PREFERRED PRACTICE PATTERN® CLINICAL QUESTIONS

















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American Academy of Ophthalmology P.O. Box 7424 San Francisco, California 94120-7424 415.561.8500 Preferred Practice Pattern® (PPP) Clinical Questions are evidence-based statements that guide clinicians in providing optimal patient care. PPP Clinical Questions answer specific questions in the "Patient, Intervention, Comparison, Outcome" (PICO) format.

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FINANCIAL DISCLOSURES

In compliance with the Council of Medical Specialty Societies' <u>Code for Interactions with Companies</u>, relevant relationships with industry occurring from December 2012 to May 2013 are listed. The Academy complies with the Code in developing PPP Clinical Questions by following the <u>Preferred Practice Patterns and Ophthalmic Technology Assessments: New Relationship with Industry Procedures</u>.

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METHODS AND KEY TO RATINGS

Preferred Practice Pattern Clinical Questions should be clinically relevant and specific enough to provide useful information to practitioners. Where evidence exists to support a recommendation for care, the recommendation should be given an explicit rating that shows the strength of evidence. To accomplish these aims, methods from the Scottish Intercollegiate Guideline Network (SIGN)¹ and the Grading of Recommendations Assessment, Development and Evaluation (GRADE)² group are used. All studies used to form a recommendation for care are graded for strength of evidence individually. To rate individual studies, a scale based on SIGN is used. GRADE is a systematic approach to grading the strength of the total body of evidence that is available to support recommendations on a specific clinical management issue. Organizations that have adopted GRADE include SIGN, the World Health Organization, the Agency for Healthcare Research and Policy, and the American College of Physicians.³

SIGN¹ Study Rating Scale

I++	High-quality meta-analyses, systematic reviews of randomized controlled trials (RCTs), or RCTs with a very low risk of bias
I+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
I-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
II++	High-quality systematic reviews of case-control or cohort studies High-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
II+	Well-conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
II-	Case-control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
III	Nonanalytic studies (e.g., case reports, case series)

GRADE² Quality Ratings

Good quality	Further research is very unlikely to change our confidence in the estimate of effect
Moderate quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Insufficient quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate Any estimate of effect is very uncertain

GRADE² Key Recommendations for Care

Strong recommendation	Used when the desirable effects of an intervention clearly outweigh the undesirable effects or clearly do not
Discretionary recommendation	Used when the trade-offs are less certain—either because of low-quality evidence or because evidence suggests that desirable and undesirable effects are closely balanced



TOPIC

Intraocular lens implantation in uveitic and cataract patients

CLINICAL QUESTION

Under what circumstances is placement of an intraocular lens (IOL) contraindicated in uveitic and cataract patients, particularly pediatric patients?

LITERATURE SEARCH

The literature search was conducted by searching the PubMed and Cochrane Review databases on January 24, 2012.

Literature search details

SYSTEMATIC REVIEW

There was one study applicable to the topic discussed in the Cochrane Review. The articles systematically reviewed for this PPP Clinical Question can be viewed here:

Articles



Recommendations for Care

SUMMARY

Visual outcomes of uveitis patients undergoing cataract surgery have dramatically improved over the past two decades. There is an increasing trend toward implantation of intraocular lenses (IOLs) in nearly all adults and in most children with uveitis, provided that complete and sustained control of inflammation is obtained pre-operatively, and the literature suggests that IOL implantation is preferable to aphakia in terms of visual acuity. However, the vast majority of studies in this field are small, uncontrolled case series, and there are few long-term data on the outcomes of either approach in patients treated with currently available immunosuppressive regimens or modern surgical techniques. Randomized controlled trials (RCTs) evaluating various types of cataract surgery in this population are also lacking. Therefore, clinicians should use their best judgment when deciding on a surgical approach.

(Study Rating Scale III, Insufficient Quality, Discretionary Recommendation)

BACKGROUND

Visual outcomes of uveitis patients undergoing cataract surgery have dramatically improved over the past two decades due to several factors, such as improved medical management (e.g., routine use of immunosuppressive therapy), refined surgical technique, and better IOL design. Numerous (but frequently uncontrolled) reports suggest that phacoemulsification with IOL implantation can be safely performed when uveitis is controlled by an appropriate anti-inflammatory regimen.

