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CATARACT SURGERY IN PATIENTS WITH HISTORY OF UVEITIS - MEDIUM TERM FUNCTIONAL OUTCOMES

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CATARACT SURGERY IN PATIENTS WITH HISTORY OF UVEITIS- MEDIUM TERM FUNCTIONAL OUTCOMES (Abstract). **Aim**: Evaluating the functional outcomes in patients with history of uveitis who previously underwent cataract surgery during 2009-2019, analysis of the best postoperative visual acuity and IOP after first day, one month, 3 months and last postoperative. **Material and methods:** Comparative/retrospective study which included cataract surgery patients with a history of uveitis evaluated between January 2009 and December 2019 in Iaşi, Department of Ophthalmology, "Sf. Spiridon" County Clinical Emergency Hospital. The study included a number of 102 eyes divided into two groups: 59 eyes from 51 patients (25 women and 26 men) the cataract and uveitis group (study group) and 43 cataract eyes (control group). All patients had cataract surgery performed by phacoemulsification and IOL-PC implantation, while the pre- and postoperative evaluation was performed according to a standardized protocol. The database was built in the *EXCEL* program and was statistically processed with the *SPSS 18.0* program. Postoperative follow-up was performed at 1 day, 1 month, 3 months and last postoperative follow up (six month). **Results:** The average age of patients of the 2 groups was 65 years. In all cases, preoperative topical steroid anti-inflammatory treatment was administered for 1 week and postoperatively, for 6 weeks. General anti-inflammatory steroids (CSR) were administered preoperatively and postoperatively in 9 patients with intermediate or posterior uveitis for 8 weeks. In two cases a capsular tension ring was used to stabilize the bag. One case required ECCE + placement of IOL in the sulcus. Only one case required IOL explantation due to severe inflammation. Among the postoperative complications, the inflammatory glaucoma and recurrent uveitis predominated. **Conclusions:** Cataract surgery with IOL implantation resulted in improved postoperative visual acuity in patients with cataract and uveitis, which was maintained at the last follow-up. In the immediate postoperative period, both groups had similar functional results. **Keywords:** CATARACT SURGERY, UVEITIS, PHACOEMULSIFICATION, CYSTOID MACULAR EDEMA, INTRAOCULAR IMPLANT.

Cataract is a major cause of vision loss in patients with uveitis, up to 40% of cases being mainly due to cataracts. Frequent complication of uveitis occurs on the one

hand due to inflammation but also due to chronic treatment with corticosteroids (CSR). The incidence of cataracts in uveitis varies from 57% in pars planitis to 78% in Fuchs' heterochromic iridocyclitis. Cataract surgery in uveitic eyes is difficult and can have many unexpected intraoperative complications. This represents a challenge for the surgeon due to the particular existing situations, namely: small pupils, posterior iris synechiae, the presence of pupillary membranes, fibrous anterior capsule (1, 2). Until the advent of corticosteroids in the early 1960s, eye inflammation was often impossible to be controlled, and articles discussing the results of cataract extraction in swollen eyes reported a high incidence of severe complications (3). In many cases, complications resulted in marked reduction of vision or even loss of the eye. Amit K Reddy *et al.* in a study that included 3,013 eyes from 2,019 patients, found a low incidence (2%) of persistent postoperative uveitis, a 29% incidence of postoperative macular edema and no case of severe granulomatous uveitis. In general, postoperative uveitis is due to the presence of inflammation at the time of surgery, cortical debris after cataract surgery and intraoperative manipulation of the iris (retractors, stretching, sphincterotomies (4). More recent publications have reported a considerable decrease in the incidence of intraoperative and postoperative complications during cataract extraction in patients with uveitis. On the one hand, this is due to a very good control of preoperative inflammation and on the other hand, to the evolution of microsurgical techniques in recent years (4, 5, 6).

