(45)

Effect of 0.1% diclofenac ophthalmic solution on inflammatory response and macular thickness following phacoemulsification cataract surgery

Wpływ 0,1% kropli diklofenaku na odczyn zapalny w komorze przedniej oka i stan plamki po operacji fakoemulsyfikacji zaćmy

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Abstract:

Purpose: To evaluate 0.1% diclofenac sodium as an adjunctive therapy with loteprednol etabonate on postoperative inflammation in the anterior chamber and on foveal and parafoveal retinal thickness.

Material and methods: Eighty eyes eligible for phacoemulsification were enrolled in a randomized clinical trial. Patients in group I (N = 40) received anti-inflammatory treatment consisting of 0.1% diclofenac with 0.5% loteprednol; group II (N = 40) patients received 0.5% loteprednol alone. Best corrected visual acuity and intraocular pressure were measured, and laser flare-photometry was done. Foveal and parafoveal thickness were assessed by optical coherence tomography.

Results: Median flare values decreased more rapidly in group I at 7 and 14 days (7.9 and 7.4 ph/ms, respectively) than in group II (13.7 and 11.8 ph/ms, respectively; $p < 0.0001$). Group II had significantly increased parafoveal thickness at 14 and 42 days (median 285.59 μm, $p = 0.001$ and 288.38 μm, $p < 0.001$, respectively). Parafoveal thickness differed significantly between groups at 14 and 42 days ($p = 0.0085$, $p = 0.0004$, respectively).

Conclusions: Eyes treated with both diclofenac sodium and loteprednol etabonate showed less inflammatory response and were less likely to develop foveal and parafoveal thickening than those treated with steroid only.

Key words: cataract surgery, steroids, NSAIDs.

Abstrakt:

Cel: określenie wpływu 0,1-procentowego diklofenaku w skojarzeniu z etabonianem loteprednolu na intensywność odczynu zapalnego w komorze przedniej oka oraz na grubość siatkówki w okolicy plamki u pacjentów po fakoemulsyfikacji zaćmy.

Materiał i metody: prospektywnym, randomizowanym badaniem objęto 80 oczu u 80 pacjentów zakwalifikowanych do operacji zaćmy. U pacjentów z grupy I (N = 40) zastosowano 0,1-procentowy diklofenak łącznie z 0,5-procentowym etabonianem loteprednolu, u pacjentów z grupy II (N = 40) – monoterapię 0,5-procentowym etabonianem loteprednolu. Analizie poddano: ostrość wzroku, ciśnienie wewnątrzgałkowe, intensywność odczynu zapalnego w komorze przedniej w badaniu flarefotometrii laserowej, grubość siatkówki w okolicy plamkowej badaną za pomocą optycznej koherentnej tomografii.

Wyniki: w dobach 7. i 14. zanotowano znamienne statystycznie zmniejszenie wartości flarefotometrii (7,9 i 7,4 ph/ms) u pacjentów z grupy I w porównaniu z pacjentami z grupy II (13,7 i 11,8 ph/ms) ($p < 0,0001$ między grupami w dobach 7. i 14.)

W okolicy plamkowej wzrost wartości grubości siatkówki po 2 i 6 tygodniach był istotnie statystycznie większy u pacjentów z grupy II: odpowiednio 285,59 i 288,38 μm – zarówno w porównaniu ze stanem przedoperacyjnym ($p = 0,001$ i $p < 0,001$), jak i ze zmianami zaobserwowanymi u pacjentów z grupy I ($p = 0,0085$ i $p = 0,0004$).

Wnioski: istotny wpływ na zmniejszenie nasilenia odczynu zapalnego w komorze przedniej ma zastosowanie 0,1-procentowego diklofenaku w skojarzeniu z etabonianem loteprednolu w porównaniu z monoterapią steroidem. Zastosowanie terapii skojarzonej ogranicza zwiększenie grubości siatkówki, doprowadzając do jej wcześniejszej normalizacji w porównaniu do stanu po zastosowaniu monoterapii steroidem.

