ICL versus SMILE in management of anisometropic myopic amblyopia in children

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ABSTRACT ●

Objective: We compare the predictability, safety, and efficacy of posterior chamber phakic intraocular lens (PCpIOL) versus small-incision lenticule extraction (SMILE) for correcting myopic anisometropia in amblyopic children.

Methods: A prospective randomized study enrolled 30 children, aged 4–12 years, with unilateral myopic anisometropic amblyopia whose refraction ranged between −5 and −10 diopters (D) and myopic astigmatic error −1 to −6 D. Patients were subdivided into group A for unilateral PCpIOL implantation and implantable collamer lens (Visian ICL/TICL) of V4C design and group B for SMILE procedure. Pre- and postoperative corrected distance visual acuity (CDVA), uncorrected visual acuity, and cycloplegic refractive spherical equivalent (CRSE) were performed in all patients and compared between both groups. Follow-up was for at least 18 months.

Results: Of the 15 children in group A, 12 (80%) revealed prevention of amblyopia and improvement in CDVA of 3–6 lines, and 3 children (20%) gained 1–3 lines. In group B, 6 (40%) eyes gained 3–5 lines, 6 (40%) eyes gained 1–3 lines, and 3 (20%) children gained 0–1 line. Stereoacuity improved in 93.33% of cases. Mean CRSE decreased in both groups 18 months postoperative ($p < 0.001$). Improvement in stereoacuity occurred in 86.66% of cases.

Conclusions: To eliminate significant anisometropic myopia in children who are noncompliant with conventional treatment, PCpIOL or SMILE may be considered as alternative modalities of treatment. Being an extraocular procedure, SMILE was found to be a safer procedure with fewer and less serious complications compared to ICL.

An eye with reduced best-corrected visual acuity with no organic pathology identified is called an amblyopic eye.[1] Anisometropic amblyopia constitutes 1% to 5% of the causes of monocular vision loss in children[2] and may be secondary to anisomyopia of more than 2 D, anisohyperopia of more than 1 D, or anisoastigmatism of more than 1.5 D.[3]

Even though correction of a refractive error with glasses or contact lenses, as well as simultaneous patching or atropinization of the nonamblyopic eye, is considered the traditional treatment of anisometropic amblyopia,[4] it fails in around 10% to 50% of amblyopic children, who may achieve a final best-corrected visual acuity of 20/40 or worse. Surgical treatment at an earlier age may be the final resort if conventional therapy fails in children with significant anisometropia.[5]

Failure of traditional nonsurgical options in high refractive errors may be attributed to the limited field of view through glasses frames, aniseikonia, and cushion- or barrel-like prismatic optical aberrations, beside the cosmetic and psychological issues.[6] Contact lenses may create problems for both children and their parents, due to difficulties with insertion and removal, infection, and intolerance.[7]

Even though photorefractive keratectomy (PRK), LASIK, and laser assisted subepithelial keratectomy (LASEK) are the approved corneal refractive procedures for management of anisometropic amblyopia, each of these treatment modalities has its own pros and cons.

In addition to common problems such as flap striae, flap displacement, limited correctable range of refractive errors, myopic regression, diffuse lamellar keratitis, and stromal haze,[8,9] all corneal excimer laser procedures carry the potential unpredictable risk of post-LASIK keratectasia when performed at very young age.

Regarding refractive lens exchange, the high incidence of retinal detachment in children with axial myopia, in addition to the disadvantage of loss of accommodation after implantation of monofocal IOL, made this procedure nonpreferable in management of myopic anisometropic amblyopia. It was replaced by phakic intra ocular lens (pIOL) surgery.[10] Nevertheless, posterior chamber phakic intraocular lens (PCpIOL) implantation may be complicated by anterior subcapsular cataract, progressive corneal endothelial cell loss, IOL capture, pigment dispersion, and secondary glaucoma, which requires proper selection of ICL overall diameter,[11] and must be performed by an experienced surgeon with minimal trauma to the clear lens and corneal endothelium.[12]

The small-incision lenticule extraction (SMILE) procedure can correct a higher refractive error compared to LASIK or PRK. An equivalent amount of biomechanical stability is achieved because the SMILE does not disrupt anterior corneal segments and grants a protective effect on the residual stromal bed (RSB) compared to LASIK. Diminished cumulative tension on the RSB is thought to potentially offer advantages such as avoiding anterior

https://doi.org/10.1016/j.jcjo.2018.01.029
ISSN 0008-4182/17

Canadian Ophthalmological Society | Société canadienne d'ophtalmologie
EYE PHYSICIANS AND SURGEONS OF CANADA | MÉDECINS ET CHIRURGIENS OPHTALMOLOGISTES DU CANADA

corneal shift resulting in myopic regression and reducing the incidence of postoperative ectasia.[13]