MATERIALS AND METHODS

It is a retrospective study that included cataract patients with a history of uveitis evaluated between January 2009 and December 2019 in the Department of Ophthalmology, from "Sf. Spiridon" County Clinical Emergency Hospital, Iasi. The study included a number of 102 eyes divided into two groups: 59 eyes from 51 patients (25 women and 26 men) the cataract and uveitis group (study group) and 43 cataract eyes (control group). Inclusion criteria for the study group were patients with uveitis who underwent cataract surgery. Presence of uveitis had to be confirmed prior surgery. There had to be at least three months with no inflammation in the absence of treatment before cataract surgery. Exclusion criteria: absence of associated uveitis; eyes with active inflammation or under corticosteroid treatment. Patients scheduled for cataract surgery had their surgery planned in advance. The surgery was performed under topical or parabulbar anesthesia. All patients underwent cataract surgery by phacoemulsification and IOL-PC implantation, the pre- and postoperative evaluation was performed according to a standardized protocol. In all cases, in the uveitis group, topical steroid and non-steroidal anti-inflammatory drugs (NSAIDs) were administered preoperative for 1 week and postoperative for 6 weeks; in some selected cases systemic anti-inflammatory corticosteroids were administered. Postoperative follow-up was performed at 1 day, 1 month, 3 months and last control after cataract surgery. The visual acuity was measured with the Snellen optotype, and the IOP was measured by Goldmann applanation tonometry (GAT); slit lamp evaluation of the anterior segment and posterior segment with the Volk 78D lens were also performed; OCT examinations were performed at Oftaprof Clinic

using Zeiss Cirrus HD-OCT to detect cystoid macular edema (CME).

Ethical Approval

During the study, the principles of the Helsinki Declaration were observed. Patients have signed an informed consent, which was attached to the observation sheets.

Statistical Analysis

The database was created in the *EXCEL* program and was statistically processed with the *SPSS 18.0* software.

RESULTS

102 eyes were divided into two groups: the study group (59 eyes from 51 patients) with cataract and uveitis and the control group (43 eyes) with cataract only.

Distribution of patients by study groups. Statistical analysis by age groups highlights the following aspects :

The mean age of patients with cataracts and uveitis (group I) was significantly lower than that of patients with cataracts alone (group II) (57.31 *vs.* 70.12 years).

- the highest frequency of patients with cataract and uveitis is found in the 60-69 age group (25.4%) and 70-79 years (41.9%)

- the incidence peak is noted in the 60-69 years (25.4%) in patients with cataract;

The average age of patients was 57.31 ± 16.30 years in those with uveitis and 70.11 +/- 11.37 in the control group, average of the groups being 65 years (fig. 1). In all cases, in the uveitis group, topical steroid anti-inflammatory and non-steroidal anti-inflammatory drugs (NSAID) were administered preoperative for 1 week and postoperative for 6 weeks, respectively. Systemic anti-inflammatory corticosteroids were administered preoperative and postoperative in 9 patients with intermediate or posterior uveitis for 8 weeks. In most cases the IOL was positioned in the capsular bag. In two cases capsular tension rings were used to stabilize the bag. One case required extracapsular extraction + placement of IOL in the sulcus. Phaco-trabeculectomy combined surgery was performed in 2 eyes. Only one case required IOL explantation due to severe inflammation. The maneuvers performed in case of intraoperative complications were: synechiolysis (in 17 eyes, 50.8%), tension ring implantation (2 eyes), small pupil requiring iris retractors, intracameral phenylephrine (mezatone) (14 eyes) and anterior vitrectomy (2 eyes) (fig. 2, tab. I). Posterior segment complications included: recurrent uveitis (23 eyes, 39%) at 3 months, inflammatory glaucoma (6 eyes, 11.9%) at 1 year, cystoid macular edema (4 eyes, 11.9%) at 6 months and opacification of the posterior capsule (4 eyes, 10.2%) at one year (fig. 3, tab. II).

In the first study group most uveitis was idiopathic (80%), followed by ankylosing spondylitis in proportion of 7.5% and other etiologies in smaller and equal proportions (sarcoidosis, TB, juvenile idiopathic arthritis, Fuchs' heterochromic iridocyclitis, etc.) (fig. 4).

In the first group (cataracts and uveitis) visual acuity varied preoperatively from 0.005 to 0.50; while at the last follow up the visual acuity ranged from 0.004 to 1.0. The mean level increased significantly at 1 day postoperatively by 145% ($p = 0.001$) and still by approximately 34% at 1 month postoperatively ($p = 0.001$). Patients gained on average 3 lines of visual acuity (fig. 5.) The mean intraocular pressure was 15.97 +/- 4.6 mmHg (SD) preoperatively, on the first postoperative day it was 16.8 +/- 5.02 mmHg (SD), and 16.12 +/- 3.89 mmHg (SD) at one month. IOP decreases at 1

