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LASER FLARE PHOTOMETRIC EVALUATION OF CATARACT SURGERY ON INTRAOCULAR INFLAMMATION IN UVEITIC EYES

ÜVEİTLİ GÖZLERDE KATARAKT CERRAHİSİNİN İNTRAOKÜLER İNFLAMASYONA ETKİSİNİN LASER FLARE FOTOMETRE İLE DEĞERLENDİRİLMESİ

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ABSTRACT
Objective: To evaluate the effect of phacoemulsification with intraocular lens (IOL) implantation on intraocular inflammation using laser flare photometer in eyes with uveitis.
Materials and Methods: Sixty-six eyes of 55 consecutive patients followed-up at Istanbul University, Istanbul School of Medicine, Department of Ophthalmology, Uveitis Service undergoing phacoemulsification with posterior chamber intraocular lens implantation between December 2009 and April 2013 were included in this retrospective study. Clinical records of patients were analyzed for demographic data, pre-operative and post-operative best-corrected visual acuity (BCVA), intraocular pressure, and quantitative measurement of inflammation with laser flare photometry. Baseline evaluations were performed 1 day before surgery and follow-up examinations took place at 1, 7, 30, and 90 days after surgery. Main outcome measures were BCVA and quantitative measurement of intraocular inflammation with laser flare photometry.
Results: Best-corrected visual acuity improved in 60 eyes and visual loss did not occur in any eye. Median intraocular flare value the day before surgery was 8.2 (range: 3.1-82.2) photons/ms. Postoperatively, median flare value initially increased to 16.8 (range: 0-158) photons/ms on day 1 which was a statistically significant increase compared to preoperative values. Thereafter decreased to 10.40 (range: 0-110) photons/ms on day 7, 11.25 (range: 4.4-145) photons/ms on day 30, and 8.1 (range: 0-84.6) photons/ms on day 90. There was no statistically significant difference between preoperative values and day 90.
Conclusion: In uveitic eyes with well-controlled ocular inflammation before surgery, phacoemulsification with IOL implantation appears safe and effective as assessed by changes in the BCVA and laser flare photometry, an objective method to measure intraocular inflammation.
Keywords: Phacoemulsification; uveitis; inflammation; aqueous flare

ÖZET
Amaç: Kronik üveiti olan gözlerde fakoemülsifikasyon ve intraoküler lens implantasyonunun intraoküler inflamasyon üzerine etkisini lazer flare fotometre ölçümü ile değerlendirmek.
Gereç ve Yöntem: Aralık 2009-Nisan 2013 tarihleri arasında İstanbul Üniversitesi, İstanbul Tıp Fakültesi, Göz hastalıkları Anabilim Dalı, Uvea ve İntraoküler İnflamasyon Departmanında takip edilen 55 üveit hastasının fakoemülsifikasyon ve arka kamara intraoküler lens implantasyonu uygulanan 66 gözü retrospektif olarak değerlendirildi. Olguların dosyaları demografik veriler, preoperatif ve postoperatif en iyi düzeltilmiş görme keskinliği, göz içi basıncı ve lazer flare fotometre ile kantitatif inflamasyon ölçümü açısından incelendi. Cerrahiden bir gün önceki bulgular bazal değerlendirme olarak ele alındı ve takipte cerrahiden 1, 7, 30 ve 90 gün sonra yapılan muayene bulguları değerlendirildi. Çalışmanın sonuç kriterleri en iyi düzeltilmiş görme keskinliği ve lazer flare fotometre ile kantitatif inflamasyon ölçümüdür.
Bulgular: Düzeltilmiş görme keskinliği 60 gözde artış gösterirken hiçbir gözde görme kaybı gelişmedi. Cerrahi öncesi ortanca flare değeri 8.2 (aralık: 3.1-82.2) foton/ms idi. Postoperatif dönemde ortanca flare değeri 1.günde 16.8 (aralık: 0-158) foton/ms düzeyine yükseldi ve bu artış istatiksel olarak anlamlı idi. Postoperatif 7.günde ortanca flare 10.40 (aralık: 0-110) foton/ms değerine inerken 30. ve 90. günlerde sırasıyla 11.25 (aralık: 4.4-145) foton/ms ve 8.1 (aralık: 0-

