Commentary review: challenges of intraocular lens implantation for congenital cataract infants

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Abstract
- As an indispensable part of congenital cataract surgery, intraocular lens (IOL) implantation in infantile patients has long-term positive impacts on visual rehabilitation, as well as postoperative complications inevitably. Timing of IOL implantation in infantile congenital cataract patients is not simply a point-in-time but a personalized decision that comprehensively takes age at surgery, risks of postoperative complications, and economic condition of family in consideration, and combines with choosing suitable IOL type and power. For infants with well-developed eyeballs and good systemic conditions, IOL implantation at six months of age or older is safe and effective. Otherwise, secondary IOL implantation may be a safer choice.
- KEYWORDS: timing of surgery; intraocular lens implantation; congenital cataract; infants
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INTRODUCTION
Congenital cataract can be defined as opacity of the crystalline lens that presents within the first year of life[1]. As the main cause of childhood blindness worldwide[2], congenital cataract is reported with an incidence of 1.8 to 3.6/10 000 persons per year by Sheeladevi et al[3], as well as a pooled global prevalence of 4.24 per 10 000 people by Wu et al[4]. For infants with dense cataract in optic axis, timely operation that relieves form deprivation is the key to prevent further damage to visual development and promote visual rehabilitation.

Intraocular lens (IOL) implantation is an indispensable part of cataract surgery to fill the vacancy of the crystalline lens power both in infants and adults. Although IOL is extensively used in adult cataract surgery, the application of IOL in infants remains controversial. Herein, we discussed the challenges, the timing of IOL implantation in congenital cataract infants and shared our own experience.

EYEBALL GROWTH IN INFANTS AND ITS IMPACT OF CATARACT SURGERY
Growth of the Eye Ball in Normal Infants As the refractive status of the human eye stays hyperopia during early childhood, defocused retinal image promotes the progress of emmetropization, coordinating ocular growth including axial elongation, corneal flattening and reduced lens power, to bring this image into focus[5]. In normal eye, axial length undergoes continuous elongation after birth. Pennie et al[6] modeled an equation of the axial elongation in millimeters during the first year of life as 17.190+0.128×(age in weeks)–0.0013×(age in weeks)². The cornea has a mean power of 51 D at birth and reduces to 45 D after 2mo. With a rate of 0.2 D/mo, the cornea then flattens until the infant is 1 year old and later stays relatively constant[7]. The crystalline lens has a mean power of 34.4 D and reduces to 26.5 D at the age of 1y[7].

Impact of Cataract Surgery on the Eyeball Growth Congenital cataract during infancy potentially influences the axial elongation, especially in patients with microcornea and microphthalmia, which makes it more difficult to predict the postoperative axial elongation. The eye of unilateral congenital cataract is usually shorter than the fellow eye[8]. Trivedi and Wilson[9] summarized the law of preoperative axial elongation in congenital cataract eyes by analyzing the biometry data of 310 unilateral cataract eyes and found axial length increased 0.62 mm/mo during the first 6mo of life, 0.19 mm/mo from 6 to 18mo and 0.01 mm/mo during 18 months to 18 years of age. Congenital cataract surgery in infants is routinely performed using vitrectomy machine and 23-gauge vitrectomy is preferred[10-13]. We can take the advantages of a vitrector for lensectomy, including anterior vitreorhexis, posterior vitreorhexis and limited anterior vitrectomy, especially in those cases concurrent with posterior capsule abnormality, such as posterior capsule defect, posterior capsule plaque, or concurrent with persistent fetal vasculature[14].
Surgery has an impact on the postoperative axial elongation in congenital cataract eyes and its growth rate is different from the equation put forward by Pennie et al[19]. Age at primary surgery shows significant impact on postoperative axial elongation. Sminia et al[20] compared the axial elongation of the cataract eyes and the fellow eyes in 45 unilateral congenital cataract patients who underwent cataract surgery at a mean age of 4.8mo. After a mean follow-up duration of 4.3y, the mean axial elongation was significantly reduced in the operated eyes compared to the fellow eyes (2.65 mm vs 2.92 mm; \( P=0.049 \)). In this regard, earlier age at surgery seemed to retard the postoperative axial elongation. Similarly, McClatchey and Parks[16] found that children who underwent cataract surgery during the first 3mo of life had reduced myopic shift compared to those who had surgery after 3mo, which indirectly indicated that surgery during early infancy retarded axial elongation. Oppositely, Fan et al[17] observed the refraction and axial length changes in thirty-four eyes of twenty congenital cataract patients who was younger than 1 year of age and underwent cataract removal and primary IOL implantation. Although twenty-two eyes had surgery during the first 6mo of life (group 1) and had a shorter axial length at surgery compared with 12 eyes that received surgery between 7 and 12mo (group 2; \( P=0.007 \)), the final axial length was greater in group 1 than that in group 2 three years after surgery (\( P=0.019 \)). To sum up, early age at surgery seems to have greater influences on axial elongation and its regularity still needs to be explored.

