Check for updates

GOPEN ACCESS

Citation: Park Y, Yum HR, Shin SY, Park SH (2022) Ocular biometric changes following unilateral cataract surgery in children. PLoS ONE 17(8): e0272369. https://doi.org/10.1371/journal.pone.0272369

Editor: Andrzej Grzybowski, University of Warmia, POLAND

Received: March 23, 2022

Accepted: July 18, 2022

Published: August 5, 2022

Copyright: © 2022 Park et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: All relevant data are within the paper.

Funding: This study was supported to SHP, the corresponding author, by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT, & Future Planning (NRF-2016R1C1B1016590) and by the Department of Ophthalmology, College of Medicine, Catholic University of Korea, Man-Soo Kim Research Fund, 2022. The funders had no role in study design, data **RESEARCH ARTICLE**

Ocular biometric changes following unilateral cataract surgery in children

Yooyeon Park¹, Hae Ri Yum², Sun Young Shin³, Shin Hae Park³*

Department of Ophthalmology, College of Medicine, Dankook University, Cheonan, Republic of Korea,
 Department of Ophthalmology, Eunpyeong St. Mary's Hospital, College of Medicine, The Catholic
 University of Korea, Seoul, Republic of Korea, 3 Department of Ophthalmology, Seoul St. Mary's Hospital,
 College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea,

* vaccine@catholic.ac.kr

Abstract

Purpose

To analyze ocular biometric changes following unilateral cataract surgery in children.

Methods

A total of 57 children aged under 13 years who underwent unilateral cataract surgery were analyzed. Groups were classified according to their age at surgery: group I (age <3), II ($3 \le$ age <6), III ($6 \le$ age <9), and IV (age \ge 9). The myopic shift, axial growth, and corneal curvature changes were compared between the pseudophakic eyes and the fellow phakic eyes.

Results

During 7.81 ± 4.39 years, the overall myopic shift (D) and the rate of myopic shift (D/year) were significantly higher at -3.25 ± 3.21 D and -0.45 ± 0.44 D/year in the pseudophakic eyes than -1.78 ± 2.10 D and -0.22 ± 0.29 D/year in the fellow phakic eyes (P = 0.01, 0.004). Group I (-1.14 ± 0.66 vs -0.02 ± 0.45 D/year) and group II (-0.63 ± 0.37 vs -0.31 ± 0.29 D/ year) showed significantly higher rate of myopic shift in the pseudophakic eyes than in the phakic eyes. The rate of myopic shift in the pseudophakic eyes decreased in the older age groups (P = 0.001). There was no significant between-eye difference in the changes in axial length and keratometric values postoperatively.

Conclusion

Following unilateral cataract surgery, a significant postoperative myopic shift was noticed in the pseudophakic eyes compared to the fellow phakic eyes in groups under 6 years old. Postoperative myopic shift and the resultant anisometropia should be considered when selecting the optimal power of IOL in young children requiring unilateral cataract surgery.

collection and analysis, decision to publish, or preparation of the manuscript.

Competing interests: The authors have declared that no competing interests exist.

Introduction

Cataracts are one of the major preventable causes of childhood amblyopia, which is preventable by early intervention before severe visual deprivation amblyopia occurs [1]. The implantation of an intraocular lens (IOL) in children undergoing cataract surgery has become widely accepted and performed at a younger age with the development of surgical instruments and techniques [2–17]. Despite the increasing frequency of IOL implantation in children, IOL selection is still challenging due to normal ocular growth, poor cooperation with biometric measurements, and the lack of a biometric formula for small-sized pediatric eyes. In contrast to adult cataract surgery, it is important to understand that children do not have a static course after cataract extraction. As pediatric eyes grow normally, the axial length (AL) typically grows, the cornea flattens, the anterior chamber gets deeper, lens thickness decreases, and vitreous chamber depth increases with age, which keeps the refractive status constant [18-20]. Rapid axial elongation occurs during the first 2 years of life and slows and stabilizes until the end of the first decade [19]. However, since cataract surgery consists of removing the lens, changes in corneal curvature alone cannot offset the effect of ocular growth. It is thought to undergo a rapid myopic shift after surgery [21-25]. Based on the anticipated development of a myopic shift after cataract surgery, it has been generally accepted to target the postoperative refraction to an initial hyperopia rather than to emmetropia, although the amount of undercorrection varies depending upon age [26]. Moreover, a myopic shift could be a more difficult issue to deal with in children with unilateral pseudophakia, as significant postoperative anisometropia following unilateral cataract surgery can lead to amblyopia and impaired binocularity.

The analysis of a postoperative myopic shift developing after pediatric cataract surgery could help set the target refraction at the time of IOL implantation more accurately and provide guidelines for the long-term care for vision development. Unfortunately, there have been a few studies regarding long-term refractive changes over 2 years in children with unilateral pseudophakia. In addition, the results from studies with Western populations should be applied with caution in Korean children, in which a higher prevalence and severity of myopia have been reported [27]. We sought to analyze ocular biometric changes and postoperative myopic shifts following unilateral cataract surgery in children of different age groups.

Materials and methods

This retrospective study was performed according to the principles of the Declaration of Helsinki after approval was granted by the Institutional Review Board (IRB) of Seoul St. Mary's Hospital, College of Medicine, the Catholic University of Korea, Seoul, Korea (KC21RISI0136). The IRB waived the requirement for informed consent and all data were fully anonymized before accessed.

The medical records of 90 children under the age of 13 years who were clinically confirmed to have cataracts and underwent cataract surgery with IOL implantation in a unilateral eye at Seoul St. Mary's Hospital were reviewed. Only children with a record of 2 years or more were included as study subjects. All types of cataracts (congenital/developmental, traumatic, and complicated cataracts) and all types of implantations of IOL were included. Thirty-three children were excluded with traumatic cataracts with corneal lacerations or retinal detachment (12 patients) and complicated cataracts associated with other ocular anomalies in the cornea, optic nerve, or retina (21 patients). Therefore, 114 eyes of 57 people were finally selected and analyzed in this study.