Słowa kluczowe: operacja zaćmy, steroidy, NLPZ.

Introduction

According to the World Health Organization, cataract is the leading cause of blindness and visual impairment in the world. The incidence rate of world blindness due to cataract was 51% in 2010, representing approximately 20 million persons (90% of them in developing countries). This number is expected to increase to 40 million by 2020 (1–5).

Refinements of cataract surgical techniques and improvements in implanted intraocular lenses have helped to lower trauma to eye tissues during surgery (6–8). As a consequence, the intensity of the postoperative inflammatory response after uncomplicated cataract surgery has been markedly decreased. Nevertheless, the surgical procedure remains a trauma that induces an inflammatory response (6, 7, 9–14).

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The blood–ocular barriers play a fundamental role in protecting and maintaining the most appropriate microenvironment for physiological cell function. These barriers include two main systems: the blood–aqueous barrier and the blood–retinal barrier (BRB). Both systems are essential in regulating the content of eye's inner fluids and protecting the internal ocular tissues from variations that continually occur in the circulation. The BRB is particularly tight and restrictive, and it serves as a physiologic barrier that regulates ion, protein, and water flux into and out of the retina.

Past these barriers, no major diffusional barriers exist between the extracellular fluid of the retina and the vitreous. In addition, the vitreous body itself does not significantly hinder diffusion exchanges between the posterior chamber and the retinal extracellular fluid. The functions of both the blood–aqueous barrier and BRB influence each other and must work in equilibrium (15–18).

Macular edema is a clinically relevant response to a changed retinal environment. In most cases, it is associated with a disruption of the BRB. The pathogenesis of cystoid macular edema (CME) involves surgical trauma to the iris, ciliary body, or lens epithelial cells. This trauma causes a release of phospholipids that induce several pathways, including the arachidonic acid cascade, which in turn generate inflammatory mediators, including prostaglandins (PGL). The mediators diffuse through the vitreous to disrupt the BRB, causing serum to pool in the macular tissue. The risk of CME is increased by conditions that affect the BRB, such as diabetes, hypertension, aging, and uveitis. The prevalence of CME after cataract surgery is increased by surgical complications (e.g., vitreous loss). However, CME is the most frequent cause of decreased postoperative vision in patients having uneventful cataract surgery (18, 19).

The clinical presentation of severe inflammation includes pain, hyperaemia, photophobia, miosis, flare in the anterior eye chamber, reduced visual acuity, elevated intraocular pressure, and CME (11, 20–22). CME is a defining characteristic of Irvine-Gass syndrome when it occurs postoperatively (23, 24). The data on CME incidence are highly variable (12, 13, 20, 25, 26), and the actual incidence of the Irvine-Gass syndrome has not been exactly established.

The diagnostic techniques for CME include high-magnification stereoscopic ophthalmoscopy using the slit lamp and several types of contact and non-contact lenses to help visualize the oedematous macula; stereoscopic retinal photography; and fluorescein angiography to visualize circulatory dynamics and the macular circulation, down to the capillary level. The most recent diagnostic technique is optical coherence tomography (OCT), a rapid, non-invasive technique that permits accurate measurement of the macular thickness and yields high-resolution tissue sections of the maculae of living subjects with almost histologic clarity.

As suggested by some authors, CME occurs after small-incision cataract surgery in 9–19% and 41% of the cases on the basis of fluorescein angiography and OCT examinations, respectively (25, 27–30). The difference underlines the importance of OCT in the diagnosis, prevention and treatment monitoring of CME.