Nonetheless, while IOL implantation is routine in the vast majority of phacoemulsification procedures, it may be problematic in patients with some forms of ocular inflammation. Failure to achieve strict, long-term control of uveitis may lead to macular edema, hypotony, glaucoma, band keratopathy, cyclitic membranes, retinal detachment, and/or the need to explant the IOL. Consequently, some experts feel that aphakia is a viable option following cataract removal. Cataract surgery in children with uveitis remains particularly challenging, and there is no consensus on the safety of primary IOL implantation in this population. This is especially true for chronic forms of uveitis, such as those associated with juvenile idiopathic arthritis (JIA) or juvenile rheumatoid arthritis (JRA). This review examines literature on contraindications to IOL implantation in patients with uveitis. This evaluation has been performed in accordance with the methods of the Scottish Intercollegiate Guideline Network (SIGN), and the body of evidence has been assessed using the system of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) group.² The Pubmed database was searched, and appropriate studies were identified; studies with particularly small sample size, poor follow-up, or other significant methodological flaws are not reviewed here for reasons of space. All other important studies are reviewed and discussed below.

REVIEW OF THE LITERATURE

Uveitis is a rare disease. No prospective, comparative trials have evaluated IOL implantation against aphakia in cataract surgery in patients with uveitis. The available literature consists largely of small, uncontrolled, retrospective case series. Data on long-term outcomes are nearly non-existent. Synthesis of study results are also complicated by variable lengths of follow-up across reports, inclusion of different uveitis syndromes, patient age differences, and historical factors, such as the availability of newer immunosuppressive regimens and different types of IOLs.

In an extensive 1990 review of IOL implantation in patients with uveitis, Hooper et al⁴ indicated that IOL implantation could be considered in patients with Fuchs heterochromic iridocyclitis (FHI) or chronic nongranulomatous uveitis of any cause, if there were no synechiae and the uveitis was "absolutely controlled." Intraocular lens implantation was "not recommended" in patients with pars planitis or lens-induced inflammation. Hooper et al⁴ also felt that IOL implantation was contraindicated in patients with JIA-associated uveitis. Milazzo et al⁵ subsequently reported results in 94 eyes of 93 adult patients with FHI who underwent cataract surgery and IOL implantation. Final visual acuity was 20/40 or better in 77% of patients. A retrospective series from the same era⁶ evaluated extracapsular cataract extraction (ECCE) and posterior chamber (PC) IOL implantation in 39 eyes in 30 adult patients with uveitis and cataract. Visual acuity improved in all but one eye, averaging 7.5 Snellen lines. Uveitis recurred in 20 eyes (51%) and post-operative cystoid macular edema (CME) developed in 18 eyes (46%).

Evidence regarding IOL implantation during cataract surgery in children with uveitis is mixed. In one series of eight children receiving IOL implantation, four eyes developed retrolental membranes and three of those eyes needed further surgery, despite posterior capsulotomy and anterior vitrectomy. BenEzra and Cohen reported a retrospective noncomparative case series of 20 eyes of 17 children with chronic uveitis undergoing cataract surgery. Eyes with JIA-associated uveitis had more complications (prolonged uveitis and secondary membranes) and poorer visual results than patients with other types of uveitis. The authors concluded that IOL implantation was preferable to aphakia in patients with unilateral uveitic cataracts because of poor contact lens tolerance, although visual outcomes in bilateral aphakic patients had visual acuity comparable to pseudophakic eyes.

Probst et al⁹ published the results of eight eyes (seven patients) with JIA-associated uveitis that underwent cataract removal by phacoemulsification with IOL implantation. Over a mean follow-up of 16.6 months, visual outcomes were better in patients older than 13 years at the time of surgery, and one pediatric patient developed chronic uveitis, posterior synechiae, and a pupillary

membrane. In a more contemporary series of cataract surgeries in 36 eyes of 25 patients with JIA-associated uveitis, ¹⁰ complications appeared less frequent in patients treated with anterior vitrectomy.

A recent paper ¹¹ described a series of 17 eyes of 16 patients with JIA-associated uveitis who underwent cataract surgery with in-the-bag IOL implantation. All operative eyes had improvement of two or more lines of acuity. Two eyes had fibrin post-operatively despite intravitreal triamcinolone acetonide (IVTA), four developed IOL deposits, and eight developed synechiae, showing that IOL implantation is not without risks. All patients had controlled inflammation preoperatively via systemic immunosuppressive drugs and/or biologic agents for three months. Nemet et al¹² reported a retrospective comparison of outcomes of IOL implantation in children with cataract and JIA-associated uveitis against outcomes in those with uveitis of other causes. Nineteen uveitic eyes were implanted with an IOL, with strict control of inflammation for three months pre-operatively. Post-operative complications were comparable in both groups, though the study was not sufficiently powered to measure differences between JIA and non-JIA patients. Quiñones et al¹³ retrospectively analyzed 41 eyes with uveitis of various types that underwent phacoemulsification prior to 2004. Intraocular lens implantation with a polymethylmethacrylate (PMMA) lens was performed in 13 eyes; the remaining 28 eyes were left aphakic. Eyes that underwent IOL implantation had better final visual acuity, although there was no significant difference in post-operative inflammation. Most patients with no post-surgical visual improvement had JIA-associated uveitis.