month postoperatively by 4% (p = 0.520) and after 3 months the decrease in intraocular pressure from one moment to another was by about 8% (p = 0.146). The IOP changes were not statistically significant (fig. 6). In patients treated with topical steroids, the mean level of postoperative visual acuity was slightly lower (0.37 *vs.* 0.45; p = 0.477), while postoperative IOP was slightly higher (15.58 *vs.* 14.43; p = 0.526). The correlation between postoperative visual acuity and the number of anti-inflammatory drugs was direct, reduced in intensity (r = +0.196; p = 0.138), but statistically insignificant. Severity of postoperative inflammation obviously leads to the use of a higher number of anti-inflammatory drugs (postoperative visual acuity and the period of administration of anti-inflammatory drugs were apparently parametrically independent r = +0.094; p = 0.477).

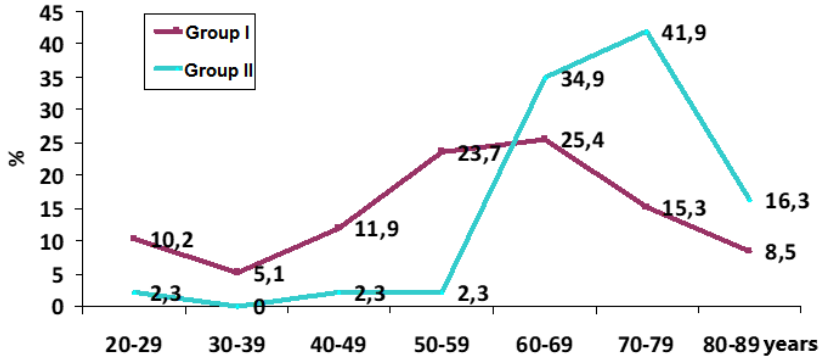


Fig. 1. Patients distribution by age group.
First study group (cataracts and uveitis) *vs.* second study group (only cataracts)

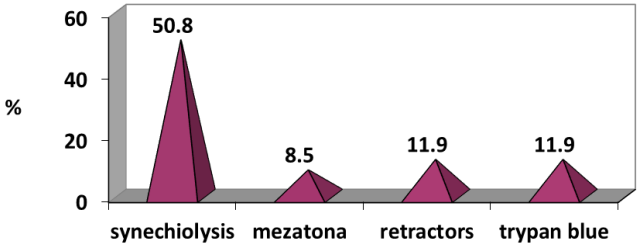


Fig. 2. Maneuvers in case of intraoperative complications

TABLE I

Maneuvers in case of intraoperative complications

Maneuvers in case of intraoperative complications	Synechiolysis	Tension ring implantation	Small pupil Iris retractors mezatona	Trypan blue
Eyes numbers	17	2	14	14

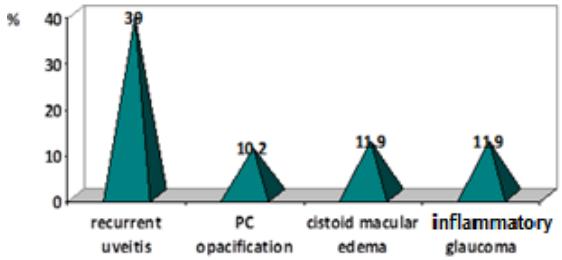


Fig. 3. Postoperative complications in the study group.

TABLE II

Postoperative complications in the study group.
CME- cystoid macular edema, PCO - posterior capsule opacification

Postoperative complications	Inflammatory Glaucoma	CME	PCO	Recurrent uveitis
Eyes numbers	6	4	4	23
Interval	1 year	6 months	1 year	3 months

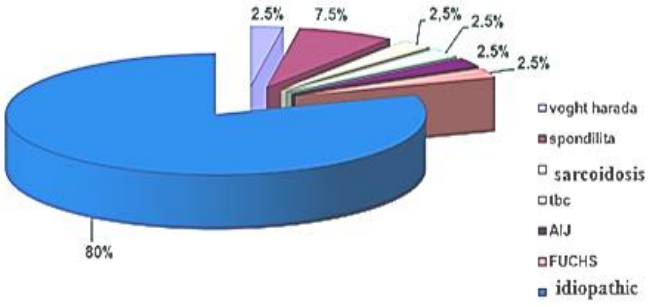


Fig. 4. Distribution of cases according to etiology of uveitis.
JIA- Juvenile Idiopathic Arthritis, TB - Pulmonary Tuberculosis