Non-steroidal anti-inflammatory drugs (NSAIDs) constitute a large and diverse class of medicines with anti-inflammatory, antipyretic and analgesic properties. Numerous studies have confirmed the anti-inflammatory action of NSAIDs used topically after cataract removal surgery (7, 9, 11, 31–34). According to some reports (6, 35–37), the anti-inflammatory efficacy of NSAIDs is at least equivalent to that of steroid drops, and in contrast to steroids, their use is not associated with a risk of certain side effects such as post-steroidal glaucoma (10, 11, 38–40). Many authors have suggested that NSAIDs and steroids are additive in their actions (7, 8, 40–42). There have been reports confirming higher efficacy of steroids in combination with NSAIDs in the treatment or prevention of CME (7, 26, 43). This allows the use of NSAIDs instead of steroids (6, 35–37) or a combination of NSAIDs with steroids to minimise the inflammatory reaction after cataract surgery (38, 39, 44, 45).

Purpose

The purpose of this study was to assess the effect of 0.1% diclofenac sodium ophthalmic solution in combination treatment on the intensity of inflammatory reaction in the anterior chamber and on foveal and parafoveal retinal thickness in patients undergoing uncomplicated cataract surgery by phacoemulsification with artificial intraocular lens implantation.

Material and methods

The prospective randomised study included 80 eyes of 80 patients, including 50 women and 30 men aged 47–90 years (mean 70 years) eligible for cataract removal surgery. All patients provided the written informed consent. The study was conducted according to the Tenets of the Declaration of Helsinki and Good Clinical Practice. All patients underwent the procedure of phacoemulsification with endocapsular implantation of a foldable intraocular lens between February 2010 and March 2012.

Patients with complicated cataract (with post-traumatic cataract, coexisting glaucoma, pseudoexfoliation syndrome, history of uveitis, degenerative myopia), as well as those with macular diseases and systemic disorders influencing postoperative inflammatory reaction (such as diabetes, bronchial asthma, collagenoses, rheumatoid arthritis, ankylosing spondylitis, gout, psoriasis) were not eligible for the inclusion in the study.

The patients were divided into 2 groups according to the postoperative anti-inflammatory treatment applied. In group I (D + L) ($N = 40$), a 0.1% diclofenac sodium ophthalmic solution (Dicloabak, Laboratoires Thea, France) was used in combination with a steroid product, 0.5% loteprednol etabonate (Lotemax, Bausch & Lomb/Dr. Gerhard Mann, Germany). In group II (L) ($N = 40$), monotherapy with 0.5% loteprednol etabonate (Lotemax, Bausch & Lomb/Dr. Gerhard Mann) was used.

The drops were administered for 6 weeks, starting 4 times daily, on the day before the surgical procedure and continuing for 2 weeks after the operation. The frequency was decreased to 3 times daily for the next 2 weeks and twice daily for the last 2 weeks. All patients also received antibiotic drops, 0.5% levofloxacin (Oftaquix, Santen Oy, Finland) for 2 weeks, and a hydrating product, 5% dexpanthenol (Corneregel, Bausch & Lomb/Dr. Gerhard Mann, Germany), tapering for 6 weeks.

Best corrected visual acuity (Snellen charts) was assessed, and intraocular pressure (mm Hg) was measured by Goldmann applanation tonometry. The severity of inflammation in the anterior chamber (ph/ms) was measured with the use of a laser flaremeter (KOWA), and foveal and parafoveal retinal thicknesses (μm) were measured by OCT (Cirrus, Zeiss).

The laser flaremeter FM-600 (KOWA) is a non-contact laser system designed to measure the protein concentration in the aqueous humour of the anterior chamber of the eye. It is a rapid non-contact examination, and it yields an average of at least 5 reliable measurements performed with mydriasis. Retinal thickness was evaluated at the central point (central retinal thickness), in the fovea (Ø 1.0 mm) and within the parafoveal ring (Ø 6.0 mm) with the use of OCT Cirrus (Zeiss).

Phacoemulsification Ozil™ was performed in a typical manner, under local anaesthesia and without complications. A 2.2 mm incision was made in the clear cornea. A one-piece acrylic foldable lens was implanted into the lens capsule, and the viscoelastic material was thoroughly removed in the final stage of surgery. The wound was tightened with Ringer fluid, without the use of sutures. Examinations were performed before surgery and after surgery on days 1, 7, 14 and 42.