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84.6) foton/ms değerlerinde idi. Cerrahi öncesi ile postoperatif 90. günlerde istatistiksel olarak anlamlı fark saptanmadı.
Sonuç: İntraoküler inflamasyon objektif değerlendirmesinde kullanılan lazer flare fotometre ölçümü ve görme keskinliğinde gözlenen sonuçlara göre oküler inflamasyon cerrahi öncesi kontrol altına alınır ise intraoküler lens implantasyonu ile fakoemülsifikasyon cerrahisi üveitli gözlerde güvenli ve etkili bir yöntem olduğu gösterilmektedir..
Anahtar Kelimeler: Fakoemülsifikasyon; üveit; inflamasyon; aköz flare

INTRODUCTION

Cataract formation is a common complication of chronic uveitis due to intraocular inflammation per se, corticosteroid usage or both (1). Uveitic cataract surgery is challenging because of band keratopathy, posterior synechiae, pupillary membranes, small pupils, iris fragility, unusual anterior capsules, and possibility of intense post-operative inflammation (2). However meticulous perioperative control of inflammation together with the advances in surgical methods and materials have led to favorable outcomes. Still visual outcome can be unpredictable due to pre-existing damages in posterior segment, ongoing inflammation, and post-operative exacerbation. Successful visual outcome in uveitic cataract surgery depends upon several key factors including careful patient selection, establishing the etiological diagnosis of uveitis, thorough eye examination, control of inflammation before and after the surgery, meticulous surgery, and postoperative control of complications (3).

Inflammation in the anterior segment of the eye causes breakdown of the blood–aqueous barrier and results in an increase in the number of cells and the protein concentration of the aqueous humor. Examination of the aqueous humor by slit-lamp biomicroscopy is the primary method used to evaluate the severity of anterior segment inflammation. However, slit-lamp microscopy grading of cells and flare is subjective and relies heavily on the experience of the examiner and is subject to considerable inter- and intra-observer variations. Laser flare photometry (LFP) provides a noninvasive, objective, and quantitative measure of aqueous humor flare (4). Increased protein content of the aqueous humor causes scattering of light and the LFP uses this principle: a laser beam of light scans a measurement window projected into the anterior chamber and light scattered by protein particles in the aqueous humor is detected by a photomultiplier and expressed in photon counts per millisecond (ph/ms). In healthy young adults, normal aqueous flare values are in the range of 2.5 to 4.5 ph/ms and increases minimally with age (5).

The aim of this study was to evaluate the impact of cataract surgery on intraocular inflammation in uveitic eyes objectively using LFP in patients with different diagnoses of uveitis.

MATERIAL AND METHOD

Sixty-six eyes of 55 consecutive patients followed-up at Istanbul University, Istanbul School of Medicine, Department of Ophthalmology, Uveitis Service undergoing phacoemulsification with posterior chamber intraocular lens implantation from December 2009 to April 2013 were included in this retrospective study. The research followed the Tenets of the Declaration of Helsinki.

Clinical records of patients were analyzed for gender, age at surgery, anatomical classification and duration of uveitis, associated systemic disease, surgical details, pre-operative and post-operative best-corrected visual acuity (BCVA), intraocular pressure (IOP), presence of posterior segment findings on indirect ophthalmoscopy, quantitative measurement of inflammation with laser flare photometry (KOWAFC-2000; KowaCo Ltd, Tokyo, Japan), and visually limiting postoperative pathologies. Baseline evaluations were performed 1 day before surgery and follow-up examinations took place at 1, 7, 30 and 90 days after the surgery. Anterior chamber laser flare measurement is a part of routine ophthalmic examination in uveitis patients in our clinic. Flare is measured about 30 minutes after pupil dilatation by 1 drop of tropicamide 1% and phenylephrine 2.5%.

Anatomical classification of uveitis was made according to Standardization of Uveitis Nomenclature (SUN) criteria (6). Diagnostic evaluation of associated systemic disease included a full medical history, clinical evaluation, and laboratory investigations. Cataract surgery was decided when decreased vision was considered to be due to cataract formation or when lens opacity limited adequate visualization of the posterior segment. Preoperative uveitis activity was determined as described by the SUN Working Group and as in Foster and Vitale's Diagnosis and Treatment of Uveitis (6,7). Inactive anterior uveitis was defined as rare cells or less. Inactivity of inflammation of the posterior segment of the eye was documented by the absence of retinal vasculitis, retinitis, choroiditis, cystoid macular edema (CME) and papillitis. All eyes were quiet under maximum anti-inflammatory therapy.

