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Macular assessment using Optical Coherence Tomography in patients after uneventful phacoemulsification treated postoperatively with bromfenac, diclofenac or dexamethasone

Ocena plamki w badaniu optycznej koherentnej tomografii u pacjentów po niepowikłanej fakoemulsyfikacji leczonych po zabiegu bromfenakiem, diklofenakiem lub deksametazonem

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Abstract: Aim: To assess macular thickness and volume using optical coherence tomography in patients treated with different anti-inflammatory agents after uneventful phacoemulsification.
Material and methods: We analysed macular parameters using optical coherence tomography in 50 consecutive patients (mean age 70.5 years) who underwent uneventful phacoemulsification cataract surgery at the Ophthalmology Department, Medical University of Warsaw between March 2012 and January 2013. Patients were divided into 3 groups, according to 3 different anti-inflammatory agents used during the postoperative period: group T receiving dexamethasone 0.1% (n=17), group Y receiving bromfenac sodium 0.09% (n=16) and group D receiving diclofenac sodium (n=17). We evaluated macular scans obtained the day before surgery and on days 1., 7., 30. and 90. postoperatively. Central subfield thickness, cube volume and cube average thickness were measured during the optical coherent tomography. The data was analysed statistically using the SAS 9.2 software. The graphs were prepared using the STATISTICA 12 software.
Results: A significant increase in central subfield thickness was observed on day 30. postoperatively. However, there were no statistically significant differences in macular thickness between the study groups.
Conclusions: Central retinal thickness increases after uneventful phacoemulsification despite active anti-inflammatory treatment and irrespective of the drug class used.

Key words: phacoemulsification, anti-inflammatory drugs, optical coherence tomography (OCT).

Abstrakt: Cel: ocena stanu plamki w badaniu optycznej koherentnej tomografii po niepowikłanej fakoemulsyfikacji u pacjentów poddanych różnej pooperacyjnej terapii przeciwzapalnej.
Materiał i metody: analizie poddano parametry plamki uzyskane metodą optycznej koherentnej tomografii u 50 chorych (średnia wieku 70,5 roku) po niepowikłanych zabiegach fakoemulsyfikacji zażmy przeprowadzonych w Klinice Okulistyki Uniwersytetu Medycznego w Warszawie w okresie od marca 2012 do stycznia 2013. Pacjentów podzielono na trzy grupy – w zależności od zastosowanej pooperacyjnej terapii przeciwzapalnej: grupa T – stosowano 0,1% deksametazon (n = 17), grupa Y – stosowano 0,09% bromfenak sodu (n = 16), grupa D – stosowano diklofenac (n = 17). Analizie poddano skany plamki wykonane przed operacją, a następnie po 1., 7., 30. i 90. dniu od zabiegu. Ocenie poddano centralną grubość siatkówki, objętość dołka i całkowitą objętość plamki. Analizę statystyczną przeprowadzono z wykorzystaniem programu SAS 9.2, a wykresy sporządzono z wykorzystaniem programu Statistica 12.
Wyniki: po 30. dniu od operacji odnotowano wzrost grubości centralnej części siatkówki. U badanych z poszczególnych grup nie stwierdzono różnic w grubościach siatkówki.
Wnioski: pomimo stosowania miejscowej terapii przeciwzapalnej po niepowikłanej fakoemulsyfikacji wzrasta grubość siatkówki w okolicy plamki, niezależnie od grupy stosowanych leków.

Słowa kluczowe: fakoemulsyfikacja, leki przeciwzapalne, optyczna koherentna tomografia (OCT).

Introduction

Cystoid macular oedema (CME) remains the most common cause of visual acuity decrease following uneventful phacoemulsification despite minimal surgical trauma associated with contemporary cataract surgery (1, 2). In most cases, vi-

sual impairment due to CME is transient, but in some patients, decreased visual acuity may become permanent. There are no strict guidelines for the prevention and treatment of CME, the majority of known algorithms provide for the use of steroidal and non-steroidal anti-inflammatory drugs or their combina-

tions to reduce postoperative inflammatory response and prevent CME (3, 4).

The aim of the study was to assess macular thickness and volume in patients after uneventful phacoemulsification and compare it depending on the post-operative anti-inflammatory treatment they received.

