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ORIGINAL ARTICLE

Cataract Management in Juvenile Idiopathic Arthritis: Simultaneous versus Secondary Intraocular Lens Implantation*

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ABSTRACT

Purpose: To compare primary versus secondary intraocular lens (IOL) implantation after cataract removal in patients with juvenile idiopathic arthritis (JIA).

Methods: Retrospective interventional study. Data were obtained for 40 children (40 eyes) with JIA-associated uveitis operated on for cataract before the age of 16 years between January 1998 and January 2005.

Results: Twenty-one patients underwent primary IOL implantation at a mean age of 13.1 ± 2.6 (9–16) years. Mean follow-up was 48.2 ± 5.4 (35–64) months. Nineteen patients underwent cataract removal at a mean age 12.3 ± 2.0 (9–16) years and secondary IOL implantation 13.6 ± 0.3 (11–16) months later. Mean follow-up was 47.2 ± 6.5 (32–64) months. BCVA difference between the two groups was significant at 24-month visit only ($p = 0.001$). Incidence of secondary glaucoma was significantly lower in the group that underwent secondary IOL implantation ($p = 0.01$).

Conclusion: Secondary IOL implantation after cataract removal in children with JIA-related uveitis provided a significantly lower incidence of secondary glaucoma.

Keywords: Arthritis, cataract, glaucoma, intraocular lens, TNF-α, uveitis

Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children.[1,2] Uveitis has been reported in 10–20% of patients with JIA and may lead to significant ocular damage and even blindness.[3,4] Cataract is among the most frequently observed ocular complications of JIA, affecting 20–30% of patients.[5,6] Occurrence of cataract may be influenced by the duration of uveitis, degree of inflammation control, and concomitant topical corticosteroid use.[7–11] Although adult uveitic cataracts are commonly managed with phacoemulsification and primary intraocular lens (IOL) implantation,[12] surgical treatment of uveitis-related pediatric cataract remains challenging, with no approach accepted as the standard one. A major point of controversy is whether to implant an IOL, because it has been thought that IOLs might aggravate inflammation, mainly in cases of juvenile idiopathic arthritis–associated uveitis in which the IOL may act as a scaffold for cyclitic membrane formation, leading to chronic hypotony and phthisis bulbi.[13] Herein, we compared outcomes after simultaneous and postponed IOL implantation after cataract removal in patients with JIA.

*The study was performed with informed consent and following all the guidelines for experimental investigations required by the Institutional Review Board or Ethics Committee of which all authors are affiliated.

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METHODS

The charts of all patients with JIA that underwent cataract surgery between January 1998 and January 2005 at the University Federico II of Naples and in private practice were retrospectively reviewed. IRB approval was obtained, the ethics committee of the University Federico II granted the approval for this study, and the patients and/or their guardians gave their informed consent to obtain the data. Inclusion criteria were diagnosis of JIA made based on International League of Associations for Rheumatology (ILAR) diagnostic criteria[14] before 16 years of age, chronic uveitis with full control of intraocular inflammation (<1+ cells in anterior chamber or vitreous body) for at least 3 consecutive months before surgery, reduced best-corrected visual acuity (BCVA) ($\leq$20/50) due to cataract or the presence of cataract that would preclude thorough posterior segment evaluation, and minimum follow-up of 2 years from last surgery. Patients older than 16 years at the time of surgery, patients who did not receive an IOL, and cases with follow-up from last surgery shorter than 2 years were excluded.

Patients randomly underwent primary implantation of the IOL at the time of lens removal, or secondary postponed implantation of the IOL after a period of contact lens use after lens removal. Before surgery, biometry was performed with IOL Master (Carl Zeiss Meditec, Dublin, CA). Intravenous corticosteroids (5–10 mg/kg) were administrated during surgery, followed by corticosteroids orally, in doses of 1–2 mg/kg/day, with an individualized tapering regimen. When postoperative inflammation was present steroids were modulated to control the inflammation.