The ophthalmologic details and medical histories were investigated for this study. The age at diagnosis and surgery, sex, birth history, family history of congenital cataracts, the type and

bilaterality of the cataract, the details of surgical procedures, and postoperative complications were reviewed. Each participant underwent a comprehensive preoperative ophthalmologic assessment, which included the measurement of best-corrected visual acuity (BCVA), intraocular pressure, refractive error (demonstrated as spherical equivalent, SE), keratometry (K), axial length (AL), slit-lamp biomicroscopy, and fundus examination. Visual acuity was expressed based on the logMAR scale (Jin's vision chart, Seoul, Korea, ISO 8596). To predict and calculate the IOL power, preoperative AL and keratometry were measured either prior to surgery or at the time of surgery. Cooperative children were examined using an auto keratorefractometer (RK-F10; Canon, Tochigi-ken, Japan) and a manual keratometer (OM-4; Topcon, Tokyo, Japan). AL measurements were performed with the IOL Master (Carl Zeiss AG, Oberkochen, Germany) or by ultrasound biometry (Storz Compuscan; Storz Ophthalmic Inc., St. Louis, MO, USA). Intraoperative evaluation under general anesthesia was performed on infants and toddlers who could not cooperate with the above examinations, using a handheld auto kerato-refractometer (Retinomax K-plus 2; Mandarin Opto-Medic Co., Singapore). IOL power was calculated using 4 different IOL formulas (Saunders Retslaff Kraft (SRK) II, SRK T, Holladay I, and Hoffer Q). The target postoperative refraction was predicted and modified by the subject's age and the refractive error of the fellow eye, based on the results from previous studies in our institution [28, 29].

All cataract surgeries were performed with a standardized technique. A 3-mm scleral corneal incision was made, then an anterior capsulotomy was done by continuous curvilinear capsulorhexis (CCC) or "can-opener" capsulotomy. Irrigation/aspiration of the lens cortex and nucleus followed. Posterior CCC with anterior vitrectomy was generally performed on patients younger than five years of age at the time of surgery. IOL insertion in the capsular bag or sulcus was done according to the subject's age or lens capsular status.

Postoperative data on the refractive error, keratometry, and AL of all patients were collected one month and one year after IOL implantation, and then yearly to measure the change in ocular biometry of the pseudophakic eyes. The predictive error using SRK II formula was calculated as absolute error between target and actual postoperative one month refraction. The myopic shift (SE change), axial eye growth (AL change), and corneal curvature (steep K and flat K) of the pseudophakic eyes were compared with the outcome data of the fellow phakic eyes at each yearly follow-up visit based on the one-month postoperative values to analyze the ocular growth following unilateral pediatric cataract surgery. The overall myopic shift and axial eye growth of the pseudophakic eyes and fellow eyes during the total follow-up period were measured and compared for each age group. The subjects were classified into four groups according to their age at IOL implantation: under 3 years (infant/toddler period, 6 eyes), 3 to 5 years (preschool period, 14 eyes), 6 to 8 years (early-school period, 18 eyes), and over 9 years of age (late-school period, 19 eyes) to analyze the age-associated ocular biometric changes.

The data are expressed as means ± standard deviations or numbers (percentages) as appropriate. Demographics were compared using the Mann-Whitney U test and Kruskal-Wallis H test or chi-squared test for continuous variables and categorical variables, respectively. The Wilcoxon signed-rank test was used for comparing data at baseline and the follow-up visits. Simple linear regression analysis using 10 years of postoperative data was performed to determine the myopic shift trends in each age group. All statistical analyses were performed using statistical analysis software (SPSS version 24.0; IBM Corp., Armonk, NY, USA). A P-value of less than 0.05 was considered to be statistically significant.

Results

A total of 114 eyes (57 pseudophakic eyes and 57 fellow phakic eyes) in 57 children were analyzed in this study. Unilateral cataract was noticed in 45 children, while 12 children with bilateral cataracts had asymmetric lens opacity, and their unoperated eyes were found to have a BCVA of more than 20/40 and did not require cataract extraction. Among the 69 eyes with cataracts, 60 eyes (87.0%) had congenital/developmental cataracts, four eyes (5.8%) had traumatic cataracts without other ocular segments affected, and five eyes (7.2%) had steroid-induced complicated cataracts (Table 1). The most common type of cataract was posterior subcapsular (65.2%), four of them had posterior lenticonus, followed by nuclear/lamellar (28.9%), and anterior subcapsular (5.8%). The detailed surgical procedures and complications after unilateral pediatric cataract surgery are shown in Table 1. A lens aspiration procedure was performed on 57 eyes, 42.1% of which had posterior CCC with anterior vitrectomy. In terms of postoperative complications, 24 eyes (42.1% of all pseudophakic eyes) showed complications of opacification in the posterior capsule (PCO), two eyes (3.5%) developed IOL opacity, two eyes (3.5%) had cortical remnants, and none showed secondary glaucoma following cataract surgery. Posterior capsulotomy was performed in 24 patients with PCO, 20 of whom were able

Clinical characteristics	No (%)
Male: Female	27: 30
Birth Hx, full-term: preterm	56: 1
Family Hx of congenital cataracts	2 (3.5%)
Bilaterality of cataract	
Bilateral	12 (21.1%)
Unilateral	45 (78.9%)
Cause of cataract (69 eyes)	
Congenital/developmental cataract	60 (87.0%)
Traumatic cataract	4 (5.8%)
Complicated cataract	5 (7.2%)
Type of cataract (69 eyes)	
Anterior subcapsular	4 (5.8%)
Nuclear or lamellar	20 (29.0%)
Posterior subcapsular or posterior lenticonus	45 (65.2%)
Surgical eye, right: left	24: 33
Surgical procedure (57 eyes)	
Posterior CCC with anterior vitrectomy	24 (42.1%)
Primary/secondary IOL implantation	55 (96.5%) / 2 (3.5%)
In the bag / sulcus insertion	50 (87.7%) / 7 (12.3%)
Complications after surgery	
PCO	24 (42.1%)
Nd-Yag laser posterior capsulotomy	20 (35.1%)
Surgical pars plana posterior capsulotomy	4 (7.0%)
IOL opacification	2 (3.5%)
Cortex remnant	2 (3.5%)
High IOP	0 (0.0%)

