



Update on Pediatric Cataract Surgery and the Delphi Panel Paper

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Abstract

Purpose of Review We review the Delphi panel paper and address topics of non-consensus in the preoperative, intraoperative, and postoperative management of pediatric cataract.

Recent Findings The Infant Aphakia Treatment Study expanded our understanding of unilateral cataract surgery in infants 6 months and younger. While primary IOL implantation is accepted for children older than 2 years, long-term data is required to determine the optimal age for primary IOL. Primary management of the posterior capsule should consider the child's unique risks and benefits. Recent benchmarking papers confirmed higher refractive prediction error than adults and there is a need for IOL calculation formulas that cater to the pediatric eye. The impact of next-generation sequencing, bag-in-the-lens, optic capture, and femtosecond laser are yet to be determined.

Summary Pediatric cataract management is challenging and questions remain on the best approach to some surgical aspects. Future long-term randomized trials will help us move toward consensus globally.

Keywords Pediatric cataract surgery · Delphi process · Practice patterns · IOL implantation · IOL power calculation · Primary posterior capsulotomy

Introduction

Pediatric cataract surgery has experienced exciting advances over the past decade. The 5-year results of the Infant Aphakia Treatment Study (IATS), a multicenter randomized trial comparing aphakic contact lenses (CL) to primary intraocular lens (IOL) implantation for infants 1 to 6 months of age with unilateral congenital cataract [1, 2•, 3•, 4–6], now serves as a benchmark for robust, high-quality empiric evidence in pediatric ophthalmology. Yet, certain aspects of the management of pediatric cataract have not been studied through randomization and lack long-term data from which to formulate strong recommendations.

Recently, Serafino et al. applied a modified Delphi process to highlight the current topics of consensus in pediatric

cataract management [7•]. A group of international experts completed a series of questionnaires and attended an in-person meeting to facilitate group consensus on areas of disagreement. Subsequently, five key areas for future research were identified from the 21.3% of non-consensus questions [7•]. In this paper, we review the outcomes of the Delphi panel and recent literature relevant to areas of agreement and non-consensus in the preoperative, intraoperative, and postoperative management of pediatric cataract.

Preoperative Considerations

Evaluation and Investigations

The diagnosis of bilateral congenital cataract should prompt the clinician to review relevant exposures during pregnancy, birth, developmental and family history, and systemic features. Although experts agree that pediatricians and geneticists play a critical role in the child's care when systemic features are identified, they disagree on whether the ophthalmologist should order investigations if no systemic findings are present [7•].

Recently, the concept of using next-generation sequencing (NGS, a novel technology that enables rapid parallel DNA

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sequencing) to analyze over 100 genes associated with bilateral congenital cataract was assessed through quality improvement techniques [8, 9]. In a study of 27 patients diagnosed before age 12, NGS was associated with improved time to diagnosis and diagnostic yield (60 versus 8% for standard investigations) [10•]. While these results are powerful, NGS is not universally available. For bilateral cataract, we routinely order TORCH screen (for congenital infections associated with toxoplasmosis, other infections such as syphilis, varicella-zoster and parvovirus B19, Rubella, cytomegalovirus, and herpes simplex virus), urinalysis, blood work and karyotype, as well as examine family members, and then refer to Medical Genetics for further assessment of positive results or systemic features.

Timing of Surgery and IOL Implantation

Timing of surgery aims to reduce the risk of deprivation amblyopia associated with visually significant congenital cataract while minimizing the risk of postoperative glaucoma. The well-accepted conventional timing of surgical intervention is age 4 to 6 weeks for unilateral and prior to 8 weeks in bilateral cases [7••, 11–13]. However, the choice of refractive correction and optimal age to primarily implant an IOL is debated.