All surgical procedures were performed under general anesthesia by the same experienced surgeon (A. M.) using a standard phacoaspiration technique. The anesthesia technique was the same in all cases. Briefly, after a clear corneal incision was made a continuous curvilinear capsulorhexis was created and phacoaspiration was performed. After complete removal of the cataract posterior capsulorhexis and wide anterior vitrectomy were performed. In patients undergoing simultaneous cataract surgery and IOL implantation, IOL was implanted into the capsular bag or in the ciliary sulcus if implantation in the bag was not possible. Secondary IOL implantation was performed as a distinct surgical access through corneal incision, 360° annular synechiotomy, posterior chamber IOL inserted into the capsular bag or in the ciliary sulcus if implantation in the bag was not possible, and 10-0 nylon suture. Before and during the 15 postoperative days after both primary and secondary IOL implantation, the operated eyes were treated with topical antibiotics, corticosteroids, and mydriatic and cycloplegic agents that were then tapered according to inflammation. In all cases a hydrophobic acrylic IOL with polymethyl methacrylate haptics (VA-60BB; 126 Hoya Corporation) was implanted.

Before and after surgery, the patients underwent a complete ophthalmological examination, including BCVA evaluation, anterior segment biomicroscopy, evaluation of cells and flare, fundus ophthalmoscopy. Standardization of Uveitis Nomenclature (SUN) Working Group Grading was used for anterior chamber reaction.[15] The intraocular pressure (IOP) was measured by applanation tonometry, but if this was not possible, noncontact tonometry, the Tono-Pen or the Icare tonometer, was used. Secondary glaucoma was defined as the presence of pathologic cupping of the optic disc, a glaucomatous visual field defect with IOP higher than 21 mmHg, or both.[16] Vertical cup/disc ratio was defined as normal when less than 0.5. Fluorescein angiography, posterior optical coherence tomography (OCT, Opko/OTI, Inc., Miami, FL), anterior segment OCT (Visante, Carl Zeiss, Germany), and echography were performed when necessary. Furthermore, the presence of synechiae formation, cell deposits on the IOL, IOL decentration, secondary capsular opacification, macular edema, and optic disc swelling was documented.

Ophthalmic examination was performed at 1 day, 2 weeks, 3, 6, and 12 months, and twice a year thereafter. Cataracts were evaluated using the Lens Opacities Classification System III.[17] Statistical calculations were performed using a statistical software (STATA version 11, STATA, Texas, USA). Visual acuity data in both groups were compared using the Kruskal–Wallis test. The Fisher test was used to compare incidence of glaucoma in the two groups. The chosen level of statistical significance was $p < 0.05$.

RESULTS

Forty patients (40 eyes) were included in the study. Mean age of all patients was 12.6 ± 2.4 (9–16) years. Clinical characteristics of the two groups are shown in Table 1.

Twenty-one patients underwent primary IOL implantation; at the time of surgery mean age of the patients was 13.1 ± 2.6 (9–16) years, mean duration of arthritis was 6.64 ± 4.71 months, mean duration of uveitis was 6.66 ± 5.34 months. Oligoarticular arthritis was present in 17 cases (80.9%), polyarticular arthritis in 4 cases (19.0%). In 10 patients (47.6%), the arthritis was diagnosed 2.7 ± 2.1 months before the diagnosis of uveitis was made. In 6 cases (28.6%), uveitis was diagnosed 3.9 ± 2.0 months before arthritis, while in 5 cases (23.8%) arthritis and uveitis were diagnosed at the same time. Nine children (42.8%) were antinuclear antibody positive (7/9 oligoarticular, 77.8%; 2/9 polyarticular, 22.2%). Before surgery a 1+ intraocular cellular reaction according to SUN classification was

TABLE 1. Cataract in juvenile idiopathic arthritis—clinical charateristics of patients after primary and secondary IOL implantation.

