·Clinical Research·

Phakic posterior chamber intraocular lens for unilateral high myopic amblyopia in Chinese pediatric patients

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Abstract

• AIM: To assess the outcomes of posterior chamber implantable collamer lens (ICL) implantation in Chinese pediatric patients with unilateral high myopic amblyopia.

• METHODS: Eleven eyes of 11 amblyopic patients aged 11.02±3.34y underwent ICL (model V4, Staar Surgical Inc.) implantation to treat unilateral anisometropia were studied. Visual acuity, cycloplegic refraction, contrast sensitivity, stereopsis, intraocular pressure (IOP), vaulting, corneal endothelial cell count and complications were evaluated. Patients completed follow-up at 3d, 1, 3mo and the last follow-up time (mean 8.18±2.82mo) after surgery.

• RESULTS: The mean myopic anisometropia was −13.70±3.25 D preoperatively and +0.69±2.63 D at 8mo postoperatively. The logMAR corrected distance visual acuity (CDVA) of the amblyopic eye was 1.51±0.72 preoperatively and 0.75±0.40 at 8mo postoperatively. The logMAR CDVA at 3d, 1, 3 and 8mo postoperatively improved by a mean of 0.64, 1.55, 1.82 and 2.64 lines and gained more than 2 lines accounted for 18%, 45%, 45%, 64%, respectively. The contrast sensitivity of 0.5, 1 and 2 cpd in amblyopic eyes was significantly increased after surgery. No patient had near stereopsis recovery. The vaulting at 3 and 8mo was significantly lower than that at 1mo postoperatively. No other intraoperative or postoperative complications were observed, except an acute pupillary block glaucoma happened in a patient at two weeks postoperatively.

• CONCLUSION: This short-term results indicate that ICL implantation can be a promising alternative therapy for high myopic anisometropic amblyopia in pediatric patients who have failed with conventional treatments and not suitable to corneal refraction surgery.

• **KEYWORDS:** phakic intraocular lens; myopic anisometropic; amblyopia; pediatric patients; refractive surgery

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INTRODUCTION

Amblyopia is a major cause of unilateral visual impairment, accounting for 33% of all the unilateral visual impairment causes in adult patients [1]. The disorder is characterized by monocular and binocular deficits, including decreased of visual acuity and contrast sensitivity, even lost of stereoacuity. There are three main different types of amblypia: refractive, strabismus and visual deprivation amblyopia. Refractive amblyopia consists of anisometropic, isoametropic and meridional amblyopia. About 50% of amblyopia patients were caused by anisometropia, 25% by strabismus and in every sixth person by mixed strabismus and anisometropia [2]. Conventional treatments for anisometropic amblyopia include refractive correction with spectacles or contact lenses and patching or penalization of the non-amblyopic eye to force the use of the amblyopic eye. However, most of children with myopic anisometropia greater than 3 diopters (D) are intolerant to aniseikonia and diplopia caused by full correction of the spectacle lens[3]. For the advantages of relieve aniseikonia and improve the quality of vision, contact lenses might be more acceptable than spectacles correction [4-5]. However, lots of children still difficult to accept wearing contact lenses everyday due to the foreign body sensation and potential complication of cornea infection[6]. Therefore, it is difficult to cure pediatric patients with severe anisometropia amblyopia by traditional non-surgical methods.

Previous studies have reported that corneal refractive surgery techniques including photorefractive keratectomy (PRK), laser *in situ* keratomileusis (LASIK), and laser-assisted subepithelial keratectomy (LASEK) are effective and safe alternatives for the treatment of unilateral high myopic amblyopia in children who have failed with conventional

approaches [7-12]. Recently, a few case reports or case series have reported that phakic intraocular lens (IOL) implantation is an effective surgical correction of high myopia in pediatric populations with anisometropic amblyopia who were not suitable to the refractive laser surgery techniques [13-17]. The aim of this study was to evaluate the short-term results regarding the effectiveness and safety of posterior chamber intraocular lens for the treatment of 11 Chinese pediatric patients with unilateral high myopic amblyopia.

