LITERATURE REVIEW

Prediction Errors and Accuracy of Intraocular Lens (IOL) Calculation Formulas in Pediatric Eyes

Fitri Muslim, Julie D. Barliana
Department of Ophthalmology, Faculty of Medicine, Universitas Indonesia
Cipto Mangunkusmo Hospital, Jakarta, Indonesia
E-mail: juliedbarliana@gmail.com

ABSTRACT

Background: Acquiring an accurate intraocular (IOL) power in children undergoing cataract surgery is challenging. Different IOL calculation formulas in children have been previously studied to achieve a precise prediction of the IOL power. Larger errors in IOL formula predictions have shown in several studies on children as future growth of the eye affects the keratometry readings and axial length. Prediction error (PE) and absolute prediction error (APE) can be effective indicators in assessing the accuracy of IOL power calculation formulas. Therefore, this review aims to investigate the accuracy of IOL power calculation formulas in pediatric eyes by measuring PE and/or APE value.
Methods: A comprehensive search was conducted from various electronic databases (Pubmed, Clinical Key, and Ophthalmology Advance) using relevant search terms. Included studies were screened using predefined inclusion and exclusion criteria to identify comparative studies comparing the accuracy of IOL calculation formulas in pediatric patients.
Result: Ten studies including 964 eyes were identified to compare different IOL formulas: Hoffer Q, SRK/T, SRK II, Holladay 1, and Holladay 2. Smaller prediction error is related to better postoperative refraction. Among included studies, Holladay 2 had the smallest mean prediction errors (PE), while SRK/T formula was the best formula of all included studies in pediatric patients as it had the smallest mean absolute prediction errors (APE). Hoffer Q also had the smallest mean APEs in shorter eyes (axial length <22 mm).
Conclusion: This study demonstrates that none of the established formulas found to be more superior than any other formulas in predicting IOL power in children. Biometry examination in patients with less than one year of age tends to show a lower accuracy.
Keywords: intraocular lens power, Prediction error, Absolute prediction error

Intraocular lens (IOL) implantation in children were firstly introduced in 1977 by Hiles.[1] A survey of American Association for Pediatric Ophthalmology and Strabismus (AAPOS) members found that IOL implantation in infants postoperative cataract surgery had increased from 4% in 1997 to 21% in 2001.[2] With improved surgical equipment and technique, the acceptable age for IOL implantation is becoming progressively younger.[2]

Measurement of an appropriate IOL power in pediatric eyes is challenging due to a number of reasons. Firstly, pediatric patients are often uncooperative thus more likely to decrease the accuracy of measurement. The second challenge is that there are various recommendations regarding the target refraction power. Last but not least, most of recent studies have shown accurate results in calculating an IOL power in adults but are essentially less precise in pediatric eyes because of narrower cornea, shorter axial lengths, and shallower anterior chambers.[3] Until now there was no universal standard guidelines for the IOL power prediction formulae in children that have been established.[1,4]

Several IOL calculation formulae that are commonly used including the Sanders–Retzlaff–Kraff (SRK) II, SRK/T, Hoffer Q, and Holladay I. In adult eyes, patients with axial length less than 22 mm are reported to be accurate with Hoffer Q and Holladay 2 formulae; axial length of 22-26 mm with Holladay I, Hoffer Q and SRK/T; axial length for more than 26 mm with SRK/T and Holladay 2.[5] Thus, several studies have compared the accuracy and prediction error of IOL formulae that are used in adults and have shown varied results in pediatric eyes.

Choosing an accurate IOL power calculation formulae for pediatric cataract surgery is one of the challenges. Accurate keratometry and biometry are important to determine the IOL power for each eye and it is easily achieved in adult eyes. However, the evidences are inconsistent due to less accurate biometry and large measurement errors of IOL formula predictions in pediatric eyes. Therefore, it is important to review which formula provides the best prediction of postoperative refraction specifically for children.

The aim of this literature review is to evaluate prediction errors and accuracy of IOL power calculation formulas and to provide the best IOL formula predictions in pediatric eyes with IOL implantation. This information should help surgeons to choose the best predictive power of an IOL during pediatric cataract surgery.

METHODS

The literature search was conducted from the electronic databases (Pubmed, Clinical Key, and Ophthalmology Advance) search using the search term: "IOL calculation in infant, OR Pediatric OR Children", "accuracy of biometry in children OR infant OR pediatric", "IOL formulae in children OR infant OR pediatric".