After congenital cataract removal, high hyperopia will persistently exist if without timely refractive correction as it is difficult to replace the vacancy of the crystalline lens power simply by axial elongation. Thus, immediate refractive correction is of great importance and significance.

**Advantages of IOL for Visual Function Rehabilitation**

The earliest way to correct the refractive status in aphakic eyes after congenital cataract surgery was wearing spectacle. Later in 1959, contact lens (CL) was applied to optically correct aphakic children and became the main choice for decades after the introduction of silicone CLs that could be worn on an extended wear basis[18]. The application of IOL in children, though later than the application of spectacle and CL, rapidly increased since 1997[19]. Although IOL was extensively used in adult cataract surgery, surgeons raised rational concerns about the long-term safety of IOL in children in consideration of the rapid growth of infantile eyes. Therefore, studies that compared the applications of CL and IOL in infantile aphakic eyes after congenital cataract surgery sprung up.

Previously, Kumar and Lambert[20] extensively evaluated the evidence for and against the use of IOL in infants and young children by reviewing the representative papers published by The Infant Aphakia Treatment Study and The IOL under 2 Cohort Study. Lambert et al[21] compared the visual outcomes of CL with primary IOL correction of monocular aphakia in patients who underwent surgery during the first 7mo of life and found no significant difference in grating visual acuity at the age of 1y between two groups, either in logMAR visual acuity at the age of 4.5y[22]. However, more than twice treated eyes in the CL group showed visual acuity better than 20/32 compared to the IOL group[23]. Focusing on visual acuity merely is not sufficient for unilateral congenital cataract patients as binocular vision is of great importance as well. In another research of Lambert et al[24], the mean interocular difference in grating visual acuity was smaller in the IOL group than that in the CL group. Autrata et al[25] evaluated the quality of binocular vision in dependence on the type of aphakic correction with a minimal of 5y follow up and found IOL was the better aphakic correction for binocular visual results, which was similar to the finding of Greenwald and Glaser[25]. Later, Autrata et al[26] made further comparisons of visual acuity, ocular alignment and binocular vision outcomes between two monocular aphakic correction modalities and better visual acuity, better binocular vision outcomes and less occurrence of strabismus were shown in the IOL group. These studies indicate that IOL correction might be advantageous to the rebuilding of binocular vision, as well as visual acuity rehabilitation.

The rate of adverse events such as postoperative complications and reoperation is another indicator to judge the superiority of the correction ways apart from visual acuity. Lu et al[27] reviewed the visual results and the complications of primary IOL implantation in infants aged 6 to 12mo and considered primary IOL implantation as a safe and effective choice for infantile cataract surgery. As optimal results depended on the skill and experience of the surgeon as well, the main disadvantage of this study was lack of control group. In addition, most representative controlled trials considered that primary IOL implantation in young infants brought a higher rate of postoperative complications than CL[21-22,28]. However, it was worth to mention that in the study of Plager et al[29], although there was a significantly higher rate of adverse events in the IOL group, the number of patients with adverse events in the CL group increased during 2-5y postoperatively compared to the first postoperative year while it decreased in the IOL group. Therefore, it is far too early to conclude which correction way is better and studies that conduct longer follow-up duration are still needed.