Surgical Technique

All eyes underwent routine clear corneal phacoemulsification with posterior chamber hydrophobic acrylic IOL (AcrySof) implantation under topical and/or peribulbar anesthesia. Pediatric patients underwent surgery under general anesthesia. Pupillary membranes were dissected when present and pupils were enlarged with dispersive ophthalmic viscoelastic devices and pupillary stretching. At completion of surgery anterior chamber was irrigated with 0.1mL triamcinolone suspension followed by 1 mg/mL cefuroxime. Two eyes did not receive triamcinolone suspension because one had a diagnosis of acute retinal necrosis and one had glaucoma.

Post-operative treatment

All patients received topical antibiotics, topical prednisolone acetate, topical non-steroidal anti-inflammatory drugs for 4 weeks, starting on the first

postoperative day. Cycloplegic and mydriatic agents were used when necessary.

Statistical Analysis

Statistical analyses were conducted using IBM SPSS 21 and $p<0.05$ was considered to be statistically significant. Data distribution was analyzed by the Kolmogorov-Smirnov test. The significance of changes across the five time points (preoperative, postoperative days 1, 7, 30, and 90) for intraocular flare values, IOP values, and BCVA were assessed using Shapiro Wilk test for data with normal distribution, and Friedman and Friedman post-hoc tests for data that were not normally distributed.

RESULTS

Twenty-seven male and 28 female uveitis patients were included in this study. Table 1 summarizes demographic data. Pupillary abnormalities including posterior synechiae, inflammatory membrane formation and miosis were found in 11 (17%) eyes and 3 patients had a history of prior pars plana vitrectomy surgery. Table 2 shows data on associated systemic diseases.

Table 1. Demographic data

Patient Characteristics (55 patients)	
Number of eyes	66
Male : Female	27:28
Mean age at surgery (years)	43.43±16.06 (7-71)
Mean duration uveitis (years)	7.66 ± 6.13 (2-35)
Post syn, pup memb, miosis, (n)	11
History of Pars plana vitrectomy (n)	3
Type of uveitis, (n)	
Anterior	19
Intermediate	8
Posterior	4
Panuveitis	22

Table 2. Table showing data of associated diseases.

Associated Disease	Number of Patients
Behçet Disease	16
Idiopathic Anterior Uveitis	6
Pars Planitis	4
Fuchs Uveitis Syndrome	9
Sclerouveitis	2
Ankylosing Spondilitis	2
Vogt Koyanagi Harada disease	2
Multifocal Choroiditis	2
Intermediate Uveitis	4
Acute Retinal Necrosis	1
Juvenile Idiopathic Arthritis	1
Idiopathic Panuveitis	2
Sympathetic Ophthalmia	1
Sarcoidosis	1
Idiopathic retinal vasculitis	1
Cytomegalovirus Anterior Uveitis	1

Best-corrected visual acuity showed improvement in 60 eyes. Best-corrected visual acuity did not improve in 6 eyes and the diagnoses of these patients were idiopathic posterior and intermediate uveitis including pars planitis, multiple sclerosis, ankylosing spondylitis, and Behçet disease. Causes of poor vision in 13 eyes were optic atrophy, macular atrophy, cystoid macular edema, epiretinal membrane, macular scar, amblyopia, and hypotony. Vision loss did not occur in any eye. Figure 1 shows the change in mean BCVA before surgery and at postoperative days 1, 7, 30, and 90. Compared to preoperative values patients showed improvement in BCVA starting from postoperative day 1 and statistically significant improvement was observed after day 7 (Table 3).

Table 3. Comparison of best-corrected visual acuity in uveitic eyes before cataract surgery and at postoperative days 1, 7, 30, and 90.