Material and methods

50 consecutive patients (age range: 56–85 years, mean age: 70.5 y.o.) after uneventful phacoemulsification and intraocular lens (IOL) implantation performed at the Ophthalmology Department, Medical University of Warsaw between March 2012 and January 2013 were enrolled in a prospective study. The exclusion criteria included: intraoperative complications, previous intraocular surgery or laser therapy, macular pathologies, uveitis, glaucoma and diabetes. The primary endpoints, that is, the changes in macular thickness and volume after phacoemulsification, were analysed with regard to different anti-inflammatory treatments the patients received. All cataract surgery procedures were performed by an experienced surgeon using the Infinity Platform (Alcon, USA). Postoperatively, the patients were divided into three groups depending on the anti-inflammatory treatment they received: group T (n=17) treated with dexamethasone 0.1% administered four times daily for four weeks, group Y (n=16) treated with bromfenac sodium 0.09% administered two times daily for two weeks and group D (n=17) treated with diclofenac sodium 0.1% administered four times daily for four weeks. Additionally, levofloxacin 0.5% was administered four times daily and tropicamide 1% was administered two times daily in all patients.

We evaluated macular optical coherence tomography (OCT) scans obtained the day before surgery and on days 1, 7, 30 and 90 postoperatively. The OCT macular map protocol was followed (Cirrus OCT, Carl Zeiss Meditec, Inc., San Francisco, CA, USA) which provides for the measurement of the central subfield thickness (CST) (µm), cube volume (CV) (mm³) and cube average thickness (CAT) (µm). Only high quality scans were included into the statistical analysis, which was performed using the SAS 9.2 software while all graphs were generated using the STATISTICA 12 software. The results were expressed as arithmetic means and standard deviations. The null hypothesis of equality of means obtained at all measurement points was verified by the two-way repeated measures ANOVA with alpha of <.05 assumed to be statistically significant.

Results

The mean values of CST at month 1. postoperatively were higher as compared to the respective baseline CST values and the differences were statistically significant.

There were no statistically significant differences in mean values of CST, CAT and CV between the groups Y, D and T at any time-point throughout the study. The measurements are presented in Figures 1, 2 and 3.

The comparison of serial measurements (on postoperative days 1 and 7, and after one month and three months) in each of the treatment groups with the baseline results (prior to cataract surgery) revealed dissimilar effects of the anti-inflammatory treatments used.

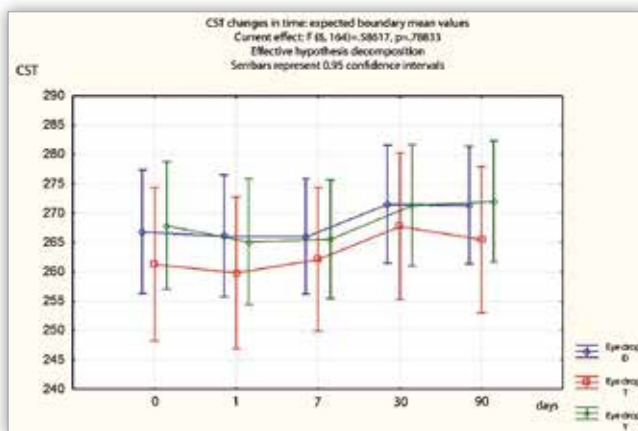


Fig. 1. Comparison of the mean values of central subfield thickness (CST) in consecutive follow-up periods in patients after uneventful phacoemulsification depending on the postoperative anti-inflammatory treatment used. The results of a two-way repeated measures ANOVA. The total effect of differences between groups $p = 0.7769$; the total effect of variance in time $p < 0.0001$; the effect of interaction (different effects of the study treatments at particular measurement points) $p = 0.7883$.

Ryc. 1. Porównanie średnich wartości centralnej grubości siatkówki (CST) w kolejnych okresach obserwacji u pacjentów po niepowikłanej operacji fakoemulsyfikacji zaćmy, w zależności od zastosowanego leczenia przeciwzapalnego. Wyniki dwukierunkowej analizy ANOVA z powtórzonymi pomiarami: łączny efekt różnic między grupami: $p = 0,7769$, łączny efekt zmienności w czasie: $p < 0,0001$, efekt interakcji (odmienne oddziaływanie analizowanych terapii w poszczególnych punktach pomiarowych) $p = 0,7883$.