Kruger et al[30] compared the cost of treatment for infants randomized to primary IOL implantation versus CL after unilateral cataract surgery and found that the total 5 years’ cost of supplies was $3204 in the IOL group versus $7728 in the CL group. Although there was no similar study conducted in developing countries, considering the truth that the cost of a
piece of IOL was about ¥2000 and that of a piece of CL was ¥4000 in China, the difference in the cost of two correction ways is even greater in developing countries. Due to lower price, wearing spectacles is another widely accepted way to correct the refractive status of aphakic eyes in developing countries\[31\]. However, the power of the spectacles to correct the aphakic status can be higher than 20 diopters and thus brings worse imaging quality and unacceptable aberration, which strongly influences binocular vision, especially in monocular aphakic patients\[32-33\]. Therefore, wearing spectacles is not an ideal choice to correct the aphakic status after congenital cataract surgery, especially for unilateral cataract infants. Although there is no convincing evidence that IOL is better than CL, IOL implantation provides better visual rehabilitation and binocular vision rebuilding, except for some adverse events. Additionally, IOL is a cost-efficient and effective choice, while CL is hard to be widely accepted by most congenital cataract families in developing countries due to its low popularization, higher financial burden, and complex care procedures.

**CHALLENGES OF IOL IMPLANTATION**

**Decision of Choosing IOL Powers and Types** Difficulties of IOL implantation in congenital cataract eyes should be mentioned. The preoperative examinations in infants are often performed under sedation or general anesthesia. Passive examinations have negative influences on the accuracy of measurement, which afterwards brings difficulties to the IOL selection. One of the challenges involved in making decision to implant IOL in infants is IOL selection itself, especially the power of IOL. Myopic shift is often observed long-term postoperatively in cataract eyes due to significant growth of the eyeball while the power of IOL is unaltered, thus the postoperative refraction is often targeted to be hyperopia. Various guidelines have been proposed to facilitate the methods for the initial undercorrection in infants in the past decades\[34-35\]. The guidelines proposed by Enyedi et al\[36\] is among the most popular ones, which recommended a postoperative refractive goal of +6 D for a 1-year-old patient, +5 D for a 2-year-old patient, +4 D for a 3-year-old patient, +3 D for a 4-year-old patient, +2 D for a 5-year-old patient, +1 D for a 6-year-old patient, plano for a 7-year-old patient and -0.75 D to plano for an 8-year-old and older patient. In fact, it is quite difficult to predict exactly how the axial length develops postoperatively. Trivedi et al\[37\] reviewed the postoperative axial length of sixty-four patients who underwent bilateral cataract surgery with primary IOL implantation at the median age of 5.1y and developed a model for predicting postoperative axial length in these children as the following equation: Postoperative AL=1.93+0.91×(baseline AL)−0.07×(baseline age)+0.14×(age at follow-up)−0.005×(baseline age)×(age at follow-up). We tested this model by using the data of sixty bilateral cataract patients who underwent surgery in our hospital and the results showed satisfactory precision. We believe this model could potentially be used to make more accurate and customized IOL calculations. However, axial elongation can be much slower than predicted in some cases, thus the excessive initial undercorrection for these cases results in high hyperopia. Oppositely, in cases with unexpected significant axial elongation, the initial undercorrection can be inadequate and results in high myopia. Unsatisfactory refraction error is the indication of IOL exchange\[38\]. For children with high myopia postoperatively, timely IOL exchange should be performed even when the axial length is still growing. For children who underwent unilateral cataract surgery, IOL exchange also needs to be performed when there is severe anisometropia. As for timing of surgery, decision should be made according to the degrees of high myopia and anisometropia in specific case. We prefer to leave a certain degree of hyperopia in infants mainly according to their ages and axial lengths, that is, a postoperative refractive goal of +6 D for a 6mo to 1-year-old patient, +3.5 