

ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

The effect of intraocular lens material and postoperative therapy on the posterior capsule opacification development after the senile cataract surgery

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SUMMARY

Introduction/Objective The most frequent postoperative complication of a successfully performed phacoemulsification cataract surgery is the development of posterior capsule opacification (PCO). It is caused by the proliferation and migration of the remaining residual epithelial cells.

The objective of this study was to investigate the influence of two different intraocular lenses and two different anti-inflammatory drugs on the development of PCO in one-year follow-up period.

Methods Investigation included 120 patients (120 eyes), equally divided into four groups. The first two groups included patients who used non-steroid anti-inflammatory drug (NSAID) postoperatively, while the other groups had corticosteroid therapy. The first and third group got hydrophilic intraocular lenses (IOL), the second and fourth group had hydrophobic IOL. Software program EPCO 2000 was used for the analysis of PCO. Student's t-test, Wilcoxon test, and ANOVA were used for data analysis and $p < 0.05$ value was accepted as statistically significant.

Results After the first three postoperative months, patients from NSAID groups had mean PCO score 0.25 ± 0.03 , which was statistically significant higher ($p = 0.042$) comparing to corticosteroid groups. At the end of the investigation, the best result in PCO preventing was seen in the group of patients with hydrophobic IOL and corticosteroid therapy, with the mean PCO score of 0.47 ± 0.08 .

Conclusion This study has revealed that IOL made of acrylic hydrophobic material seemed to be the right choice when choosing intraocular lens to prevent PCO development. On the other hand, NSAID and corticosteroid therapy have showed similar results in preventing postoperative intraocular inflammation. This fact can be very useful in situations when corticosteroids must be used with great caution.

Keywords: posterior capsule opacification; intraocular lens; nonsteroidal anti-inflammatory drugs; corticosteroids

INTRODUCTION

Cataract represents blur of the eye lens, which affects everyone over the age of 65. This process is physiological and occurs due to the morphological and biochemical processes of the eye lens that appear with aging. Cataract developed in this manner is known as a senile cataract [1]. The only possible cataract treatment is a surgical one, and that procedure is entitled phacoemulsification [1, 2]. Cataract surgery is one of the most commonly performed surgical procedures worldwide [3]. Although it represents a routine procedure, this surgery is neither without risk, nor without complications. Those complications could be temporary and mild, such as corneal edema, or temporary postoperative intraocular pressure increase, but also very serious like posterior capsule rupture, suprachoroidal hemorrhage, and postoperative endophthalmitis [3]. The most frequent postoperative complication of a

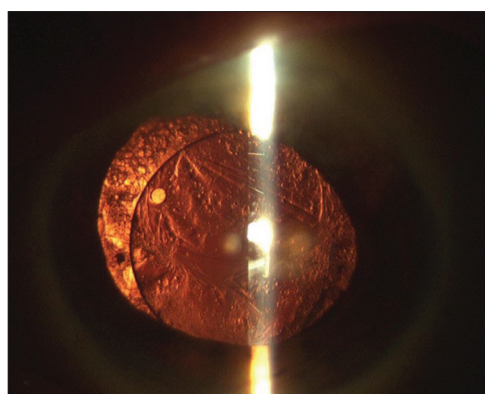


Figure 1. Posterior capsule opacification

successfully performed cataract surgery is the development of posterior capsule opacification (PCO), also known as the secondary cataract [4] (Figure1). It could provoke the decrease of the best-corrected visual acuity, reduction of contrast sensitivity, glare occurrence, or monocular diplopia [4].

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PCO is caused by proliferation and migration of the remaining residual epithelial cells. These cells are divided into “A” cells, which are situated under the anterior lens capsule, and “E” cells situated near the lens equator [1]. Phacoemulsification breaks down the blood-aqueous barrier and releases inflammatory cytokines. This local inflammatory reaction activates “E” cells that proliferate, migrate, and lead to PCO [1, 2]. Many methods are used to reduce inflammation and cells migration. They are performed during the phacoemulsification, such as emphasized hydrodissection, in-the-bag intraocular lenses (IOL), implantation, capsulorhexis size, or postoperative by picking adequate IOL and anti-inflammatory therapy [5–8].

The aim of this study was to investigate the influence of two different intraocular lenses and two different anti-inflammatory drugs on the development PCO in the one-year follow-up period.

METHODS

This study was a prospective, randomized study, conducted at the Clinic of Ophthalmology, Kragujevac Clinical Centre, Serbia, done from June 1, 2017 until June 1, 2018. It included 120 patients (120 eyes), who were selected for the cataract surgery. After the successfully performed phacoemulsification, patients were divided into four groups according to the implanted IOL and postoperative anti-inflammatory therapy.