Time	Mean±Standard Deviation	Median	Minimum	Maximum	p	post-hoc
Preoperative n=66	0.22±0.17	0.20	0.01	0.60		
Postoperative day 1 n=66	0.39±0.28	0.40	0.01	1.00		Preop vs Postop day 7 Preop vs Postop day 30 Preop vs Postop day 90
Postoperative day 7 n=66	0.54±0.32	0.60	0.01	1.00	<0,001	Postop day 1 vs day 7 Postop day 1 vs day 30
Postoperative day 30 n=66	0.67±0.35	0.80	0.01	1.00		Postop day 7 vs day 30 Postop day 7 vs day 90
Postoperative day 90 n=66	0.69±0.35	0.80	0.01	1.00		

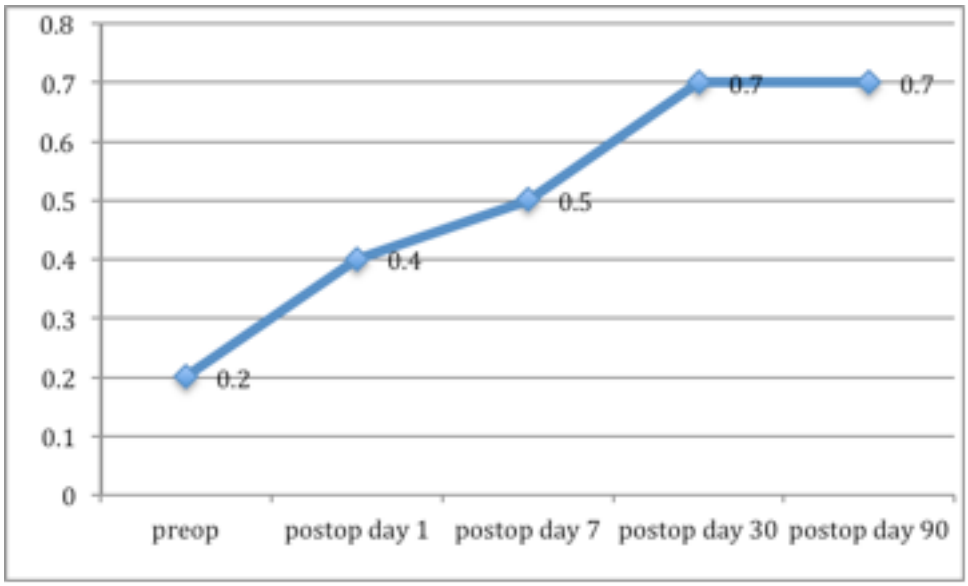

Figure 1. Line chart showing the change in mean best-corrected visual acuity before surgery and at postoperative days 1, 7, 30 and 90.

Preoperatively, uveitis was inactive in all patients, which was also confirmed by laser flare meter. Median intraocular flare value the day before surgery was 8.2 (range: 3.1-82.2) ph/ms. Postoperatively, median flare value initially increased to 16.8 (range: 0-158) ph/ms on day 1 which was a statistically significant increase compared to preoperative values. Thereafter decreased to 10.4 (range: 0-110) ph/ms on day 7, 11.25 (range: 4.4-145) ph/ms on day 30, and 8.1 (range: 0-84.6) ph/ms on day 90 (Figure 2). There was no statistically significant difference between preoperative values and day 90 (Table 4). All the eyes except 2 received intracameral 0.1mL triamcinolone injection at the end of the surgery. Six patients received intravenous methylprednisolone 20-60 mg per-operatively. Systemic methyl-prednisolone dosage was increased from with an

average of 8 mg to 17 mg in 8 patients postoperatively which was then tapered to preoperative dosage in 30 days.

Nine eyes had been receiving anti-glaucoma medication before surgery. Increase in post-op IOP above 21mmHg was noted in 10 eyes that responded well to topical anti-glaucomatous treatment. Change in mean IOP over time is shown in Figure 3 and Table 5.

