (mo) (P Value)
	LogMAR UDVA [Snellen]	LogMAR CDVA [Snellen]	
Preoperative	1.10±0.17 (1.00 to 1.30) [20/250 (20/200 to 20/400)]	0.84±0.52 (0.22 to 2.00) [20/120 (20/100 to 20/2000)]	Preop-24 (.01)
6 months	0.90±0.46 (0.40 to 1.30) [20/160 (20/50 to 20/400)]	0.78±0.76 (0.10 to 1.82) [20/120 (20/25 to 20/2000)]	Preop-6 (.35)
24 months	0.61±0.56 (0.15 to 1.30) [20/80 (20/30 to 20/400)]	0.39±0.35 (0.10 to 1.00) [20/50 (20/25 to 20/200)]	6-24 (.27)
60 months	0.65±0.49 (0.30 to 1.00) [20/80 (20/40 to 20/200)]	0.36±0.38 (0.10 to 1.00) [20/30 (20/20 to 20/50)]	24-60 (.99) Preop-60 (.01)

UDVA = uncorrected distance visual acuity, CDVA = corrected distance visual acuity

patients (strabismus deviation >15 prism diopters) to achieve orthophoria and maintain binocular vision.

VISUAL AND REFRACTIVE OUTCOMES

Table 1 summarizes the pre- and postoperative visual and refractive outcomes. As shown, all patients experienced visual improvement, except one patient (no. 1) who presented with microtropia (exotropia).

Table 2 summarizes the statistical analysis of the visual outcomes achieved. Mean preoperative sphere was -9.63±6.94 D (range: +8.00 to -18.00 D). Cylinder ranged from 0.00 to 3.00 D preoperatively and

mean preoperative spherical equivalent refraction (SE) was -10.14±6.96 D (range: +8.00 to -18.00 D). Mean postoperative sphere 6 months postoperatively was -0.30±0.45 D (range: -1.00 to 0.00 D), and mean SE was -1.30±0.45 D (range: -1.75 to -0.75 D). At 24 months, mean sphere was -0.25±0.97 D (range: -1.75 to +1.50 D), and SE was -1.16±1.03 D (range: -2.38 to +0.75 D). Regarding the 60-month outcomes, mean sphere was -1.06±1.70 D (range: -3.00 to +2.75 D) and mean cylinder was 2.17±1.11 D (range: 0.75 to 3.00 D). The difference between preoperative and 6-month postoperative sphere and cylinder was statis-

TABLE 3

Endothelial Cell Count for 9 Eyes of 9 Children* Implanted With Phakic Intraocular Lens for Treatment of Anisometropic Amblyopia

Patient (Age [y])	Endothelial Cell Count (cells/mm ²)		Endothelial Cell Loss (%)
	Preop	5 Years Postop	
1 (7)	2245.39	2095.62	6.67
2 (8)	2624.72	2338.05	10.92
3 (2)	2423.96	2195.26	10.42
4 (15)	2396.90	2242.00	6.46
5 (12)	3165.80	2770.00	12.50
6 (5)	3567.00	3101.05	13.06
7 (2)	1832.29	1681.00	8.26
8 (8)	3100.00	2750.00	11.29
9 (6)	3100.00	2710.00	12.58
Mean overall (SD)	2717.34 (549.92)	2431.44 (435.66)	10.24 (2.53)

SD = standard deviation

*Although 10 children were enrolled in the study, patient 10 was excluded from endothelial cell loss analysis due to ocular trauma during the postoperative follow-up period.

tically significant ($P=.04$), with no further significant changes ($P\geq.23$). An increase in refractive cylinder at the end of follow-up was observed in six (60%) eyes.

As shown in Table 2, statistically significant differences were found in logMAR CDVA between the preoperative and 24-month postoperative values. In addition, a progressive improvement of CDVA was observed during follow-up, with the best mean value at 60 months. Regarding UDVA, an improvement was also observed over time but it did not reach statistical significance. A comparison between pre- and postoperative UDVA values could not be done because preoperative values were not available due to the high refractive errors present (all patients had visual acuity of counting fingers).

Safety and efficacy indices at 60 months postoperative were 3.90 ± 2.98 (range: 1.00 to 10.00) and 1.42 ± 0.82 (range: 0.83 to 2.00), respectively.