The search was limited to research articles published in English language and conducted in human. If the full text articles were not available online, manual search in the Central Library and Department of Ophthalmology Library Faculty of Medicine Universitas Indonesia were then conducted. In the initial screening, the title and abstract of all studies found were reviewed to choose articles that were relevant to the study purpose. Reference list from the included studies were also checked for potentially relevant articles. Relevant studies were then screened based on the inclusion and exclusion criteria. The inclusion criteria for studies were: (i) IOL power calculation formula used in pediatric patients, (ii) eyes undergoing uncomplicated cataract and IOL implantation, (iii) the accuracy (prediction error (PE) or absolute prediction error (APE) of IOL power calculation formulas studied. Exclusion criteria for studies were: (i) full text unavailable, (ii) PE or APE data unavailable.

All relevant studies were reviewed based on Level of Evidence developed by Oxford Centre for Evidence-based Medicine Levels of Evidence 2011. Study characteristics extracted from the retrieved studies were demographic data (mean age, axial lengths, sample size), the postoperative refraction time, methods of biometry measurement, the formula used and its PE and/or APE. Prediction error (PE) is defined as the difference between the predicted and the observed postoperative IOL refractive power and it considers the sign of error into account. Absolute prediction error (APE) is defined as the predicted IOL refractive power minus the actual postoperative IOL refractive power and it does not consider the sign or direction of the error into account. PE AND APE are presented as mean in all studies. The accuracy of the biometry measurement results was indicated by PE and APE. The closer the mean of PE and APE value to zero, the better its accuracy.

RESULT

The initial search yielded 18 articles. After screening the abstract, articles with potentially relevant trials were reviewed. Subsequently, 10 full- text articles that met the inclusion criteria were included in this review. The characteristics of the eligible studies are summarized in **Table 1**. A total of 964 eyes were enrolled in this review. Nine of ten studies compared the accuracy and PE of different IOL calculation formulas in children, whilst a study by Jasman et al[6] compared SRK II with pediatric IOL calculator, which is a computer software for IOL calculation using a modification of SRK II with a Holladay algorithm model. The follow- up period ranged from 2-24 weeks. There were various biometry measurements found in this review, including applanation and immersion methods.

Table 1. Characteristics of review articles

Study No.	Author	Year	Level of evidence	Mean Age (year old)	Number of eyes	IOL Formulae Calculation	Time of post-operative measurement	Methods of biometry Measurement
1	Vasavada et al[5]	2016	IV	2,97 ± 2.97	117	Holl 2, Holl 1, HQ, SRK/T	4-6 weeks	Immersion
2	Vanderveen et al[7]	2013	IV	0*	43	HQ, Holl 1, Holl 2, SRK II, SRK/T	4 weeks	Immersion & Applanation
3	Jasman et al[6]	2010	IV	6.84± 3.42	31	SRK II and other paediatric IOL calculator	12 weeks	Applanation
4	Trivedi et al[8]	2011	IV	3.9 ± 2.9	54	Holl 2, Holl 1, HQ, SRK/T	2 weeks - 8 weeks	Immersion
5	Kekunnaya et al[9]	2012	IV	0*	128	SRK II, SRK/T, Holl 1, HQ	4 weeks	Applanation
6	Nihalani et al[10]	2010	IV	6.4 ± 5.4	135	SRK II, SRK/T, Holl 1, HQ	4-8 weeks	Applanation
7	Neely et al[3]	2005	IV	5.7 ± 4.4	101	SRK II, SRK/T	4-8 weeks	Applanation
8	Moore et al[11]	2008	IV	5.3 ± 3.6	203	SRK II, SRK/T, Holl 1	4-8 weeks	Immersion & Applanation
9	Tromans et al[12]	2001	IV	0*	52	SRK II, SRK/T	12 weeks	Applanation
10	Mezer et al[13]	2004	IV	7 ± 5	93	SRK, SRK II, SRK/T, Holl 1, HQ	8-24 weeks	Applanation

HQ = Hoffer Q; Holl 1 = Holladay 1; Holl 2 = Holladay 2
* 0 means age of the subject less than 1 year