D to +4 D for a 2-year-old patient, +2.5 D to +3 D for a 3-year-old patient, +2 D for a 4-5-year-old patient, +1 D for a 6-year-old patient, plano for a 7-year-old patient and -0.75 D to plano for an 8-year-old and older patient. For unilateral cataract infants we also refer to the refraction status of the contralateral healthy eye to determine the initial undercorrection. After years of follow-up, most of these young patients reached to emmetropia at the age of 7y, although high hyperopia and high myopia somewhat occurred. There is still a long way to go to leave optimal initial undercorrection. It has been demonstrated that pediatric cataract patients have worse precision and prediction error of IOL power calculation compared to adult cataract patients\[39-40\]. Our team enrolled a total of 68 eyes (68 patients) that underwent congenital cataract surgery and IOL implantation in the capsular bag and compared the calculation accuracy of eight formulas (SRKII, SRK/T, Holladay 1, Holladay 2, Hoffer Q, Olsen, Barrett and Haigis)\[41\]. We found in patients younger than 2 years old or with an AL≤21 mm, SRK/T formulas were relatively accurate, while Barrett and Haigis formulas were better in patients older than 2 or with an AL>21 mm. Later, we made further research to compare the accuracy of five IOL power calculation formulas (SRK/T, Holladay 1, Holladay 2, Hoffer Q and Haigis) for pediatric eyes in children of different ages, finding that SRK/T and Holladay 1 formulas were relatively accurate in patients younger than 2 years old, while the Haigis formula performed better in patients older than 2\[42\]. In the study of O’Gallagher et al\[43\], SRK/T was also the
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The most accurate formula in predicting postoperative refraction for patients younger than 8 years old. Similarly, SRK/T and Holladay 1 formulas showed better precision in the study of Infant Aphakic Treatment Study, while Hoffer Q tended to overcorrect eyes and SRKII tended to undercorrect eyes[44-45]. The choice of IOL also depends on the material and design. Acrylic lenses have been proven to have lower rates of posterior capsule opacification (PCO) when compared to silicone or polymethylmethacrylate (PMMA) IOL in children[46-47], which indicates the better material biocompatibility of acrylic lenses. Both hydrophilic and hydrophobic acrylic IOLs have been reported to have good outcomes in children[48-49] although no controlled trial has been conducted. In terms of design, single-piece acrylic lenses seem to be superior to three-piece acrylic lenses in the rates of perioperative and postoperative complications[50]. Considering that the capsular bag diameter of infants is limited, IOLs with two open haptics are the first choice because of their good deformability and adaptive capacity in capsular bag. Furthermore, about the application of multifocal IOLs and toric IOLs, although it has been reported occasionally, the safety and effectiveness of these IOLs in children still remains unclear[51-52].

Positions of IOL Implantation Capsular bag and sulcus are the most common positions to place IOL. For children who undergo primary IOL implantation, capsular bag is the optimal position. As for those who are left aphakic and undergo secondary IOL implantation, in-the-bag IOL implantation is still the most ideal if the residual capsule is reopened successfully. As an alternative of in-the-bag IOL implantation, sulcus IOL implantation in infants is also widely performed. However, postoperative complications of sulcus IOL implantation, such as IOL decentration and secondary glaucoma, are the threats that deteriorate visual acuity and require additional operation. In extreme cases with unsatisfactory capsular outcomes after primary congenital cataract removal, some surgeons choose iris-claw IOL implantation. Although satisfactory visual outcomes are reported postoperatively, in view of the concerns about the rate of corneal endothelial cell loss especially in pre-pupillary IOL implantation[53], the use of iris-claw IOL in children will continue to be a moot point and is unlikely to be widely adopted[54]. This prompts us that in primary congenital cataract removal, it is essential to refer to cornea diameter for making an appropriate vitreorehesis opening diameter. We made an anterior vitreorhesis opening diameter of about 4.0-5.0 mm and a posterior vitreorhesis opening diameter of about 3.0-4.0 mm, and most of our infantile patients accepted secondary in-the-bag IOL implantation.