SUBJECTS AND METHODS

Eleven patients (7 males and 4 females) diagnosed as unilateral high myopic amblyopia from December 2013 to February 2015 in Zhongshan Ophthalmic Center of Sun Yat-sen University were studied. Inclusion criteria were as follows: 1) age between 5 to 18y; 2) refractive difference between two eyes equal to or more than 6.00 D; 2) the corrected distance visual acuity (CDVA) of the amblyopia eye below 20/50 (Snellen) and the CDVA of the fellow eye above 20/25 (Snellen); 3) the amblyopic eye was not successfully treated with spectacles and/or contact lenses (CL) combinations with standard occlusion therapy; 4) not suitable for corneal laser refractive surgery; 5) central anterior chamber depth (ACD) more than 2.8 mm. Exclusion criteria were patients with active inflammation, glaucoma, cataracts and other ocular organic disease; the history of intraocular surgery or severe ocular trauma; developmental, neurobehavioral, or neurological disorders; severe systemic disease.

The amblyopic eyes were treated with an implantable contact lens (ICL; model V4, Staar Surgical Inc.). The parents or guardians were given a detailed explanation of the procedure of ICL surgery and the risk and potential complications. The surgery could not stop the progression of myopia and amblyopia treatment was still needed after surgery. The aim of the surgery was to correct refractive errors of the amblyopic eye, which could play a fundamental role in treating unilateral anisometropia amblyopia. All parents or guardians were signed a detailed informed consent before surgery. All the study procedures were conducted in accordance with the tenets of the World Medical Association's Declaration of Helsinki. Ethical approval was obtained from the Ethics Committee of Zhongshan Ophthalmic Center (ethical approval number: 2014MEKY001). All parents provided written informed consent for US Food and Drug Administration (FDA) off-label use of the ICL.

Preoperative Management All patients underwent a complete preoperative ophthalmic examination inclusive of a detailed anterior and posterior segment examination with a slit lamp, ocular alignment by Hirschberg method and alternate cover test, intraocular pressure (IOP) with noncontact tonometry, corneal topography with OrbscanIIz, corneal endothelial cell count by corneal endothelial cell photography. Other ancillary studies, such as corneal diameter gauge and optical coherence tomography (OCT), were performed whenever indicated. The size of the ICL was determined with a STAAR sizing calculation formula that based on the measurement of horizontal corneal diameter [white to white (WTW) distance] and ACD with Orbscan II Topographer. Uncorrected and corrected distance visual acuity (UDVA and CDVA) using Early Treatment of Diabetic Retinopathy Study (EDTRS) converted to logarithm of the minimum angle of resolution (logMAR) notation for statistical analysis, cycloplegic refraction, contrast sensitivity by Psykinematix psychophysics software, stereoacuity at near fixation by Randot Preschool Stereoacuity Test were also evaluated preoperatively.

Surgical Method Eleven amblyopic eyes had standard implantation of ICL by the same surgeon (Yu KM). Briefly, two peripheral iridectomies were created at the 10:30 and 1:30 clock-hour position using Nd:YAG laser to prevent postoperative pupillary block for the older patients whose surgery was performed under surface anesthesia. Patients were given cycloplegic agents 3 times at 10-minute intervals before surgery. A 3.2-mm corneal incision was created at the 9-o'clock (right eye) or 3-o'clock (left eye) limbus position and an auxiliary incision was made at the 12-o'clock (right eye) or 6-o'clock (left eye) limbus position. The anterior chamber was filled with a hyaluronic acid material (STERILE, Hangzhou, China). An injector cartridge (STAAR Surgical) was used to insert ICL through the corneal incision. A specially designed intraocular spatula was used to place 4 footplates of ICL on the ciliary sulcus. The remaining viscoelastic material was entirely washed out with balanced salt solution. Three younger patients who underwent general anesthesia with intubation were performed peripheral iridotomy after ICL implantation with miosis.