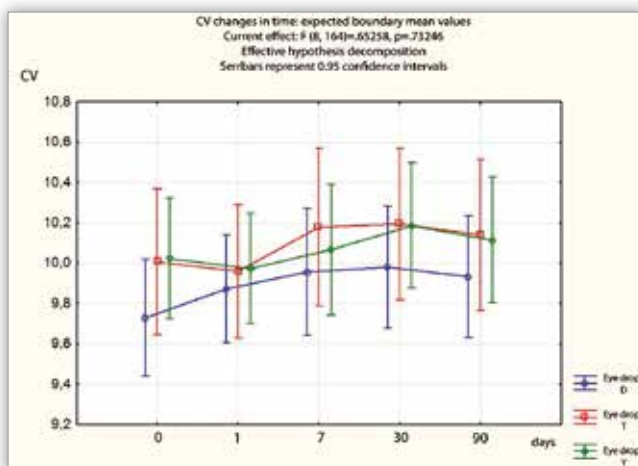


Fig. 2. Comparison of the mean values of cube volume (CV) in consecutive follow-up periods in patients after uneventful phacoemulsification cataract surgery depending on the postoperative anti-inflammatory medication used. The results of a two-way repeated measures ANOVA. The total effect of differences between groups $p = 0.5636$; the total effect of variance in time $p < 0.0001$; the effect of interaction (different effects of the study treatments at particular measurement points) $p = 0.7325$.

Ryc. 2. Porównanie średnich wartości objętości dołka (CV) w kolejnych okresach obserwacji u pacjentów po niepowikłanej operacji fakoemulsyfikacji zaćmy, w zależności od zastosowanego leczenia przeciwzapalnego. Wyniki dwukierunkowej analizy ANOVA z powtórzonymi pomiarami: łączny efekt różnic między grupami: $p = 0,5636$, łączny efekt zmienności w czasie: $p < 0,0001$, efekt interakcji (odmienne oddziaływanie analizowanych terapii w poszczególnych punktach pomiarowych) $p = 0,7325$.

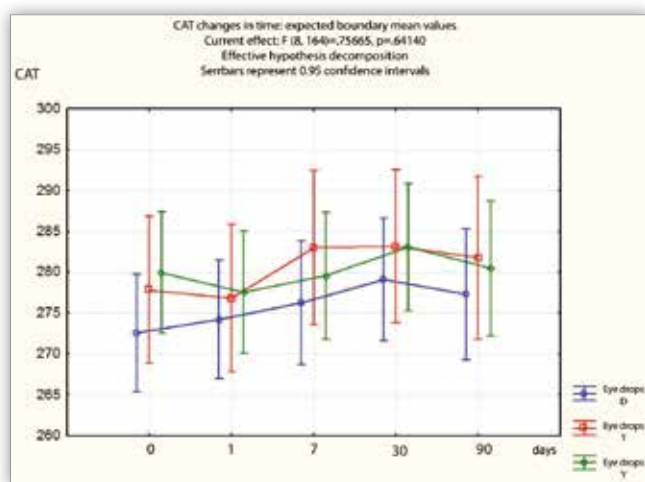


Fig. 3. Comparison of the mean values of cube average thickness (CAT) in consecutive follow-up periods in patients after uneventful phacoemulsification cataract surgery depending on the postoperative anti-inflammatory treatment used. The results of a two-way repeated measures ANOVA. The total effect of differences between groups $p = 0.6230$; the total effect of variance in time $p < 0.0001$; the effect of interaction (different effects of the study treatments at particular measurement points) $p = 0.6414$.

Ryc. 3. Porównanie średnich wartości całkowitej grubości płamki (CAT) w kolejnych okresach obserwacji u pacjentów po niepowikłanej operacji fakoemulsyfikacji zaćmy, w zależności od zastosowanego leczenia przeciwzapalnego. Wyniki dwukierunkowej analizy ANOVA z powtórzonymi pomiarami: łączny efekt różnic między grupami $p = 0.6230$; całkowity efekt zmienności w czasie $p < 0.0001$; efekt interakcji (odmienne oddziaływanie analizowanych terapii w poszczególnych punktach pomiarowych) $p = 0.6414$.

However, the postoperative changes in CST, CV and CAT from baseline in all treatment groups, observed at different time-points were not clinically relevant and fell in the measurement error range.

Discussion

Unexplained decrease of visual acuity after cataract surgery with intraocular lens implantation was first described by Irvine in 1953, while a few years later Gass and Norton linked it to macular oedema with the characteristic fluorescein angiography findings (5, 6). The incidence rate of CME decreased from approximately 60% to approximately 20% with the change of surgical technique from intracapsular to extracapsular cataract extraction, having reached 9-19% confirmed with fluorescein angiography since the advent of small incision cataract surgery. Although CME is OCT-detectable in approximately 41% of patients, significant deterioration of visual acuity is reported only in approximately 0.1–2.0% of cases (2, 5–7). This complication usually occurs 4–12 weeks after cataract surgery (8, 9). In our study, statistically significant increase in retinal thickness without signs of CME, was observed on day 30 after surgery.