Table 2. Mean prediction error and mean absolute prediction error

Author	Formulae	Mean PE	Mean APE
Vasavada et al[5]	Hol 1 Hol 2 Hoffer Q SRK/T	0.41 ± 1.76 0.36 ± 1.87 0.69 ± 2.30 0.28 ± 1.64	1.29 ± 1.25 1.23 ± 1.18 1.43 ± 1.37 1.19 ± 1.15
Vanderveen et al[7]	Hoffer Q Hol 1 Hol 2 SRK/T SRK II	2.3 ± 2.4 N/A N/A -2.3 ± 2.0 0.3 ± 1.8	2.6 ± 2 1.7 ± 1.3 1.9 ± 1.5 1.4 ± 1.1 2.4 ± 1.8
Jasman et al[6]	SRK II	1.03 ± 0.69	N/A
Trivedi et al[8]	Hol 1 Hol 2 Hoffer Q SRK/T	-0.21 ± 0.90 0.02 ± 0.91 0.07 ± 1.01 -0.47 ± 0.98	0.71 ± 0.58 0.68 ± 0.61 0.72 ± 0.71 0.84 ± 0.69
Kekunnaya et al[9]	SRK II SRK/T Hol 1 Hoffer Q	-1.39 ± 2.47 -2.83 ± 2.72 -3.39 ± 2.74 -4.39 ± 3.42	2.27 ± 1.69 3.23 ± 2.24 3.62 ± 2.42 4.61 ± 3.12
Nihalani et al[10]	SRK II SRK/T Hol 1 Hoffer Q	-0.77 ± 1.24 -0.54 ± 0.96 -0.41 ± 0.91 -0.27 ± 0.93	1.11 ± 0.94 0.84 ± 0.71 0.76 ± 0.64 0.76 ± 0.61
Neely et al[3]	SRK II & SRK/T	0.3 ± 1.5+	1.18 1.12
Moore et al[11]	SRK II, SRK/T, Holladay 1	0.05 ± 1.42+	1.08 ± 0.93+
Tromans et al[12]	SRK II & SRK/T	2.63 ± 2.65 1.07 ± 0.98	N/A N/A
Mezer et al[13]	SRK	Group 1* : 1.22 ± 1.13 Group 2**: 1.79 ± 1.47	N/A
	SRK II	Group 1* : 1.08 ± 1.11 Group 2**: 1.58 ± 1.55	N/A
	SRK/T	Group 1* : 1.06 ± 0.89 Group 2**: 1.37 ± 1.22	N/A
	Hol 1	Group 1* : 1.06 ± 0.79 Group 2**: 1.35 ± 1.23	N/A
	Hoffer Q	Group 1* : 1.1 ± 0.78 Group 2**: 1.37 ± 1.22	N/A

+ : Separated outcomes from each formulae is not available
* : Represent a group of 59 eyes with duration of follow up 2-3 month (axial length: 19.79 mm- 25.41mm)
** : Represent a group of 34 eyes with duration of follow up 2-6 month (axial length: 19.24- 26.69 mm)
N/A : Not available

From all the studies that presented the mean PE of each formula, “the closest to zero” mean of PE for the SRK/T formula group was found in Vasavada[5] study, which is 0.28 ± 1.64 (Table 2). Meanwhile, the lowest mean of PE for Holladay 2 formulae was found in a study by Trivedi et al.[8] However, the lowest mean PE in this review was found in the study by Moore et al[11] 0.05 ± 1.42 in SRK II, SRK/T, and Holladay 1 formulae.

From ten studies, only six studies reported the mean APE of each formulae. Two studies reported that SRK/T was the most accurate formulae with the lowest mean APE (Vasavada et al[5] and Neely et al[3]). Two other studies otherwise reported that SRK II was the most accurate formula to be used (Vanderveen et al[7] and Kekunnaya et al[9]). Trivedi et al[8] and Nihalani et al[10] were reported that Holladay formula as the most accurate formula. However, both of these studies had short axial length in their subjects. In contrast, three of six studies reported that the least accurate formula based on the highest mean of APE was Hoffer Q (Vasavada et al[5], Vanderveen et al[7], Kekunnaya et al[9]).

DISCUSSION

Intraocular lens (IOL) power determination is unique and may be difficult in pediatric cataract surgery. Selection of the IOL calculation formula and the postoperative refraction target may vary from one surgeon to another. As a matter of fact, post-operative growth of children’s eyeballs is rather significant, and in effect changes the refractive status.[9] Gul et al reported axial length in children, that expand with age, gradually reached maturity by the age of 9-10 years, whilst the lens thickness gradually reduced until 12 years of age.[14]

In general, IOL power calculation formulas are divided into 2 major categories; empirically-determined by regression formulas and theoretical formulas. Regression formula, e.g. the Sanders-Retzlaff- Kraff (SRK) formula, is derived from a mathematical analysis of a large sampling data of postoperative results in adult patients. The SRK formula (first generation of linear regression formula) is suitable for eyes with average AL range (22.5-25.0 mm) and does not work well in longer eyes (more than 25 mm) or shorter eyes (less than 22.5 mm). The second generation of this regression formula is SRK II and it is considered as the most accurate formula for normal range of axial length. The third generation of formulas were SRK/T, Holladay I, and Hooffer Q. These regression formulas were modified empirically and theoretically by also taking the following factors, such as retinal thickness, corneal curvature, and anterior chamber depth, into consideration.[15]