Table 1.	Clinical	characteristics	of 57	children	who un	derwent	unilateral	cataract	surger	y.
----------	----------	-----------------	-------	----------	--------	---------	------------	----------	--------	----

Hx, history; CCC, continuous curvilinear capsulorhexis; IOL, intraocular lens; PCO, posterior capsular opacity; IOP, intraocular pressure

https://doi.org/10.1371/journal.pone.0272369.t001

Group	All	I (Infant/toddler) age <3	II (Preschool) $3 \le age < 6$	III (Early-school) 6 \leq age $<$ 9	IV (Late-school) age \geq 9	P-value
Number of eyes	57	6	14	18	19	
Age at IOL implantation (year)	7.55 ± 3.57	1.77 ± 0.78	4.25 ± 0.72	7.93 ± 0.75	11.46 ± 1.62	< 0.001 ^a
AL (mm)	22.78 ± 1.47	20.43 ± 1.69	22.32 ± 1.38	23.16 ± 1.08	23.58 ± 0.87	0.001 ^a
Mean K (D)						
Preoperative	43.29 ± 1.58	43.79 ± 2.63	42.95 ± 1.85	43.37 ± 1.20	43.36 ± 1.65	0.734
Postoperative 1-month	43.76 ± 1.60	45.50	43.75 ± 1.40	43.58 ± 1.15	43.79 ± 2.36	0.601
SE (D)						
Preoperative	-0.46 ± 4.16	-4.31 ± 7.51	$+0.45 \pm 3.36$	$+0.47 \pm 4.33$	-1.16 ± 4.18	0.278
Postoperative 1-month	$+0.50 \pm 1.97$	$+1.92 \pm 4.71$	$+1.25 \pm 1.52$	$+0.49\pm0.99$	-0.50 ± 1.08	0.011 ^a
Anticipated target (SRK II)	$+0.67 \pm 1.45$	$+3.00 \pm 2.28$	$+1.24\pm1.18$	$+0.74\pm0.64$	-0.52 ± 0.90	$< 0.001^{a}$
P-value ^b	0.882	0.715	0.861	0.394	0.691	
BCVA (logMAR)						
Preoperative	0.87 ± 0.63	N/A	0.94 ± 0.67	0.73 ± 0.29	0.95 ± 0.82	0.679
Postoperative 1-month	0.37 ± 0.30	0.60	0.57 ± 0.31	0.35 ± 0.21	0.24 ± 0.30	0.003 ^a
P-value	< 0.001 ^b	N/A	0.036 ^b	$< 0.001^{b}$	<0.001 ^b	

Table 2. Ocular biometric findings of pseudophakic eyes at the time of IOL implantation and one-month postoperatively.

AL, axial length; K, keratometry; D, diopter; SE, spherical equivalent; BCVA, best-corrected visual acuity; N/A, not applicable

The data are expressed as means \pm standard deviations.

^aComparison was performed using the Kruskal Wallis H test. Significant values at P < 0.05.

^bPostoperative 1-month SE and anticipated target were compared, and preoperative BCVA was compared with postoperative BCVA. Comparison was performed using the Wilcoxon signed-rank test. Significant values at P < 0.05.

https://doi.org/10.1371/journal.pone.0272369.t002

to achieve clear vision after Nd-YAG laser therapy. Surgical pars plana posterior capsulotomy was chosen in the other four patients since they were too young to cooperate with the laser procedure.

Table 2 shows the early postoperative biometric change of pseudophakic eyes, at the time of IOL implantation and one month postoperatively. Children with older age had longer AL (P = 0.001), with a mean of 20.43 mm for group I, 22.32 mm for group II, 23.16 mm for group III, and 23.58 mm for group IV. One month after the IOL implantation, significant VA improvement was seen in all age groups. In a comparison of postoperative SE with the preoperative anticipated target using SRK II principles, no statistical differences were found in any age group (P = 0.882).

Long-term yearly biometric data of the subjects were analyzed (Table 3). The mean followup period of 57 children was 7.81 (2.2–21.6) years and the final follow-up age was 15.4 ± 6.19 years. During the total follow-up period, the overall myopic shift (D) and the yearly rate of myopic shift (D/year) were significantly higher with -3.25 ± 3.21 D and -0.45 ± 0.44 D/year in the pseudophakic eyes than with -1.78 ± 2.10 D and -0.22 ± 0.29 D/year in the fellow phakic eyes (P = 0.01 and P = 0.004, respectively). In the comparison of each age group, group I and group II showed a more rapid myopic shift in the pseudophakic eyes than in the fellow phakic eyes, as -1.14 ± 0.66 D/year versus (vs.) -0.02 ± 0.45 D/year in group I (P = 0.009) and -0.63 ± 0.37 D/year vs. -0.31 ± 0.29 D/year in group II (P = 0.014). The amount and rate of myopic shift in the pseudophakic eyes decreased in the older age groups (P = 0.001), and no significant between-eye difference in the myopic shift was found in children who underwent unilateral cataract surgery at the age of 6 or older. Ten years of SE data on the pseudophakic and fellow phakic eyes in the four groups divided by age are shown in Fig 1. Using linear

