USE OF OPTICAL COHERENCE TOMOGRAPHY IN DETECTION OF CYSTOID MACULAR EDEMA AFTER TREATMENT WITH NONSTEROIDAL ANTI-INFLAMMATORY DRUGS

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The development of cystoid macular edema (CME) remains an important complication and the commoncause of reduced visual acuity after cataract surgery. Based on scientific literature , the incidence of clinicaly significant CME varies from 0.1% to 2% in patients without any predisposingrisk factors.However, some clinical trials have reported up to 9% angiographically-proven, clinically undetected CME and increased mean foveal thickness after uncomplicated cataract surgery measured by optical coherence tomography.

Even the postoperative CME is believed to be a self-limiting condition, it may cause irreversible retinal damage in some cases, eventually leading to poor visual outcome and it can become a major source of patients' dissatisfaction. Although the exact pathogenesis of CME is yet to be fully determined,chronic intraocular inflammation with the release of prostaglandins (PG), disruption and hyperpermeability of blood-aqueous and blood-retina barrier thought to be a major contributing risk factors in the pathogenesis of CME. This explains why the utilization of non-steroidal anti-inflammatory drugs (NSAIDs) shows high success rates in treatment of pseudophakic CME [1,3].

Although NSAIDs only inhibit COX, they provide excellent anti-inflammatory properties. NSAIDs also help to maintain intraoperative mydriasis andrelieve postoperative ocular pain. Based on the mechanism of action, steroids seem to be superior than NSAIDs in regards of inflammation control, since they act on a preliminary step in the inflammatory cascade. However, the usage of corticosteroid eye drops may have significant adverse effects, such as steroid-induced intraocular pressure elevation, delayed wound healing, increased risk of infection.In contrast, NSAIDs provide excellent safety profile with minor side effects.

With the development of surgical techniques and biomaterial science, cataract surgery with intraocular lens (IOL) implantation has brought great benefits to the patients . Approximately 10 million cataract surgeries are being performed worldwide each year.

The performance of intraocular lenses is determined by several factors, from which biocompatibility of IOL material has a major importance.The biocompatibility of IOL is based on two major criteria: uveal and capsular biocompitabulity. Uveal biocompatibility is determined by inflammatory foreign body response of the eye against the implant. In terms of capsular biocompatibility, it includes the proliferation and migration of lens epithelial cells, which eventually leads to posterior capsule opacification, or ongrowth of epithelial cells onto the anterior surface of IOL.Various clinical studies are conducted to compare the uveal and capsular biocompatibility afterimplantation of different biomaterials in the eye. Materials used in intraocular lenses should provide a long-term uveal and capsular biocompatibility and safety profile [2,6].

Acrylic IOLs with hydrophobic surfaces are safe for intraocular implantation, as they have been widely used in clinical practice all around the world for decades and it has been proven by different clinical studies, that these type of IOLs have excellent uveal biocompatibility and significantly lower rates of posterior capsule opacification.Studies have shown, that acrylic material has a relatively low propensity to induce lens epithelial cell proliferation in the capsular bag. Whether the hydrophilic or hydrophobic IOLs are better for PCO prevention, still remains under active investigation. Risk factors for PCME development are mostly associated with surgical complications during cataract surgery,such as: posterior capsular rupture, vitreous loss, vitrectomy for retained lens fragments, iris trauma, intraocular lens dislocation, early postoperative capsulotomy (YAG capsulotomy), iris fixed intraocular lenses and anterior chamber lenses [4,7].

It has been shown, that optical-coherence tomography (OCT) is very effective tool in diagnosing pseudophakic CME, providing excellent *in vivo* exposureto the retinal layers and gives us the possibility to discover changes on microscopic level. Intraretinal cystoid spacesinitially develop in the inner nuclear layer and progressesinto outer plexiform layer; Ultimately, accumulation of fluid in the subretinal space can be observed.Optical-coherence tomography allows quantitative evaluation of retinal changes and hashigh diagnosticyield. By giving the opportunityto imageretinal layers noninvasively, OCT hasbecome a rapid and favorabletool for eye physicians to analyzethe retinal changes occurringin pseudophakic CME [5,13].