The main inclusion criterion was the existence of the senile cataract. The patients with other types of cataracts, such as traumatic, iatrogenic, complicated, or presenile cataract were excluded from the study. The patients with previous history of intraocular surgery, trauma, inflammatory diseases of anterior eye segment, zonular weakness, glaucoma were also excluded. Those patients who were on a chronic topical, intraocular, or systemic anti-inflammatory therapy were excluded. The study involved only participants who underwent uncomplicated phacoemulsification.

With the approval of institutional Committee on Ethics and according to the tenets of the Declaration of Helsinki, all the patients gave their written consent at the beginning of the investigation.

A complete ocular examination was performed before the surgery as well as at every postoperative visit for every patient. That included visual acuity, intraocular pressure measurement, slit lamp evaluation, retinal examination, and ocular ultrasonography. Five days before the surgery, topically 0.3% solution of ofloxacin was administrated, five times per day.

The patients were randomized by picking two unmarked, opaque envelopes. The first envelope determined which IOL would be implanted. We used two acrylic, single-piece, square-edged IOL: hydrophilic – Eyecryl plus 600 (Biotech visioncare, Luzern, Switzerland) and hydrophobic – SA60AT (Alcon-Couvreur NV, Puurs, Belgium). The second envelope was about postoperative therapy: NSAID – nepafenac ophthalmic suspension 0.1% or dexamethasone phosphate 0.1%.

When all preoperative protocols were satisfied, the phacoemulsification was performed by two experienced surgeons. Phaco machine for all surgeries was Stellaris (Bausch & Lomb, Rochester, NY, USA). Adequate mydriasis was achieved using topical phenylephrine hydrochloride ophthalmic solution 2.5%. Tetracaine eye drops was the only anesthetic drug used during the surgery. Paracentesis and clear corneal incisions were made. Viscoelastic sodium hyaluronate ophthalmic solution 1.4% fulfilled the anterior chamber and continuous curvilinear capsulorhexis, hydrodissection and nucleus rotation followed. Then the nucleus was cracked and aspirated using the “stop and chop” technique. Irrigation and aspiration were performed to aspirate the remaining lens cortex. Capsular bag was fulfilled with viscoelastic and intraocular lens was implanted with adequate injector. When the viscoelastic was removed, intracameral solution of cefuroxime with 1 mg / 0.1 ml balanced salt solution was injected. Corneal incisions hydrated by balanced salt solution using a blunt injection needle. Postoperatively patients instilled topically 0.3% solution of ofloxacin five times daily, for one postoperative week, and one of two possible anti-inflammatory drugs, four times a day, during the first postoperative month.

After the randomization and phacoemulsification, 120 patients were equally divided into four groups (n = 30). The first two groups included patients who used postoperatively non-steroid anti-inflammatory drug with the difference that patients in the first group got hydrophilic intraocular lens, and the patients in the second group got hydrophobic intraocular lens. The other two groups were the corticosteroid groups. Hydrophilic IOL were implanted in group three, while the patients from the fourth group got hydrophobic IOL (Table 1).

Table 1. Distribution of the groups

Groups	Types of intraocular lenses	Medication used
Group I	Eyecryl plus 600	nepafenac ophthalmic suspension 0.1%
Group II	SA60AT	nepafenac ophthalmic suspension 0.1%
Group III	Eyecryl plus 600	dexamethasone phosphate 0.1%
Group IV	SA60AT	dexamethasone phosphate 0.1%

After the discharge from the Clinic, follow-up examinations were performed one, three, six and 12 months after the cataract surgery. During these visits, digital high-resolution images were taken for each patient during the slit lamp examination in a full mydriasis and retroillumination. All images were analyzed by using Evaluation of Posterior Capsule Opacification 2000, a standard software program for analysis of PCO [6]. The boundaries of each opaque area noticed at the posterior capsule were marked using a computer mouse. According to the density of these areas, opacification was scaled from grade 0 to 4. Posterior capsule without any opacification was considered as grade 0. Other grades included minimal (grade 1), mild (grade 2), moderate (grade 3), and severe (grade 4) PCO. The PCO score for each area was calculated by multiplying the

opacification density grade with the fraction of the capsule area. The sum of all these individual PCO scores defined the total PCO score for the analyzed image.