In view of the fact that SMILE can safely and effectively correct myopia, it is logical to replace LASIK for the correction of anisometropia in children with amblyopia. Potential advantages of the extraocular SMILE procedure for children include the decreased risk of future unpredictable ectasia after this tissue-saving procedure and use of a single-laser platform to complete the procedure, and all flap-related complications in children could be avoided. The avoidance of corneal flap creation represents a less invasive technique with implications that potentially improve corneal biomechanical stability, as well as corneal nerve integrity.[14]

In our study, we avoided LASIK and refractive lens exchange owing to the reasons mentioned. The purpose of the current study is to compare the efficacy and safety of PCpIOL implantation and SMILE for correcting myopic anisometropia in amblyopic children.

Methods

This prospective randomized comparative study included 30 children with refractory amblyopia who have been endorsed for SMILE procedure or ICL implantation at a specialized eye hospital, Magrabi Eye Hospital (M.E.H), in the period between October 2013 and July 2014. Anisometropic myopic eyes were prospectively randomized either to PCpIOL procedure (group A) or SMILE procedure (group B).

The mean age of the 15 children in the SMILE group was 9.47 ± 1.73 years (range 5–12 years); the mean age of the 15 children in the PC pIOL group was 8.73 ± 2.55 years (range 4–12 years). The study protocol adhered to the tenets of the Declaration of Helsinki and was approved by the ethics committee of M.E.H. Comprehensive discussion with parents was undertaken preoperatively, explaining the details of surgery, its benefits, and its complications. Informed written consent, including the off-label use of SMILE and PCpIOL, was obtained from all parents. Two surgeons, S.E. and M.W., performed all surgeries.

Inclusion criteria were myopic anisometropic amblyopic children aged 4–12 years who had refractive spherical error from −5 to −10 D and myopic astigmatism of −1.0 to −6.0 D, with unsuccessful conventional amblyopia therapy (using varying combinations of spectacles, contact lenses, and occlusion therapy).

Our protocol in management of myopic anisometropic amblyopia was refractive/optical correction using spectacles or contact lens for 1 month, followed by amblyopia management for a period of 2 months. Children with moderate to severe amblyopia should receive part-time patch occlusion of the sound eye for 6 hours per day, and those with mild amblyopia should be patched 4 hours per day for 6 weeks, combined with at least 1 hour of near visual activity during patching. Parental medical advice and strong recommendation of amblyopia therapy over several clinical visits was performed for up to 3 months preoperatively.

Decision of surgical refractive correction in the current study was taken if patients and/or parents failed to comply with our strategy of refractive correction (spectacles/contact lenses) and amblyopia management (patch therapy), or if corrected distance visual acuity (CDVA) failed to improve by >0.1 logMAR after 3 months of following the recommended therapy guidelines.

Exclusion criteria of the study included the presence of congenital cataract, and deep amblyopia in children older than 12 years. As explained by the randomized design of the current prospective study, patients with anterior chamber depth (ACD) less than 3.00 mm and endothelial cell count less than 2600/mm^2 were excluded, owing to the contraindication of phakic IOL implantation in these patients. Also, patients with hypermetropic amblyopia, preoperative corneal thickness of <475 μ or residual stromal thickness of <275 μ,[15] cycloplegic refractive spherical equivalent (CRSE) over −10.00 D, and abnormal or suspicious corneal topography were not candidates for SMILE procedure and were excluded from the study.

All patients were evaluated for manifest refraction spherical equivalent (MRSE), CRSE, CDVA, uncorrected visual acuity (UCVA), ocular alignment, stereoacuity, and endothelial cell count (ECC).

Additional baseline testing included anterior chamber depth (ACD), white-to-white (W-W) distance, and keratometry readings using Scheimpflug imaging system (Pentacam HR; Oculus Optikgerate).

We adjusted the power and size of ICL using the STAAR company online calculator and ordering system, which uses a modified vertex calculation formula for phakic IOL calculation, using the patients' data; ACD, CRSE, back vertex distance, and K readings.

To achieve a target postoperative vault of 530 ± 50 μ, the system was supplied by the following data; W-W measurement, ACD, CCT, and birth date, with ICL overall diameter selected between 0.50 mm increments (12.1, 12.6, 13.1, and 13.7) according to (W-W) measurements. Target postoperative refraction was −0.75 D in both groups.