The purpose of this study was to determine (OCT analysis) the rate of postoperative cystoid macular edema in patients undergoing uncomplicated cataract surgery(phacoemulsification) and implantation of acrylic hydrophobic intraocular lens (IOL) (Lifeline Medical Devices Ind) treated with or without postoperative anti-inflammatory drugs.

Material and methods. Study involved 94 eyes of 72 patients,between 60-70 of age (women-65%, men-35%). Eyes were equally divided into two groups (I and II)(n-47 in each). Post-operatively treatment regimen for participants from Group I included antibiotic and NSAID eye drops, while participants from group II weretreated only with antibiotic eye drops. Acrylic hydrophobic intraocular lens (IOL) (Lifeline Medical Devices Ind) was implanted in all patients comprising both groups.

All patients underwent uncomplicated cataract surgery. Patients diagnosed with senile cataracts, with nuclear sclerosis up to +2 or +3 were included in the study. Patients with the history of diabetes mellitus, arterial hypertension, any type of ischemic maculopathy, age-related macular degeneration, epi-retinal membrane, uveitis, topical use of prostaglandin analogs, were excluded from the study. Both groups were operated by a single surgeon at eye clinic "AkhaliMzera", Tbilisi, Georgia. Patients were operated under peribulbar anesthesia. Tropicamide 1% and phenylephrine 5% were administered for papillary dilatation. A single planar clear corneal incision was created using 2.2 mm metal tip knife at 12 o'clock. Two side port paracentesis were made using a 1.0 mm clear-cut side port knife. 5.5 mm continuous curvilinear capsulorhexis (CCC) was initiated using Utrata forceps. Phacoemulsification was done using Infinity Vision System (Alcon Laboratories, inc.), operating in burst mode. The nucleus was cracked with direct chop technique. Effective phaco time was (EPT) 6.4+-2.8 seconds and ultrasound time (UST) 49.3±16.7 seconds, respectively. After complete removal of lens material, anterior chamber was filled with an ophthalmic viscosurgical device (OVD). Foldable hydrophobic IOL was

implanted in the capsular bag. OVD was completely removed from anterior chamber using bimanual irrigation and aspiration hand-piece. The anterior chamber was formed and clear corneal incision was sealed.

In order to participate in the study, informed consent forms were obtained from all patients prior to surgery. The baseline OCT scan of macular anatomy and central retinal thickness was acquired on the dayprior to surgery. For comparison analysis, OCT scan of macula was performed after one week and one month postoperatively.

Results and discussion. No patient developed cystoid macular edema from either group (CME). In both groups (with or without NSAID eye drops cover) mean central retinal thickness (CRT) was 230±0.005micronsbefore the surgery. MM6 scans of OCT showed moderate increase of CRT and accounted for 15±0.080microns ($p<0.05$)at 7th postoperative day. One month postoperatively, mean CRT change was 5±0.09 microns ($p<0.05$). No statistically significantchanges of CRT was noted in both groups ($p<0.5$) (Fig.).

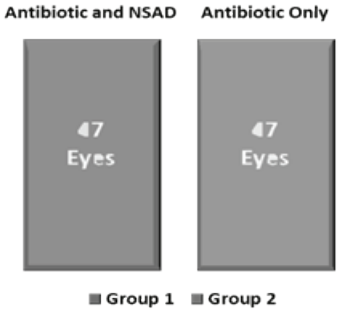

Fig. No significant statistical change of CRT growth was noted in both groups

Risk-factors of pseudophakic cystoid macular edema, are primarily related to surgical complications, such as posterior capsule rupture, vitreous loss, vitrectomy, surgical trauma of iris, IOL dislocation, early post-operative capsulotomy (Nd:YAG capsulotomy), Iris fixated IOLs and anterior chamber IOLs. Loss of vitreous body increases the risk of cystoid macular edema by 10-20%. Prolapse of vitreous body into the wound prolongs cystoid macula edema and may be associated to poor visual prognosis . Incarceration of iris, additional risk-factor of CME, may have significant association with decreased vision in patients with chronic pseudophakic CME compared to other intra-operative complications. Specific IOLs are associated withthe increasedrisk of cystoid macular edema development. Meta-analysis has shown, that prevalence of CME is the highest in eyes with implantation of iris fixated IOLs; Anterior chamber IOLs increase the risk of CME compared to posterior chamber IOLs [9,11,14].