	Primary IOL implantation	Secondary IOL implantation
n	21	19
Age (years)	13.1 ± 2.6 (9–16)	12.3 ± 2.0 (9–16)
Duration of uveitis (months)	6.66 ± 5.34	6.54 ± 3.18
BCVA (logMAR) at baseline	0.72 ± 0.2	0.69 ± 0.11
BCVA (logMAR) at 24-month visit	0.32 ± 0.1	0.20 ± 0.08
IOP at last visit (mmHg)	20.3 ± 3.3	17.6 ± 2.7
Follow-up	48.2 ± 5.4 (35–64)	47.2 ± 6.5 (32–64)

BCVA, best-corrected visual acuity; IOP, intraocular pressure; IOL, intraocular lens.

present in all patients, while after surgery a 2+ intraocular cellular reaction was present in 12/21 patients (57.1%).

Patients were treated with adalimumab alone (40 mg subcutaneously) in 12 cases, and adalimumab and methotrexate (15 mg/m^2 up to 20 mg weekly) in 9 cases. Of the latter, in 2 cases methotrexate was withheld due to gastrointestinal side effects, but a constant clinical improvement was present. The mean dose of oral prednisone was 30.4 ± 6 mg/day preoperatively, 15.2 ± 5.3 mg/day 6 months postoperatively, and 7.23 ± 5.4 mg/day at the end of the follow-up period ($p < 0.05$).

IOL was implanted in the ciliary sulcus in 13 cases (62%) and in the capsular bag in 8 cases (38%). The impossibility of implanting in the bag was due to glued sheets of the bag. Mean follow-up was 48.2 ± 5.4 (35–64) months. Mean BCVA was 0.72 ± 0.2 logMAR preoperatively, 0.28 ± 0.1 logMAR 1 month postoperatively, 0.16 ± 0.09 logMAR at 3 months, 0.25 ± 0.12 logMAR at 6 months, 0.23 ± 0.08 logMAR at 12-month visit, and 0.32 ± 0.1 logMAR at 24-month visit. The difference between the preoperative BCVA and the postoperative BCVA was statistically significant at all time points ($p < 0.05$). At month 24, BCVA was significantly lower when IOL was implanted in the ciliary sulcus rather than in the capsular bag (0.38 vs. 0.21 logMAR, respectively, $p < 0.05$).

Before surgery, IOP, gonioscopy, vertical/disc ratio, and visual field were normal in all eyes. Secondary open-angle glaucoma was observed in 13 of the 21 patients (61.9%) and was associated with goniosynechiae at gonioscopy. In all these cases IOP was >21 mmHg and glaucomatous optic disc excavation and visual field defects (superior or inferior arcuate defects, arcuate nasal scotomas) were present. Of them, 5 patients underwent trabeculectomy with mithomicin C and are still on antiglaucomatous treatment. The remaining 8 patients are on antiglaucomatous treatment with brimonidine 0.2%, timolol 0.5%, and brinzolamide 10 mg/mL. Cystoid macular edema developed in 3 cases (14.3%), papillitis in 1 case (4.8%), IOL decentration in no cases, and retrolental membrane formation in 15 cases (71%). All patients who developed retrolental membrane formation underwent a vitrectomy procedure.

Nineteen patients underwent secondary IOL implantation. Secondary implantation was performed after a mean period of 13.6 ± 0.3 (11–16) months from cataract removal. IOL was implanted in the ciliary sulcus in 11 cases (57.9%) due to glued sheets of the bag and in the capsular bag in 8 cases (42.1%). At the time of cataract extraction the mean age of patients was 12.3 ± 2.0 (9–16) years, mean duration of arthritis was 6.21 ± 4.12 months, and mean duration of uveitis was 6.54 ± 3.18 months.

Oligoarticular arthritis was present in 13 cases (68.4%) and polyarticular arthritis in 6 cases (31.6%). In 11 patients (57.9%), the arthritis was diagnosed 2.7 ± 2.1 months before the diagnosis of uveitis was made. In 7 cases (36.8%), uveitis was diagnosed 3.9 ± 2.0 months before arthritis, while in 1 case (5.3%) arthritis and uveitis were diagnosed at the same time. Thirteen children (68.4%) were antinuclear antibody positive (10/13 oligoarticular, 77%; 3/13 poliarticular, 23%). Before surgery a 1+ intraocular cellular reaction was present in all patients, while after surgery a 2+ intraocular cellular reaction was present in 7/19 patients (36.8%).