Unilateral Cataract

The IATS transformed our understanding of the management of visually significant unilateral cataract in infants 6 months and younger. At both 1 and 4.5 years of follow-up, there was no significant difference in visual acuity with primary IOL versus aphakic CL [2••, 14]. However, the IOL group had significantly more adverse events (81 versus 56% having at least one) and additional surgeries (72 vs 16%), most commonly related to visual axis opacification (VAO) [3••, 15]. Thirty-one percent had glaucoma-related adverse events at 4.8 years, with no difference between groups and greater risk with earlier surgery [4]. IOL implantation was overall 5.5% more expensive, despite higher patient costs for CL [6]. Other outcome measures included the overall prevalence of strabismus, which increased during follow-up with rates of strabismus surgery similar at 5 years between groups, as were stereopsis outcomes [2••, 5, 16]. Thus, aphakic CL are recommended for infants under 6 months if feasible for the child and caregivers.

Two recent survey studies suggest global practice patterns support these findings, with over 80% of respondents managing unilateral cataract younger than 6 months with aphakic CL [12••, 17]. While IATS is a pivotal study, it is not broadly generalizable given only unilateral cataracts were included and some methodological concerns have been raised. It has been suggested that the minimum postoperative topical steroid regime of four times daily was less aggressive than other studies; however, the IATS authors

reported that the frequency was often increased based on postoperative inflammation [18, 19]. Furthermore, other markers of visual function, such as contrast sensitivity and visual fields, were not assessed, although these may be difficult to test in young children [20, 21].

The optimal timing for primary IOL in unilateral cataract has not been elucidated. While primary IOL facilitates continuous visual stimulation through partial refractive correction, aphakic CL enable flexibility and power adjustment as the child grows. There is relatively equal preference globally for primary IOL versus CL after 6 months of age, with North American surgeons favoring aphakic CL [12••]. While approximately half of surveyed Indian ophthalmologists prefer primary IOL for infants aged 6 to 12 months, it is accepted by the majority after 1 year [17]. Differences in regional practice patterns may reflect surgical volumes, availability of CL, and access to specialists, with environmental conditions also impacting CL wear. Primary IOL has been advocated in children aged 7 to 22 months, based on a lower rate of adverse events at 5 years compared to the IATS [22•]. However, direct comparison is limited as this retrospective study was of small sample size and included both unilateral and bilateral cases.

Finally, a meta-analysis suggested that surgery within the first month of life significantly increases the risk of secondary glaucoma, while pseudophakia was associated with reduced risk [23]. However, the median age at surgery was significantly higher in these children and only 22.6% had IOL implantation of which only two eyes developed secondary glaucoma. Furthermore, the studies were nonrandomized and retrospective. Thus, long-term prospective randomized trials are needed to better understand the optimal age for primary IOL in children older than 6 months.

Bilateral Cataract

Refractive error following bilateral cataract surgery can be managed with primary IOL implantation, aphakic CL, or spectacles, as there is less risk of aniseikonia. Secondary IOL implantation may be considered once axial elongation has stabilized, or earlier if compliance with aphakic correction is of concern. Superior visual outcomes have been reported following bilateral compared to unilateral cataract surgery [24, 25], with approximately 75% of children having long-term visual acuity 20/40 or better [26, 27]. This relates to the greater amblyogenic stimulus of monocular deprivation. Worse outcomes are associated with baseline nystagmus, absence of primary IOL, and surgery prior to age 1, likely secondary to amblyopia in congenital cases [26].

IoLunder2, a prospective cohort study from the British Isles of children undergoing cataract surgery with or without primary IOL before 2 years of age, found similar results to the IATS for unilateral cataract. However, primary IOL for bilateral cases was associated with better visual outcomes, although reoperation was

significantly higher at 1 year [28••]. Younger age at surgery was a predictor of secondary glaucoma in bilateral cases and significant microphthalmos (axial length less than 16 mm) increased the risk in unilateral disease, while IOL implantation did not reduce the risk [28••]. Globally, most surgeons select aphakic refractive correction to manage bilateral cataract before 6 months, while practices are variable for older children, with a trend toward favoring primary IOL after 1–2 years [12••, 17]. In a multicenter registry of children younger than 13 years of age, the odds of primary IOL implantation were significantly greater in children 2 years or older, and were lower in bilateral compared to unilateral cases younger than 2 years [29•]. There is no accepted minimum age for implantation, highlighting the need for high-quality prospective studies [7••]. In our practice, children will receive a primary IOL in most cases above the age of 1. But given the absence of published long-term data on this population, primary IOL implantation prior to age 2 years requires thorough informed consent with the parents highlighting the child's individualized risks.