Systemic diseases also increase the risk of postoperative CME in patients undergoing cataract surgery. Diabetes Mellitus andsystemic hypertension are well-established systemic risk factors. In regards of ocular pathology, active uveitis is the most significant contributing risk factor in development of CME and is the major cause of decreased postoperative vision in patients with uveitis. History of retinal vein occlusion, diabetic macular edema, presence of epi-retinal membrane and local usage of prostaglandin analogs also increase the risk of postoperative CME.

Conclusion. Study analysis has shown, that cystoid macular edema has not developed in patients, who underwent uncomplicated cataract surgery with hydrophobic IOL implantation, with or without NSAID eye drop cover. There was no statistically and clinically significant difference between the groups in terms of CRT.

Implantation of acrylic hydrophobic intraocular lens (IOL) (Lifeline Medical Devices Ind.) has shown to provide high uveal biocompatibility.

Major risk factors of CME in cataract surgery are intraoperative surgical complications. Certain systemic and local ophthalmic diseases, as well as topical use of prostaglandin analogs are also strongly linked to postoperative CME development.

In order to reduce the rate of postoperative CME and maximize the visual outcome, right preventive measures should be taken. It is essential to look through the pharmacokinetic and pharmacodynamic characteristics of NSAIDs and determine the role, capacity and efficiency of these drugs in control of postoperative inflammation and pain. In a comparative trial, Bucci et al studied the efficiency of ketorolac and nepafenac in the inhibition of prostaglandin E_2 (PGE_2) and their concentration in aqueous humor. They concluded, that ketorolac is more capable to inhibit PGE_2 and higher concentration levels of ketorolac is being reached in the anterior chamber. However, Bucci et al's findings were challenged by Walters et al. They conducted prospective, multicenter, double-blind clinical trial comparing the pharmacokinetics and pharmacodynamics of nepafenac, ketorolac and bromfenac. Walters concluded, that nepafenac has better bioavailability and greater capacity to inhibit COX2 thanks to amfenac, the active metabolite of nepafenac.

In conclusion, a prophylactic usage of NSAID eye drops in combination with the standard postoperative antibiotic regimen in eyes undergoing cataract surgery, showed to have a beneficial effect on prevention of postoperative CME, while patients, who underwent uncomplicated phacoemulsification without NSAID eye drop cover and acrylic hydrophobic intraocular lens (Lifeline Medical Devices Ind) implantation, also had excellent visual outcome and no changes in retinal architecture.

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SUMMARY

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The aim of the study was to determine the correlation between implanted IOL material type to detect CME after NSAID use in cataract surgery. Study involved 94 eyes of 72 patients. Eyes were equally divided into two groups (n-47 in each). Post-operatively treatment regimen for participants from Group I included antibiotic and NSAID eye drops, while participants from group II were treated only with antibiotic eye drops. Acrylic hydrophobic intraocular lens (IOL) was implanted in all patients comprising both groups. No patient developed cystoid macular edema from either group (CME). In both groups (with or without NSAID eye drops cover) mean central retinal thickness (CRT) was 230±0.005 microns before the surgery. No statistically significant changes of CRT was noted in both groups (5± 0.09 microns) ($p<0.5$).

Study analysis has shown, that cystoid macular edema has not developed in patients, who underwent uncomplicated cataract surgery with hydrophobic IOL implantation, with or without NSAID eye drop cover. There was no statistically and clinically significant difference between the groups in terms of CRT.

Implantation of acrylic hydrophobic intraocular lens(IOL) has shown to provide high uveal biocompatibility.

Major risk factors of CME in cataract surgery are intraoperative surgical complications. Certain systemic and local ophthalmic diseases, as well as topical use of prostaglandin analogs are also strongly linked to postoperative CME development.

In conclusion, usage of NSAID eye drops in combination with antibiotic regimen in eyes undergoing cataract surgery, showed to have a beneficial effect on prevention of postoperative CME.

Keywords: cystoid macular edema, Non-steroidal anti-inflammatory drugs (NSAIDs), Intraocular lens (IOL).