Patients were treated with adalimumab alone in 10 cases and adalimumab and methotrexate in 9 cases. The mean dose of oral prednisone was 34.5 ± 5.1 mg/day preoperatively, 15.5 ± 3.0 mg/day 6 months postoperatively, and 7.12 ± 5.8 mg/day at the end of the follow-up period ($p < 0.05$). Mean follow-up from secondary IOL implantation was 47.2 ± 6.5 (32–64) months. Mean BCVA was 0.69 ± 0.11 logMAR preoperatively, 0.31 ± 0.12 logMAR 1 month postoperatively, 0.14 ± 0.08 logMAR at 3 months, 0.21 ± 0.08 logMAR at 6 months, 0.21 ± 0.07 logMAR at 12-month visit, and 0.20 ± 0.08 logMAR at 24-month visit. The difference between the preoperative BCVA and the postoperative BCVA was statistically significant at all time points ($p < 0.05$). The difference between BCVA in the primary IOL implantation group and BCVA in the secondary IOL implantation group was significant at 2 years ($p = 0.001$). The eyes in which the IOL was implanted in the ciliary sulcus rather than in the capsular bag showed similar BCVA at baseline ($p > 0.05$) but significantly lower BCVA at month 24 (0.15 logMAR at baseline vs. 0.32 logMAR at month-24 visit, $p = 0.01$), due to formation of retrolental membranes.

Before surgery IOP, gonioscopy, vertical cup/disc ratio, and visual field were normal in all eyes. Secondary open-angle glaucoma was observed in 4 of the 19 patients (21%), and was associated with

goniosynechiae. In all these cases IOP was >21 mmHg and glaucomatous optic disc excavation and visual field defects, such as superior or inferior arcuate defects and arcuate nasal scotomas, were present. Of them, 3 patients underwent trabeculectomy with mithomicin C and are still on antiglaucomatous treatment, while the other patient is on antiglaucomatous treatment with brimonidine 0.2% and timolol 0.5%. Cystoid macular edema developed in 3 cases (20%), papillitis in no cases, IOL decentration in no cases, and retrolental membrane formation in 4 cases (21%). All patients who developed retrolental membrane formation underwent a vitrectomy procedure. Incidence of secondary glaucoma and retrolental membrane formation was significantly lower in the group that underwent secondary implantation ($p = 0.01$ and $p = 0.001$, respectively).

DISCUSSION

To our knowledge, this is the first reported comparison of outcomes after simultaneous and secondary IOL implantation after cataract removal in JIA patients. A significantly greater incidence of secondary open-angle glaucoma and retrolental membrane formation was present 48.2 months after primary IOL implantation. Retrolental membrane originates from the exudates that form a membrane behind the lens, also known as retrolental cyclitic membrane. Several authors agree that IOLs should not be routinely implanted in patients with JIA-associated uveitis, as a high rate of postoperative complications has been described, such as formation of fibrin, posterior synechiae, hypotony, macular edema, and giant cell IOL deposits.[5,18–20] However, outcomes from cataract surgery can differ depending on the etiology of the uveitis.[21] Children with JIA who have undergone cataract surgery show worse visual outcomes and a more complicated postsurgical course compared with children with uveitis secondary to other causes (i.e., idiopathic), likely due to more severe intraocular inflammation and younger age.[22,23]

A recent study by Terrada et al. on primary IOL implantation in uveitis from JIA, Behçet disease, sarcoidosis, and varicella zoster suggested that uveitis is not a contraindication for primary IOL implantation when full control of intraocular inflammation with oral steroids is obtained.[24] However, the different etiologies of uveitis considered in the aforementioned study are a limitation to consider. Grajewski et al. suggested that in JIA-associated uveitis IOL implantation may be performed when a maximum perioperative control of inflammation with intravitreal steroids is obtained.[25] In our series, secondary open-angle glaucoma was due to occlusion of the trabecular meshwork by goniosynechiae rather than to systemic side effects of oral steroids.