In patients with bilaterally dense cataracts, immediate sequential bilateral surgery is an alternative to minimize amblyogenic delay for the second eye surgery or when the child is at increased risk from general anesthesia. It is associated with similar visual outcomes and rate of adverse events compared to consecutive operations, while offering potential economic advantages [30, 31]. There is a low but finite risk for bilateral endophthalmitis or toxic anterior segment syndrome, which needs to be discussed with the family on a case-by-case basis, and this needs to be weighed against the anesthetic risk. In such cases, it is our practice to treat each eye as individual cases, with separate instruments, surgical scrub, prep and drapes, and different batch numbers for consumables for each eye.

IOL Power Calculation

Preoperatively, it is important to consider factors influencing the refractive outcome following primary IOL implantation, including baseline axial length, age at surgery, future axial elongation of the infant eye, and laterality. In the IATS, baseline axial length was on average 0.6 mm shorter in cataractous eyes compared to fellow eyes, with significantly increased axial growth following IOL implantation compared to aphakia at 1 year [32]. However, both groups had similar change in axial length and refractive growth rate at 5 years [33, 34]. Multiple studies have demonstrated a progressive myopic shift following primary IOL, with rates significantly higher in younger children and within the first few years of life [35–38]. Myopic shift is also accelerated in unilateral compared to bilateral pseudophakia [37, 39].

Target Refraction

While some may aim for immediate postoperative emmetropia to avoid the potential amblyogenic stimulus of

uncorrected ametropia, myopic shift throughout life may later necessitate an IOL exchange. Thus, undercorrection using age-adjusted target refractions has been proposed in planning for future axial growth [36, 40], coupled with spectacle correction of residual hyperopic ametropia. The Enyedi et al. guidelines, targeting postoperative refraction of +6 for a 1-year-old, +5 for 2-year, +4 for 3-year, +3 for 4-year, +2 for 5-year, +1 for 6-year, plano for 7-year, and –1 to –2 for patients 8 years and older, were recently validated, with almost half of the cohort within 1.0 D of expected refraction at 7 years [40, 41••]. Myopic shift was not significantly different for unilateral pseudophakic children aged 2 to 6 years who were targeted for emmetropia or undercorrected by two or more diopters [42]. While the Delphi panel agreed on targeting residual hyperopia adjusted for age [7••], refractive goals must consider likelihood of wearing spectacle overcorrection for immediate significant hyperopia, as well as family history of refractive error.

IOL Power Calculation and Formulas

Compared to adults, pediatric power calculations are prone to several errors. Baseline office axial length and keratometry measurements are the gold standard, as lack of fixation under general anesthesia may introduce inaccuracies [43]. However, pediatric cases frequently necessitate intraoperative A-scan, with immersion technique preferred as contact yields significantly shorter measurements by mean 0.27 mm [7••, 44]. This is particularly important when patient cooperation or cataract morphology limit accurate preoperative refraction. Furthermore, the formulas commonly employed are based on adult normative data, which are not reflective of pediatric intraocular dimensions.

Non-consensus in IOL power calculation formula selection is an important area for future study [7••]. Comparison of refractive outcome studies is limited by considerable variability in mean age at surgery, follow-up duration, and axial length, as well as use of different biometry techniques, prediction formula, A-constants and IOLs. Significantly lower prediction error (the difference in predicted and actual postoperative spherical equivalent refraction, PE) has been reported for Holladay 1 [45] and SRK/T [45, 46], while others report improved PE with Hoffer Q [43], Holladay 2 [47], and SRK II [48], yielding no consensus on which is superior. Significantly higher prediction error has been reported for shorter eyes [45, 49••], manufacturer lens constants [45, 46], and ciliary sulcus IOL placement [50], while others suggest no factors influence calculation accuracy [51]. Nihalani et al. recently established benchmark standards for pediatric PE, with 66% of children older than 2 years within 1D of expected refraction [49]. This may serve as an important comparison for future studies. With adult power formulas leading to greater PE in pediatric eyes, the development of a validated pediatric-specific formula would be valuable.