Spherical equivalent change								
Group (age at IOL implantation)	Follow-up period (year)	Overall r	nyopic shift (D)		Rate of myopic shift (D/year)			
		Pseudophakic eye	Phakic eye	P-value	Pseudophakic eye	Phakic eye	P-value	
All	7.81 ± 4.39	-3.25 ± 3.21	-1.78 ± 2.10	0.01 ^a	-0.45 ± 0.44	-0.22 ± 0.29	0.004^{a}	
I (age <3)	6.65 ± 3.36	-6.46 ± 4.12	-0.52 ± 2.09	0.009 ^a	-1.14 ± 0.66	-0.02 ± 0.45	0.009 ^a	
II (3≤ age <6)	6.94 ± 3.05	-5.07 ± 3.91	-2.46 ± 2.82	0.056	-0.63 ± 0.37	-0.31 ± 0.29	0.014 ^a	
III (6≤ age <9)	8.13 ± 5.28	-2.43 ± 2.00	-1.93 ± 1.98	0.496	-0.30 ± 0.21	-0.23 ± 0.30	0.339	
IV (age ≥ 9)	8.52 ± 4.70	-1.62 ± 1.63	-1.55 ± 1.43	0.908	-0.23 ± 0.27	-0.21 ± 0.20	0.977	
P-value		0.001 ^b	0.429		$< 0.001^{b}$	0.502		
		Axial length c	hange					
Group (age at IOL implantation)	Follow-up period (year)	Overall axia	l eye growth (mr	n)	Rate of axial e	ye growth (mm/y	vear)	
		Pseudophakic eye	Phakic eye	P-value	Pseudophakic eye	Phakic eye	P-value	
All	6.33 ± 2.98	1.49 ± 1.14	1.42 ± 0.91	0.94	0.23 ± 0.16	0.26 ± 0.15	0.504	
I (age <3)	7.35 ± 3.02	2.83 ± 1.16	2.15 ± 1.69	0.486	0.32 ± 0.07	0.25 ± 0.17	0.886	
II (3≤ age <6)	6.26 ± 2.90	2.11 ± 1.34	1.66 ±0.93	0.512	0.33 ± 0.15	0.29 ± 0.10	0.468	
III (6≤ age <9)	6.02 ± 3.19	0.98 ± 0.51	1.12 ± 0.53	0.606	0.17 ± 0.12	0.25 ± 0.19	0.243	
IV (age ≥ 9)	6.32 ± 2.92	0.88 ± 0.65	0.99 ± 0.29	0.743	0.18 ± 0.18	0.23 ± 0.18	0.583	
P-value		0.006 ^b	0.494		0.015 ^b	0.787		

Table 3. Comparison of myopic shift and axial eye growth of pseudophakic eyes and fellow phakic eyes during the total follow-up period after unilateral pediatric cataract surgery.

IOL, intraocular lens; D, diopter

The data are expressed as means \pm standard deviations.

^aComparison was performed using the Mann-Whitney U test. Significant values at P < 0.05.

^bComparison was performed using the Kruskal Wallis H test. Significant values at P < 0.05.

https://doi.org/10.1371/journal.pone.0272369.t003

regression analysis, group I was revealed to have the steepest yearly change in SE ($R^2 = 0.954$) among the 4 age subgroups of pseudophakic eyes with -1.11 D/year, followed by group II at -0.91 D/year ($R^2 = 0.979$), group III at -0.42 D/year ($R^2 = 0.975$), group IV at -0.20 D/year ($R^2 = 0.674$) (P < 0.001, Fig 1A). However, the phakic eyes did not show any significant difference in yearly SE changes in any age subgroup (P = 0.502, Fig 1B).

Long-term postoperative changes in axial length were also evaluated (Table 3). Younger age groups had a larger amount and higher yearly rate of axial growth in the pseudophakic eyes. The overall axial growth was more prominent in the younger age groups in the pseudophakic eyes (P = 0.006), whereas all age groups showed similar axial growth patterns in the phakic eyes (P = 0.494). However, neither the overall amount nor the yearly rate of axial eye growth showed any significant difference between the pseudophakic and phakic eyes (P = 0.504, respectively), even in groups I and II that showed significant myopic shifts in the pseudophakic eyes.

The keratometry values of the pseudophakic and phakic eyes at postoperative one month and at final follow-up are shown in Table 4. No statistical differences between the eyes or among the age groups were found. Corneal astigmatism (steep K–flat K difference) increased over time at 0.56 ± 0.83 D in the pseudophakic eyes vs. 0.36 ± 0.69 D in the phakic eyes, but no significant between-eye difference was found (P = 0.559).

Discussion

This study investigated the long-term ocular biometric changes between pseudophakic and the fellow phakic eyes after unilateral pediatric cataract surgery with an average follow-up of 7.81 years. Following unilateral cataract surgery, the pseudophakic eyes showed a higher overall



Fig 1. Ten years of spherical equivalent values on the pseudophakic and fellow phakic eyes in the four groups divided by age. (A) Group I had the steepest yearly change in spherical equivalent in the pseudophakic eyes among the four age groups at -1.11 D ($R^2 = 0.954$), followed by group II at -0.91 D ($R^2 = 0.979$), group III at -0.42 D ($R^2 = 0.975$), and group IV at -0.20 D ($R^2 = 0.674$) (P < 0.001). (B) No significant difference was shown in yearly SE changes in the phakic eyes among the age groups (-0.39 D in group I; -0.52 D in group II; -0.29 D in group III; and -0.14 D in group IV, P = 0.502).

https://doi.org/10.1371/journal.pone.0272369.g001

amount and rate of myopic shift than the fellow phakic eyes, with the absence of any significant between-eye differences in axial length and keratometric values. A significant postoperative myopic shift was found in children who underwent unilateral cataract surgery under 6 years of age. These findings have an important clinical implication that postoperative myopic shift and the resultant anisometropia should be considered when setting the target refraction and selecting the optimal IOL power at the time of unilateral cataract surgery in children.