In our study all patients were receiving TNF-α blockers at the time of surgery. According to previous reports the intraocular inflammation should be under control for a minimum of 3 months before surgery.[13,23,25,26] TNF-α blockers have been used to treat uveitis and juvenile idiopathic arthritis, and especially uveitis associated with juvenile idiopathic arthritis in children who have failed conventional topical and second-line disease-modifying antirheumatic drug (DMARD) therapy.[27–29] Despite the utilization of a similar therapy in both groups and quiescence of uveitis at the time of surgery, secondary implantation provided better outcomes in terms of complications. According to our data, primary implantation likely increases inflammatory levels despite medical management of JIA. Secondary implantation likely allows reduction of inflammation following cataract removal before the IOL is inserted. Our results agree with data by Lundvall and Zetterstrom, who observed complications in 70% of patients with uveitis from juvenile rheumatoid arthritis after cataract extraction with primary IOL implantation and posterior capsulorhexis.[30] Again, the higher incidence of complications after primary implantation in our study could be due to the increased severity JIA-associated uveitis.

Posterior capsulorhexis and wide anterior vitrectomy were performed in all patients. A significantly greater incidence of secondary retrolental membrane formation was noted in the patients who underwent primary IOL implantation (71% versus 21%). Ben Ezra and Cohen observed retrolental membranes in 80% of eyes with JIA despite posterior capsulotomy and vitrectomy, and a second surgical intervention was required in all cases.[23] As suggested by Ben Ezra and Cohen,[23] by Terrada et al.[24], and by Jensen et al.[31], primary opening of the posterior capsule during initial surgery allows better visual acuity to be obtained. A posterior capsulotomy in the absence of vitrectomy should be avoided.[31]

In conclusion, despite the retrospective design and relatively short follow-up, our data showed that secondary postponed IOL implantation after cataract removal in children with JIA-related uveitis was associated with a significantly lower incidence of secondary glaucoma and retrolental membrane formation. While we agree that full control of the uveitis at the time of surgery is essential to obtaining good outcomes, a delay of 1 year before secondary implantation seems sufficient to limit inflammation-related complications.

DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

REFERENCES

1. Levinson JE, Wallace CA. Dismantling the pyramid. *J Rheumatol Suppl.* 1992;33:6–10. Review.
2. Ruperto N, Levinson JE, Ravelli A, et al. Long-term health outcomes and quality of life in American and Italian inception cohorts of patients with juvenile rheumatoid arthritis, I: outcome status. *J Rheumatol.* 1997;24: 945–951.
3. Kanski JJ. Juvenile arthritis and uveitis. *Surv Ophthalmol.* 1990;34:253–267.
4. Kotaniemi K, Savolainen A, Karma A, Aho K. Major review: recent advances in uveitis of juvenile idiopathic arthritis. *Surv Ophthalmol.* 2003;48:489–502.
5. Edelsten C, Lee V, Bentley CR, et al. An evaluation of baseline risk factors predicting severity in juvenile idiopathic arthritis associated uveitis and other chronic anterior uveitis in early childhood. *Br J Ophthalmol.* 2002;86: 51–56.
6. Packham JC, Hall MA. Long-term follow-up of 246 adults with juvenile idiopathic arthritis: functional outcome. *Rheumatology (Oxford).* 2002;41:1428–1435.
7. Kotaniemi K, Kautiainen H, Karma A, Aho K. Occurrence of uveitis in recently diagnosed juvenile chronic arthritis: a prospective study. *Ophthalmology* 2001;108:2071–2075.
8. Kotaniemi K, Arkela-Kautiainen M, Haapasaari J, Leirisalo-Repo M. Uveitis in young adults with juvenile idiopathic arthritis: a clinical evaluation of 123 patients. *Ann Rheum Dis.* 2005;64:871–874.
9. Grassi A, Corona F, Casellato A, et al. Prevalence and outcome of juvenile idiopathic arthritis-associated uveitis and relation to articular disease. *J Rheumatol.* 2007;34: 1139–1145.
10. Heiligenhaus A, Niewerth M, Ganser G, et al. Prevalence and complications of uveitis in juvenile idiopathic arthritis in a population-based nation-wide study in Germany: suggested modification of the current screening guidelines. *Rheumatology (Oxford).* 2007;46:1015–1019.
11. Skarin A, Elborgh R, Edlund E, Bengtsson-Stigmar E. Long-term follow-up of patients with uveitis associated with juvenile idiopathic arthritis: a cohort study. *Ocul Immunol Inflamm.* 2009;17:104–108.
12. Estafanous MFG, Lowder CY, Meisler DM, Chauhan R. Phacoemulsification cataract extraction and posterior chamber lens implantation in patients with uveitis. *Am J Ophthalmol.* 2001;131:620–625.
13. Foster CS, Barrett F. Cataract development and cataract surgery in patients with juvenile rheumatoid arthritis associated iridocyclitis. *Ophthalmology.* 1993; 100:809–817.
14. Giannini EH, Ruperto N, Ravelli A, et al. Preliminary definition of improvement in juvenile arthritis. *Arthritis Rheum.* 1997;40:1202–1209.
15. Jabs DA, Nussenblatt RB, Rosenbaum JT; Standardization of Uveitis Nomenclature (SUN) Working Group. Standardization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop. *Am J Ophthalmol.* 2005;140:509–516.
16. Merayo-Lloves J, Power WJ, Rodriguez A, et al. Secondary glaucoma in patients with uveitis. *Ophthalmologica.* 1999; 213:300–304.
17. Chylack Jr LT, Wolfe JK, Singer DM, et al; for the Longitudinal Study of Cataract Study Group. The Lens Opacities Classification System III. *Arch Ophthalmol.* 1993; 111:831–836.
18. Kanski JJ. Lensectomy for complicated cataract in juvenile chronic iridocyclitis. *Br J Ophthalmol.* 1992;76:72–75.
19. Probst LE, Holland EJ. Intraocular lens implantation in patients with juvenile rheumatoid arthritis. *Am J Ophthalmol.* 1996;122:161–170.
20. Okhravi N, Towler HM, Lightman SL. Cataract surgery in patients with uveitis. *Eye (Lond).* 2000;14 (Pt 5):689–690.
21. Van Gelder RN, Leveque TK. Cataract surgery in the setting of uveitis. *Curr Opin Ophthalmol.* 2009;20:42-45.
22. Quinones K, Cervantes-Castaneda RA, Hynes AY, et al. Outcomes of cataract surgery in children with chronic uveitis. *J Cataract Refract Surg.* 2009;35:725–731.
23. Ben Ezra D, Cohen E. Cataract surgery in children with chronic uveitis. *Ophthalmology* 2000;107:1255–1260.
24. Terrada C, Julian K, Cassoux N, et al. Cataract surgery with primary intraocular lens implantation in children with uveitis: long-term outcomes. *J Cataract Refract Surg.* 2011; 37:1977–1983.
25. Grajewski RS, Zurek-Imhoff B, Roesel M, et al. Favourable outcome after cataract surgery with IOL implantation in uveitis associated with juvenile idiopathic arthritis. *Acta Ophthalmol.* 2012;90:657–662.
26. Acevedo S, Quinones K, Rao V, et al. Cataract surgery in children with juvenile idiopathic arthritis associated uveitis. *Int Ophthalmol Clin.* 2008;48:1–7.
27. Smith JR, Levinson RD, Holland GN, et al. Differential efficacy of tumor necrosis factor inhibition in the management of inflammatory eye disease and associated rheumatic disease. *Arthritis Rheum.* 2001;45:252–257.
28. Lovell D. Biological agents for the treatment of juvenile rheumatoid arthritis: current status. *Paediatric Drugs.* 2004; 6:137–146.
29. Biester S, Deuter C, Michels H, et al. Adalimumab in the therapy of uveitis in childhood. *Br J Ophthalmol.* 2007;91: 319–324.
30. Lundvall A, Zetterstrom C. Cataract extraction and intraocular lens implantation in children with uveitis. *Br J Ophthalmol.* 2000; 84:791–793.
31. Jensen AA, Basti S, Greenwald MJ, Mets MB. When may the posterior capsule be preserved in pediatric intraocular lens surgery? *Ophthalmology* 2002;109:324–327.