IOL Selection

Several IOL designs and materials have been used in pediatric cataract surgery. Foldable hydrophobic acrylic IOLs are the most preferred for implantation in the capsular bag [17, 52–55]. While similar rates of PCO are reported compared to PMMA, deposits on the IOL surface and posterior synechiae are significantly less frequent [53]. Furthermore, the flexible nature enables implantation through smaller corneal incisions. However, whether to place a one-piece or three-piece hydrophobic acrylic in the capsular bag is a point of debate, with no comparative studies in the pediatric literature [7•]. While the association of some hydrophobic acrylic IOLs with glistenings is of concern, there is only one report in the pediatric literature [56, 57]. We have now adopted the use of lens implants that are not associated with glistenings.

Recently, hydrophilic acrylic IOLs have also been proposed for use in children, but there have been no direct comparative studies to hydrophobic implants [58, 59]. The “bag-in-the-lens” is a unique monofocal spherical hydrophilic IOL with an encircling groove in the optic to secure equally sized anterior and posterior capsular leaflets, to prevent lens epithelial cell migration [60]. It is associated with VAO in less than 10% of cases at long-term follow-up [61•].

Other selection considerations include aspheric and multifocal IOLs. In a recent randomized prospective study of 23 children (40 eyes), higher order aberrations and contrast sensitivity were significantly better with an aspheric compared to a spherical IOL, but the visual and refractive outcomes were similar [62]. Multifocal IOLs have also been proposed for children (aged 2–14 years, follow-up 27.4 months) [63]. A study of children older than 5 years (1 year follow-up) reported similar visual outcomes, contrast sensitivity, and stereopsis, but improved distance-corrected near acuity with a multifocal compared to a monofocal IOL [64]. Then, 30.5% of respondents in a survey of AAPOS members would consider using multifocals [54]. However, decreased contrast sensitivity and the presence of multiple blurred, superimposed images from the focal points of a multifocal are potential amblyogenic stimuli [65, 66]. Accurate preoperative biometry and IOL centration required for multifocals may not be feasible in children [66]. Furthermore, multifocal IOLs require a postoperative refraction near emmetropia [65], yet axial growth continues into the second decade [67]. Given no currently available long-term data from prospective randomized trials, we do not offer multifocals as standard of care for children of amblyogenic age or before axial growth has stabilized.

Intraoperative Considerations

Anterior Capsule Management

Various techniques have been described for managing the anterior capsule (AC) in children, including manual continuous

curvilinear capsulorhexis (MCCC), two-incision push-pull (TIPP), and vitrectorhexis. TIPP capsulorhexis is a reliable method of producing a circular rhexis by joining two opposite semicircular tears and is less dependent on surgeon experience [68–70]. A four-incision approach has also been described [71]. Vitrectorhexis is another alternative, with low reported AC tear rate of approximately 4–5% [72, 73]. In a retrospective review of 339 eyes, the risk of AC tear was higher with vitrectorhexis in children older than 6 years and with MCCC in the younger cohort [72]. Thus, vitrectorhexis is preferred to manage the highly elastic infant AC, while the finer control of MCCC offers superior outcomes in older children. This was confirmed in a survey of AAPOS member preferences [74]. There was also consensus among the Delphi panel that MCCC offers advantages when primarily implanting an IOL, while vitrectorhexis is favored when planning for aphakia in children 2 years and younger [7•]. Anterior and posterior capsulorhexis diameters of 4 to 5 mm are associated with reduced anterior capsular contraction and VAO [75]. Although anterior capsular elasticity, visualization, and success of MCCC improve with use of Trypan blue [76, 77], there is no clear consensus on its use in pediatric AC management [7•]. While not routine, we prefer to use it in the context of significant opacity of the anterior capsule or lens substance.

Femtosecond laser has also been proposed for the management of both anterior and posterior capsules in children. An early case series reported increased capsulotomy diameters than were programmed due to inherent capsule elasticity [78]. The Bochum formula was proposed to account for significantly greater capsular deviations in younger children [79]. Fung et al. recently applied this formula to a new femtosecond laser platform, with final median BCVA 0.20 logMAR and median duration of laser process under 3 min [80]. However, use of femtosecond laser may be limited by lack of availability and cost of the laser platform, learning curve, and potential increase in case duration.