On the upside, Holladay I also calculates the surgeon factor. Meanwhile, Holladay II was the fourth generation formula that contains seven factors to improve predictability including axial length, horizontal cornea thickness, corneal power, anterior chamber depth, lens thickness, preoperative refractive status, and patient age. All of these IOL formulas are the options for calculating IOL power in children.[15]

In this literature review, nine from ten studies used SRK/T formula as one of their IOL power calculation tools. It may imply a tendency towards the usage of SKR/T formula, which may be due to the superiority in combining advantages between theoretical and empirical analysis.[2] SRK/T is actually derived from SRK II where the “A” constant is modified to predict the effectiveness of lens position. Tromans et al compared formula between SRKII and SRK/T and it showed that SRK/T was more superior as it is shown the smaller mean APE in SRK/T than SRK II.[12]

Studies by Trivedi et al[8] and Nihalani et al[10] were reported Holladay as the most accurate IOL formulas. This finding is consistent with previous study by Andreo et al[16] showing Holladay is more accurate than SRK/II and SRK/T in shorter eyes.

Kekunaya et al finding showed the highest mean PE and mean APE compared to other studies. A possible interpretation of this finding is that the mean age of sample is 11.7 months (<1 year of age). This finding is less surprising since a significant decrease of refractive power up-to 24-27 D occurred in the first year of life.[17] Thus, one month follow-up in Kekunaya et al study may prove the significant changes in refractive status.[9]

There were many methods that can be used to choose the target refraction by considering the growth of axial length in pediatric eyes. A study by Al Shamrani et al[18] mentioned recommendations in selecting IOL power for congenital cataract from various studies. One common method is called the "Rule of Seven" where target refraction status is calculated by subtracting the number of seven with age in years of the children (7 – age in years). From all included studies in this review, none of the studies mentioned the methods of the target refraction determination. However, a possible assumption for this discrepancy might be the accuracy of the IOL calculation predictions were not affected by the target refraction determination.

From the included studies, the shortest duration of follow-up was 2 weeks and the longest follow up was 24 weeks. Most studies had 4-8 weeks follow-up duration. Only a study by Mezer et al[13] which conducted follow up duration to 6 months. Most studies suggested to assess the accuracy of IOL power calculation in 4 to 6 weeks postoperatively because there were significant changes in postoperative refraction status in 6 months due to increasing axial length in pediatric eyes less than two years old.

Calculating an accurate measurement of keratometry and biometry is essential in determining the IOL power for each eye in adult or children.[12] A-Scan ultrasound biometry is the customary technique for estimating the axial length in children.[19] Ultrasound can be performed by utilizing applanation or immersion methods. The applanation strategy is where placing the ultrasound probe straightforwardly on the cornea, which marginally indents the surface leading to estimation errors into value in axial length. The immersion technique utilizes a drop of fluid between the probe and cornea anticipating the indentation of cornea. When the probe is lined up with the optical axis of the eye and the ultrasound beam is opposite to the retina, the retinal spike is shown as a straight, steeply rising echo-spike.[20] Conversely, when the probe is not appropriately lined up with the optical axis of the eye, the retinal spike is shown as a barbed, moderate rising echo-spike.[20] This finding is also reported by Moore et al[11] in which the immersion A-scan biometry was slightly more accurate than contact biometry in relation to APE. The lower accuracy in applanation technique has been attributed to the indentation of the cornea surface by the ultrasound probe, thus may shorten the actual AL.

Beside choosing the most appropriate formulas, other factors may contribute to the accuracy of IOL power calculation, especially in children. Patient's state of consciousness may relate to the precision of measurement. Axial length and keratometry measurement under general anesthesia may help when the patient is uncooperative in precise fixation and centration.[2,21] However, error results in axial length measurements under general anesthesia in the supine position may translate to fixation and centration errors due to the applanation biometry technique. This applanation technique cause indention of the surface of cornea by an ultrasound probe which results in reducing the axial length.[9] Biometry measurement in conscious state is preferable. However, it suggests a need for further research and studies regarding this.

CONCLUSION

Based on this review, none of the established formulas were shown to be more accurate in predicting IOL power in pediatric eyes. This review demonstrates that the accuracy of each formula was not much different from one to another. Furthermore, biometry examination in patients less-than-one year of age tends to show lower accuracy compared to older children or adults. Further study to predict IOL power postoperative refraction is suggested.