Statistical methods

A generalised estimating equation was used to analyse the significance of investigated parameters in subsequent measurements. Normality of distribution of the tested parameters in the treatment groups was examined with the use of the Shapiro-Wilk test. In the case of deviations from normality assumptions, logarithmic transformation of the given parameter was performed or a continuous parameter was replaced with an indicator variable (0/1). Linear regression was used for continuous variables, and logit regression was used for indicator variables.

The models took into account the measurement time (0, 1, 7, 14, 42 days), the treatment type (L *vs* D + L) and the interaction between the treatment and measurement time. In linear models, the differences between the mean values in subsequent measurements and for different treatment types were expressed as β. A positive β means an increase of the value of the parameter analysed between the specified measurements or treatment types; a negative β indicates a decrease. The value of β for the interactions between the measurement type and treatment time, if significantly different than 0, indicates that the observed changes over time in the L group differ from those in the D + L group.

Logit models analyse differences in frequency of an event (success) defined as obtaining the values of the specified parameter above the adopted cut-off point. Thus, the odds ratio of this event to occur measures the discussed difference. The odds ratio is the quotient of number of observations with values above the cut-off point per 1 observation and the number of observations with values below the cut-off point, i.e. success/failure ratio ("success" and "failure" used here are used figuratively and should not be understood as a therapeutic success or failure).

To measure the differences between subsequent measurements and the odds for success, the success odds are determined at each point in time (0, 1, 7, 14, 42 days), and then the odds ratio (OR) is calculated for the given measurement against, for example, the baseline measurement. An OR of 1 means the same odds of success as in the compared groups; OR $>$ 1 means that for one measurement, success odds are greater than for the other one; and OR $<$ 1 means the opposite result. The same applies to the comparison between groups differing by the treatment. Calculations were performed in Stata, v.10. (Stata Statistical Software: Release 10, College Station, TX, Stata Corporation LP 2007).

Results

The best corrected distance visual acuity was similar in patients in both groups, and intraocular pressure also did not differ significantly in patients in the study groups during study observation (L *vs*. D + L, $p > 0.1$). A significant decrease was observed in the intensity of the inflammatory reaction on days 7 and 14 in patients treated with diclofenac in combination with the steroid product (D + L), in comparison with those treated with only loteprednol etabonate (L) (Fig. 1). It is worth mentioning that already at 14 days the value of the inflammatory response in the D + L group did not differ significantly from the value before the surgical procedure (Tab. I). The β values in the model correspond to the differences between log(FLARE).

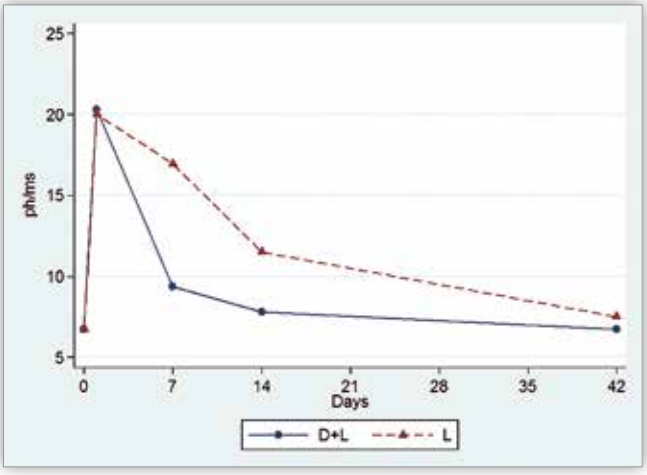

Fig. 1. Severity of inflammatory response in the anterior chamber.
Ryc. 1. Intensywność odczynu zapalnego w komorze przedniej oka.