Two studies have since provided longer-term follow-up data on IOL implantation in children with uveitis. Terrada et al¹⁴ described 22 eyes in 16 children with uveitis who underwent phacoemulsification with in-the-bag implantation of a heparin surface-modified (HSM) PMMA IOL. Median follow-up was six years. Visual acuity was improved in 19 eyes, unchanged in two eyes, and worse in one eye. The authors concluded that good visual outcomes are possible if excellent control of the inflammation is maintained and there are no posterior segment uveitic complications. Sijssens et al¹⁵ reported their 17-year experience in the management of cataract surgery in 29 uveitic children (48 eyes). Better visual results were reported in pseudophakic patients up to seven years after surgery. With maximum control of perioperative inflammation and intensive follow-up, IOL implantation in children with JIA-associated uveitis was not associated with an increased risk of ocular hypertension, secondary glaucoma, cystoid macular edema, or optic disc swelling, and showed better visual results up to seven years later.

Evidence on outcomes of cataract surgery with IOL implantation in children with JIA-associated uveitis is very limited. Lam et al ¹⁶ reported a series of six eyes of five children aged 12 years or less with JIA uveitis. A PMMA lens was placed in four eyes and an acrylic PC IOL in one eye. Visual acuity improved an average of seven Snellen lines after surgery. No posterior synechiae were noted during follow-up. Adan et al ¹⁷ reported two children with oligoarticular, ANA-positive, JIA-associated uveitis and cataract who underwent cataract removal with IOL implantation at the age of seven years and subsequently required IOL explantation because of persistent uveitis, hypotony, and macular edema. The first patient had not been treated with systemic corticosteroids or immunosuppressive therapy, while the second had been treated with both methotrexate and etanercept.

DISCUSSION

The evidence base in the management of pediatric uveitic cataracts is limited, with no RCTs evaluating IOL implantation against aphakia. Uncontrolled retrospective studies suggest that IOL implantation can be considered in most pediatric patients with well-controlled uveitis, and that JIA-associated uveitis should not be considered an absolute contraindication. The best visual outcomes are likely to occur when there is excellent control of the underlying uveitis, regardless of the exact techniques of surgery performed. The ideal duration of pre-operative quiescence is unknown, but most clinicians recommend a minimum of three months in patients with chronic

uveitis (especially JIA-associated uveitis). Because such a delay in cataract surgery may take place during the period of amblyogenesis, consultation with a pediatric ophthalmologist and aggressive management of amblyopia following cataract surgery is essential. Amblyopia risks with aphakia must be balanced against the possible longer-term need for immunosuppressive therapy to control inflammation in pseudophakic patients.

Most series on pediatric cataract and uveitis were performed prior to the routine use of anti-TNF therapy¹⁸ as well as availability of approved forms of local corticosteroid therapy, such as the two-three year fluocinolone acetonide implant, the shorter acting dexamethasone implant, preservative-free IVTA, and topical difluprednate. While corticosteroids are themselves cataractogenic and should be used sparingly in children, they can play an essential role in treatment of acute uveitis flare-ups as well as sequelae of uveitis, such as macular edema. The use of steroid-spanning immunosuppressive therapy may allow for a reduction of corticosteroid therapy and should be initiated early in the course of therapy when uveitis appears to be chronic. ^{13,19,20}

Controversy also exists over the most appropriate IOL to implant in pseudophakic patients. Oneor three-piece acrylic hydrophobic IOLs are most commonly used by pediatric cataract surgeons, and evidence exists to support the use of HSM PMMA IOLs. ^{21,22} Multifocal lenses are relatively contraindicated in patients with uveitis, especially children, because of the greater difficulty in obtaining precise IOL calculations. ²¹ In younger children, posterior capsulorrhexis and anterior vitrectomy should be considered in order to reduce the rate of post-operative capsular opacification, since YAG laser capsulotomy may be difficult in the pediatric population.

The available studies are limited by small numbers of subjects, age differences among patients, retrospective analyses, use of different types of IOLs, variations in surgical technique, and lack of controlled anti-inflammatory regimens. Most of the studies reviewed are short-term studies and long-term results extending over several years are very limited. Thus, clinicians should use their best judgment when deciding on a surgical approach.



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