Review

Significance of Axial Length Monitoring in Children with Congenital Cataract and Update of Measurement Methods

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Abstract

Congenital cataract is the main cause of blindness in children, with significantly varying treatment effects. The development of axial length is an important factor that affects the prognosis of these children. However, when compared with the eyes of normal children, the mechanism of growth of the axial length is so complicated that the reported findings differ significantly in terms of the measuring apparatus, assessment methods, and statistical outcome, making the rule of axial length development still unclear. In this paper, we first review the process of axial length development in normal healthy children and compare different hypotheses about certain factors that could affect the development of axial length. The results of some current research about the characteristics of axial length development in congenital cataract children are then reviewed. Lastly, the advantages and disadvantages of current axial length measurements methods are compared and analyzed. The purpose of this review is to improve our understanding of the complexity and importance of axial length development and to suggest better use of axial length monitoring measurements in congenital cataract children for pediatric ophthalmologists, with the hope of offering assistance that will enhance long-term therapeutic effects for these children. (***Eye Science 2013*; *28*:*95-102***)

Keywords: congenital cataract; axial length; measurement method

Congenital cataract is a serious disease that causes blindness and asthenopia in children. Its complex diversity and varying surgical response have made this condition a considerable challenge to ophthalmologists. The developmental pattern of the ocular axis and determination of effective and safe approaches for dioptric correction require urgent resolution.

The structural and functional growth of the ocular system in children with congenital cataract has unique characteristics. Besides "congenital insufficiency", "acquired development" is also subject to influence from multiple factors[1,2]. Postoperative long-term refractive error is mainly ascribed to a myopic shift induced by axial growth and to an early refractive error primarily resulting from intraocular lens (IOL) power calculation[3]. Along with widespread application of IOL implantation for cataracts, the selection of IOL (IOL power and implantation time) is of significance to postoperative visual recovery in affected children.

Recently, substantial progress has been made in the technique of cataract extraction, whereas similar progress is lacking in the accurate calculation of IOL power. Accurate selection of IOL for children mainly depends upon precise measurement of axial length and comprehensive understanding of eye developmental patterns. Consequently, proper methods for axial length measurement should be selected to explore the developmental pattern of the eyeball and to analyze the changes in axial length in children with congenital cataract. This will not only provide instructions for dates of surgery and surgical approaches, but also will provide personalized formulas for IOL power calculations and supply of IOLs that specifically target children.

Development of the eyeball and eye axis

At birth, the human visual system (intraocular substance and nervous system) has not attained maturity and only reaches 82% maturity at 12 months

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later; therefore, it is likely to be affected by a variety of factors and undergo developmental changes[1]. Axial length also increases after birth, being approximately 16 to 17 mm at birth and rapidly increasing up to 20 to 21 mm at 1 year of age. It slowly decreases at the age of 2 to 3 years and reaches approximately 23 mm by age 6, almost equivalent to that of adults. It then more or less stabilizes from age 10 to 15[4–6]. In normal children, axial growth probably correlates with heredity, environment, development, and nutrition, *etc*.[7–9]. In children with congenital cataract, axial development is associated with formation of cataract, implementation of surgery, and IOL implantation, *etc*. At present, emmetropization is widely accepted as the mechanism underlying changes in axial length and refractive status after birth[10], while the underlying mechanisms of pathological changes include theories involving regulation, defocus, and form deprivation. Previous studies found that the early incidence of ocular hypertension in normal infants is likely to cause an excessive increase in axial length. However, the subjects with ocular hypertension are typically excluded from studies on the growth of axial length in patients with congenital cataract[11]. In the present study, we therefore discuss mainly defocusing and form deprivation, which are potentially associated with axial length development in patients with congenital cataract.

1. Emmetropization: Bilateral refractive indexes in newborns were approximately +2.00D ±2.75D, equivalent to hyperopia. The bilateral refractive indexes gradually altered over age and reached 0.00D ±1.00D until adulthood, defined as “emmetropization”[10]. At 3 to 12 months after birth, emmetropization rapidly progressed and the intraocular substance also presented with a variety of alterations, such as declines in corneal curvature, decreases in lens thickness, and enlargement of the vitreous cavity. The regulation of axial growth is the most pivotal factor affecting emmetropization. A higher degree of hyperopia induced more rapid axial growth, which stimulated the process of bilateral emmetropization[12].