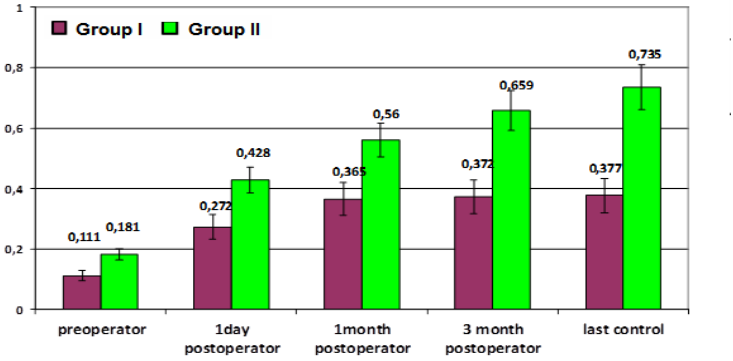


Fig. 5. Evolution of the mean level of visual acuity on study groups
The last control period (six month)

In the cataract control group, visual acuity varied preoperatively from 0.004 to 0.50; whereas at the last follow up, this ranged from 0.10 to 1.0, being significantly higher than that recorded in patients with uveitis (p = 0.001). The average level of visual acuity increased significantly at 1 day postoperatively by 136% (p = 0.001), an approximately extra 31% at 1 month postoperatively (p = 0.001), while after 3 months the visual acuity increased from one follow-up to another by 11-18% (p <0.001). Patients gained on average 5 lines of visual acuity (fig. 6). There is a statistically significant difference in final postoperative visual acuity between the two groups (p = <0.001).

The mean intraocular pressure was 15.88 +/- 3.68 mmHg (SD) preoperatively, the first postoperative day was 16.44 +/- 3.49 mmHg (SD), and at 1 month it was 15.05 +/- 3.49 mmHg (SD) (p <0.039) (fig. 6).

In all cases, in the uveitis group, topical steroid and non-steroidal anti-inflammatory drugs (NSAIDs) were administered preoperative for 1 week and postoperative for 6 weeks, in some selected cases systemic anti-inflammatory corticosteroids were administered.

There was no correlation in the uveitis cases between visual acuity and inflammation-free time interval (fig. 7).

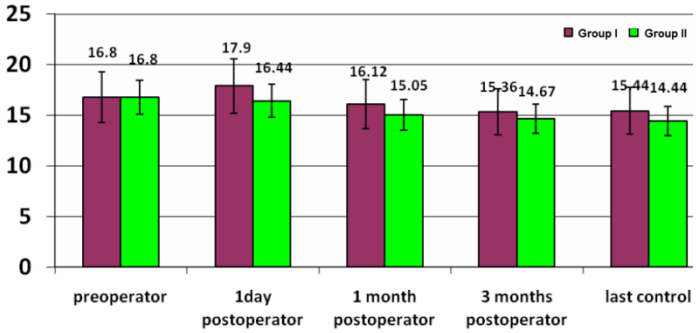


Fig. 6. Evolution of the mean level of intraocular pressure on study groups

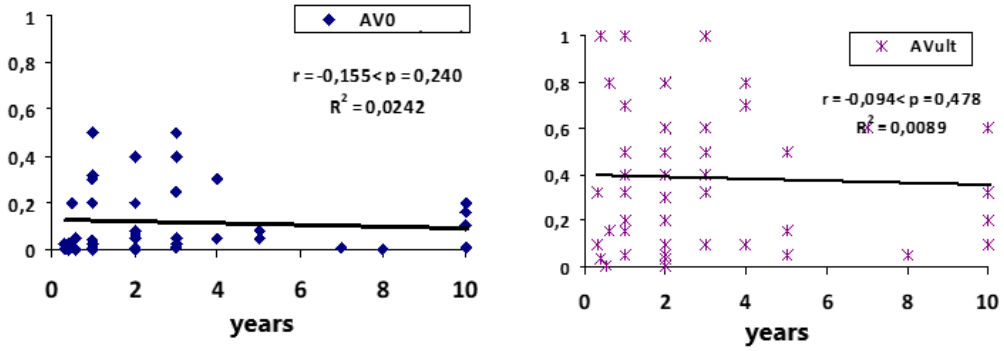


Fig. 7. Visual acuity and inflammation-free time interval correlation

There was no statistical significance between IOP and inflammation-free time interval (fig. 8).