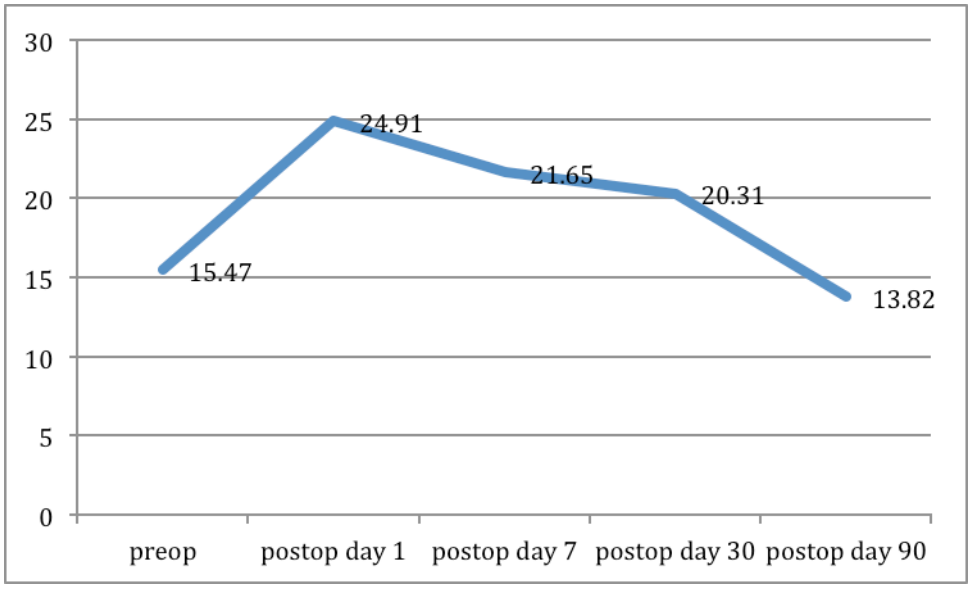

Figure 2. Line chart showing mean anterior chamber flare readings (photon/ms) by laser flare photometry before surgery and at postoperative days 1, 7, 30 and 90.

Table 4. Comparison of anterior chamber flare readings (photon/ms) by laser flare photometry in uveitic eyes before cataract surgery and at postoperative days 1, 7, 30 and 90.

Time	Mean± Standard Deviation	Median	Minimum	Maximum	p	post-hoc
Preoperative n=63	15.47±16.53	8.20	3.10	82.20		
Postoperative day 1 n=65	24.91±27.62	16.80	0.00	158.00		Preop vs Postop day 1
Postoperative day 7 n=65	21.65±25.93	10.40	0.00	110.00		Postop day 1 vs day 30
Postoperative day 30 n=56	20.31±30.21	11.25	4.40	145.00	<0,001	Postop day 1 vs day 90
Postopoperative day 90 n=65	13.82±15.37	8.10	0.00	84.60		Postop day 7 vs day 90
						Postop day 30 vs day90

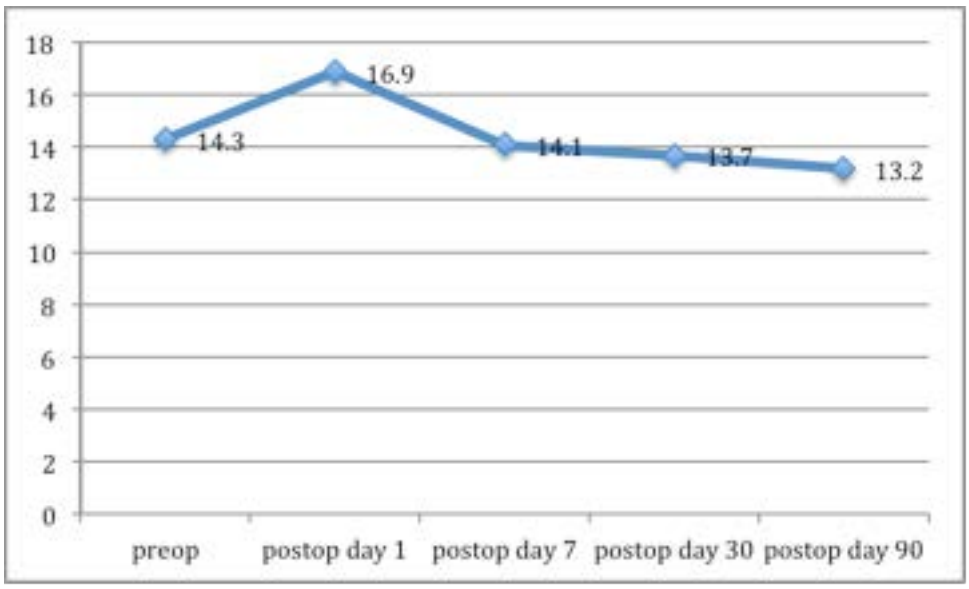

Figure 3. Line chart showing changes in mean intraocular pressure (mmHg) before surgery and at postoperative days 1, 7, 30 and 90..

Table 5. Comparison of intraocular pressure (mmHg) in uveitic eyes before cataract surgery and at postoperative days 1, 7, 30 and 90.