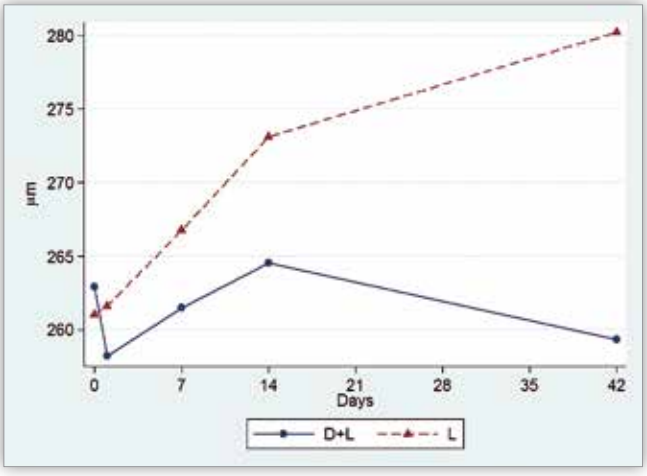

Fig. 2. Foveal retinal thickness.
Ryc. 2. Grubość siatkowki w dołku środkowym.

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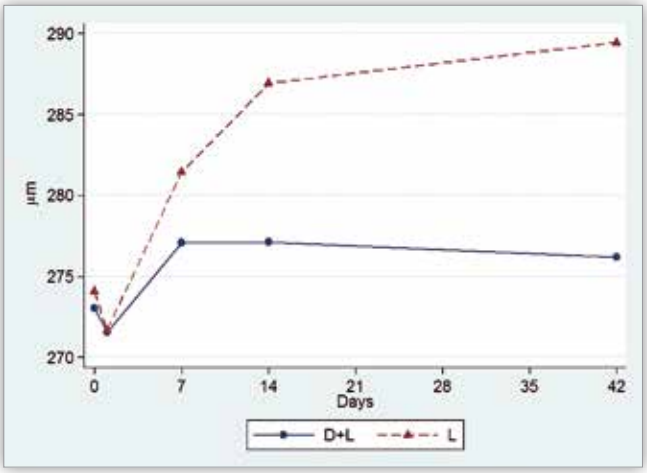

Fig. 3. Parafoveal retinal thickness.
Ryc. 3. Grubość siatkówki w obszarze plamkowym.

In the D + L group, in measurements at 1 and 7 days, the mean values of log(FLARE) were higher than at the baseline by 1.07 and 0.25, respectively. The differences in measurements at 7 and 14 days in the L group were higher than the differences in the D + L group by 0.78 and 0.59 (statistically significant interactions). The difference in log(FLARE) between measurements at 1 and 0 days in both groups was the same: 1.07. In the D + L group, the difference between measurements at 7 and 0 days was 0.25, and in the L group it was 1.03 (including β value 0.78). The difference between measurements at 14 and 0 days in the D + L group was not statistically significant ($p > 0.1$) and in the L group was 0.59 ($p < 0.001$). The difference between measurements at 42 and 0 days in both groups was insignificant ($p > 0.1$). The mean values of log(FLARE) in the L and D + L groups at time 0 did not differ (L *vs*. D + L, $p > 0.1$) as shown in Table II.

The values of foveal retinal thickness (Ø 1.0 mm) and of parafoveal retinal thickness (Ø 6.0 mm) are presented in Figures 2 and 3 and in Tables III–VI, respectively. The values of β in the model represent differences in foveal retinal thickness (Ø 1.0 mm).