2. Defocus: Animal experiments[13,14] showed that the fitting of animal eyes with positive or negative lenses induced defocus. Animal axial length could change to relocate the defocused image on the retina and was probably associated with the migration of retina to the imaging plane caused by the growth of the sclera and changes in the choroidal thickness[15]. The growth of the eyeball is proposed to be affected by peripheral retinal defocus, while hyperopic defocus is thought to lead to continuous increases in axial length. Previous studies suggested that the changes in human axial length after a 60-min defocus treatment were consistent with the results obtained from animal experiments. In addition, the underlying mechanisms of axial changes might be similar between animal and human studies. However, long-term defocus experiments are still needed[16].

3. Form deprivation: This refers to the insufficient or stagnant development of visual acuity during the critical period in infants with congenital cataract, corneal leucoma, and ptosis. These conditions prevent light from the entering pupil so that adequate visual stimulation is not provided to the macular area. In form deprivation infants, the eyeball growth tends to be accelerated and an excessive increase in axial length may be induced, forming a vicious cycle of visual damage, increased axial length, and aggravated myopia[1]. Zongyin Gao et al[17]. reviewed a total of 36 children with unilateral form deprivation-induced ocular illnesses and concluded that axial length in the affected eye and the difference in axial length between the two eyes were positively correlated with the course of the diseases. This indicated that unilateral form deprivation tends to result in axial length extension and that a longer course of disease induces a more significant increase in axial length in both acquired and congenital form deprivation groups. However, a variety of studies obtained different outcomes for the axial length of the affected eye in patients with congenital cataract, which was shorter compared with the axial length in normal controls in some studies[18,19] but showed no significant difference between two groups in another[20]. The relationship with the severity and onset time of form deprivation was questioned, as was the effect that form deprivation has on the development of axial length. The relationship that form deprivation has with other related factors is also unresolved. All these questions remain to be answered by large-sam-

ple investigations.

Changes in the eye axis in children with congenital cataract

The factors inducing changes in the eye axis of children with congenital cataract include preoperative onset of form deprivation, date of surgery, postoperative degree of amblyopia, whether stereopsis and image fusion function normally, and IOL implantation. However, evaluation of the effect of each individual influential factor is difficult. A host of investigations have analyzed the axial growth and development of eyes with congenital cataract, and in aphakic and phakic eyes. However, these studies vary greatly in terms of sample size, inclusion and exclusion criteria, research methods, and postoperative follow-up. No consensus has yet been reached, but the findings establish a foundation and provide guidance for exploring the underlying pattern of axial growth and development in children with congenital cataract.

1. Eyes with congenital cataract: Capozzi et al[20]. statistically analyzed the axial length in 180 infants with congenital cataract (younger than 42 months old) prior to surgery and revealed that the axial length of the affected eye was significantly longer in the monocular group than in the binocular group. No statistical significance was observed between the affected and fellow eyes in the monocular group. The Infant Aphakia Treatment Study (IATS) conducted by American scholars analyzed a total of 114 infants aged 1 to 7 months with monocular congenital cataract (diameter of central opacity >3 mm). The axial length was shorter in the affected eye (18.0 mm) than in the normal fellow eye (18.6 mm). Ping Xie et al[21]. measured the axial length of the affected eye in children[20] (aged 3 to 16 years) with monocular congenital cataract and found that the axial length was 0.07 to 2.64 mm longer in the affected eye than in the fellow eye and this difference in axial length increased significantly with age with a positive correlation [aged 3 to 6 years group: (0.70±0.07) mm; aged 7 years above group: (1.39±0.16) mm)]. Lixin Xie et al[19]. demonstrated that the preoperative axial length in children (aged 1 to 3) with monocular congenital cataract was significantly longer in the affected eye than in the normal fellow eye, and the axial length in 64.4% cases of congenital cataract exceeded the mean value found in counterparts of same age. However, they also noted that 7 of the 18 children aged above 10 years with monocular congenital cataract had shorter axial length in the affected eyes than in the normal fellow eyes. Consequently, they proposed that form deprivation is simply one of the multiple influential factors related to the development of the eye axis in children with congenital cataract. Other factors including heredity, development, and unknowns probably also play a role and deserve more attention. Previous research revealed that the development of axial length presented with different patterns that changed in response to multiple factors. The association between accelerated or reduced axial growth and form deprivation remains to be elucidated.