Postoperative Complications Related to IOL Implantation Visual axis opacification (VAO) is the most common postoperative complication widely reported in various studies. The rate of VAO in these studies varies from each other, which in the study of Lambert et al[22] was about 40%, while in the study of Lundvall and Zetterström[55] the rate was about 67%. Plager et al[56] conducted a prospective randomized clinical trial in infants younger than 7 months of age and found that the occurrence of postoperative complications including VAO was more commonly seen in the IOL group than the CL group. They also gave the explanation that this phenomenon should be attributed to the fact that the fused anterior and posterior lens capsules in aphakic patients prevented the lens material spilling from the Soemmerring ring into the pupillary axis, while in pseudophakic patients, the presence of the IOL prevented the fusion of the anterior and posterior axis capsule, thereby facilitating the repopulating lens material spilling into the visual axis[57]. The risk factors of VAO after IOL implantation includes early age at surgery and IOL model. Solebo et al[58] found increasing age at surgery and the use of a 3-piece IOL model were independently protective against the development of proliferative VAO. Because of the dense follow-up after surgery, the occurrence of VAO can be discovered in time and be removed by appropriate treatments including reoperation or YAG laser capsulotomy.

Glaucoma is another postoperative complication that greatly threatens visual function[57], although its rate is much lower than VAO. Corticosteroids are reported to have association with ocular hypertension in human eyes[58]. Topical corticosteroids such as dexamethasone are routinely used after surgery, for over 4-6wk in usual[59]. Published studies reported that up to one fifth of children developed raised intraocular pressure, with onset at weeks or months after starting using topical steroids[60-61]. Before we establish a diagnosis of glaucoma after surgery, we need to exclude steroids-induced ocular hypertension by distinguishing the timing of ocular hypertension and stopping using the dexamethasone eye drop instead of simply according to intraocular pressure. Choosing appropriate topical steroids is also of importance. Taking the advantage of its strong anti-inflammation effect, we routinely use 0.1% tobramycin-dexamethasone eye drops four times per day and taper it for 4-6wk postoperatively, monitoring intraocular pressure at 1, 2, and 4wk. For individual patients who develop ocular hypertension, we will adopt 0.5% loteprednol etabonate ophthalmic suspension 2-3 times per day and taper it for 3-5wk to replace 0.1% tobramycin-dexamethasone eye drops. The relationship was established between certain preoperative characteristics that predisposed to a higher risk of glaucoma, such as persistent fetal vasculature, microcornea and early age at surgery[62-63]. Besides these preoperative characteristics, IOL implantation, whose role in the progress of glaucoma after congenital cataract surgery remains controversial, might be another factor...
that influences the occurrence of glaucoma. In the research by Asrani et al\textsuperscript{[64]}, they proved the hypothesis that primary IOL implantation might decrease the incidence of open angle glaucoma in children. In their results, only 1 case of open angle glaucoma was found among 377 eyes with primary pseudophakia while 14 eyes developed glaucoma among 124 aphakic eyes after four years of follow-up. Similarly, the long-term incidence of secondary glaucoma was lower in eyes with primary IOL implantation (9.5%) than those without primary IOL implantation (15.1%) according to the Meta-analysis of Zhang et al\textsuperscript{[65]}. However, there was no statistically significant difference in the risk of glaucoma between patients in the CL group and the IOL group in the studies of Infant Aphakia Treatment Study\textsuperscript{[62-63]}. Thus, convincing randomized controlled trials are still urgently needed to settle the disputes. Besides VAO and glaucoma, surgeons also need to pay close attentions to various other postoperative complications, avoiding severe influences on patients if without timely treatment. Relatively common postoperative complications include IOL decentration, iris pigment dispersion, ocular hypertension and pupillary membrane\textsuperscript{[66-67]}. Although there are various complicated postoperative complications, we can still try our utmost for the benefit of patient via utilizing improved medical conditions, frequent follow-ups, as well as early discovery, early diagnosis and early treatment of the complications.