ICL procedure was performed under general anaesthesia (GA). Benoxinate hydrochloride (0.4%) was used to induce pre-emptive analgesia after loss of consciousness. In group A, ICL implantation was performed as described by Assetto et al.[16] A 3.20 mm tunnelled temporal clear cornea incision was created, and the anterior chamber was filled with viscoelastic material (Viscoat; Alcon Laboratories, Inc, Fort Worth, Tex.). The V4C ICL (Visian; STAAR Surgical Inc, Monrovia, Calif.) was loaded into the cartridge, as specified by the manufacturer and injected intraocularly. An iris manipulator was used to place the lens within the posterior chamber. The viscoelastic

material was then removed using the aspiration/irrigation mode of the Ocutome (Storz; Premiere, St. Louis, Mo.). Toric ICLs were implanted in 5 eyes of 5 patients with myopic astigmatism (−1.0 to −6.0 D). In cooperative children, marking of horizontal meridian was done whenever possible using a pendular marker at 180°. According to preoperative company diagram/plan, clockwise/counterclockwise rotation of the toric ICLs was done after sulcus implantation. Intraoperative complications included upside down intracameral insertion of ICL that required lens explantation, re-loading, and re-implantation.

All patients were treated with moxifloxacin 0.5% eye drops (Vigamox; Alcon Laboratories, Inc) 4 times daily, prednisolone acetate 1% (Pred Forte; Allergan, Inc, Irvine, Calif.) 4 times daily, and tropicamide 0.5% (Mydriacyl®; Alcon Laboratories) once a day for 2 weeks. Pred Forte was tapered over a period of 2 additional weeks.

SMILE procedure was performed under sedation in 15 children using the Visumax femtosecond laser system (Carl Zeiss-Meditec, Jena, Germany). The diameter and thickness of the caps were 7.50 mm and 120 μm, respectively, and the diameter of the optical zone was 6.50 mm. The posterior part of the lenticule was created by laser scanning in spirals from the centre of the pupil to the periphery of the optical zone. The anterior part of the lenticule was created by laser scanning in spirals from the periphery to the centre of the pupil. Through a small incision of 50° in chordal length, a femto-lamellar Siebel dissector was used to dissect the cleavage plane anterior and posterior to the intrastromal lenticule, till the lenticule is totally freed, which is then extracted through the peripheral incision using a nontoothed serrated forceps.[17] The same nomogram used in adults was adopted in our study; for example, an error of −8.00 D was corrected by 120 μ-lenticule removal. Postoperatively, moxifloxacin 0.5% (Vigamox), and rimexolone 1% (Vexol; Alcon Laboratories Inc) 4 times daily for 2 weeks were prescribed.

Because the correction of the refractive error alone was not sufficient to treat the anisometropic amblyopia as recommended by PEDIG in 2006,[18] patching therapy was applied soon after the refractive correction was done.

The importance and need of postoperative patching of the sound eye was explained to the parents in both groups. Patching the sound eye was recommended in mild amblyopia for 4 hours per day postoperatively for 3 weeks followed by 2 hours daily for another 3 weeks until the visual acuity improved and established near to the level of nonamblyopic eye. In moderate to severe amblyopia, patching was done for 6 hours daily for 4 weeks, followed by 4 hours daily for 2 weeks then 2 hours daily for another 2 weeks.

Follow-up examinations were scheduled at 3 days; 1 week; 1, 3, 9, and 18 months; and then as needed. All included patients completed the 18 months follow-up. Postoperative Scheimpflug imaging was performed in both groups at 1, 3, 9, and 18 months postoperatively to detect any evidence of early corneal ectasia in group B, to measure ICL vault in group A, and to measure ACD in both groups.

Statistical Methods

Data were coded and entered using the statistical package SPSS version 24. Data were summarized using mean and standard deviation. Comparisons between groups were done using the unpaired *t* test. Comparison between preoperative and postoperative values in each group was done using the paired *t* test.[19] *p*-Values less than 0.05 were considered as statistically significant.

Results

Endothelial cell count (ECC), MRSE, CRSE, CDVA, UCVA, ocular alignment, and stereoacuity were evaluated in both groups before and after each procedure.

Preoperative and postoperative visual acuity was measured at 4 m with ETDRS logMAR Number Charts (Precision Vision, Inc, La Salle, Ill.). An experienced optometrist was assigned for masked assessment of visual acuity (i.e., unaware of the child's surgical state).

Stereoacuity was assessed using Frisby and Lang stereotests. Endothelial cell counts were measured using specular microscopy (Konan Medical, Torrance, Calif).