Statistical analysis was done by using SPSS Statistics for Windows software (IBM Corp., Armonk, NY, USA). The significance at different time intervals during the study was tested with the Student's t-test or by the Wilcoxon equivalence test in case where the distribution was not normal. Examination of the incidence of opacification in dependence on the type of intraocular lens was done by using the χ^2 test and ANOVA ($p < 0.05$ value was accepted as statistically significant).

RESULTS

The mean age of the examined patients was 76.4 ± 6.8 years (range 66–88 years) without statistical significance among the groups. A total of 64 females and 56 males were equally divided into four groups. During the study, four patients from corticosteroid groups had temporary intraocular pressure increase, which was efficiently treated with antiglaucomatous eye drops. Two patients developed postoperative macular edema (both from the corticosteroid groups) and one patient died, so they were excluded from the investigation.

At the first follow-up, one month after the phacoemulsification, the mean PCO score among the groups was I = 0.12 ± 0.03 , II = 0.08 ± 0.02 , III = 0.06 ± 0.01 , IV = 0.05 ± 0.01 (Table 2). Groups II–IV had first grade opacification, while some patients from the first group developed second grade opacification. Statistically significant difference was noticed between the first and other groups, as well as between NSAID and corticosteroid groups ($p = 0.032$).

Table 2. The mean posterior capsule opacification score during one year of follow-up period

Group	1 month	3 months	6 months	12 months
I	0.16 ± 0.03	0.26 ± 0.04	0.48 ± 0.10	0.64 ± 0.12
II	0.08 ± 0.02	0.23 ± 0.03	0.37 ± 0.05	0.49 ± 0.06
III	0.06 ± 0.01	0.21 ± 0.03	0.42 ± 0.08	0.57 ± 0.09
IV	0.05 ± 0.01	0.18 ± 0.05	0.32 ± 0.04	0.47 ± 0.08

At the next visit, more participants from NSAID groups had worse mean PCO score (I = 0.26 ± 0.04 ; II = 0.23 ± 0.03) compared to those with topical corticosteroid (III = 0.21 ± 0.03 ; IV = 0.18 ± 0.05), with calculated statistical significance ($p = 0.042$). Comparing all four groups separately, statistically significant difference was detected only between groups I and IV ($p = 0.03$).

After six months postoperatively, the mean PCO score in the fourth group was statistically different from other groups (I = 0.44 ± 0.10 ; II = 0.37 ± 0.05 ; III = 0.42 ± 0.08 ; IV = 0.32 ± 0.04). The difference between hydrophilic IOL groups was not significant, $p = 0.069$.

Twelve months after the cataract surgery, the fourth group had the lowest mean PCO score, 0.47 ± 0.08 . The mean PCO score in other groups was I = 0.64 ± 0.12 , II = 0.49 ± 0.06 and

III = 0.57 ± 0.09 . No statistically significant difference was found between groups II and IV ($p = 0.061$). Statistical significance was noted between the first and other groups, as well as between hydrophobic vs. hydrophilic groups ($p < 0.001$).

DISCUSSION

According to many previous studies, PCO still remains the most common complication of successfully performed cataract surgery [6, 9, 10]. The only known treatment of formed PCO is Nd:YAG capsulotomy. This procedure is not without risk. Some of the possible complications are IOL damage, retinal detachment, macular edema, intraocular pressure increase [11]. Therefore, all researchers agree that the best treatment of PCO is prevention [10, 11].

Corticosteroids are well known to have anti-inflammatory effect, but they can cause severe ocular side effects: intraocular pressure increase, cataract development, disturbance of the corneal wound healing [12]. For this reason, not a small number of phaco surgeons are interested in some alternatives. NSAID for ocular use are mostly administrated in the management of ocular inflammation with non-infectious origin. During the postoperative period, they reduce anti-inflammatory reaction, and consequently the development of PCO [13]. Corticosteroids block the release of arachidonic acid by the suppression of the enzyme phospholipase A2. That action stops the production of inflammatory mediators, such as leukotrienes and prostaglandins [14]. NSAID act through the inhibition of the enzyme cyclooxygenase, which causes the suspension of prostaglandin production. Thereby, NSAID are mostly in use as antipyretic, anti-inflammatory, and analgesic drugs [15].

Intraocular lens material and design have an important impact on preventing PCO. Acrylic material is associated with reduced PCO rate by causing a lower postoperative inflammation than the previously used materials [9]. In addition, lenses with sharp edge design have better outcomes by the inhibition of lens epithelial cells' (LECs) migration [16].