Postoperative Treatment and Assessment Postoperatively, tobramycin 0.3% dexamethasone 0.1% eyedrops (Tobradex) was administered locally 4 times daily for one week and then 2 times daily for one week. The postoperative follow-up included visits at 1, 3d, 1wk, 1, 3, 6mo, and 1y, then six months thereafter. At each follow-up visit except 1d and 1wk, complete eye examinations were performed, including UDVA, CDVA, refraction, contrast sensitivity, stereoacuity, IOP and the ICL position, where possible, endothelial cell counts, repeat anterior segment and fundus evaluations. WaveLight Oculyzer anterior segment analysis system (Alcon, Fort Worth, Texas, USA) was used to measure the objective vaulting after surgery. The residual error was measured one month postoperatively and full correction by glasses were prescribed (if needed) based on the cycloplegic refraction. All patients continued postoperative amblyopia therapy one month after surgery with occlusion of the

Table 1 Preoperative demographics of patients with unilateral high myopic amblyopia

Patient No.	Eye	Gender	Age at surgery (a)	Refraction (D)	Ocular alignment	logMAR (Snellen)		Preoperative evaluation of amblyopic eyes				
						UCVA	CDVA	Kmax/Kmin (D)	ACD (mm)	WTW (mm)	ICL length (mm)	ICL power (D)
1	Right	F	17.3	-14.00-0.50×80	Ortho	1.7 (20/1000)	0.4 (20/50)	41.5/40.9	2.90	12.5	12.0	-18.5
	Left			-2.50-0.75×160		1.0 (20/200)	0.0 (20/20)					
2	Right	F	12.4	-4.00-0.50×5	Ortho	0.5 (20/63)	-0.1 (20/16)					
	Left			-20.00		2.4 (20/2500)	1.1 (20/250)	44.8/44.4	2.95	11.1	11.5	-23.0
3	Right	M	13.4	-1.00	Ortho	0.3 (20/40)	-0.1 (20/16)					
	Left			-13.00-0.75×15		1.7 (20/1000)	1.5 (20/670)	44.1/43.1	3.26	11.5	12.0	-18.5
4	Right	F	10.3	+1.50	Ortho	-0.1 (20/16)	-0.1 (20/16)					
	Left			-17.00-2.25×16		2.4 (20/2500)	2.0 (20/2000)	44.0/41.5	2.88	11.3	12.0	-21.0
5	Right	M	7.0	-11.00-0.25×85	Ortho	2.4 (20/2500)	2.4 (20/2500)	42.3/42.0	2.83	11.4	12.0	-14.5
	Left			+0.25+0.50×55		0.0 (20/20)	0.0 (20/20)					
6	Right	M	5.2	-15.00-1.25×130	Ortho	2.4 (20/2500)	2.4 (20/2500)	43.6/41.9	2.89	11.5	12.0	-20.0
	Left			+1.00+0.50×165		0.2 (20/32)	0.1 (20/25)					
7	Right	F	10.8	-3.50-0.50×180	Ortho	1.0 (20/200)	0.0 (20/20)					
	Left			-20.00-2.50×170		2.4 (20/2500)	1.5 (20/670)	44.4/42.2	2.81	11.6	12.0	-23.0
8	Right	M	8.8	-14.50-2.00×175	Ortho	2.4 (20/2500)	2.4 (20/2500)	44.7/42.5	3.30	11.7	12.0	-20.0
	Left			-1.25-1.50×5		0.2 (20/32)	0.0 (20/20)					
9	Right	M	11.0	-14.50-2.50×20	Ortho	1.7 (20/1000)	0.7 (20/100)	44.7/42.5	3.10	11.7	12.0	-19.0
	Left			-3.00-5.50×180		0.5 (20/63)	0.0 (20/20)					
10	Right	M	14.0	-12.00-1.00×30	Exotropia	1.7 (20/1000)	0.88 (20/150)	44.1/42.7	3.32	11.5	12.0	-17.0
	Left			-2.50		0.6 (20/80)	-0.1 (20/16)					
11	Right	M	11.0	+0.25+1.00×70	Ortho	0.1 (20/25)	0.0 (20/20)					
	Left			-10.00-2.50×175		2.4 (20/2500)	1.3 (20/400)	47.7/45.6	3.26	11.5	12.0	-15.0

D: Diopters; UDVA: Uncorrected distance visual acuity; CDVA: Corrected distance visual acuity; Ortho: Orthophoria; logMAR: Logarithm of the minimum angle of resolution; Kmax: Keratometric readings at the steepest; Kmin: Keratometric readings at the flattest; ACD: Anterior chamber depth; WTW: White to white; ICL: Implantable collamer lens.

dominant eye for 4-6h daily, with optical refractive correction as necessary, and physical training included Haidinger's Brush, red light flashing, *etc*.