REFERENCES

1. O'Hara MA. Pediatric intraocular lens power calculations. Current opinion in ophthalmology. 2012;23:388-93.
2. Eibschitz-Tsimhoni M, Archer SM, Del Monte MA. Intraocular lens power calculation in children. Survey of ophthalmology. 2007;52:474-82.
3. Neely DE, Plager DA, Borger SM, Golub RL. Accuracy of intraocular lens calculations in infants and children undergoing cataract surgery. Journal of AAPOS : the official publication of the American Association for Pediatric Ophthalmology and Strabismus. 2005;9:160-5.
4. Whitmer S, Xu A, McClatchey S. Reanalysis of refractive growth in pediatric pseudophakia and aphakia. Journal of AAPOS : the official publication of the American Association for Pediatric Ophthalmology and Strabismus. 2013;17:153-7.
5. Vasavada V, Shah SK, Vasavada VA, Vasavada AR, Trivedi RH, Srivastava S, et al. Comparison of IOL power calculation formulae for pediatric eyes. Eye (London, England). 2016;30:1242-50.
6. Jasman AA, Shaharuddin B, Noor RA, Ismail S, Ghani ZA, Embong Z. Prediction error and accuracy of intraocular lens power calculation in pediatric patient comparing SRK II and Pediatric IOL Calculator. BMC ophthalmology. 2010;10:20.
7. Vanderveen DK, Trivedi RH, Nizam A, Lynn MJ, Lambert SR, Infant Aphakia Treatment Study G. Predictability of intraocular lens power calculation formulae in infantile eyes with unilateral congenital cataract: results from the Infant Aphakia Treatment Study. Am J Ophthalmol. 2013;156:1252-60 e2.
8. Trivedi RH, Wilson ME, Reardon W. Accuracy of the Holladay 2 intraocular lens formula for pediatric eyes in the absence of preoperative refraction. Journal of cataract and refractive surgery. 2011;37:1239-43.
9. Kekunnaya R, Gupta A, Sachdeva V, Rao HL, Vaddavalli PK, Om Prakash V. Accuracy of intraocular lens power calculation formulae in children less than two years. American journal of ophthalmology. 2012;154:13-9.e2.
10. Nihalani BR, VanderVeen DK. Comparison of intraocular lens power calculation formulae in pediatric eyes. Ophthalmology. 2010;117:1493-9.
11. Moore DB, Ben Zion I, Neely DE, Plager DA, Ofner S, Sprunger DT, et al. Accuracy of biometry in pediatric cataract extraction with primary intraocular lens implantation. Journal of cataract and refractive surgery. 2008;34:1940-7.
12. Tromans C, Haigh PM, Biswas S, Lloyd IC. Accuracy of intraocular lens power calculation in paediatric cataract surgery. The British journal of ophthalmology. 2001;85:939-41.
13. Mezer E, Rootman DS, Abdolell M, Levin AV. Early postoperative refractive outcomes of pediatric intraocular lens implantation. Journal of cataract and refractive surgery. 2004;30:603-10.
14. Gul A, Caglar C, Cinal A, Yasar T, Kilic A. Ocular biometry and central corneal thickness in children: a hospital-based study. Arq Bras Oftalmol. 2014;77:152-4.
15. Hoffer KJ. Dalam: Hoffer KJ, editor. Formulas and programs: formula history and basics. New Jersey: SLACK Incorporated; 2011.h.137-42.
16. Andreo LK, Wilson ME, Saunders RA. Predictive value of regression and theoretical IOL formulas in pediatric intraocular lens implantation. Journal of pediatric ophthalmology and strabismus. 1997;34:240-3.
17. Shenoy BH, Mittal V, Gupta A, Sachdeva V, Kekunnaya R. Refractive outcomes and prediction error following secondary intraocular lens implantation in children: a decade-long analysis. The British journal of ophthalmology. 2013;97:1516-9.
18. Al Shamrani M, Al Turkmani S. Update of intraocular lens implantation in children. Saudi J Ophthalmol. 2012;26:271-5.
19. Yam JC, Wu PK, Ko ST, Wong US, Chan CW. Refractive changes after pediatric intraocular lens implantation in Hong Kong children. Journal of pediatric ophthalmology and strabismus. 2012;49:308-13.
20. Shammas HJ, Shammas MC, Garabet A, Kim JH, Shammas A, LaBree L. Correcting the corneal power measurements for intraocular lens power calculations after myopic laser in situ keratomileusis. American journal of ophthalmology. 2003;136:426-32.
21. Hoevenaars NE, Polling JR, Wolfs RC. Prediction error and myopic shift after intraocular lens implantation in paediatric cataract patients. Br J Ophthalmol. 2011;95:1082-5.