Refractive changes following unilateral pediatric cataract surgery have been investigated in several studies (Table 5). Some studies with different ethnicities have demonstrated a greater

Group (age at IOL implantation)	Steep K (I) at postop. 1-month	1	Flat K (D) at postop. 1-month			
	Pseudophakic eye	Phakic eye	P-value ^a	Pseudophakic eye	Phakic eye	P-value ^a	
All	44.78 ± 1.77	43.87 ± 1.39	0.058	42.73 ± 1.63	42.57 ± 1.60	0.671	
I (age <3)	47.50	45.25	N/A	43.50	43.00	N/A	
II (3≤ age <6)	44.44 ± 1.66	43.90 ± 1.83	0.556	43.06 ± 1.14	42.80 ± 1.81	0.73	
III (6 \leq age $<$ 9)	44.59 ± 1.23	44.08 ± 1.16	0.173	42.57 ± 1.37	42.63 ± 1.45	0.809	
IV (age \geq 9)	44.89 ± 2.48	43.15 ± 1.43	0.202	42.68 ± 2.39	42.15 ± 2.09	0.755	
P-value ^b	0.517	0.4		0.769	0.988		
Group (age at IOL implantation)	Steep K (D) at final follow-up		Flat K (D) at final follow-up			
	Pseudophakic eye	Phakic eye	P-value ^a	Pseudophakic eye	Phakic eye	P-value ^a	
					•		
All	44.37 ± 2.09	43.68 ± 1.94	0.096	41.93 ± 1.94	42.18 ± 1.86	0.772	
All I (age <3)	$\frac{44.37 \pm 2.09}{44.93 \pm 1.84}$	43.68 ± 1.94 43.75 ± 1.41	0.096 0.533	41.93 ± 1.94 42.74 ± 1.56	42.18 ± 1.86 41.88 ± 1.59	0.772 0.533	
All I (age <3)	$\begin{array}{c} 44.37 \pm 2.09 \\ \\ 44.93 \pm 1.84 \\ \\ 44.74 \pm 2.11 \end{array}$	$\begin{array}{c} 43.68 \pm 1.94 \\ \\ 43.75 \pm 1.41 \\ \\ 44.48 \pm 3.06 \end{array}$	0.096 0.533 0.927	41.93 ± 1.94 42.74 ± 1.56 42.60 ± 2.25	42.18 ± 1.86 41.88 ± 1.59 42.42 ± 2.53	0.772 0.533 1.0	
All I (age <3)	$\begin{array}{r} 44.37 \pm 2.09 \\ 44.93 \pm 1.84 \\ 44.74 \pm 2.11 \\ 44.33 \pm 1.49 \end{array}$	$\begin{array}{c} 43.68 \pm 1.94 \\ \\ 43.75 \pm 1.41 \\ \\ 44.48 \pm 3.06 \\ \\ 43.66 \pm 1.63 \end{array}$	0.096 0.533 0.927 0.21	$41.93 \pm 1.94 42.74 \pm 1.56 42.60 \pm 2.25 41.89 \pm 1.50$	$\begin{array}{r} 42.18 \pm 1.86 \\ \hline 41.88 \pm 1.59 \\ \hline 42.42 \pm 2.53 \\ \hline 42.38 \pm 1.62 \end{array}$	0.772 0.533 1.0 0.547	
$\begin{tabular}{c} All \\ \hline I (age <3) \\ \hline II (3 \le age <6) \\ \hline III (6 \le age <9) \\ \hline IV (age \ge 9) \\ \end{tabular}$	$\begin{array}{c} 44.37 \pm 2.09 \\ \\ 44.93 \pm 1.84 \\ \\ 44.74 \pm 2.11 \\ \\ 44.33 \pm 1.49 \\ \\ 44.02 \pm 2.74 \end{array}$	$\begin{array}{r} 43.68 \pm 1.94 \\ \hline 43.75 \pm 1.41 \\ \hline 44.48 \pm 3.06 \\ \hline 43.66 \pm 1.63 \\ \hline 43.33 \pm 1.95 \end{array}$	0.096 0.533 0.927 0.21 0.471	41.93 ± 1.94 42.74 ± 1.56 42.60 ± 2.25 41.89 ± 1.50 41.37 ± 2.26	$\begin{array}{c} 42.18 \pm 1.86 \\ 41.88 \pm 1.59 \\ 42.42 \pm 2.53 \\ 42.38 \pm 1.62 \\ 41.97 \pm 2.09 \end{array}$	0.772 0.533 1.0 0.547 0.695	

Table 4. Keratometry values of pseudophakic and fellow phakic eyes at postoperative one-month and at final follow-up after unilateral pediatric cataract surgery.

IOL, intraocular lens; K, keratometry; D, diopter; postop., postoperative day; K-diff, difference in steep-flat K; N/A, not applicable

The data are expressed as means ± standard deviations.

^aComparison was performed using the Mann-Whitney U test. Significant values at P < 0.05.

 $^{\rm b}$ Comparison was performed using the Kruskal Wallis H test. Significant values at P < 0.05.

https://doi.org/10.1371/journal.pone.0272369.t004

References	Ethnic population	No. of eyes	Age at IOL implantation (years), mean (range)	Mean rate of refractive change (D/year)		Follow-up years, mean (range)	
				Pseudophakic eye	Fellow eye		
Enyedi et al. ^b [4]	United States	83	6.3 (0.75-17)	-0.65	-0.12	2.2 (0.5-6.6)	
				(-1.2 in age≤2)			
Yam et al. ^b [6]	Hong Kong Chinese	32	7.3 (1.5–17)	-0.84	-0.24	4.4 (2-9)	
				(-0.91 in age≤2)			
Sminia et al. ^{a, b} [11]	Netherlands	20	4.1 (2.2–8)	-0.21	-0.23	4.8 (1.8–11.1)	
		25	0.4 (0.06–1.4)	-1.40 ^b	-0.40	4.3 (1.0–11.9)	
Weakley et al.* [16]	United States	108	0.2 (0.08–0.6)	-2.12	-	4.9 (0.9–5.4)	
Yang et al. [17]	Taiwanese	62	5.6 (1-9.8)	-0.46	-0.23	3.6 (1-9.75)	
Present study ^b	Korean	114	7.6 (0.5–15.6)	-0.45	-0.22	7.8 (2.2–21.6)	
				(-1.14 in age<3)			

Table 5.	Previous	studies of	n refractive	changes at	ter unilateral	pediatric	cataract	surgery
				· · · · · · · · · · · · · · · · · · ·				· · · · ·

IOL, intraocular lens; D, diopter

*The Infant Aphakia Treatment Study

^a The patients were divided into two groups based on an age of 18 months.