РЕЗЮМЕ

ВЫЯВЛЕНИЕ ЦИСТОИДНОГО МАКУЛЯРНОГО ОТЕКА ПОСЛЕ ЛЕЧЕНИЯ НЕСТЕРОИДНЫМИ ПРОТИВОВОСПАЛИТЕЛЬНЫМИ ПРЕПАРАТАМИ С ПОМОЩЬЮ ОПТИЧЕСКОЙ КОГЕРЕНТНОЙ ТОМОГРАФИИ

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Целью исследования явилось определить корреляцию между типом материала имплантированных интраокулярных линз с цистоидным отеком сетчатки при инстилляции нестероидных противовоспалительных препаратов в хирургии катаракты.

В иследовании включены 72 пациента (94 глаза), которые были разделены на равные группы, по 47 в каждой. Пациенты I группы принимали антибиотик и нестероидные противовоспалительные препараты, во группе II - только антибиотик.

Анализ результатов клинических исследований показал, что в постоперационный период после имплантации гидрофобной линзы цистоидный отек сетчатки не развился ни в одной из групп (230±0,005 микрон). Степень изменений центральной толщины сетчатки клинически была незначительной (5±0,09 микрон, $p<0.05$). Акриловый гидрофобный хрусталик показал, что обладает высокой увеальной биосовместимостью. Риск-факторами развития цистоидного макулярного отека после хирургии катаракты являются системные заболевания глаза, интраоперационные осложнения, высвобожденные во время операции простагландины и свободные радикалы. Анализ проведенного клинического исследования выявил, что после неосложненной факоэмульсификации применение нестероидных противовоспалительных капель вместе с антибиотиками понижают риск развития цистоидного макулярного отека в постоперационном периоде.

რეზიუმე

მაკულის ცისტოიდური შეშუპების გამოვლენა ოპტიკური კოგერენტული ტომოგრაფიის მეშვეობით არასტეროიდული ანთებისსაწინააღმდეგო წვეთებით მკურნალობის შემდეგ

მ.დვალი, ო.ცერცვაძე, შ.სხირტლაძე

თბილისის სახელმწიფო სამედიცინო უნივერსიტეტი, თვალის სნეულებათა დეპარტამენტი; თვალის კლინიკა „ახალი მზერა", თბილისი, საქართველო

კვლევის მიზანს წარმოადგენდა იმპლანტირებული ინტრაოკულარული ლინზების მასალის ტიპსა და ბადურის ცისტოიდურ შეშუპებას შორის კორელაციის განსაზღვრა ანთებისსაწინააღმდეგო არასტეროიდული პრეპარატების გამოყენების შემდეგ კატარაქტის ქირურგიაში.

კვლევაში ჩართული იყო 72 პაციენტი (94 თვალი), რომლებიც თანაბრად განაწილდა ორ ჯგუფად (n=47). I ჯგუფში შემავალი პაციენტები პოსტოპერაციულ პერიოდში იწვეთებდნენ ანტიბიოტიკის და ანთებისსაწინააღმდეგო არასტეროიდულ წვეთებს, II ჯგუფის პაციენტები - მხოლოდ ანტიბიოტიკის წვეთებს.

კლინიკური კვლევის შედეგების ანალიზმა აჩვენა, რომ კატარაქტის ოპერაციის დროს ჰიდროფობური თვალშიდა ლინზის იმპლანტაციის შემდეგ პოსტოპერაციულ პერიოდში ბადურის ცისტოიდური შეშუპება არ განვითარდა არც ერთ ჯგუფში - 230±0.005 მიკრონი. ბადურის ცენტრალური სისქის ცვლილების ხარისხი კლინიკურად უმნიშვნელო იყო - 5±0.09 მიკრონი ($p<0.05$). აკრილის ჰიდროფობურმა ბროლმა აჩვენა, რომ აქვს მაღალი უვეალური ბიოთავსებადობა. კატარაქტის ქირურგიის შემდეგ განვითარებული მაკულის ცისტოიდური შეშუპების გამომწვევი ფაქტორებია თვალის სისტემური დაავადებების, ინტრაოპერაციული გართულებების, ოპერაციის დროს გამოთავისუფლებული პროსტაგლანდინები და თავისუფალი რადიკალები.

ჩატარებული კლინიკური კვლევის ანალიზის შედეგად ავტორებს გამოტანილი აქვთ დავასკვნა, რომ გაურთულებელი ფაკოემულსიფიკაციის შემდგომ ანთებისსაწინააღმდეგო არასტეროიდული წვეთების გამოყენება ანტიბიოტიკებთან ერთად ამცირებს მაკულის ცისტოიდური შეშუპების განვითარების რისკს ადრეულ პოსტოპერაციულ პერიოდში.