POSTOPERATIVE ENDOTHELIAL CELL COUNTS AND KERATOMETRY

Endothelial cell count was >2000 cells/mm² in all patients 60 months after surgery, except in two (Table 3); one patient had reduced postoperative corneal endothelial cell count as a result of chronic eye

rubbing due to long-standing spring catarrh allergic conjunctivitis (8.3% endothelial loss), and the other patient suffered an ocular trauma during the follow-up period (42% endothelial loss). Preoperatively, mean endothelial density was 2717.34 ± 549.92 cells/mm², whereas 60 months postoperatively, density was 2431.44 ± 435.66 cells/mm² ($P=.04$). Mean endothelial cell loss was $4.25\pm 6.29\%$ (range: 1.57% to 10.92%) 2 years after surgery whereas it was $10.24\pm 2.53\%$ (range: 6.46% to 13.06%) 60 months after surgery. Endothelial cell count was >2000 cells/mm² in 90% of patients preoperatively and at 5 years was 80% (Table 3). The patient who suffered ocular trauma was excluded from the endothelial cell loss statistics to evaluate the endothelial cell effect solely due to the PIOL implant.

No significant changes in mean keratometry were detected during follow-up ($P=.69$).

COMPLICATIONS

One child developed acute iridocyclitis after implantation, which was detected 24 hours after surgery and resolved with steroid administration and follow-up. Otherwise, no major postoperative complications were encountered, and the biomicroscopic appearance of the anterior segment at 60 months was excellent. One patient implanted with an Artisan lens suffered a blunt ocular trauma during follow-up and it was necessary to reposition the PIOL, resulting in residual astigmatism, coloboma of the iris, and a more significant endothelial cell loss (final endothelial count >1500 cells/mm²).

CASES WITH LONGER FOLLOW-UP

In three patients, 84-month follow-up was completed. In these patients, postoperative UDVA and CDVA were excellent (0.85 ± 0.21 [0.70 to 1.00] and 0.22 ± 0.25 [0.05 to 0.40] logMAR, respectively), thus maintaining the improvement achieved in the previous visits. Specifically, in one patient a gain of nine lines of logMAR CDVA was observed. The endothelial cell count in these three cases was >2000 cells/mm² (endothelial cell loss was 8.67%, 20.24%, and 20.76%, respectively).

DISCUSSION

Twenty percent of the general population with high refractive errors develops visual impairment due to severe anisometropic amblyopia.¹⁸ Refractive surgery can be useful in such cases for reducing the refractive error, creating isometropia, and then facilitating the visual recovery with conventional amblyopic treatments. However, there is no clear consensus on pediatric refractive surgery¹⁹⁻²² and it is still considered controversial.

Several reports on this topic have been published but are limited in addressing the controversies, especially regarding the medium- to long-term outcomes.^{2,3,5-7,9-15} A number of recently published studies, some through Pediatric Eye Disease Investigator Group (PEDIG; National Eye Institute, Bethesda, Maryland) trials, have challenged traditional thinking on the limitation of pediatric age in reversing amblyopia and gaining visual function in children aged 6 to 17 years.²³⁻²⁷ Specifically, one PEDIG trial demonstrated that patching 2 to 6 hours per day with near visual activities and atropine in amblyopic patients aged 7 to 12 years could improve visual acuity even if the amblyopia has been previously treated.²⁵ However, the same authors demonstrated that patching 2 to 6 hours per day with near visual activities could modestly improve visual acuity in patients aged 13 to 17 years when amblyopia has not been previously treated.²⁵

When refractive surgery is considered for treating a case of anisometropic ametropia with severe amblyopia, the associated refractive error is normally high in the affected eye (≥ 10.00 D of myopia or ≥ 6.00 D of hyperopia). For this reason, excimer laser refractive surgery is not possible in a great number of patients because significantly large amounts of tissue ablation would be necessary, which can lead to corneal weakening and to an increase in corneal higher order aberrations resulting in a decrease of visual quality.^{28,29} Phakic IOL implantation is a good option in such cases because these types of lenses have proven to provide excellent visual recovery and postoperative visual quality.^{30,31} As stated previously, different models of IOLs have been successfully implanted in children with severe anisometropic amblyopia, but the concern remains regarding unforeseen long-term side effects.

The postoperative functional visual results in these 10 children were rewarding. As expected, better UDVA was observed in all patients due to the effective correction of the refractive error, although in some patients the target refraction was not zero. The CDVA in all 10 operated eyes improved gradually over 60-month follow-up. One factor accounting for this visual improvement is the elimination of anisometropia, which was contributing to the development of amblyopia. Another factor was the application of additional treatments such as patching therapy or strabismus surgery (eyes with a combined anisometropic and strabismic anisometropia) during postoperative follow-up. Our visual results are in concordance with those reported previously for children with anisometropic amblyopia implanted with PIOLs.^{2,9-15,32} In these previous series or case reports, small samples of eyes were also used, with larger samples only in the studies by Lesueur