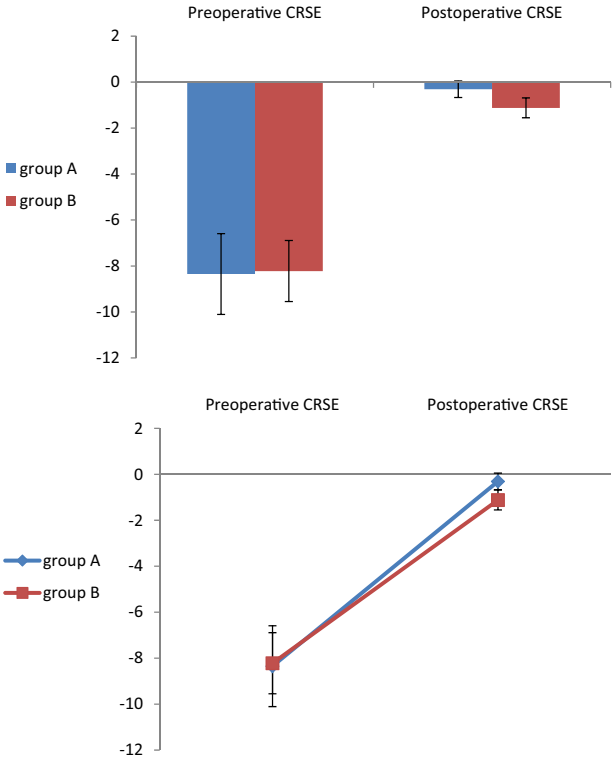

Fig. 1—Comparison between pre- and postoperative CRSE in both groups. CRSE improved significantly in both groups but more in group A. CRSE, cycloplegic refractive spherical equivalent.

Eye alignment was assessed by cover-uncover test at distance, and microtropia was excluded using a 4 prism base out test.

The mean preoperative CRSE was −8.35 D in group A and −8.22 D in group B. At 18 months postoperative, CRSE improved significantly to −0.31 D in group A ($p \leq 0.001$) and −1.12 D in group B ($p \leq 0.001$). At 1, 3, 9, and 18 months postoperative, CRSE improved significantly in both groups compared to baseline. CRSE was statistically compared in PIOL and SMILE groups in Figure 1.

Regarding predictability, postoperative CRSE was within 0.5 D of the intended target refraction in 60% of cases in group A and in 47.4% of cases in group B, and within 1.00 D of the intended target refraction in 100% of cases in group A and 93.3% of cases in group B.

The ICL group showed improvement in CDVA for up to 3–6 lines in 86.6% of children and less than 3 lines in only 2 children with an average improvement from 1.02 logMAR preoperative to 0.61 logMAR at 18 months postoperative ($p \leq 0.001$). As for the SMILE group, CDVA improved by 3–5 lines in 13.3% of children, 6 eyes gained 1–3 lines, and 7 eyes gained 0–1 line. Mean CDVA improved from 0.77 logMAR preoperative to 0.56 logMAR at 18 months postoperative. This change was statistically significant ($p < 0.001$). logMAR CDVA was statistically compared in both groups in Figure 2.

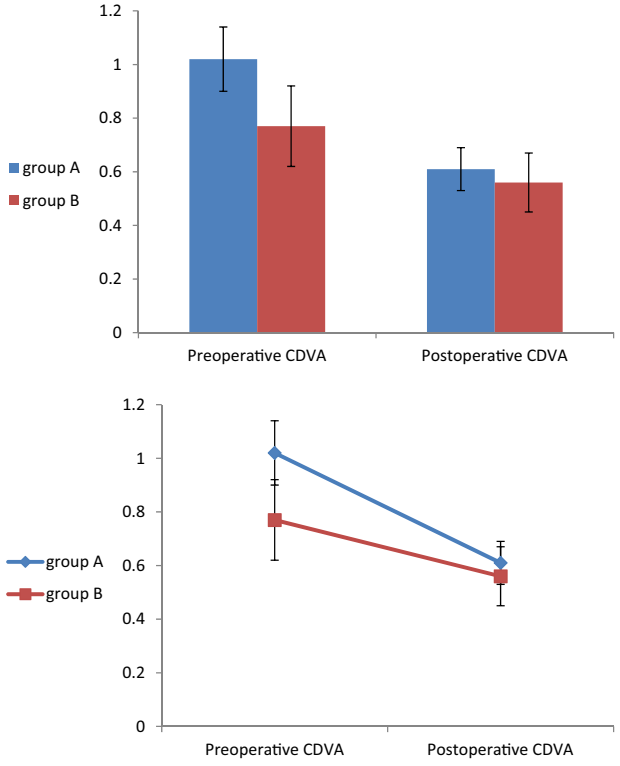

Fig. 2—Comparison between pre- and postoperative logMAR CDVA in both groups. CDVA improved significantly in both groups but more in group A. CDVA, corrected distance visual acuity.