2. Aphakic eye: In previous animal experiments, the authors removed the lens from one eye on the day of birth and found that the axial length was shorter in the aphakic eye than in the fellow eye at 1 to 2 years postoperatively[22,23]. However, human research yielded contrasting results. Wei Xiao et al[24]. analyzed 49 consecutive patients (89 eyes) who underwent cataract surgery at 3 months after birth and IOL implantation at age 2.5 years and observed that the axial length was longer in the aphakic eyes of children with early congenital cataract (aged <2.5 years old) than in normal controls. McClatchey et al[25]. showed a higher increase in refractive index (−5.7 diopter) in the aphakic eyes of patients with congenital cataract than in those receiving IOL implantation after surgery (4.6 diopter, $P=0.03$). The association between the higher increase in axial length of aphakic eyes vs. normal eyes and postoperative high degree of hyperopia and long-term status of hyperopic defocus is unclear.

3. Eyes implanted with IOLs: An animal experiment showed that performing cataract surgery in combination with IOL implantation immediately after birth inhibited the development of eyeballs[22], whereas human studies revealed relatively complicated outcomes. Vasavada et al[26]. conducted a prospective observational case study of congenital cataract children and noted that the infants who underwent

cataract extraction combined with IOL implantation before age 1 showed accelerated axial growth within 2 years after surgery. The children with monocular congenital cataract had a higher rate of increase in their surgical eyes than in their fellow eyes while those with binocular congenital cataract had an increased rate equivalent to normal controls.

The IATS[11] included two groups of infants with congenital cataract undergoing cataract extraction before age 1: in group A, the infants received cataract extraction combined with IOL implantation and in group B, the subjects wore a corneal contact lens after cataract extraction alone. Postoperative refractive index was consistent between two groups. The axial length was 0.6 mm shorter in group B than in group A (P=0.009). This discrepancy may have arisen because the children in group A received more surgeries than did their counterparts in group B, such as removal of opacity near the optical axis, glaucoma surgery, and iridectomy, which could have increased the levels of intraocular chemical substances (prostaglandin, *etc.*) and altered the growth of the eyeball. A significant difference was also noted between the actual and estimated refractive indexes in children with short axes following IOL implantation, probably due to rapid axial growth.

Multivariate analysis also revealed that the eye axis is the unique independent factor associated with this difference[27]. However, other scholars proposed that this difference may result from the changes in the position of the implanted IOL in infants[28]. Yusen Huang et al[29]. analyzed 49 children aged > 2 years who underwent bilateral cataract extraction combined with IOL implantation and found that IOL implantation had no apparent effect on accelerating the development of the eye axis of the affected children; the axial length of the majority of the children at 5-year postoperatively was almost equivalent to that of healthy counterparts of the same age. Similarly, Yong Pan et al[30]. conducted a 10-year follow-up of 64 children (64 eyes) aged from 5 to 12 years who underwent monocular cataract extraction combined with posterior chamber IOL implantation and found that selecting those IOLs with the same refractive index with healthy children yielded no significant difference between surgical and fellow eyes at 10 years postoperatively. Hussin et al[31]. analyzed the eye axis in children (aged < 5 years) with congenital cataract after IOL implantation and found no statistical significance in axial length between the surgical and fellow eyes from the monocular group. In addition, the average eye axis was slightly longer in the monocular group than in the binocular group with no statistical significance; no significant difference was noted in the eye axis between congenital cataract children and normal counterparts.