^b Studies with different ethnicities that have demonstrated a significantly higher rate of refractive change (D/year) in pseudophakic eyes than in fellow phakic eyes.

https://doi.org/10.1371/journal.pone.0272369.t005

myopic shift in pseudophakic eyes [4, 6, 11, 16]. They found a more rapid myopic shift of -0.65 to -2.12 D/year in pseudophakic eyes compared to -0.12 to -0.40 D/years in the fellow eyes. However, a Taiwanese study [17] with a mean age of 5.6 years at surgery did not find any significant difference in refractive changes between the pseudophakic eyes and the fellow phakic eyes. In a study by Sminia et al. [11], there was no difference in an older age group at a mean of 4.1 years. The results of the present study revealed a significantly higher rate of refractive change in the pseudophakic eyes at an average of -0.45 D/year, compared to -0.22 D/year in the fellow phakic eyes. The subgroup analysis according to age at surgery showed that children who underwent cataract surgery earlier had a larger (groups I and II) and more rapid (group I) postoperative myopic shift. The overall amount and myopic shift rate in the pseudophakic eyes decreased in the older age groups (P = 0.001), and no significant between-eye difference in myopic shift was found in children who underwent unilateral cataract surgery at the age of 6 or older. In particular, a postoperative myopic shift was noticeable in children with an IOL implanted before 3 years of age. They showed a mean myopic shift of -6.46 ± 4.12 D in the pseudophakic eyes and -0.52 ± 2.09 D in the fellow phakic eyes during a mean follow-up period of 6.65 years after cataract surgery. These findings imply that children with unilateral pseudophakia who underwent cataract surgery earlier are at risk of developing significant anisometropia due to a large myopic shift occurring in the pseudophakic eyes. A recent prospective study, which included infants who underwent unilateral IOL implantation at a median age of 2.2 months, pointed out that the majority of them had significant anisometropia at an age of 5 years [16].

We could not find any significant between-eye differences in the changes of axial length and keratometric values following unilateral cataract surgery, in contrast to the large myopic shift observed in the unilateral pseudophakic eyes. Differences in the amount and yearly rate of axial eye growth showed no statistical significance between the pseudophakic and phakic eyes (P = 0.94 and P = 0.504, respectively) in any age subgroup. Similar findings were found in previous studies [11, 12, 30], these findings provide supportive evidence that the myopic shift in the operated eye is an optical phenomenon. In developing phakic eyes, progressive flattening of the crystalline lens decreases the refractive consequences of axial elongation [19, 20]. After lens removal, a myopic shift in pseudophakic eyes could occur if the fixed power of the IOL fails to offset the axial growth. As the eye grows, the IOL moves farther from the retina. Similar to the effect of vertex distance with high-power lenses, the anterior movement of the IOL as the child grows induces a myopic shift by itself [12, 30]. Our study found that the younger age groups showed more rapid axial eye growth compared to the older age groups, consistent with the previous studies [13, 15, 19, 31, 32]. Although there were no between-eye differences in axial elongation following surgery, the large axial growth observed in younger children might lead to significant refractive changes in the pseudophakic eyes with fixed IOL power. Moreover, the incidence and severity of myopia have been increasing in several Asian countries, including Korea. A recent population-based study reported that the prevalence rates of myopia (≤ -0.5 D) and high myopia (≤ -6.0 D) among 13–18-year-old Korean adolescents were 80.1% and 8.9%, respectively [33]. These ethnic variations could make a greater impact on the pattern of long-term myopic shifts in Korean children and require further research.

IOL selection is still challenging in growing children who do not have a static course after cataract extraction. It is more difficult to choose targeted refraction in children who require unilateral cataract surgery to minimize anisometropia and the following amblyopia and prevent the future development of high myopia in the long perspective. An analysis of the longterm refractive change of unilateral pseudophakia enables us to anticipate a myopic shift developing after surgery. Kraus et al. [34] reported 10 cases that required an IOL exchange for high myopia in children with unilateral pseudophakia. A recent randomized clinical trial of the Infant Aphakia Treatment Study group (IATS) [16] revealed significant anisometropia with a median value of -3.5 D in 5-year-old children after unilateral IOL implantation in infants. The authors found that the immediate postoperative refractive targets of +8 D or +6 D were not sufficient to compensate for the actual myopic shifts observed in that study [16]. The major findings in the present study were: (1) more rapid myopic shift in pseudophakic eves in children aged 6 years and younger at the time of cataract surgery, (2) approximately -6.0 D greater myopic shift in the pseudophakic eyes than in the fellow phakic eyes at an average follow-up of 6.65 years in children younger than 3 years of age at surgery, and (3) no significant betweeneye difference in the overall amount and rate of myopic shift in children who underwent unilateral cataract surgery at age over 6 years old. These findings should be considered differently depending upon the age at surgery in optimizing IOL selection in children requiring unilateral cataract surgery. For children older than 6 years of age, an IOL power could be selected with the target refraction matched to the refractive error of the fellow eye. For younger children under 6 years of age, since they are susceptible to developing amblyopia, efforts should be given to facilitate visual development in the treated pseudophakic eye. According to the 2018 American Academy of Ophthalmology (AAO) guidelines [35], the threshold for the correction of aniso-hypermetropia was +2.5 D for children younger than one year, +2.0 D for children 1-2 years old, and +1.5 D for children older than 2 years. Also, in a long-term perspective, the power of an IOL should be selected that will not develop significant anisometropia and high myopia following the period of ocular growth [34]. Based on the large myopic shift observed in young children, it could be reasonable to determine an optimal IOL power of < +2.0 D more hyperopic than the refractive error of the fellow phakic eye. These guidelines could be practically useful in treating children who require unilateral cataract surgery due to acquired cataracts related to trauma or drugs as well as congenital causes.