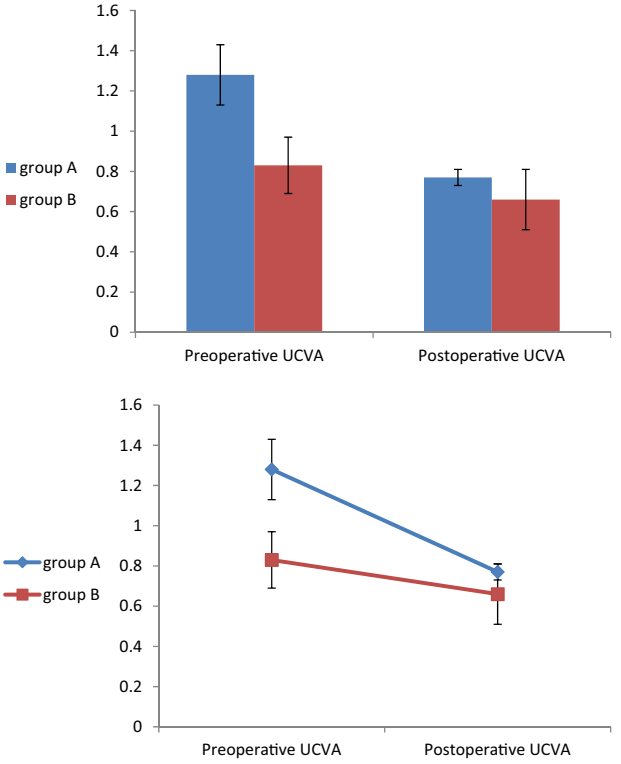

Fig. 3—Comparison between pre- and postoperative logMAR UCVA in both groups. UCVA showed statistically significant improvement in both groups more in group A. UCVA, uncorrected visual acuity.

Mean logMAR UCVA showed a statistically significant improvement ($p \leq 0.001$) in the ICL group from 1.28 preoperative to 0.77 after 18 months, whereas for the SMILE group at 18 months postoperation, the mean UCVA was 0.66, compared to baseline value of 0.83 ($p \leq 0.001$) (Fig. 3).

Table 1 describes the individual preoperative and postoperative refractive, corrected, and uncorrected visual outcomes of the 30 myopic anisometropic amblyopic eyes. The final postoperative CDVA of the 2 groups at 18 months postoperative was found to be statistically insignificant ($p = 0.202$) (Table 2).

Patient number 12 in this study was the only patient without postoperative improvement in UCVA or CDVA. No single patient did show a decrease in CDVA or UCVA postoperatively in either group. Overall, the safety index, which is the ratio of mean postoperative decimal CDVA to mean preoperative decimal CDVA, at the final visit was 2.5 in the ICL group and 1.64 in the SMILE group.

The ratio of mean postoperative logMAR UCVA converted to decimal to mean preoperative logMAR CDVA converted to decimal (efficacy index) was 1.8 in group A and 1.27 in group B. Preoperatively, 93.33% of cases in group A and 86.66% of cases in group B showed an improvement in stereo-acuity (to smaller than 1200 sec arc) compared to 49.07% and 68.00%, respectively. Preoperative exotropia encountered in 4 children in group

Table 1—Individual preoperative and postoperative refractive, corrected, and uncorrected visual outcomes of the 30 myopic anisometropic amblyopic eyes

	Group A						Group B					
	Preoperative			Postoperative			Preoperative			Postoperative		
	UCVA	CRSE	CDVA	UCVA	CRSE	CDVA	UCVA	CRSE	CDVA	UCVA	CRSE	CDVA
1	1.22	−10.0	1.00	0.78	−0.85	0.60	0.60	−8.50	0.54	0.40	−0.20	0.40
2	1.30	−9.0	1.00	0.70	−0.75	0.60	0.70	−7.25	0.54	0.54	−1.75	0.48
3	1.30	−10	1.10	0.70	−0.15	0.50	0.88	−7.00	0.78	0.60	−1.30	0.58
4	1.22	−10	0.92	0.78	+0.20	0.60	1.00	−9.75	0.90	0.92	−1.35	0.60
5	1.5	−9.5	1.00	0.80	−0.73	0.70	0.92	−8.25	0.90	0.78	−1.30	0.60
6	1.00	−10.00	0.90	0.78	−0.50	0.70	0.90	−9.50	0.88	0.60	−1.20	0.54
7	1.30	−8	1.10	0.70	−0.20	0.60	1.08	−9	1.00	0.70	−1.75	0.54
8	1.22	−7.25	1.00	0.80	−0.45	0.70	0.80	−8	0.78	0.54	−0.75	0.48
9	1.22	−5.0	1.10	0.80	−0.33	0.60	0.82	−7	0.78	0.54	−1.00	0.48
10	1.40	−9.5	1.00	0.78	0	0.50	0.92	−10	0.90	0.90	−1.50	0.80
11	1.40	−8.75	1.08	0.80	−0.10	0.70	0.80	−9.50	0.78	0.54	−1.00	0.52
12	1.50	−9.75	1.18	0.78	−0.81	0.60	0.70	−8.75	0.60	0.70	−0.85	0.60
13	1.40	−6	1.10	0.80	−0.25	0.70	0.90	−5.00	0.80	0.80	−1.00	0.50
14	1.00	−6.75	0.70	0.78	0	0.50	0.60	−7.50	0.54	0.54	−0.50	0.52
15	1.22	−5.75	1.10	0.80	+0.26	0.50	0.88	−8.25	0.82	0.82	−1.35	0.78