IOL Placement

Implantation in the capsular bag is preferred for primary IOL when there is adequate support. Ciliary sulcus IOL positioning evaluated by UBM is associated with significantly increased vertical IOL decentration, IOL tilt, and crowding of the anterior chamber, although visual outcomes are similar to in-the-bag placement [81•]. Furthermore, sulcus fixation may increase the risk of secondary glaucoma [81•]. Yet, it offers a good alternative when there is poor capsular support or in cases of secondary IOL when the bag cannot be opened. However, in-the-bag placement is also preferred for secondary IOL when the residual capsule may be opened and the Soemmerings ring is debulked, particularly essential for one-piece lens implants. Posterior chamber IOL placement is preferred to anterior chamber IOLs, which are associated with

corectopia, haptic migration, and implant pigment deposits [82] and should not be used in children.

Posterior Capsule Management

Visual axis opacification (VAO) is one of the most common long-term complications of pediatric cataract surgery. VAO occurs at extremely high rates when the posterior capsule is left intact, and ranges from 4 to 100% depending on whether posterior capsulotomy and anterior vitrectomy are performed [3•, 24, 83–86]. Whether implantation of an IOL influences VAO is controversial, with some reports of higher rates in pseudophakic children [3•, 25], while others suggest no difference with aphakia [24]. Proliferation of residual lens epithelial cells is more common in younger children, post-traumatic cataract, and in the presence of other ocular anomalies [84, 87–89].

Primary posterior curvilinear capsulorhexis (PCC) with or without anterior vitrectomy (AV) aims to remove the “scaffold” onto which lens epithelial cells can grow. Secondary Nd:YAG laser capsulotomy is an option if the posterior capsule (PC) is left intact, although this may necessitate a second anesthesia if the child is uncooperative in clinic. Primary PCC/AV significantly decrease postoperative lens repopulation [83, 90]. However, the upper age limit for performing PCC/AV is debated. Most experts prefer PCC/AV for all children younger than 5 years and uncooperative children aged 5 to 8. The Delphi panel did not reach consensus on the management of cooperative children aged 5 to 8 or those older than 8 years who are likely uncooperative, highlighting an important question for further research [7•]. The PC is typically left intact for cooperative children 8 years and older who have less significant epithelial proliferation and may undergo secondary laser capsulotomy successfully. The risk versus benefits of PCC, including general anesthesia concerns and developmental considerations, should be discussed in detail with caregivers preoperatively.

PCC and AV can be performed before or after IOL implantation via a limbal or pars plana approach. Both vitrectorhexis or manual technique using intraoperative forceps are effective [91, 92]. A recent randomized trial reported faster performance of pars plana vitrectorhexis and AV after IOL implant with a 25 compared to 20-gauge system, but some difficulty in maneuvering the 25-gauge system was associated with smaller posterior rhexis size [93•]. Both anterior and posterior vitrectorhexis approaches are associated with similar intraoperative stability and 1-year outcomes with a 25-gauge system [94•]. An endoilluminator used externally may aid in visualization of the posterior capsule and anterior hyaloid face [95]. Trypan blue may also facilitate posterior capsulorhexis through changes to intrinsic capsular elasticity [96]. Finally, although it is not essential in standard practice, two recent papers have reported using triamcinolone acetonide to visualize the anterior vitreous face and residual strands in the anterior chamber [7•, 97, 98].

Posterior optic capture, in which the optic is placed through the posterior capsulorhexis with haptics in-the-bag or the sulcus, has been proposed as an alternative to anterior vitrectomy. A meta-analysis of 10 studies (282 eyes) found significantly improved rates of IOL decentration and VAO with optic capture, although visual outcomes were similar [99•]. It is hypothesized that fusion of the two capsular surfaces may limit the growth of epithelial cells onto the visual axis. Since publication of this meta-analysis, a prospective randomized trial found no difference in the development of VAO or deposits on the IOL [100•]. A recent retrospective case control study (52 eyes) also found similar rates of VAO and other complications with in-the-bag IOL and vitrectomy compared to optic capture [101].