There were some limitations to our study. First, since the causes and types of cataracts among patients enrolled were diverse, it may have influenced the results to some extent. Second, the predictive error was calculated using the SRK-II formula only. Third, our series was

performed retrospectively and had relatively small subject numbers in some subgroups. The younger age groups did not have sufficient numbers of children to perform a parametric statistical analysis. Limited numbers of patients have undergone unilateral cataract extraction and primary IOL implantation before 3 years old due to the complexity of the surgical techniques and the risk of various intraoperative and postoperative complications [36]. Further prospective studies with a larger sample size and long-term follow-up are required to confirm the results observed in the present study, especially focusing on very young children.

Conclusion

A significant postoperative myopic shift was noticed in pseudophakic eyes following unilateral cataract surgery compared to the fellow phakic eyes, especially in young children under 6 years of age. Axial length and keratometric changes did not accompany a myopic shift. Pediatric cataract surgeons should be aware of the long-term ocular biometric changes developed in pseudophakic eyes during ocular growth following cataract surgery.

Supporting information

S1 Data. Study data. All patient results and demographics information. (XLSX)

Author Contributions

Conceptualization: Yooyeon Park, Shin Hae Park.

Data curation: Yooyeon Park, Hae Ri Yum, Sun Young Shin, Shin Hae Park.

Formal analysis: Yooyeon Park.

Funding acquisition: Shin Hae Park.

Investigation: Yooyeon Park, Hae Ri Yum, Sun Young Shin.

Methodology: Yooyeon Park, Shin Hae Park.

Supervision: Sun Young Shin, Shin Hae Park.

Validation: Hae Ri Yum, Shin Hae Park.

Writing - original draft: Yooyeon Park.

Writing - review & editing: Yooyeon Park, Shin Hae Park.

References

- Stone RA, Lin T, Desai D, Capehart C. Photoperiod, early post-natal eye growth, and visual deprivation. Vision Res. 1995; 35(9):1195–1202. https://doi.org/10.1016/0042-6989(94)00232-b PMID: 7610580
- Weakley DR Jr, Lynn MJ, Dubois L, Cotsonis G, Wilson ME, Buckley EG, et al. Myopic Shift 5 Years after Intraocular Lens Implantation in the Infant Aphakia Treatment Study. Ophthalmology. 2017; 124 (6):822–827. https://doi.org/10.1016/j.ophtha.2016.12.040 PMID: 28215452
- Ahmadieh H, Javadi MA. Intra-ocular lens implantation in children. Curr Opin Ophthalmol. 2001; 12 (1):30–34. https://doi.org/10.1097/00055735-200102000-00006 PMID: 11150078
- Enyedi LB, Peterseim MW, Freedman SF, Buckley EG. Refractive changes after pediatric intraocular lens implantation. Am J Ophthalmol. 1998; 126(6):772–781. https://doi.org/10.1016/s0002-9394(98) 00247-5 PMID: 9860000
- Plager DA, Kipfer H, Sprunger DT, Sondhi N, Neely DE. Refractive change in pediatric pseudophakia: 6-year follow-up. J Cataract Refract Surg. 2002; 28(5):810–815. https://doi.org/10.1016/s0886-3350 (01)01156-7 PMID: 11978460