DIAGNOSIS AND TREATMENT OF PATIENTS WITH SINONASAL INVERTED PAPILLOMA

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Inverted papilloma is a benign epithelial tumor that refers to Schneider's sinonasal papilloma. According to the classification of the World Health Organization (2005), Schneiderian papillomas includes three subtypes: inverted, exophytic (fungiform) and oncocytic papilloma ("oncocytic Schneiderian papilloma") [1].

The frequency of occurrence of inverted papilloma (IP) ranges from 0.4% to 7% of all neoplasms of the nasal cavity and paranasal sinuses [1]. According to the literature data, the incidence of IP ranges from: 0.2 - 1.5 per 100,000 of the population per year [2,3,4]. This tumor is more prevalent in male (male-to-female ratio=2-5:1) [1]. The vast majority of inverted papillomas occur in adults, with a mean age at diagnosis of 55 years [2,5].

In 1854, Ward first described the occurrence of papillomas in the sinonasal cavity [6]. However, in 1935, Reingertz, histologically described the presence and nature of an IP in the paranasal sinuses [7].

IP arises from the Schneiderian epithelium of the nasal cavity and paranasal sinuses, mainly from the lateral wall of the nose, and, as a rule, has a one-sided nature of the lesion [2,8,9]. Growth of the lesion is characterized by invagination of the integumentary epithelium into the underlying stroma. There are three characteristics, which distinguish an inverted papilloma from other benign synonasal tumors: a high recurrence rate (up to 70%), a high potential of local bone erosion, and a risk of malignancy (5-13%) [9].

The etiology of inverted papillomas has not been fully elucidated [10]. Epidemiological and meta-analytical studies indicate that the human papillomavirus (HPV), in particular HPV-18, and the Epstein-Barr virus may be one of the causes of IP [11-13]. Although the alleged involvement of the Epstein-Barr virus in some studies has not been confirmed [1].Unfortunately, the possibility of recurrence of the disease and the malignant potential of the tumor persist for many years. It has been suggested that the human papillomavirus plays a main role in the pathophysiology of IP over the past 30 years, but the literature data remain controversial. Smoking and allergic sensitization are other factors that have also been debated as possible causes for the development of IPs, so the specific cause of this lesion has not yet been established [3,11,14].

According to published data, the most common site of tumor origin was the ethmoid (48.0%). Tumors originated less frequently within the maxillary sinus (28.0%), lateral nasal wall (10.0%), sphenoid sinus (7.5%), inferior turbinate (2.5%), frontal sinus (2.5%), nasal septum (2.5%) [15]. A number of studies have demonstrated that using computed tomography (CT), allows visualize some focal bone hyperostosis or sclerosis, which indicate the zone of origin of the IP [16]. In 2011, Badaai et al. used an independent radiologists to determine the location of the IP, based on an assessment of the degree of osteitis (areas of hyperostosis). The results of the study confirmed the prognostic value of the radiological localization of the origin of IPs in 41% cases [17].

IP is usually diagnosed in the late stages in average, 1–4 years after the first appearance of sinonasal symptoms [18,19]. Patients' complaints are non-specific, including nasal congestion, anterior and/or posterior rhinorrhea, headache, hyposmia or anosmia, epistaxis or facial pain. The disease is asymptomatic in 4–23% of cases, and the neoplasm is detected accidentally [18, 20].

During endoscopic examination of the nasal cavity and paranasal sinuses, an inverted papilloma usually looks like a reddish-gray, heterogeneous, "lobed" polypoid growths, with a convoluted or wrinkled surface. Tissues affected by the tumor are loose in texture and bleed upon contact with instrumentation [1].

Radiological methods have two main goals: determination the spreading of the tumor and determination the site of the tumor attachment to the bone. CT examination of the paranasal sinuses is the gold standard in the investigation this pathology. The tumor shows nonspecific signal and has an iso-intense, homogeneous character. In a CT scan, microcalcification areas within the neoplasm are detected in approximately 20% of cases, being a pathognomonic sign for diagnosis [21].