UCVA, uncorrected visual acuity; CRSE, cycloplegic refractive spherical equivalent; CDVA, corrected distance visual acuity.

A and 3 children in group B improved by orthoptic treatment to orthophoria at the last follow-up visit, without the need for surgical intervention. Mean baseline Pentacam ACD was 3.15 ± 0.13 mm and 2.89 ± 0.19 mm in groups A and B, respectively. A nonstatistically significant change in ACD was recorded 18 months postoperatively, with a mean ACD of 2.97 ± 0.17 mm in group A and 2.87 ± 0.34 mm in group B.

In the present study, the SMILE group did not show any statistically significant change in ECC at any time point, with preoperative ECC of 2843 cells/mm^2 and 18-month postoperative ECC of 2826 cells/mm^2. In the ICL group, ECC did not change significantly at postoperative 1, 3, and 9 months compared to preoperative counts. However, the 18-month ECC loss was statistically significant ($p < 0.05$) compared to the preoperative counts, representing a loss of 1.54% (from preoperative ECC of 2857 to 2813 cells/mm^2 at 18 months). There was no statistically significant change in ECC in the SMILE group at any time point after the surgery.

The mean ICL vault in group A after 18 months, as measured by Scheimpflug tomography at the 90° axis, was 517 ± 92 μ. Postoperative vault was within the range of the intended vault (480–580 μ) in 12 cases.

The postoperative ICL vault was lower than the target vault (476 μ) in one eye. That was not associated with cataract or rotatory/torsional ICL movements or iris pigment dispersion. It did not require exchange or explantation of the ICL and was higher (593 μ) in 1 eye, with no angle closure or elevation of intraocular pressure.

No single case did present with early topographic post-SMILE corneal ectatic changes throughout the 18 months of follow-up. Complications encountered in the SMILE group included intraoperative suction loss in 2 eyes and early postoperative stage 2 diffuse lamellar keratitis (DLK) in 1 eye. The 2 procedures that were interrupted with suction loss were resumed and managed successfully. The single eye presenting with DLK was managed by frequent topical steroids (Pred Forte 1%; Allergan) every 2 hours for 4 days, and the granular white deposits inside the pocket resolved completely.

In group A, we encountered 2 cases of faint anterior subcapsular cataract with an ICL vault of 546 μ and 573 μ in patients 4 and 9, respectively, which did not require ICL explantation or exchange. A single case presented with acute anterior uveitis and acute IOP elevation, which resolved with topical steroids and beta-blocker for 5 days.

Table 2—Comparison between pre- and postoperative logMAR UCVA, CRSE, and logMAR CDVA in both groups A and B

	Group A				Group B				*p*
	Mean	SD	Minimum	Maximum	Mean	SD	Minimum	Maximum	
Preoperative UCVA	1.28	0.15	1.00	1.50	0.83	0.14	0.60	1.08	<0.001
Preoperative CRSE	−8.35	1.76	−10.00	−5.00	−8.22	1.33	−10.00	−5.00	0.817
Preoperative CDVA	1.02	0.12	0.70	1.18	0.77	0.15	0.54	1.00	<0.001
Postoperative UCVA	0.77	0.04	0.70	0.80	0.66	0.15	0.40	0.92	0.016
Postoperative CRSE	−0.31	0.36	−0.85	0.26	−1.12	0.43	−1.75	−0.20	<0.001
Postoperative CDVA	0.61	0.08	0.50	0.70	0.56	0.11	0.40	0.80	0.202

UCVA, uncorrected visual acuity; CRSE, cycloplegic refractive spherical equivalent; CDVA, corrected distance visual acuity.

Discussion

Uncorrected refractive errors, during the critical visual period (age <12 years), represent a paramount cause of amblyopia,[20] especially in the presence of anisometropia. Anisometropia leads to projection of unequal images on the fovea with subsequent brain suppression of the eye, which provides the blurred image, owing to inability of the cortex to fuse different retinal images.[21]

The principle of change in the retinal image size and magnification by the ocular-optical system lies behind the success of refractive surgical correction in amblyopia management.[22] It follows the modifications of corneal curvature in corneal refractive surgery or the implantation of a corrective contact lens in a more physiological position close to the nodal point.