D + L	N	Min.	Max.	Mean/ Średnia	SD	Median/ Mediana	p25	p75
0	40	1.00	14.70	6.82	2.60	6.70	5.30	7.60
1	40	7.60	76.90	20.59	11.88	17.50	13.65	24.55
7	40	1.40	21.30	8.91	3.92	7.90	6.40	10.35
14	40	2.70	24.80	7.76	3.49	7.40	5.80	9.05
42	40	1.20	17.00	6.78	2.69	6.45	4.95	8.75
L								
0	40	2.30	11.70	6.33	2.44	5.85	4.70	7.85
1	40	6.80	52.7	21.23	11.32	18.80	13.60	27.90
7	40	6.50	52.20	19.96	13.63	13.70	9.90	23.75
14	40	3.20	31.90	13.71	6.92	11.80	9.05	16.75
42	40	1.70	13.80	7.82	3.05	7.65	5.60	9.85

Inter-group comparisons at subsequent points in time, based on the model/ Porównanie wartości u pacjentów z obu grup w kolejnych punktach w czasie, na podstawie modelu.

Time/ Punkt czasowy	0	1	7	14	42
L *vs* D + L	$p > 0.1$	$p > 0.1$	$p < 0.0001$	$p < 0.0001$	$p > 0.1$

Tab. II. Flaremeter value (ph/ms).
Tab. II. Wartości flarefotometrii laserowej (ph/ms).

In the D + L group, no statistically significant differences were observed in subsequent measurements compared with measurements at 0 days. In the L group, the difference between measurements at 14 and 0 days was 10.46, and the difference between measurements at 42 and 0 days was 22.75 (statistically significant interaction). The mean values of foveal retinal thickness (Ø 1.0 mm) in the L and D + L groups at time 0 did not differ (L *vs*. D + L, $p > 0.1$). No stati-

Log(Flare)	ß	95% CI for ß	*p*
L *vs* D + L			>0.1
Differences in D + L and L/ Różnice w D+L i L			
Measurement 1 *vs* 0/ Pomiar 1. *vs* 0	1.07	(0.91,1.24)	<0.001
Measurement 7 *vs* 0/ Pomiar 7. *vs* 0	0.25	(0.09, 0.41)	0.002
Measurement 14 *vs* 0/ Pomiar 14. *vs* 0			>0.1
Measurement 42 *vs* 0/ Pomiar 42. *vs* 0			>0.1
Additional differences in L/ Dodatkowe różnice w L			
Measurement 1 *vs* 0/ Pomiar 1. *vs* 0			>0.1
Measurement 7 *vs* 0/ Pomiar 7. *vs* 0	0.78	(0.55, 1.00)	<0.001
Measurement 14 *vs* 0/ Pomiar 14. *vs* 0	0.59	(0.36, 0.82)	<0.001
Measurement 42 *vs* 0/ Pomiar 42. *vs* 0			0.08

Tab. I. Linear model for flaremeter, after logarithmic transformation.
Tab. I. Flarefotometria laserowa – model liniowy po zastosowaniu transformacji logarytmicznej.

D + L	N	Min.	Max.	Mean/ Średnia	SD	Median/ Mediana	p25	p75
0	40.00	201.23	280.25	262.91	33.27	260.50	249.00	282.71
1	40.00	214.81	323.46	258.19	23.03	259.75	243.00	270.80
7	40.00	204.00	333.00	261.46	28.35	262.75	240.12	273.92
14	40.00	219.75	319.75	264.54	24.18	265.50	251.50	278.12
42	40.00	220.99	297.00	259.35	20.38	260.00	243.00	273.50
L								
0	40.00	188.89	346.91	261.02	29.60	259.50	251.43	276.00
1	40.00	198.77	332.10	261.60	26.95	260.13	245.68	278.00
7	40.00	187.65	330.86	266.75	29.62	264.00	255.56	278.50
14	40.00	216.05	371.00	273.10	33.45	269.69	257.00	290.18
42	40.00	225.93	371.60	280.20	31.46	275.00	260.00	295.68

Inter-group comparisons at subsequent points in time, based on the model/ Porównanie wartości u pacjentów z obu grup w kolejnych punktach czasowych, na podstawie modelu.

Time/ Punkt czasowy	0	1	7	14	42
L *vs* D + L	$p > 0.1$	$p > 0.1$	$p > 0.1$	$p > 0.1$	$p < 0.0009$

Tab. III. Foveal retinal thickness – Ø 1.0 mm (μm).
Tab. III. Grubość siatkówki w dołku środkowym – Ø 1,0 mm (μm).