- Yam JC, Wu PK, Ko ST, Wong US, Chan CW. Refractive changes after pediatric intraocular lens implantation in Hong Kong children. J Pediatr Ophthalmol Strabismus. 2012; 49(5):308–313. https://doi. org/10.3928/01913913-20120501-04 PMID: 22588728
- Ashworth JL, Maino AP, Biswas S, Lloyd IC. Refractive outcomes after primary intraocular lens implantation in infants. Br J Ophthalmol. 2007; 91(5):596–599. https://doi.org/10.1136/bjo.2006.108571 PMID: 17179164
- Lambert SR, Buckley EG, Plager DA, Medow NB, Wilson ME. Unilateral intraocular lens implantation during the first six months of life. J AAPOS. 1999; 3(6):344–349. https://doi.org/10.1016/s1091-8531 (99)70043-1 PMID: 10613578
- Astle WF, Ingram AD, Isaza GM, Echeverri P. Paediatric pseudophakia: analysis of intraocular lens power and myopic shift. Clin Exp Ophthalmol. 2007; 35(3):244–251. https://doi.org/10.1111/j.1442-9071.2006.01446.x PMID: 17430511
- McClatchey SK, Dahan E, Maselli E, Gimbel HV, Wilson ME, Lambert SR, et al. A comparison of the rate of refractive growth in pediatric aphakic and pseudophakic eyes. Ophthalmology. 2000; 107 (1):118–122. https://doi.org/10.1016/s0161-6420(99)00033-0 PMID: 10647729
- Sminia ML, de Faber JT, Doelwijt DJ, Wubbels RJ, Tjon-Fo-Sang M. Axial eye length growth and final refractive outcome after unilateral paediatric cataract surgery. Br J Ophthalmol. 2010; 94(5):547–550. https://doi.org/10.1136/bjo.2009.160192 PMID: 19692358
- Inatomi M, Kora Y, Kinohira Y, Yaguchi S. Long-term follow-up of eye growth in pediatric patients after unilateral cataract surgery with intraocular lens implantation. J AAPOS. 2004; 8(1):50–55. https://doi. org/10.1016/j.jaapos.2003.08.008 PMID: 14970800
- Leiba H, Springer A, Pollack A. Ocular axial length changes in pseudophakic children after traumatic and congenital cataract surgery. J AAPOS. 2006; 10(5):460–463. <u>https://doi.org/10.1016/j.jaapos.</u> 2006.06.006 PMID: 17070483
- Vasavada AR, Raj SM, Nihalani B. Rate of axial growth after congenital cataract surgery. Am J Ophthalmol. 2004; 138(6):915–924. https://doi.org/10.1016/j.ajo.2004.06.068 PMID: 15629281
- 15. Kora Y, Shimizu K, Inatomi M, Fukado Y, Ozawa T. Eye growth after cataract extraction and intraocular lens implantation in children. Ophthalmic Surg. 1993; 24(7):467–475. PMID: 8351094
- Weakley D, Cotsonis G, Wilson ME, Plager DA, Buckley EG, Lambert SR. Anisometropia at Age 5 Years After Unilateral Intraocular Lens Implantation During Infancy in the Infant Aphakia Treatment Study. Am J Ophthalmol. 2017; 180:1–7. https://doi.org/10.1016/j.ajo.2017.05.008 PMID: 28526552
- Yang ML, Lin KK, Hou CH, Liang YS, Lee JS. Primary intraocular lens implantation for unilateral idiopathic cataract in children. Chang Gung Med J. 2008; 31(1):52–58. PMID: 18419053
- Twelker JD, Mitchell GL, Messer DH, Bhakta R, Jones LA, Mutti DO, et al. Children's Ocular Components and Age, Gender, and Ethnicity. Optom Vis Sci. 2009; 86(8):918–935. <u>https://doi.org/10.1097/opx.0b013e3181b2f903</u> PMID: 19650241
- Gordon RA, Donzis PB. Refractive development of the human eye. Arch Ophthalmol. 1985; 103 (6):785–789. https://doi.org/10.1001/archopht.1985.01050060045020 PMID: 4004614
- Munro RJ, Fulton AB, Chui TY, Moskowitz A, Ramamirtham R, Hansen RM, et al. Eye growth in termand preterm-born eyes modeled from magnetic resonance images. Invest Ophthalmol Vis Sci. 2015; 56 (5):3121–3131. https://doi.org/10.1167/iovs.14-15980 PMID: 26024095
- Wildsoet CF. Active emmetropization—evidence for its existence and ramifications for clinical practice. Ophthalmic Physiol Opt. 1997; 17(4):279–290. PMID: 9390372
- Kugelberg U, Zetterström C, Lundgren B, Syrén-Nordqvist S. Eye growth in the aphakic newborn rabbit. J Cataract Refract Surg. 1996; 22(3):337–341. https://doi.org/10.1016/s0886-3350(96)80246-x PMID: 8778367
- Kugelberg M, Shafiei K, Zetterström C. Single-piece AcrySof in the newborn rabbit eye. J Cataract Refract Surg. 2004; 30(6):1345–1350. https://doi.org/10.1016/j.jcrs.2003.10.023 PMID: 15177615
- Lambert SR, Fernandes A, Grossniklaus H, Drews-Botsch C, Eggers H, Boothe RG. Neonatal lensectomy and intraocular lens implantation: effects in rhesus monkeys. Invest Ophthalmol Vis Sci. 1995; 36 (2):300–310. PMID: 7843901
- Lambert SR. The effect of age on the retardation of axial elongation following a lensectomy in infant monkeys. Arch Ophthalmol. 1998; 116(6):781–784. https://doi.org/10.1001/archopht.116.6.781 PMID: 9639448
- 26. Al Shamrani M, Al Turkmani S. Update of intraocular lens implantation in children. Saudi J Ophthalmol. 2012; 26(3):271–275. https://doi.org/10.1016/j.sjopt.2012.05.005 PMID: 23961005
- 27. Lim DH, Han J, Chung TY, Kang S, Yim HW; Epidemiologic Survey Committee of the Korean Ophthalmologic Society. The high prevalence of myopia in Korean children with influence of parental refractive

errors: The 2008–2012 Korean National Health and Nutrition Examination Survey. PLoS One. 2018; 13 (11):e0207690. https://doi.org/10.1371/journal.pone.0207690

- 28. Sim JO, Park MR, Park SH. Changes in Refraction following Pediatric Cataract Surgery. J Korean Ophthalmol Soc 2005; 46(5):768–774.
- Kim YD, Kim DH, Park SH. Comparison of IOL Formulas in Pediatric Intraocular Lens Implantation. J Korean Ophthalmol Soc. 2007; 48(2):251–258.
- McClatchey SK, Parks MM. Myopic shift after cataract removal in childhood. J Pediatr Ophthalmol Strabismus. 1997; 34(2):88–95. https://doi.org/10.3928/0191-3913-19970301-07 PMID: 9083953
- **31.** Lambert SR, Lynn MJ, DuBois LG, Cotsonis GA, Hartmann EE, Wilson ME. Axial elongation following cataract surgery during the first year of life in the infant Aphakia Treatment Study. Invest Ophthalmol Vis Sci. 2012; 53(12):7539–7545. https://doi.org/10.1167/iovs.12-10285 PMID: 23074203
- **32.** Hussin HM, Markham R. Changes in axial length growth after congenital cataract surgery and intraocular lens implantation in children younger than 5 years. J Cataract Refract Surg. 2009; 35(7):1223–1228. https://doi.org/10.1016/j.jcrs.2009.03.015 PMID: 19545812
- Choi JA, Han K, Park YM, La TY. Low serum 25-hydroxyvitamin D is associated with myopia in Korean adolescents. Invest Ophthalmol Vis Sci. 2014; 55(4):2041–2047. <u>https://doi.org/10.1167/IOVS.13-12853</u> PMID: 24699557
- Kraus CL, Trivedi RH, Wilson ME. Intraocular lens exchange for high myopia in pseudophakic children. Eye (Lond). 2016; 30(9):1199–1203. https://doi.org/10.1038/eye.2016.152 PMID: 27419831
- Wallace DK, Morse CL, Melia M, Sprunger DT, Repka MX, Lee KA, et al. Pediatric Eye Evaluations Preferred Practice Pattern[®]: I. Vision Screening in the Primary Care and Community Setting; II. Comprehensive Ophthalmic Examination. Ophthalmology. 2018; 125:P184–P227. <u>https://doi.org/10.1016/j.ophtha.2017.09.032</u> PMID: 29108745
- McClatchey SK, Hofmeister EM. Intraocular Lens Power Calculation for Children. In: Wilson ME, Trivedi RH, Pandey SK (eds) Pediatric Cataract Surgery: Techniques, Complications, and Management. Wolters Kluwer Health, Philadelphia; 2005. pp 30–38.