After the appropriate surgical technique, our results indicated that the satisfactory PCO prophylaxis could be provided by implanting acrylic hydrophobic IOL. These results are in accordance with earlier studies [9, 10, 11, 17]. Intraocular lenses made of hydrophobic material can adhere to collagen membrane and fibronectin. That creates less space between IOL and posterior lens capsule, making it difficult for LECs to migrate and to develop PCO [18]. Some investigators advocate that the difference between these two materials is associated with less sharp edges of the hydrophilic lenses [9]. During the manufacture of hydrophilic IOL, they are primarily produced dehydrated, and then rehydrated which can lead to the loss of sharpness [19].

The results we collected highly indicated a strong anti-inflammatory potential of administrated corticosteroids in the first three postoperative months. This fact is similar to some earlier studies [14, 15]. During the final six months of the study, it seemed to be, that IOL material had the main influence on preventing the PCO development.

Anti-inflammatory drugs have a huge effect on controlling the inflammation in early postoperative period. LECs cannot be completely removed during phacoemulsification even using advanced surgical techniques. After a few months, because of the chronic inflammation, LECs start to proliferate and migrate towards the lens posterior capsule. During that period, IOL block the further migration of the LECs. Therefore, the finest results in preventing the PCO development can be reached by the synergistic act of anti-inflammatory therapy and aqueous intraocular lens implantation.

CONCLUSION

PCO still represents the most frequent postoperative complication of the uncomplicated cataract surgery. This

condition causes decreased visual acuity and patients' dissatisfaction. In accordance with the results presented in this study, we believe that the adequate prevention of PCO forming is provided by the implantation of acrylic hydrophobic IOL in a capsular bag. Similar scores in PCO development one year after the phacoemulsification in hydrophobic IOL groups with NSAID or corticosteroid, provide the new possibilities in the prevention of postoperative inflammation. These results can be particularly useful in situations when corticosteroids must be used with great caution, such as glaucoma patients, the presence of active infection, or conditions with the delayed corneal healing.

Conflict of interest: None declared.

REFERENCES

1. Wang Y, Guan H. The role of DNA methylation in lens development and cataract formation. *Cell Mol Neurobiol.* 2017;37(6):979–84.
2. Morya AK, Bhandari S, Naidu A. Retrospective study on outcomes of terminal chop technique of nuclear fragmentation in phacoemulsification and combined surgery: An observational study. *Indian J Ophthalmol.* 2019;67(2):217–20.
3. Veselinovic A, Cvetanovic M, Milosevic Z, Veselinovic D. Intraoperative and postoperative complications of phacoemulsification in cataract eyes with pseudoexfoliation syndrome. *Srp Arh Celok Lek.* 2017;145(3–4):124–8.
4. Johansson B. Glistenings, anterior/posterior capsular opacification and incidence of Nd:YAG laser treatments with two aspheric hydrophobic acrylic intraocular lenses – a long-term individual study. *Acta Ophthalmol.* 2017;95(7):671–7.
5. Lin Q, Tang J, Han Y, Xu X, Hao X, Chen H. Hydrophilic modification of intraocular lens via surface initiated reversible addition-fragmentation chain transfer polymerization for reduced posterior capsular opacification. *Colloids Surf B Biointerfaces.* 2017;151:271–9.
6. Haripriya A, Chang DF, Vijayakumar B, Niraj A, Shekhar M, Tanpreet S, et al. Long-term posterior capsule opacification reduction with square-edge polymethylmethacrylate intraocular lens: Randomized controlled study. *Ophthalmology.* 2017;124(3):295–302.
7. Kim SJ, Schoenberger SD, Thorne JE, Ehlers JP, Yeh S, Bakri SJ. Topical nonsteroidal anti-inflammatory drugs and cataract surgery: a report by the American Academy of Ophthalmology. *Ophthalmology.* 2015;122(11):2159–68.
8. Malik A, Sadafale A, Gupta YK, Gupta A. A comparative study of various topical nonsteroidal anti-inflammatory drugs to steroid drops for control of post cataract surgery inflammation. *Oman J Ophthalmol.* 2016;9(3):150–6.
9. Lu C, Yu S, Song H, Zhao Y, Xie S, Tang X, et al. Posterior capsule opacification comparison between morphology and objective visual function. *BMC Ophthalmol.* 2019;19(1):40.
10. Chang A, Kugelberg M. Posterior capsule opacification 9 years after phacoemulsification with a hydrophobic and a hydrophilic intraocular lens. *Eur J Ophthalmol.* 2017;27(2):164–8.
11. Ton Van C, Tran THC. Incidence of posterior capsular opacification requiring Nd:YAG capsulotomy after cataract surgery and implantation of enVista[®] MX60 IOL. *J Fr Ophtalmol.* 2018;41(10):899–903.
12. Al Hanaineh AT, Hassanein DH, Abdelbaky SH, El Zawahry OM. Steroid-induced ocular hypertension in the pediatric age group. *Eur J Ophthalmol.* 2018;28(4):372–7.
13. Jung JW, Chung BH, Kim EK, Seo KY, Kim TI. The effects of two non-steroidal anti-inflammatory drugs, bromfenac 0.1% and ketorolac 0.45%, on cataract surgery. *Yonsei Med J.* 2015;56(6):1671–7.
14. Murakami M, Nakatani Y, Atsumi GI, Inoue K, Kudo I. Regulatory functions of phospholipase A2. *Crit Rev Immunol.* 2017;37(2–6):121–79.
15. Duan P, Liu Y, Li J. The comparative efficacy and safety of topical non-steroidal anti-inflammatory drugs for the treatment of anterior chamber inflammation after cataract surgery: a systematic review and network meta-analysis. *Graefes Arch Clin Exp Ophthalmol.* 2017;255(4):639–49.
16. Joshi RS. Postoperative posterior capsular striae and the posterior capsular opacification in patients implanted with two types of intraocular lens material. *Indian J Ophthalmol.* 2017;65(6):466–71.
17. Leydolt C, Schartmüller D, Schwarzenbacher L, Schranz M, Schriefl S, Menapace R. Comparison of posterior capsule opacification development with 2 single-piece intraocular lens types. *J Cataract Refract Surg.* 2017;43(6):774–80.
18. Chassain C, Chamard C. Posterior capsule opacification, glistenings and visual outcomes: 3 years after implantation of a new hydrophobic IOL. *J Fr Ophtalmol.* 2018;41(6):513–20.
19. Koshy J, Hirnschall N, Vyas AK, Narendran R, Crnej A, Gangwani V, et al. Comparing capsular bag performance of a hydrophilic and a hydrophobic intraocular lens: A randomised two-centre study. *Eur J Ophthalmol.* 2018;28(6):639–44.