**Timing of IOL Implantation** Choose the optimal timing of IOL implantation for congenital cataract patients is a challenging work for surgeons, which asks for comprehensive considerations of various factors including age at surgery and laterality of cataract eyes. Published studies proposed different opinions on the outcomes of IOL implantation at different ages. The choices of age at primary IOL implantation in infants were strict and conservative in some studies, which postponed the timing to 2 years of age or older. Sukhija et al\textsuperscript{[68]} took an active attitude towards IOL implantation in patients younger than 2 years old as there were excellent long-term outcomes in their retrospective research with a follow-up of at least 8 y. Solebo et al\textsuperscript{[69]} conducted a prospective observational cohort study with a total of 256 eligible children. According to their results, primary IOL implantation was not associated with better visual outcome but was associated with a five times higher risk of reoperation for VAO requiring general anesthesia in children with bilateral cataract and a 20 times higher risk in children with unilateral cataract, which indicated more cautious attitude should be held towards primary IOL implantation for children younger than 2 y.

Negalur et al\textsuperscript{[70]} performed primary IOL implantation in infants under 6mo who met the selection criteria as follows: 1) with minimum corneal horizontal white-to-white diameter of 10 mm; 2) without associated anterior-segment dysgenesis or increased intraocular pressure. According to their postoperative visual acuity, complications and myopia shift, primary IOL implantation seemed to be reasonably safe in appropriately selected infants under 6mo. However, Lambert et al\textsuperscript{[71]} raised objections to perform primary IOL implantation in infants under 6mo as in his research IOL implantation was not recommended for children of 6mo or younger because this treatment would bring about a higher incidence of VAO with this treatment compared with aphakia. Thus, for those who could accept CL to correct aphakic after congenital cataract surgery, seeking opportunities for IOL implantation during early childhood is unnecessary.

Although age at primary IOL implantation is still full of controversies, what needs to be understood is that the choice of timing of IOL implantation depends on not only age, but also laterality of cataract eyes. For infants with unilateral congenital cataract, the age at IOL implantation could be conducted at suitably earlier time. Kumar and Lambert\textsuperscript{[72]} shared their experience that they preferred to leave 3-month-old or younger infants with a unilateral cataract under aphakic conditions and to optically correct their visual acuity with CLs while they did not implant IOL in infants with bilateral cataracts until they were at least 7 months of age. As for bilateral congenital cataract patients, the timing of IOL implantation should be put off a little later to lower the rate of postoperative complications. To sum up, age at surgery and laterality of cataract eyes are both key factors to determine the optimal timing of IOL implantation during early childhood. As unilateral congenital cataract strongly worsens the establishment of binocular vision, it is worthwhile to take the corresponding risks for earlier primary IOL implantation. As for bilateral congenital cataract infants, the timing of IOL implantation should be put off to an older age to lower the rate of postoperative complications. In our opinion, for infants with well-developed eyeballs and good systemic conditions, IOL implantation at 6 months of age or older is safe and effective, especially for those with unilateral congenital cataract. Otherwise, secondary IOL implantation is a better choice for young infants and can be performed at one and a half years old for unilateral patients and at two years old for bilateral patients. For secondary IOL implantation, we prefer residual capsular bag reopening and capsular bag positioning.

**SUMMARY** With the developments of surgical instruments and IOLs, for medical teams with good surgical skills and care ability, we recommend IOL implantation at six months of age or older for congenital cataract infants with well-developed eyeballs, especially for those with unilateral cataract infants. Otherwise,
we perform secondary IOL implantation at one and a half years old for unilateral patients and at two years old for bilateral patients. For congenital cataract patients with microcornea and microphthalmia, IOL implantation also needs to be postponed. With regard to IOL type selection, we prefer to choose acrylic IOL with two open haptics. As for IOL power, we prefer to leave a certain degree of hyperopia, while for unilateral cataract infants we should also refer to the refraction of the contralateral healthy eye.

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