Intraoperative Medications

A major area of non-consensus in the management of pediatric cataract is the routine use of intracameral prophylactic pharmacotherapy, given a lack of high-quality evidence in the literature. While intracameral antibiotic was not found to reduce postoperative fibrin formation in a pediatric cohort [102], a recent large meta-analysis demonstrated reduced endophthalmitis rates with intracameral cefuroxime and moxifloxacin and good safety profile in adults [103]. Approximately 70% of AAPOS members recently reported using intracameral antibiotic for endophthalmitis prophylaxis, although there was no consensus on drug of choice [104•].

In a retrospective case control study, the use of intracameral triamcinolone acetonide was associated with significantly less VAO and inflammation, with no reports of elevated postoperative IOP or endophthalmitis [105]. However, it is difficult to assess causality as both the triamcinolone and control groups received systemic and topical steroids postoperatively. One case series (24 eyes) reported no increased glaucoma risk with intracameral dexamethasone and rate of significant VAO was high at 34 months [106].

Postoperative Considerations

Postoperative Medications

Postoperative pharmacotherapy regime should include topical steroid, antibiotic, and dilating drops. We frequently use topical moxifloxacin four times daily, prednisolone 1% 4–6 times daily with taper based on clinical response, and atropine 0.5–1% twice daily. A combination drop may be substituted to facilitate ease for the caregiver. A recent randomized phase 3B trial comparing difluprednate 0.05% to prednisolone 1% four times daily for children younger than 3 years showed similar safety and efficacy [107•]. Difluprednate was associated with transient IOP elevation during treatment, but

inflammatory control was faster. Topical ketorolac 0.5% for children with intact PC demonstrated similar rates of VAO compared to PCC/AV alone [108]. However, the feasibility of caregivers outside of a study protocol instilling topical ketorolac for 3 months, as frequently as 12 times daily in the early postoperative period, is questionable.

Intracameral triamcinolone acetonide (1.2 mg/0.03 mL) injection has also been compared to postoperative oral prednisolone (1 mg/kg/day), with similar incidence of VAO, signs of inflammation, and IOP at 1 year [109]. We prefer to only utilize oral prednisolone on postoperative day 1 if the child has a fibrinous anterior chamber reaction, with taper based on clinical improvement and close IOP monitoring.

Visual Rehabilitation

Amblyopia therapy is critical to success following pediatric cataract surgery, particularly in unilateral cases, and should begin shortly after lensectomy. A multidisciplinary approach involving pediatric ophthalmologists, orthoptists, nurses, optometrists, opticians, and contact lens specialists facilitates long-term monitoring and care of these children. Parents should be well-informed of the intensive follow-up required after surgery, the different options for visual rehabilitation, and potential compliance issues must be identified and addressed immediately.

When possible, aphakia is managed with silicone elastomer (SE), rigid gas permeable (RGP), or hydrogel CL. A regression formula and modified A-constant were validated to estimate initial CL power based on preoperative biometry, when refraction is difficult postoperatively [110, 111]. The IATS reported similar visual outcomes irrespective of CL type, although RGP necessitated more frequent replacement [112]. SE lenses may be worn for extended periods but are less effective at correcting astigmatism, while RGP offer more customization but are limited to daily wear [113••]. While experts prefer SE lenses for children under age 3, practices are variable for older children [7••]. Frequent postoperative refractions are imperative to confirm accuracy of CL power, as residual ametropia is amblyogenic. Although the capacity to regularly change CL power is an advantage, this must be balanced with local availability of CL services, as well as economic implications for caregivers.

Conclusions

Two years after publication of the Delphi paper, we have yet to fully answer questions of uncertainty in pediatric cataract management despite a growing literature. There is a need to clarify the optimal age for primary IOL implantation, as well as appropriate windows for managing the posterior capsule primarily. Furthermore, an IOL power calculation formula derived from pediatric normative data may improve prediction

error in this cohort. The impact of advances such as next-generation sequencing, bag-in-the-lens, optic capture, and femtosecond laser on our understanding and outcomes of pediatric cataract surgery are yet to be determined. Targeted multicenter randomized controlled trials with rigorous methodology and long-term follow-up like the IATS will enable us to move toward consensus worldwide.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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