Contrast Sensitivity Test Contrast sensitivity measurements were performed using previous described method [18-19]. Briefly, the sinusoidal gratings stimuli, which generated by a Mac Pro laptop (Apple Inc., California, USA) with Psykinematix software (KyberVision, Quebec, Canada), was presented within a circular aperture with a diameter of 48 on an EIZO 21-inch CRT monitor (EIZO Corporation, Ishikawa, Japan, resolution=1280 (1024 pixels, refresh rate=85 Hz), with the 120 cm viewing distance in a dark room. The algorithms allows for 10.8 bits of contrast resolution. Contrast was expressed as a Michelson Contrast percentage. During 200ms stimulus presentation time, patients had to judge the orientation of the grating as vertical or horizontal following a two-alternative, forced-choice method. The interstimulus interval was 500ms. The test was measured using a 3-down 1-up interleaved staircase procedure with six reversals converging on 79.4% accuracy. Following a familiarization procedure, contrast sensitivity of amblyopic eye was assessed at 0.5, 1, 2 cpd and fellow eye at 0.5, 2, 8 cpd, with the nonviewing eye covered by an opaque eyepatch.

Statistical Analysis This study uses IBM SPSS Statistics 19 statistical software (SPSS Inc., Chicago, IL, USA) for data analysis. The Pearson correlation coefficient was used as a measure of correlation. The data was presented as the mean± standard deviation (SD). Paired t-test or Wilcoxon-signed rank test was used to compare each postoperative value to the baseline value. For multiple comparisons of 3d, 1, 3, 8mo postoperative quantitative results, the repeated measures analysis of variance was applied to normal distribution, homogeneity of variance parameters data while nonparametric data was analyzed using the related-samples Friedman test. All tests were two tailed, and P values less than 0.05 were considered statistically significant. For postoperative pair comparison, Bonferroni correction was used to adjust the significance test level.

RESULTS

Preoperative patient demographics are summarized in Table 1. The mean age of the patients at the time of surgery was 11.02±3.34y (range: 5 to 17y). The logMAR UCVA and CDVA of the un-operated fellow eyes were 0.39±0.37 (range: -0.10 to 1.00) and -0.03±0.06 (range: -0.10 to 0.10), respectively. All patients completed follow-up at 3d, 1, 3mo and the last follow-up time [mean 8.18±2.82mo (range: 6 to 13mo)] after surgery.

Table 2 Changes in manifest refraction over time in patients with ICL implantation n=11

Time	Spherical equivalent (D)		Anisometropia (D)
	Operated eye	Un-operated eye	
Preop.	-15.34±3.35 (-11.13, -21.25)	-1.65±2.44 (+1.50, -5.75)	-13.70±3.25 (-10.00, -19.63)
Postop. 1mo	-0.55±0.66 (+0.38, -1.50)[a]	-1.39±2.43 (+1.25, -5.50)	+0.84±2.41 (+5.38, -2.00)[a]
Postop. 3mo	-0.63±0.76 (+0.38, -2.00)[a]	-1.43±2.47 (+1.25, -5.50)	+0.81±2.40 (+5.38, -2.00)[a]
Postop. 8mo	-0.90±0.73 (+0.38, -2.00)[a]	-1.59±2.63 (+1.38, -5.50)	+0.69±2.63 (+5.00, -2.25)[a]
[b]P	0.046	0.168	0.557

Preop.: Preoperation; Postop.: Postoperation; D: Diopters; [a]P<0.05 compared with preop.; [b]P represent difference among postop. follow up time.

Refraction The attempted and achieved spherical equivalent (SE) refraction in amblyopia eyes for ICL implantation was positive correlated (Pearson r=0.980, P=0.000). The achieved SE refraction at 1mo postoperatively was within ±0.50 D of the attempted power in 6 eyes (55%), within ±1.00 D in 7 eyes (64%), and within ±1.50 D in 11 eyes (100%). Table 2 shows the changes of manifest refraction over time after ICL implantation in children with high myopic anisometropia. There was a significant reduction in both the mean SE of amblyopic eye and SE anisometropia at 1, 3 and 8mo postoperatively (P=0.000 for all). Eight months postoperative follow up, there was significant changes in SE refraction of amblyopic eye, suggesting an ongoing trend of myopic shift (P =0.046), however, anisometropia was not significantly changed (P =0.557). The mean refraction of un-operated eyes was stable for the entire follow-up period (P =0.168).