In the current study, we aimed to compare the outcomes and complications of SMILE and PCpIOL in patients with myopic anisometropic amblyopia. The present study found a statistically significant improvement in CRSE in both groups 18 months postoperation compared to baseline. This suggests successful refractive correction in both groups and improvement in CDVA, in agreement with the previous literature supporting the fair outcomes of PIOL and SMILE in the treatment of myopic anisometropic amblyopic children.

The advantages of PIOLs are numerous, including reversibility of the procedure with the ability to exchange IOL or add a piggyback lens in sulcus to correct future errors. PC pIOLs have a wider range of refractive error correction (up to −17.00 D) compared to corneal refractive surgery. Other advantages include quick visual rehabilitation, lack of regression, higher predictability, high visual quality, preservation of accommodation, and preservation of corneal surface for potential application of bioptics in the future period of refractive stability.[6] However, an experienced surgeon is required to choose and to implant a PCpIOL in children.

Eissa[23] described a case series of 14 pediatric eyes with pseudophakic myopic anisometropic amblyopia that were successfully managed with piggyback Visian collamer lens. Uncorrected distance visual acuity improved in all cases, and CDVA improved in 11 amblyopic eyes (2–4 lines). Mean preoperative (Piggyback) MRSE of −5.23 ± 1.13 decreased to mean postoperative MRSE of −0.30 ± 0.5 after 2 years, with a statistically significant difference ($p < 0.05$).

Lesueur and Arne[24] monitored a series of 5 pediatric eyes with severe anisometropia, which were managed with Visian ICL implantation. Follow-up for a mean period of 11.8 months was complete. The mean preoperative CRSE was −12.8 D, and the mean CDVA was counting fingers (CF) to 20/200. They reported an achievement of ≥3 lines in 2 children.

In 2002, Lesueur and Arne[25] reported the outcomes of Visian ICL implantation in a larger case series of 12 pediatric eyes with refractive amblyopia, who were followed up for 20.5 months. Mean preoperative MRSE was −12.70 and CDVA ranged from CF to 20/63, compared with the mean postoperative CDVA of 20/63.

BenEzra et al.[26] reported Visian ICL implantation in 3 female children with myopic anisometropic amblyopia (−6 to −16 D). The study showed significant improvement in visual acuity and stereoacuity after 18 months of follow-up, without any statistically significant change in ECC.

Another study by Khalid et al.[27] involved ICL implantation in 11 patients (5–15 years old) with anisometropic amblyopia, and preoperative mean CRSE of −11.07 D in 9 myopic eyes and +8.87 in the 2 hyperopic eyes. In myopic eyes, the mean preoperative CDVA improved from 20/171 to 20/51. Hyperopic eyes showed an improvement in preoperative CDVA of 20/130 to a postoperative best-corrected vision of 20/25.[27]

The ICL-implanted eyes in our study showed an improvement in CDVA by 3–6 lines in 86.6% of children, and mean baseline CRSE improvement from −8.35 to −0.31 D after 18 months. Our promising results regarding improvement in CDVA and CRSE in the ICL group are comparable to studies by Lesueur and Arne,[25] BenEzra et al.,[26] and Khaled et al.[27] However, the current prospective study was designed in a comparative protocol between ICL and SMILE procedures, with a larger number of patients.

Phakic IOLs have been reported in the literature to cause glaucoma, corneal endothelial cell loss, chronic uveitis, and cataract development.[28] Despite low incidence of cataract (1.3%) after ICL implantation in adults,[28] pediatric patients theoretically have a higher risk of cataract and glaucoma after PIOL implantation because of shallow anterior chamber depth and tendency of children to rub their eyes.[8]

We encountered in the current study 2 eyes with faint anterior subcapsular cataract, 1 week after ICL implantation. The early incidence of cataract may be explained by intraoperative lens capsule trauma during explantation of upside-down lens and re-implantation.

Given the long life expectancy of s child as well as a high tendency for eye rubbing, the long-term corneal endothelial cell loss proved to be a serious complication of PIOL implantation in children.[28] However, the rate of endothelial cell loss with PCpIOL was much lower compared with postoperative anterior chamber pIOL endothelial cell loss.[29]

In the present study, group B did not show any statistically significant change in ECC at any time point. Similarly, in group A, ECC did not change significantly at postoperative 1, 3, and 9 months compared to preoperative counts. However, at 18 months postoperation, ECC loss was statistically significant compared to the preoperative counts, representing a loss of 1.54% (from preoperative ECC of 2857–2813 cells/mm^2 at 18 months). As such, the endothelial cell loss after PIOL implantation in

our study is less than that previously documented by Jimenez et al.,[30] who reported 4.83% and 5.17% ECC after 6 and 12 months of PC pIOL implantation, respectively. Our results in ECC loss are also promising compared to the studies of Pirouzian and Ip[29] and Alio et al.[31] in which the endothelial cell loss rate ranged between 6.5% and 15.2% but over the course of 3–5 years.