	ß	95% CI for ß	*p*
L *vs* D + L			>0.1
Differences in D + L and L/ Różnice w D + L i L			
Measurement 1 *vs* 0/ Pomiar 1. *vs* 0			>0.1
Measurement 7 *vs* 0 / Pomiar 7. *vs* 0			>0.1
Measurement 14 *vs* 0 / Pomiar 14. *vs* 0			>0.1
Measurement 42 *vs* 0 / Pomiar 42. *vs* 0			>0.1
Additional differences in L/ Dodatkowe różnice w L			
Measurement 1 *vs* 0/ Pomiar 1. *vs* 0			>0.1
Measurement 7 *vs* 0/ Pomiar 7. *vs* 0			>0.1
Measurement 14 *vs* 0/ Pomiar 14. *vs* 0	10.46	(–0.03, 20.96)	0.051
Measurement 42 *vs* 0/ Pomiar 42. *vs* 0	22.75	(12.26, 33.25)	<0.001

Tab. IV. Linear model for foveal retinal thickness – Ø 1.0 mm.
Tab. IV. Model liniowy dla grubości siatkówki w dołku środkowym – Ø 1,0 mm.

stically significant increase in retinal thickness was observed in patients in the D + L group. In patients in the L group, after 14 and 42 days of treatment, a persistent increase in foveal (Ø 1.0 mm) retinal thickness was observed in comparison with the baseline. Also, in the parafoveal region, within a 6-mm-diameter ring, a statistically significant increase in the retinal thickness was found in patients in the L group at 7, 14 and 42 days after treatment, in comparison with the baseline value. The values of β in the model represent differences in parafoveal retinal thickness (Ø 6.0 mm). In the D + L group, in measurements at 7 and 14 days, retinal thickness was higher than in the baseline measurement by 4.04 and 4.10 ($p = 0.027$, $p = 0.025$, respectively). The differences in measurements at 14 and 42 days in the L group were higher than the differences in the D + L group by 8.75 and 12.18 ($p = 0.001$, $p < 0.001$ respectively). The difference between measurements at 42 and 0 days in the D + L group was insignificant ($p > 0.1$) and in the L group was 12.18 ($p < 0.001$). The mean values of parafoveal retinal thickness (Ø 6.0 mm) in the L and D + L groups at time 0 did not differ (L *vs*. D + L, $p > 0.1$). The difference in retinal thickness in the parafoveal ring (Ø 6.0 mm) between measurements on days 1 and 0 in both groups was the same and statistically insignificant ($p > 0.1$).

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D + L	N	Min.	Max.	Mean/ Średnia	SD	Median/ Mediana	p25	p75
0	40	231.18	306.18	273.02	16.80	275.84	261.32	281.49
1	40	228.82	300.50	271.56	15.76	272.40	260.21	282.40
7	40	240.00	344.71	277.06	19.22	274.85	262.43	288.39
14	40	245.88	303.82	277.12	14.49	279.00	266.91	289.85
42	40	231.76	300.29	276.21	15.32	277.55	265.84	287.26
L								
0	40	231.47	309.00	274.07	16.51	273.97	266.88	282.25
1	40	240.25	307.65	271.67	15.14	272.97	261.75	280.50
7	40	255.88	308.53	281.42	14.03	281.34	270.44	292.97
14	40	241.47	351.76	286.92	20.51	285.59	273.50	298.24
42	40	254.41	352.06	289.44	19.53	288.38	276.38	300.63

Inter-group comparisons at subsequent points in time, based on the model/ Porównanie wartości u pacjentów z obu grup w kolejnych punktach czasowych, na podstawie modelu.