Visual Acuity Figure 1A and Table 3 show the mean logMAR visual acuity changes in the operated eyes. UDVA and CDVA of the amblyopic eye at 3d, 1, 3 and 8mo after surgery was significantly improved compared with preoperative (P<0.05 for all). During 8mo postoperative follow up, both UDVA and CDVA of the amblyopic eye were significantly increased (P =0.000, P =0.008). UDVA at 3 and 8mo postoperatively was significantly greater than that at 3d postoperatively (P =0.008, P =0.007). CDVA at 8mo postoperatively was significantly improved than that at 3d, 1 and 3mo after surgery (P =0.006, P =0.003, P=0.007). Figure 1B shows the logMAR CDVA of 3d, 1, 3 and 8mo after surgery was improved mean 0.64 ±1.29 (0-4) lines, 1.55±1.81 (0-5) lines, 1.82±1.78 (0-5) lines, 2.64±2.42 (0-6) lines, and gained more than 2 lines accounted for 18% (2 eyes), 45% (5 eyes), 45% (5 eyes) and 64% (7 eyes), respectively. No patients lost any lines of visual acuity after surgery.

Contrast Sensitivity One patient was too young to finish contrast sensitivity test and the visual acuity of amblyopic eyes in other patients was so poor that only 0.5, 1 and 2 cpd spatial frequencies were measured (Table 4). The contrast sensitivity of 0.5, 1, 2 cpd at 3d, 1, 3 and 8mo in amblyopic eyes was significantly increased after surgery (all P<0.05). The contrast sensitivity of 2, 8 cpd at 3d and 0.5, 2 cpd at 3 and 8mo after surgery in un-operated fellow eyes was

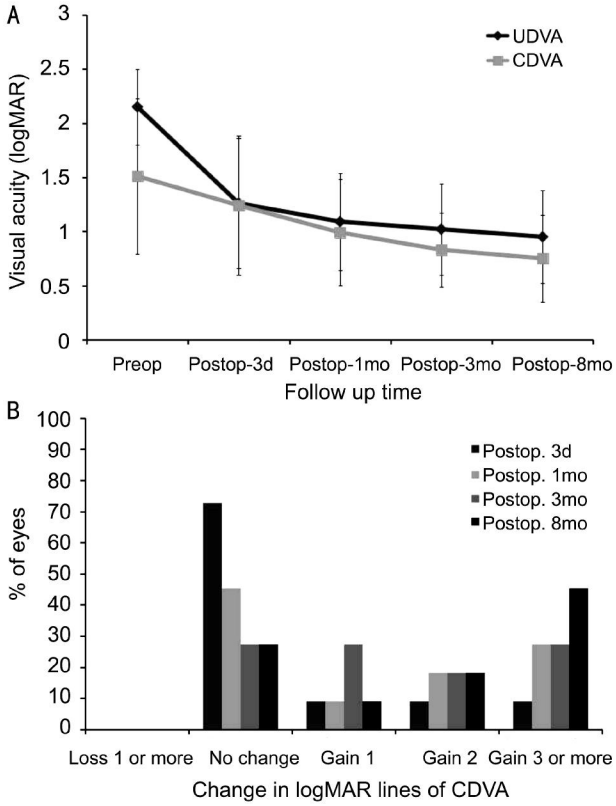

Figure 1 LogMAR visual acuity changes in the operated eyes
A: Changes of UDVA and CDVA in amblyopic eye after surgery; B: Changes in lines of logMAR CDVA after ICL implantation.