The aetiology of CME is not fully understood. Surgically-induced trauma seems the most likely cause, since it induces the release of inflammatory mediators responsible for the weakening of the blood-aqueous and blood-retinal barriers.

At present, standard management of inflammation after cataract surgery includes the topical use of two classes of drugs, i.e.

steroids and non-steroidal anti-inflammatory drugs (NSAIDs). Steroids act on the inflammatory process by inhibiting phospholipase A2 in the arachidonic acid cascade (reduced production of leukotrienes and prostaglandins), inhibiting macrophage and neutrophil migration, decreasing the permeability of blood vessels and producing vasodilation. NSAIDs, on the other hand, act on cyclooxygenases, inhibiting the production of prostaglandins and thromboxane. Thus, they reduce blood vessel permeability and vasodilation and inhibit leucocyte migration. When topically used in ophthalmology, NSAIDs have a proven effect of maintaining pupil dilation (5 – 7, 13–19). Accordingly, increasingly more clinicians advocate the use of NSAIDs after cataract surgery. There are numerous published studies comparing the use of steroids, NSAIDs and combination therapies as well as particular agents. These comparisons address such aspects as the effect on the inflammatory response in the anterior eye segment, as well the role in preventing and managing CME. The most frequently discussed drugs include such NSAIDs as diclofenac sodium 0.1%, ketorolac 0.5%, nepafenac 0.1% or bromfenac 0.09% and corticosteroids such as prednisolone 0.25/1.0%, dexamethasone 0.1%, betamethasone or fluorometholone 1.0% (2, 7, 14–22).

Although both classes of drugs have been found to control the postoperative inflammatory response in patients undergoing cataract surgery to a similar extent, studies by fluorophotometry demonstrated that NSAIDs are more effective than corticosteroids in stabilizing the blood-vitreous barrier (17–20). When different NSAIDs were compared, diclofenac was found to have more potent anti-inflammatory effect than indomethacin and flurbiprofen, but similar to that of ketorolac (6). Bromfenac is a 3–18 times more potent inhibitor of COX2 than amfenac, diclofenac or ketorolac, but ketorolac achieves higher concentrations in the vitreous than bromfenac with the resulting more effective inhibition of prostaglandin production in the anterior segment (6, 17, 21).

Review of studies on adverse events associated with the use of anti-inflammatory drugs reveals increased risks for elevated intraocular pressure, posterior capsule opacity, infection and delayed surgical wound healing in patients using steroids. The most common adverse events-reported with the long-term use of NSAIDs are local and include corneal punctate epitheliopathy, increased inflammatory response with less frequent severe keratitis and iritis, as well as single cases of poor healing or liquefactive necrosis of the cornea.

We did not observe adverse events associated with anti-inflammatory drugs which would require treatment discontinuation in our cohort. Studies comparing steroids and NSAIDs usually consider their effect on intraocular pressure finding its steroid-induced elevation to be significantly higher. Walter et al. observed postoperative macular oedema in 1% of 200 patients treated with prednisolone and in 0.5% of a similar number of patients receiving bromfenac, while elevated intraocular pressure was significantly more frequent in the patients treated with prednisolone (8% vs 3.5%, respectively) (23).

When evaluating the effects of treatment on prevention and management of CME, it is necessary to consider both their efficacy in inhibiting inflammatory mediators and the concentrations achieved in the posterior eye segment after topical administration. Studies in animals did not detect any ketorolac in the vitreous after topical administration, while diclofenac and indomethacin achie-

ved concentrations sufficient to inhibit prostaglandin production in the retina and uvea only to a very small extent. On the other hand, topically administered nepafenac and bromfenac were detected in the retina at concentrations effectively inhibiting prostaglandin production (17, 20). Almeida et al. reported similar efficacy of ketorolac and nepafenac in preventing CME after uneventful cataract surgery (24). One metaanalysis reviewing the efficacy of steroids in preventing CME took into consideration the potency of particular agents (dexamethasone, betamethasone, fluorometholone, rimexolone), but did not find any evident differences between them (6). Kessel et al. analysed the results of published studies comparing NSAIDs and steroids to find that NSAIDs were more effective in preventing and treating CME. The authors emphasized that the studies were carried out in Asian patients and more research is needed in non-Asian patient populations. That is why a study is being conducted in collaboration with the European Society of Cataract and Refractive Surgeons to compare the effects of topical bromfenac and dexamethasone (6, 24). In our study, we did not observe any significant differences in macular thickness and volume between patients after uneventful phacoemulsification cataract surgery treated with dexamethasone 0.1% or bromfenac 0.09% or diclofenac 0.1%. However, the study groups were small and further research in a bigger patient population is needed.

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