Time	Mean± Standard Deviation	Median	Minimum	Maximum	p	post-hoc
Preoperative n=66	14.34±2.61	14.00	7.00	19.00		
Postoperative day 1 n=66	16.90±5.90	15.00	5.00	33.00		
Postoperative day 7 n=66	14.02±4.23	14.00	7.00	34.00	<0,001	Postop day 1 vs day 7 Postop day 1 vs day 30 Postop day 1 vs day 90
Postoperative day 30 n=66	13.66±2.64	14.00	7.00	19.00		
Postopoperative day 90 n=66	13.19±2.32	14.00	3.00	18.00		

DISCUSSION

The results of this study in patients with a wide range of uveitis etiology with good preoperative control show that phacoemulsification with IOL implantation using current technology and management modalities is safe and efficient in terms of postoperative intraocular inflammation as measured by LFP.

Important prognostic factors for successful visual outcome are etiology of uveitis, visual potential of the eye and appropriate timing of the surgery. Preoperative control of inflammation is critical in the management of patients with uveitic cataracts for the achievement of a good visual outcome (8-10). Measurement of intraocular inflammation with slit-lamp examination remains subjective with considerable intra- and inter-observer variations, however quantitative evaluation of inflammation is essential in deciding the appropriate timing of the surgery and during follow-up. Laser flare

photometry is a sensitive, non-invasive instrument that allows detection of subclinical alterations in the blood-ocular barriers, identifying subtle pathological changes that are otherwise impossible to detect (4). Despite the remission of inflammation before cataract surgery, most uveitic eyes have higher flare values before surgery than normal eyes with cataract due to primary blood aqueous barrier damage (11). Therefore a normative value should be assessed for each patient and the timing of cataract surgery regarding the level of inflammation should be made in patient basis. In our study the eyes undergoing surgery were relatively quiet however still preoperative flare values of the patients were higher than normative values due to the breakdown of the blood aqueous barrier in uveitic eyes. The results of this study show that further breakdown of the blood aqueous barrier in uveitic eyes following phacoemulsification surgery is reversible. In our study aqueous flare was highest on the first postoperative day, declined rapidly in the first week and returned to preoperative levels by month 3 as shown before in normal eyes (12).

Besides careful pre-operative management, cataract surgery in uveitic eyes also requires meticulous surgical technique and aggressive post-operative treatment. Eyes with anterior uveitis require management of pupil abnormalities including synechiae, miosis and iris fragility, which also may increase aqueous flare. The surgical technique may need to be modified according to these factors. Cataract extraction in eyes with uveitis also carries an increased risk for postoperative exacerbation of inflammation and macular edema (13). Therefore, at the end of the surgery intracameral instillation of triamcinolone acetonide is recommended for an efficient control of post-operative inflammation. It has been shown in previous studies that intracameral triamcinolone injection in combination with postoperative low-dose topical steroids is effective in preventing fibrin formation after cataract surgery in patients with juvenile idiopathic artritis (14). However, in the present study to minimalize postoperative inflammation, systemic steroid dosage of all the pediatric uveitis patients undergoing surgery was also increased postoperatively.

Still successful visual outcome does not depend only on surgery itself. Eyes with posterior uveitis require careful monitoring of the posterior segment before and after the surgery to establish the degree of prior permanent structural damage that uveitis may have caused such as retinal detachment, optic atrophy, vitreous opacity, cystoid macular edema, epiretinal membrane, and macular scar. These concurrent pathologies may limit the visual outcome therefore the patient should be informed before surgery if there is a guarded prognosis (15). In the present study although majority of the eyes showed improvement in BCVA, causes of poor vision were optic atrophy, macular atrophy, cystoid macular edema, epiretinal membrane, macular scar, amblyopia and hypotony due to probable complications of uveitis. Still most eyes in this study benefited from surgery, showed improved visual acuity and did not demonstrate intense post-operative intraocular inflammation.

Our study suffers from certain limitations. These include its retrospective and uncontrolled nature with potential bias factors. Since the study included uveitic eyes with a large diagnostic range, the study group was also not homogenous. However, this study provides quantitative data on change in aqueous flare values after cataract surgery in uveitic eyes.

CONCLUSION

Phacoemulsification with IOL implantation appears to have favorable visual effect on eyes with uveitis where meticulous control of preoperative intraocular inflammation is achieved. Laser flare photometric measurements showed that there is a significant increase in LFP at the first postoperative day that decreases to preoperative levels by postoperative day 90. Laser flare photometry may be a useful tool to assess for timing of cataract surgery and objective assessment of postoperative intraocular inflammation.

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