Table 3 Changes in logMAR visual acuity over time in patients with ICL implantation n=11

Time	UDVA	CDVA
Preop.	2.15±0.35 (1.70, 2.40)	1.51±0.72 (0.40, 2.40)
Postop. 3d	1.26±0.60 (0.44, 2.40)[a]	1.24±0.64 (0.24, 2.40)[a]
Postop. 1mo	1.09±0.45 (0.40, 1.50)[a]	0.99±0.49 (0.20, 1.50)[a]
Postop. 3mo	1.02±0.42 (0.40, 1.50)[a,b]	0.83±0.34 (0.30, 1.30)[a]
Postop. 8mo	0.95±0.43 (0.30, 1.50)[a,b]	0.75±0.40 (0.20, 1.30)[a,b]
[c]P	0.000	0.008

Preop.: Preoperation; Postop.: Postoperation. [a]P<0.05 compared with preop.; [b]P<0.01 compared with postop. 3d, 1 or 3mo; [c]P represent difference among postop. follow up time.

significantly increased compared with preoperative (all P< 0.05). During 8mo postoperative follow up, the contrast sensitivity of 1, 2 cpd in amblyopic eyes were significantly increased (P =0.007, P =0.005). However, the contrast sensitivity of 0.5, 2, 8 cpd in fellow eyes were not significantly changed (all P>0.05).

Table 4 Changes in contrast sensitivity over time in patients with ICL implantation *n*=10

Time	Un-operated eye (space frequency)			Operated eye (space frequency)		
	0.5 cpd	2 cpd	8 cpd	0.5 cpd	1 cpd	2 cpd
Preop.	104.90±46.09	141.65±48.14	42.70±21.27	29.59±22.50	11.64±14.61	6.74±9.60
Postop. 3d	124.23±32.46	197.65±71.16[a]	68.39±24.48[a]	45.87±21.00[a]	29.89±24.76[a]	23.18±28.80[a]
Postop. 1mo	137.82±56.30	184.21±83.87	49.46±32.68	48.62±14.48[a]	40.27±22.83[a]	27.38±28.77[a]
Postop. 3mo	134.43±29.77[a]	219.72±96.88[a]	47.86±17.84	57.89±27.71[a]	61.65±39.78[a]	42.53±26.89[a]
Postop. 8mo	149.44±30.48[a]	209.77±76.48[a]	57.43±40.08	62.41±28.79[a]	63.56±50.34[a]	53.69±54.71[a,b]
[c]*P*	0.112	0.615	0.284	0.069	0.007	0.005

Preop.: Preoperation; Postop.: Postoperation. [a]$P<0.05$ compared with preop. significantly difference; [b]$P<0.01$ compared with postop. 1mo; [c]*P* represent difference among postop. follow up time.

Stereopsis All patients without near stereopsis both preoperatively and the last follow up time postoperatively.

Intraocular Pressure The IOP for the amblyopic eye was not significantly changed from 13.75±4.26 mm Hg preoperatively to13.45±4.34 mm Hg at 3d, 11.88±3.09 mm Hg at 1mo, 13.64±2.87 mm Hg at 3mo, 13.45±2.73 mm Hg at 8mo after surgery, respectively ($F=1.606$, $P=0.192$).

Vaulting The mean vaulting was 0.75±0.17 (range: 0.45 to 1.04) mm at 1mo, 0.69±0.16 (range: 0.38 to 0.96) mm at 3mo, 0.65±0.17 (range: 0.33 to 0.96) mm at 8mo after surgery, with significant difference ($F=19.294$, $P=0.000$). The vaulting at 3 and 8mo were significantly lower than that at 1mo postoperative ($P=0.007$, $P=0.000$).

Endothelial Cell Count The mean endothelial cell count (ECD) was 3054.78±369.31 (range: 2261.40 to 3532.50) cells/mm^2 preoperatively and 3007.75±429.89 (range: 2077.40 to 3558.30) cells/mm^2 at the last follow up time postoperatively, without any significance endothelial cell loss ($T=0.685$, $P=0.510$).

Complications Only one eye had acute pupillary block glaucoma at two weeks postoperatively and successfully treated by laser peripheral iridotomy, and no other intraoperative or postoperative complications happened. No general anesthesia complications were observed.