Many authors reported the outcomes of laser corneal refractive surgery in children. However, the current literature rarely documented the results of correction of refractive errors and management of anisometropic amblyopia in children using femtosecond-assisted SMILE. In a meta-analysis of 15 articles on corneal laser refractive surgery in 213 pediatric eyes, Alió et al.[32] found a significant increase in logMAR UDVA and CDVA in the overall sample of amblyopic eyes after PRK, LASEK, and LASIK surgery ($p < 0.001$). Corneal haze was reported in 5.3% of LASIK and 8.5% of surface ablation cases, representing the principal complication.

Limitations for SMILE surgical candidacy in adults, including myopic error of ≤10.00 D, cylindrical error of ≤6.00 D,[33] residual stromal bed thickness 250–275 μm, and minimum corneal thickness 475–500 μm,[14] should be applied on anisometropic children eyes recruited for SMILE. Using the SMILE procedure, we can overcome intraoperative and postoperative flap-related problems, as well as complications like severe postoperative pain, stromal haze, and decentration, which are encountered with other flapless corneal refractive procedures: PRK/LASEK. Corneal stromal haze, explained by stromal wound healing after excimer LASER ablation,[34] is a common complication in PRK but not a paramount problem in SMILE.

Owing to its performance under GA, the problem of decentration with corneal refractive procedure in children remains an issue. A 5% decentration in visual axis can cause a 17% to 20% undercorrection of refractive error.[35] However, globe immobilization with the suction ring during the SMILE procedure reduces the incidence of decentration and subsequent undercorrection.

A study by Samir and Lotfy[36] in 2014 enrolled 18 eyes of 18 children with myopic anisometropic amblyopia that were not successfully treated with the standard amblyopia treatment for 6 months. These children were divided equally and randomly into the LASIK group and the SMILE group. Enrolled children were followed up for 6 months. The mean spherical equivalent refraction in the SMILE operated eye had reduced significantly from −9.25 ± 1.54 D preoperatively to −0.87 ± 0.96 D after 6 months. There was no statistically significant difference between the 2 groups as regard to the postoperative refraction.

From the results of the current study, it is reasonable to conclude that in children with anisometropic amblyopia who are noncompliant with spectacle/contact lens wear, both ICL implantation and SMILE are viable surgical treatments. ICL implantation procedure in children showed high predictability and a wide range of CRSE correction (up to −17.00 D), with salvage of corneal integrity and strength. Furthermore, ICL exchange and the reversibility of the procedure add to its potential advantages. Applying bioptics principle is possible by excimer LASER correction of residual refractive error at the age of refractive stability, in contrast to retreatment after SMILE procedure, which remains an issue. However, the SMILE procedure remains a safe alternative with no risk of cataract, glaucoma, or uveitis.

One of the limitations of this study was lack of assessment of the effect of higher-order aberrations on the quality of vision and CDVA in either group. In addition, late complications such as post-SMILE ectasia or cataract after ICL procedure render the 18-months follow-up a relatively short period. The possible role of phakic IOLs and SMILE in slowing myopic progression secondary to improved retinal image[37]—compared to other traditional forms of correction—should be studied through a longer follow-up period. A third disadvantage was the lack of structured quantitative reading assessment of recruited children under binocular conditions.

To our knowledge, this is the first study comparing the outcomes of SMILE and PCpIOL implantation in children with anisometropic amblyopia. Future prospective randomized double-blinded studies with larger data set and longer follow-up are recommended to evaluate the long-term safety, efficacy, predictability, and benefits of SMILE and ICL implantation in amblyopic children and the role of unilateral refractive surgery in upgrading learning ability of amblyopic children.

The current study may contribute with future prospective trials to settle solid inclusion criteria for refractive amblyopic children who will benefit most from refractive surgery and help to select the ideal surgical co-adjuvant for the treatment and prevention of refractive amblyopia.

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Footnotes and Disclosure:

The authors have no proprietary or commercial interest in any materials discussed in this article.

We are very thankful to Dr. Ahmed Ibrahim, pediatric ophthalmology specialist, and Mohamed Daood, optometrist, for their help in preoperative and postoperative care of patients.

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Originally received Aug. 12, 2017. Final revision Jan. 10, 2018. Accepted Jan. 11, 2018.

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