Ефекат материјала интраокуларног сочива и постоперативне терапије на развој замућења задње капсуле сочива после операције сенилне катаракте

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САЖЕТАК

Увод/Циљ Најчешћа постоперативна компликација успешно изведене операције катаракте факоемулзификацијом је развој замућења задње капсуле сочива. То је проузроковано пролиферацијом и миграцијом преосталих резидуалних епителних ћелија.

Циљ ове студије је испитивање утицаја два различита интраокуларна сочива и два различита антиинфламаторна лека на развој замућења задње капсуле сочива током једног-дишњег периода праћења.

Метод Истраживање је обухватило 120 болесника (120 очију), подједнако подељених у четири групе. Прве две групе укључивале су болеснике који су користили постоперативно нестероидни антиинфламаторни лек (*NSAID*), док су остале групе добиле кортикостероидну терапију. Прва и трећа група добиле су хидрофилна интраокуларна сочива (ИОС), а друга и четврта хидрофобна ИОС. За анализу замућења задње капсуле сочива коришћен је софтверски програм *EPSCO 2000*. Студентов т-тест, Вилкоксон тест и *ANOVA* коришћени су за анализу података, а вредност $p < 0,05$ је прихваћена као статистички значајна.

Резултати После три постоперативна месеца болесници из група *NSAID*-а имали су средњу вредност замућења задње капсуле сочива $0,25 \pm 0,03$, што је било статистички значајно више ($p = 0,042$) у поређењу са кортикостероидним групама. На крају студије, најбољи резултати у спречавању настанка замућења задње капсуле сочива забележени су у групи болесника са хидрофобним ИОС и кортикостероидном терапијом, са средњом вредношћу $0,47 \pm 0,08$.

Закључак Ова студија је показала да су интраокуларна сочива израђена од акрилатног хидрофобног материјала била прави избор приликом одабира интраокуларног сочива у спречавању развоја замућења задње капсуле сочива. С друге стране, *NSAID* и терапија кортикостероидима су показале сличне резултате у спречавању постоперативне, интраокуларне инфламације. Ова чињеница може бити веома корисна у ситуацијама када се кортикостероиди морају употребљавати са великим опрезом.

Кључне речи: замућење задње капсуле сочива; интраокуларна сочива; нестероидни антиинфламаторни лекови; кортикостероиди