and Arne¹⁴ (11 eyes) and Tychsen et al¹⁰ (12 eyes). The age range in these studies of PIOL implantation in children was also similar (3 to 16 years). A third potential factor for the improvement in CDVA is change in ocular magnification and higher order aberrations with PIOL implantation.³³ Calculations performed by our group using the Kooijman eye model corrected with spectacles and with a PIOL in high refractive errors proved that most of the increase in visual acuity could be explained by the increase in magnification (a factor of 1.2) and reduction in the retinal spot size (a factor of 2).³³ Spherical refraction was reduced significantly in all patients, which confirms the excellent correction potential of PIOLs, but cylinder increased in some cases. It should be noted that the corneal incision required for insertion of the angle-supported PIOL used in the current study was large, which is a factor that could lead to unexpected astigmatic changes.³⁴ In future studies, flexible and toric angle-supported PIOLs should be evaluated for the use in children to achieve better control of postoperative cylinder.

In the current study, the majority of patients (9 of 10) were implanted with the anterior chamber iris-fixated Artisan lens. Iris-fixated PIOLs have been documented to be well tolerated in the eyes of both adult³⁵⁻³⁷ and pediatric patients with a maximum follow-up of 48 months.^{2,9-13} Specifically, the Artisan model seems a good option because the incidence of complications of cataract or significant endothelial cell loss are rare³⁵ if safety criteria are followed. Saxena et al³⁸ found a negative significant correlation between endothelial cell loss and anterior chamber depth. However, the use of posterior chamber PIOLs in children seems to be more concerning. Although the efficacy of the refractive correction in children with such lenses has been confirmed,^{13,14} there is evidence of the higher risk of cataract formation with this type of PIOL.^{39,40} In the current series, only one patient was implanted with a posterior chamber PIOL and no signs of cataract formation were observed during 5-year follow-up. To the best of our knowledge, this is the first pediatric case reported that was implanted with the PRL model of posterior chamber PIOL. Previous reported cases were all implanted with the Implantable Collamer Lens (ICL) posterior chamber PIOL (STAAR Surgical Co AG, Nidau, Switzerland). It should be noted that subluxation of a phakic refractive lens into the vitreous body has been described and is considered the most serious complication with this type of IOL.⁴¹

Regarding corneal endothelial changes, as expected, a reduction in the endothelial cell density was observed in all cases. However, the values were not indicative of the need for PIOL explantation in any patient and

were in the range of endothelial cell loss reported in adult patients⁴²⁻⁴⁷ and pediatric patients⁹⁻¹⁵ implanted with PIOLs. One limitation of the current retrospective study was the use of different instrumentation to measure the endothelial cell count pre- and postoperatively. This could introduce some bias in the calculation of the endothelial cell loss. Future prospective studies of endothelial damage in pediatric patients implanted with PIOL are mandatory to confirm outcomes from retrospective studies.

Considering the outcomes obtained in the current study, we can conclude that PIOL implantation appears to be an effective option in treating severe cases of anisometropia leading to amblyopia in children in whom conventional treatment methods are not satisfactory and laser refractive surgery is not possible. A better quality of vision compared with keratorefractive surgery with excimer laser is achieved by implanting an anterior chamber PIOL in patients with moderate and high spherical refractive errors.^{48,49} In 60-month follow-up as well as 84-month follow-up (three patients only), the complication rate in our series was very low, with no cataract formation or severe corneal endothelial cell loss requiring PIOL explantation. Few patients were included and longer follow-up is necessary to determine the potential longer term complications. However, our case series presents the longest follow-up that has been reported to date. Regular follow-up is mandatory and eye patching therapy or strabismus surgery after PIOL implantation is crucial for achieving complete visual rehabilitation in these cases. In addition, endothelial cell density must be monitored annually in these patients. Long-term monitoring for endothelial cell density and stability of eye alignment for both motor and sensory is indicated. A number of factors, including proper amblyopia treatment following PIOL implantation, are critical in achieving the optimal clinical results in pediatric patients. Randomized, multicenter, prospective, clinical studies of various ages would greatly enhance our understanding of the efficacy and safety of PIOL implantation in the treatment of anisometropic ametropia in children.

AUTHOR CONTRIBUTIONS

Study concept and design (J.L.A.); data collection (J.L.A., B.T.T.); analysis and interpretation of data (C.L., D.P.P.); drafting of the manuscript (B.T.T., D.P.P.); critical revision of the manuscript (J.L.A., C.L.); statistical expertise (D.P.P.); administrative, technical, or material support (J.L.A.); supervision (J.L.A., B.T.T., C.L.)

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