DISCUSSION

Corneal refractive surgery using excimer laser technology has been considered as an alternative to correct high myopic anisometropia for the patient who was failed with conventional refractive correction such as spectacles, contact lenses. Several studies also reported that BCVA and binocular vision improvement were better in children who received permanent surgical correction (PRK or LASEK or anterior chamber IOLs implantation) for high myopic anisometropia with amblyopia than in those who were treated by contact lens [6,20]. PRK was the earliest refractive surgery that has been performed effectively initially in children, however, it need to comply with long term steroid regimen postoperatively and limited to refractive errors below -6.00 D [7-8]. LASEK has also been performed with good results. However, corneal haze formation has been reported as a major concern for receiving cornea surface ablation surgery, especially in high myopic correction [11-12]. LASIK have demonstrated as a safe, predictable, and effective method for correction of myopic anisometropia in refractive amblyopia children. Nonetheless, flap-related problem similar to adult LASIK surgery was the major complication occurred in children after LASIK surgery [10]. Owing to the advantages of avoiding corneal related complications and reversibility, ICL has become the preferred refractive surgical approach for the correction of high myopia in adult patients who was not suitable for corneal refractive surgery [21-23]. Several previous studies also concluded that ICL have optical advantages, fewer ocular higher order aberrations (HOAs), better contrast sensitivity, safer and more effective than LASIK, suggesting that it may be a better surgical option for the treatment of myopia[24-25].

The encouraging progress in implanting IOLs in adult phakic eyes led us to propose this surgical treatment for anisometropia with amblyopia in children. The US FDA approved two pIOLs: one iris-fixated pIOL (AC-pIOLs) and one posterior-chamber IOL (PC-pIOLs) for correction of ametropia in adult. In our review of the literature, previous only few case series of PC-pIOLs implantation for the treatment of unilateral high myopia and severe amblyopia in children. Lesueur and Arne [13] reported the first clinical application of PC-pIOLs to treat severe anisometropia in 5 eyes of 4 children aged 3 to 16 years. There was no complication reported in this study with mean follow-up of 11.8mo (range: 4 to 21mo) and the CDVA improved 3 or more Snellen lines with recovery of binocular vision in 2 patients and orthotropia achieved in 3 patients. In the follow up time, Lesueur and Arne [14] reported twelve eyes of 11 children underwent insertion of ICL for treatment of high myopia amblyopia. After a mean period of follow-up of 20.5mo (range: 3 to 48mo), the ICL position was stable in all eyes without any significant clinical complications. Recovery of binocular vision was achieved in six patients and orthotropia was reestablished postoperatively in seven patients with strabismus. BenEzra *et al* [15] reported PC-pIOLs performed in the anisometropic amblyopia eyes of 3 female children (ages 9 to 18). CDVA was improved in all cases and fusional abilities and stereopsis were observed in two

cases at 9mo postoperatively. No major clinical complication was observed, except the temporary pigment dispersion in one case. Althomali [16] reported 6 amblyopic children underwent toric PIOL implantation for refractory anisometropic amblyopia. Five of the 6 eyes gained more than 3 lines of corrected distance visual acuity with a maximum gain of 8 lines in one eye and all PIOLs remained well centered after a mean follow-up of 23mo.

Corneal refractive surgery was not a suitable option for our patient given their level of myopia (mean SE -15.58±3.11D). ICL was performed in the 11 amblyopic eyes to reduce refractive error and eliminate anisometropia. Eight months postoperative follow up, although there was a myopic shift in amblyopic eye, however, anisometropia was not significantly changed. The myopic shift in children after refractive surgery was also reported in previous studies, the authors thought that axial growth, vigorous healing response and not fully developed visual systems might be the reasons[10]. The visual acuity continued to improve considerably from 3d to 8mo after ICL implantation without anyone lost one line of the vision test, which was consistent with previous researches. Contrast sensitivities of amblyopic eyes in the low and mild spatial frequencies (0.5, 1, 2 cpd) postoperative were better than preoperative, and also significantly increased with follow up time postoperatively. Due to the poor visual acuity of amblyopic eyes, no one had stereopsis been recovered. ICL implantation for the treatment of unilateral myopic anisometropia might eliminate the biocular retinal image size differences and much closer to the physiological conditions. We believe the improvement of visual acuity and contrast sensitivity can result from refractive correction and/or elimination of anisometropia alone, and further benefits from amblyopia therapy postoperatively. Zhou *et al* [26] reported that perceptual learning in the amblyopic eyes can transfer contrast sensitivity improvement in the untrained fellow eyes. The un-operated fellow eyes in our study had better contrast sensitivity postoperative compared with preoperative might result from the learning effect and the transfer effect of improvement in amblyopic eyes.