In patients with synechiolysis, visual acuity significantly increased from 0.14 to 0.33 (p = 0.05), and intraocular pressure dropped significantly from 18.2 to 14.9 mmHg (p = 0.05). In patients with recurrent uveitis, visual acuity increased significantly from 0.09 to 0.33 (p = 0.05), and intraocular pressure dropped slightly from 17.3 to 16.65 mmHg (p = 0.623) (fig. 9).

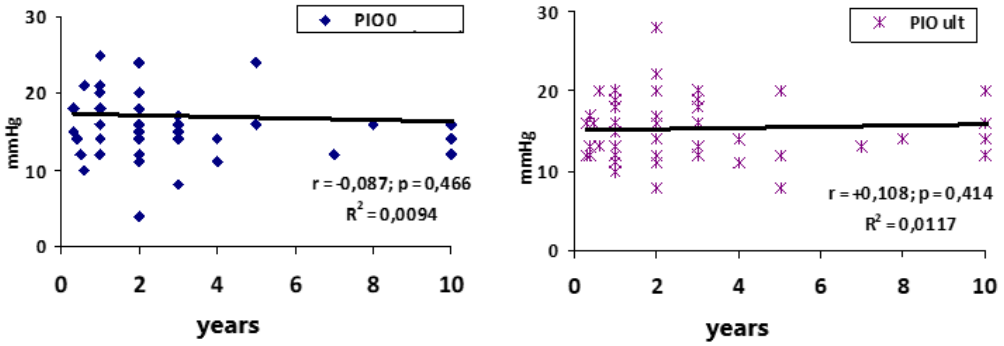


Fig. 8. IOP and inflammation-free time interval correlation

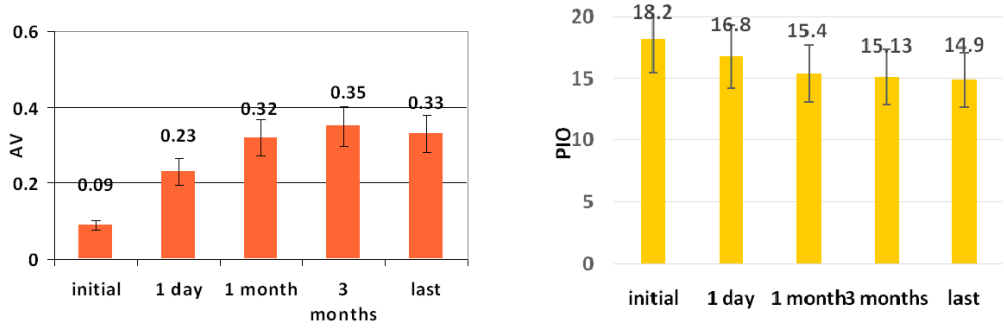
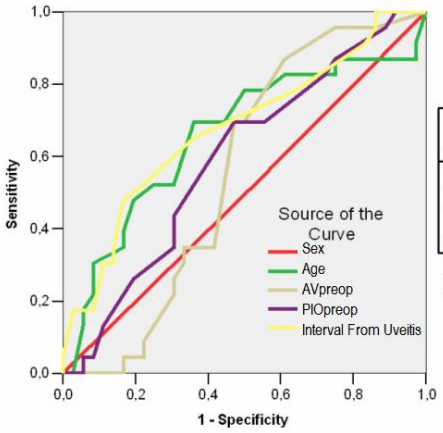


Fig. 9. Functional results of patients with recurrent uveitis

Logistic regression (multivariate analysis) provides a useful means to highlight the relationship between a presumed dependent variable and one or more explanatory variables called “predictors” which can be categorical or continuous. Risk is mathematically modeled as an equation as a collection of predictor variables. Linear regression models showed that visual acuity was significantly determined, in general, by gender, age, preoperative visual acuity - model 3 (y = 0.347 - 0.095 sex + 0.001 age + 0.924 AV0; p = 0.029), but model 5 also highlights the influence of the preoperative IOP and the interval from subsidence of inflammation as parameters that influence the visual acuity result at the last evaluation (y = 0.492 - 0.081 sex +0.001 age +0.914 AV0 - 0.07 PIO0 - 0.002 interval; p = 0.016). Of the preoperative factors, only gender is a good predictor of synechiolysis (AUC = 0.644; 95% CI: 0.501-0.786). Of

the preoperative factors, age (AUC = 0.659; 95% CI: 0.508-0.809) and the interval from extinction of the uveitis (AUC = 0.678; 95% CI: 0.534-0.821) seem to be good predictors of recurrent uveitis determinism (fig. 10).