Further in-depth study in multiple investigations of the growth of eyeball after congenital cataract surgery has included another vital variable: differences in axial length between both eyes. The differences in axial length between both eyes seldom exceeded 0.5 mm in a normal population[32], but differences greater than this were commonly seen in patients with congenital cataract[33]. Previous research indicated that the association between the differences in axial length between both eyes and visual acuity after congenital cataract surgery is of extremely vital significance. The best corrected visual acuity was constantly poor when the difference in axial length exceeded 0.5 mm[34]. Smaller differences in axial length between the two eyes, younger age at operation, and better amblyopia treatment were essential factors for good clinical prognosis[32]. Trivedi et al[35]. retrospectively analyzed a total of 49 children who underwent congenital cataract extraction combined with IOL implantation between 1994 and 2004 and found that the differences in axial length between the surgical and fellow eyes gradually decreased. The axial length of the fellow eye tended to increase faster if it was shorter than the surgical eye and vice versa. The growth pattern between both eyes tended to achieve symmetry. Thus, the idea of symmetric development of the eye axis between both eyes was proposed. Consequently, whether the refractive index and axial length of the fellow eye should be considered when selecting the power of IOL requires further study.

The changes and regulation of axial length that occur after congenital cataract surgery are complex. Prediction of the pattern of axial growth and changes in refractive index remains a challenge in children undergoing cataract surgery combined with IOL implantation. Accurate measurement of axial length prior to surgery is crucial for obtaining the estimated postoperative power and selecting a suitable IOL for children with congenital cataract. Previous studies indicated that the error of IOL power induced by axial length measurement was 4–14D/mm for children and 3–4D/mm for adults[36]. Therefore, obtaining an accurate axial length, as one of the vital factors, is critical for the success of congenital cataract surgery in combination with IOL implantation and this aspect is now attracting increasing attention from clinicians.

Measurement of the eye axis

Accurate measurement of axial length is of vital importance for IOL power calculation and for yielding sound visual acuity post-IOL implantation. Common methods utilized for measuring axial length employ three physics principles: ultrasound, optics, and magnetic resonance imaging as follows:

1. A- and B-mode ultrasound examination: Ultrasound examination is one of the most common methods for measuring axial length, and is even regarded as the gold standard for axial length measurement. In clinical practice, the A-mode ultrasonic instrument is mainly utilized to measure the distance between the corneal anterior surface and the vitreoretinal interface and uses a 10 MHz transducer with a resolution approximately from 200 to 300 μm and a precision of approximately 150 μm. The A-mode ultrasonic instrument has two types of transducers: contact and immersion. Previous research found that anterior chamber depth and axial length measured by A-mode ultrasound were relatively smaller with a contact transducer than with an immersion transducer, and resulted in an approximately 1D error when calculating IOL power[3]. However, Ben-Zion et al[37]. found no statistical significance in the refractive error measured by the two types of instruments. Compared with the A-mode ultrasound with a contact transducer, the immersion ultrasonic instrument is relatively more complex to operate and has a limited application range.

B-mode ultrasound can be applied into measuring the axial length of eyes with high myopia or vitreoretinopathy and yields more accurate results by detecting the presence and position of posterior staphyloma and the vitreo-retinal condition[38]. Some scholars have recommended the combined use of A- and B-mode ultrasound to obtain accurate measurement results for axial length[39]. However, other scholars found a high degree of variation when employing the combined method of A- and B-mode ultrasound, probably resulting from different positions of the eye axis displayed on B-ultrasound images, relatively rough frozen images, and an inability to determine whether the image is along the direction of optical axis, *etc.*[40].

During ultrasound examination, relatively great variations were found between measurements made by one single operator and multiple operators. The incidence of corneal injury and infection could also be elevated if the probe was not properly disinfected. In recent years, non-contact and easy-to-operate optical coherence interferometry has gradually replaced ultrasound in clinical practice.

2. Zeiss IOLMaster: The IOLMaster separates a laser into two independent beams of axial light that reach different layers of the ocular structure along the direction of the optical axis. The beams are then reflected, captured by an imaging detector, and the measurement results are automatically yielded. The IOLMaster was reported to measure the distance between the anterior cornea (the anterior surface of tear film) and pigment epithelia with a precision of 0.01 mm. The measurement outcomes of posterior staphyloma and macular edema were automatically obtained. In terms of measurement reproducibility, some Chinese researchers suggested that the reproducibility of the IOLMaster was relatively high and the measurement accuracy resembled average postoperative error<0.1D[41]. As a form of non-contact optical coherence interferometry, IOLMaster is a simple method for measuring axial length and prevents mutual infection among patients.