We also found a handful of peer-reviewed published articles on iris-fixated pIOL for high anisometropic myopia in children demonstrated that it can improve visual acuity and stereopsis without severely complications [27-31]. Many of the risk factors associated with an iris-fixated pIOL are similar for adults and children[32]. A major concern in children is the potential long-term risk for endothelial cell loss associated with eye rubbing. The second concern is the risk for increased intraocular inflammation and development of chronic uveitis. Iris-fixated pIOL can also lead to complications such as retinal changes and pupil ovalization in adult patients. Previous randomized comparative eye study demonstrated that both iris-fixated pIOL and PC pIOLs have equally satisfactory visual outcomes after surgery[33]. Another study concluded monocular UDVA was similar for both groups, whereas binocular UDVA was better in the PC-IOL[34]. The PC-IOL group had more accurate refractive outcomes than the iris-fixated pIOL group. A significant advantage of PC pIOLs over iris-fixated pIOL seems to stem from a decreased rate of corneal endothelial cell loss with the former. Saxena *et al* [28] reported of iris-fixated pIOL implantation for correction of anisometropic amblyopic for children had a significant endothelial cell loss at 3y postoperative. Assil *et al* [29] reported 7 children with high anisometropia performed iris-fixated pIOL, no intraoperative or postoperative complications were identified, but the endothelial cell loss ranging from 6.5% to 15.2% over 3y. Alió *et al* [35] retrospective study of 10 children who underwent PIOL implantation (9 eyes with iris-fixated pIOL and 1 eye with a PC pIOL), CDVA improved in all children. Five years after surgery, endothelial cell count was >2000 cells/mm^2 in eight (80%) patients; for the remaining two patients, one reported frequent eye rubbing and the other suffered ocular trauma. In our study, there was no significance endothelial cell loss at 8mo after surgery, however, regularly long term follow ups were still needed.

Several potential complications happened in the adult PC-pIOLs implantation such as cataract formation, pupillary-block glaucoma, spontaneous dislocation of pIOL into the vitreous cavity, and retinal detachment have been rare reported in pediatric PC-pIOL implantation due to the handful cases in previously literature. Cataract formation was the major complications of ICL implantation and FDA studies have reported that the incidence of secondary cataract was 2.1% within 1y and 2.7% within 3y after surgery [20]. A continuous reduction of central vault was observed over time after ICL implantation, and insufficient vaulting was responsible for the development of anterior subcapsular cataract [36-37]. Some authors previously defined an excellent vaulting as 0.25 to 0.75 mm. Excessive and insufficient vaulting were the risk factors of complications [38]. In our study, the mean vaulting at 8mo ranged 0.33 to 0.96 mm were significantly lower than at 1mo ranged 0.45 to 1.04 mm postoperative. ICL length selection for children should consider the reduction of central vault over time and accurate formula that yield ideal vault need further study.

There was no significant clinical adverse event except one case with acute pupillary block glaucoma happened at two weeks postoperatively. The IOP was dropped from 50 mm Hg to normal limits after laser iridectomy and remained during the follow up time. Although visual acuity was improved, corectasis still can be observed at 1y follow up. The combination of ICL implantation and iridectomy was performed for this patient who was too young to receive laser iridotomy under local anesthesia. The ICL was

implanted under pharmacological mydriasis, and then miosis was needed for iridectomy surgery. Inadequate miosis was one of the important risk factors for not enough layer incision of iris. Recently, several studies have reported the new ICL with the a central hole design seems to provide similar results to conventional ICL for the correction of moderate to high myopia and it does not require iridotomy or iridectomy and may also reduce the risk of pupillary block and cataract formation [39-40]. This newly developed hole ICL implantation appears to be a good option for anisometropia with amblyopia in children.

Our preliminary results shows that phakic posterior chamber IOL implantation can be a promising alternative treatment for high myopic anisometropic amblyopia in children in whom conventional treatments have failed and cornea refraction surgery was not suitable. However, there were only a small group of patients and short term results observed in our study. Longer term follow-ups and more patients are still necessary to evaluate the efficacy and safety of ICL implantation for young pediatric patients.

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