Multivariate analysis revealed that a greater number of anti-inflammatory drugs administered for a significantly longer period can change the postoperative visual acuity (y = 0.709 + 0.646 AIN number - 0.274 Per Adm; p = 0.042) and postoperative IOP (y = 19.42 + 0.431 AIN number - 0.786 Per Adm; p = 0.008).



Area Under the Curve

Test Result Variable(s	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
Sex	,497	,078	,969	,345	,649
Age	,659	,077	,041	,508	,809
AVpreop	,556	,075	,470	,409	,703
PIOpreop	,594	,075	,228	,447	,740
Interval From Uveitis	,678	,073	,022	,534	,821

The test result variable(s): Sex, Varsta, AVpreop, PIOpreop, IntervalDelaUveita has at least between the positive actual state group and the negative actual state group. Statistics may b biased.

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Fig. 10. ROC curve - preoperative parameters which influence the evolution of recurrent uveitis

DISCUSSION

Cataracts are a common complication of uveitis, which occurs on one hand due to inflammation but also due to chronic treatment with corticosteroids. Cataract surgery in patients with uveitis is a serious challenge for the anterior segment surgeon. Today, phacoemulsification with intraocular lens implantation (IOL) in the capsular bag is the care standard for most patients with uveitis. However, despite the remarkable advances in surgical techniques and IOL materials, certain specific considerations should be made in terms of patient selection, preoperative preparation, as well as preoperative and postoperative management for long-term successful outcomes (7, 8). Studies show that there is a number of peculiarities regarding surgery of patients with uveitis, which determine the reduction of inflammation in the postoperative period: minimum number of maneuvers during surgery, short duration of surgery, small instead of large incisions, phacoemulsification with IOL implantation instead of extracapsular extraction of the lens and so on.

Preoperative management depends on the type and etiology of the uveitis, uveitis activity, the absence or presence of preoperative CME - there is no consensus of experts, several protocols being available (5, 6, 9). Thus, in non-granulomatous anterior uveitis Prednisolone acetate 1% eyedrops are administered 4 times/day 3-7 days preoperatively and in anterior uveitis associated with IJA (idiopathic juvenile

arthritis), severe granulomatous, intermediate or posterior uveitis, prednisone is recommended with dosage of 1mg/ kg bw/day, 3 days preoperatively. Also, in all cases, nonsteroidal anti-inflammatory drugs (NSAID) eyedrops 4 times/day 3-7 days before surgery, are proved to be more efficient in preventing the development of cystoid macular edema.

Postoperatively corticosteroid and antibiotic eyedrops are administered, NSAID eyedrops are continued 4 times/day for 6-8 weeks, up to 6 months depending on the case; in severe forms it is continued, tapering the treatment with Prednisone up to a minimum dose of 10 mg/day and combination of cycloplegic-mydriatic eyedrops (tropicamide 1% and phenylephrine 5%) 4times/day 5-7 days (6, 8, 9, 10, 11). Studies show an incidence of only 4% of CME in patients receiving oral and postoperative corticosteroids versus 27% in those without treatment (10, 12). Idan Hecht *et al.* exemplified in a study of 13,368 patients with a mean age of 73 years, who underwent cataract surgery, treated only with corticosteroids, only with NSAIDs or combination of the two, that postoperative treatment with steroids among patients undergoing treatment for uncomplicated cataract surgery was associated with lower rates of opacification of the posterior capsules compared with NSAID-only treatment (10).

The presence of inflammatory glaucoma should be established before surgery and anti-glaucoma therapy (avoiding prostaglandin derivatives) should be initiated. In the case of herpetic uveitis, prophylactic antiviral therapy with acyclovir or valaciclovir should be given at least 1 week before surgery to prevent recurrent viral infection (5, 8). Functional outcomes may be influenced by immediate and late postoperative complications: CME with an increased incidence after ECCE (33-66%) *vs.* Phaco (12-59%); severe anterior segment inflammation (posterior synechia, pupillary membranes); postoperative IOP increase - anti-glaucoma medication + corticosteroids; Posterior Capsule Opacification (PCO) (23-48% at 1 year) - the most common with variable incidence in different studies - requiring Nd: Yag capsulotomy - are prevented through postoperative inflammation control, well-centered circular capsulorhexis, square edge design of the IOL, meticulous removal of OVDs, etc. (5, 8, 10, 11, 13).