As shown in Table 1, most researchers found significant differences in the axial length measured by the IOLMaster v.s. A-mode ultrasound. Some studies found a higher accuracy for the IOLMaster than for A-mode ultrasound and other researchers revealed that although the axial length is longer when measured with the IOLMaster than with A-mode ultrasound, the results between the two methods were highly correlated[41]. Some scholars noted superior reproducibility in measuring the axial length in children for the IOLMaster compared to A-mode ultrasound[42,43]. In addition, the IOLMaster is advantageous for measuring the axial length in complicated cases. Deviation existed in the axial lengths measured by A-mode ultrasound and IOLMaster in patients with macular edema, with the IOLMaster proving more suitable for measuring the axial length in these types of clinical cases[44,45].

Table 1 Comparison of the measurement of axial length by the IOLMaster and A-mode ultrasound

Source	Sample number（n）	Mean age（year）	IOLMaster（mm）	A-scan(mm)	P
J Cataract Refract Surg 2010[47]	18	7.4	22.14±1.37	22.27±1.26	0.002
Optom Vis Sci 2004[42]	179	10.6	24.14±1.06	24.00±1.05	<0.001
Chinese Journal of Practical Ophthalmology 2007[41]	46	53.6	24.06±2.36	23.87±2.11	<0.001
Clin Experiment Ophthalmol 2003[48]	46	72	23.36±1.24	23.21±1.30	<0.01
Clin Experiment Ophthalmol 2009[49]	55	76	23.37±0.87	23.25±0.90	<0.0001

Note：$P<0.05$ was considered as statistically significant

The IOLMaster also has promising application prospects in measuring the indexes of IOL- and silicone oil-implanted eyes. The difference of speed of ultrasound in silicone oil and normal eyes can a discrepancy between the actual and measured data. Albeit a correction formula for the measurement of silicone oil-filled eyes by A-mode ultrasound was proposed based on the attenuation ratio of ultrasonic speed, the axial length of the affected eye in the normal IOP group measured by IOLMaster had less measurement errors compared with that measured by A-mode ultrasound with the correction formula before removal of silicone oil for patients with good fundus status and stable IOP[46], which mainly results from silicone oil gap in vitreous cavity[53].

The IOLMaster also has certain limitations in its accuracy of measurement of the axial length of patients with a number of conditions including leukoma, mature or hypermature cataract, posterior capsular opacification, severe vitreous hemorrhage, and nystagmus. A higher detection rate for axial length in cataract patients is now reported for the modified IOLMaster compared to the original IOLMaster; however, posterior capsular opacification remains the primary factor affecting detection rate and the influence can not be thoroughly removed[50].

To sum up, IOLMaster and A-mode ultrasound can both be applied in different situations but they cannot completely replace each other.

Other devices, including the BioGraph/LENSTAR LS900 biometer and the Orbscan Ⅱ can also be used to measure axial length. However, the accuracy of measurement remains to be validated due to the short clinical application time of this equipment.

3.Magnetic resonance imaging（MRI）：MRI is a medical imaging technique used in radiology to visualize details of the internal structures of the body. MRI makes use of the property of nuclear magnetic resonance to image the nuclei of atoms inside the body, and has been widely applied in modern medicine. At present, MRI has a widespread application in ophthalmologic examinations as it provides more precise measurement of spatial biological parameters such as posterior segment, inner diameter of eyeball cavity and 3 dimensional parameters of eyeball[51]. In addition, MRI can be applied in the measurement of axial length of silicone oil-filled eyes because it is not affected by refractive medium, the degree of silicone oil filling, the position of silicone oil and silicone oil emulsion[52]. Xiaochun Mao et al[53]. conducted MRI to 32 patients undergoing vitrectomy combined with silicone oil filling and observed the vitreous cavity was not fully filled with silicone oil with a vitreous gap in all cases with a higher detection rate compared with A-mode ultrasound. However, the relatively expensive cost of MRI limits its application scope[52].

Each measurement device has its own features and is applied in different modes. Thus, no measurement instrument can be completely replaced by alternative devices. During the treatment of congenital cataract in children, it is difficult to perform measurements in children under anesthesia and in those with nystagmus because they lose fixation. Ophthalmologists should select suitable measurement methods for the highest measurement accuracy. Meanwhile, proper surgery time and rational power of the implanted IOLs should be determined according to the pattern of axial growth in children with congenital cataract, thereby providing the optimal prognosis for visual acuity.

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