In our study, similarly to other literature studies, postoperative visual acuity increased significantly and was maintained at the last follow up. Sonia Mehta and colleagues in a review of literature using a database of 89 articles found that patients with a history of uveitis but no inflammation before surgery had a visual acuity of 20/40 or better in 69% cases especially if cataract surgery was performed through phacoemulsification (2). However, the presence of active uveitis at the time of phacoemulsification was associated with poor visual results (2, 13). In our study, the most frequent postoperative complication was recurrent uveitis (39%), which occurred on average at 3 months, 6 months and the latest at 2 years postoperatively. Most often this was due to intraoperative maneuvers at the pupillary level (stretching, synechiolysis, etc.).

The incidence of CME was 11% in cases with complicated surgery, intermediate or posterior uveitis and prior history of CME. Marie-Lyne Belair and co-workers evaluated the incidence of cystoid macular edema in two groups of patients who underwent cataract surgery, one that associates uveitis (41 eyes) *vs.* the one without

associated uveitis (52 eyes), similar to our study finding an 8% incidence of edema in those with uveitis and its absence in those without. In those treated with preoperative and postoperative corticosteroids the risk of edema was very low (14). In general, PCO occurred at 8 months - 2 years postoperatively, with an incidence of 10%. In a retrospective study of 3,013 eyes Amit K. Reddy evaluated the incidence of persistent anterior uveitis after cataract surgery, which was found in 2% while cystoid macular edema appeared in 29.4% of cases. Regardless of race (Caucasian or African American), uveitis persisted at one year postoperatively, despite moxifloxacin and topical corticosteroid therapy, periocular and intravitreal dexamethasone implant placement. A small percentage showed opacification of the posterior capsule. Visual acuity increased postoperatively in the study group similar to the control group, in accordance with low intraoperative and postoperative complications, as well as prompt treatment with pre- and postoperative anti-inflammatory depending on the cause of ocular inflammation (4). In a study on 111,641 eyes, of which 1,173 with associated uveitis, which underwent cataract surgery, Colin J Chu *et al.* found poorer visual acuity in the uveitis group postoperatively on the first day and at 12-24 weeks and increased intraocular pressure at the same intervals as opposed to the group without uveitis, with an increased frequency of anti-glaucoma procedures (7). In our study in the immediate postoperative period (one day) both groups had almost similar functional results; after one month the functional results in the control group are much better, with statistically significant differences between groups. The presence of a high percentage of recurrent postoperative uveitis (39%) in the study group would be an explanation of the weaker functional outcomes in this group compared to the control group. Preoperative inflammation control and the correct treatment of pre-operative CME can lead to good functional results after surgery. The reached data are comparable to those in the literature. Currently there are no studies comparing the level of visual acuity and intraocular pressure in patients with inflammation *vs.* non-inflammation who have undergone the same type of surgery. Thus, cataract surgery in eyes with uveitis can result in normal or near-normal visual acuity in most cases, at least in the short term, although it is not so common with regard to age-related (non-uveitic) cataracts. Further research is needed on a significant number of patients, in order to increase the level of confidence on which we can make decisions regarding the surgical treatment of cataract in uveitic eyes, and in particular to develop evidence that is specific to the individual clinical entities that make up this heterogeneous group of disease.

The limits of the study consist in the retrospective nature, the small number of enrolled cases and, most importantly, lack of uniformity of the evaluation period from surgery to the last follow-up. The absence of visual acuity results and intraocular pressure at longer intervals postoperatively also represents a serious limitation, and the results cannot be extrapolated to the general population.

CONCLUSIONS

Cataract surgery with artificial lens implantation resulted in improved postoperative visual acuity in patients with cataract and uveitis, which was maintained at the last follow up. In the immediate postopera-

tive period, both groups had similar functional results. Preoperative and postoperative inflammation control was a key factor in achieving relevant functional results. There is a statistically significant difference in final postoperative visual acuity between the two groups. Cataract surgery in uveitis patients requires careful evaluation of the diagnosis to determine the cause of uveitis, adequate patient selection, zero tolerance to preoperative inflammation, vigilant use of drugs to control preoperative inflammation, meticulous surgery, correct decision for implantation of IOL, control of postoperative inflammation and early detection and aggressive management of complications.

CONFLICT OF INTEREST AND FUNDING

The authors declare that there is no conflict of interest, and they received no specific funding regarding this scientific research.

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