Time/ Punkt czasowy	0	1	7	14	42
L *vs* D + L	$p > 0.1$	$p > 0.1$	$p > 0.1$	$p < 0.0085$	$p < 0.0004$

Tab. V. Parafoveal retinal thickness – Ø 6.0 mm (μm).
Tab. V. Grubość siatkówki w obszarze plamkowym – Ø 6,0 mm (μm).

	ß	95% CI for ß	*p*
L *vs* D + L			>0.1
Differences in D + L and L/ Różnice w D + L i L			
Measurement 1 *vs* 0/ Pomiar 1. *vs* 0			>0.1
Measurement 7 *vs* 0/ Pomiar 7. *vs* 0	4.04	(0.46, 7.62)	0.027
Measurement 14 *vs* 0/ Pomiar 14. *vs* 0	4.10	(0.52, 7.68)	0.025
Measurement 42 *vs* 0/ Pomiar 42. *vs* 0			0.081
Additional differences in L/ Dodatkowe różnice w L			
Measurement 1 *vs* 0/ Pomiar 1. *vs* 0			>0.1
Measurement 7 *vs* 0/ Pomiar 7. *vs* 0			>0.1
Measurement 14 *vs* 0/ Pomiar 14. *vs* 0	8.75	(3.68, 13,81)	0.001
Measurement 42 *vs* 0/ Pomiar 42. *vs* 0	12.18	(7.11, 17.24)	<0.001

Tab. VI. Linear model for parafoveal retinal thickness – Ø 6.0 mm.
Tab. VI. Model liniowy dla wartości grubości siatkówki w obszarze plamkowym – Ø 6,0 mm.

Discussion

Along with dynamic progress in surgical methods, a rapid decrease has occurred in the intensity of postoperative inflammatory response after uncomplicated cataract surgery in recent years (6, 7, 37). However, we cannot definitely rule out the possibility of significant postoperative inflammatory response in individual cases. Therefore, routine use of anti-inflammatory agents after cataract removal surgery is widely adopted practice (10, 11, 21, 32, 41). The surgical trauma can activate phospholipase A_2 (PLA-2), which can also trigger the arachidonic acid cascade and lead to PGL production. The transformation of arachidonic acid into PGL depends on cyclooxygenase (COX). Various anti-inflammatory drugs block the individual stages of the transformation. Through their effect on PLA-2, steroids inhibit arachidonic acid release and the production of its metabolites, including PGL. In contrast, NSAIDs irreversibly inhibit PGL synthesis through their effect on COX-1 and COX-2 activity (19, 46–48). NSAIDs inhibit PGL production more effectively than steroids (49). In view of the different molecular targets of steroids and NSAIDs, their synergistic action can be used in combined anti-inflammatory therapy (39).

The results of our study suggest that diclofenac sodium paired with loteprednol etabonate significantly contributes to lowering

the inflammatory response in the anterior chamber after phacoemulsification. Many reports also confirm the efficacy of topical NSAIDs in treating the postoperative inflammatory response (7, 10, 11, 33, 38–40). Interestingly, studies conducted by Laurell and Zetterström (6) as well as Miyake et al. (43) demonstrated that diclofenac monotherapy is as effective as dexamethasone or fluorometholone. El-Harazi et al. (35) showed that the anti-inflammatory action of diclofenac does not significantly differ from that of prednisolone. Biro et al. (50) and Georgopoulos et al. (51) observed a postoperative increase in retinal thickness that had no significant effect on visual acuity after uncomplicated phacoemulsification.

Questions arise about how often subclinical CME develops and whether CME prevention, not just treatment of the existing condition, is justified. As shown by our study, diclofenac sodium used in combination with loteprednol etabonate prevents a significant increase in retinal thickness after uneventful phacoemulsification. Whereas in patients treated with local steroid only, a persistent increase in foveal retinal thickness in comparison with the baseline was observed during follow-up visits.

The beneficial effect of NSAIDs in the prevention and treatment of Irvine-Gass syndrome has been confirmed by numerous studies (11, 12, 20–22, 43, 47). Flach (41) suggested a clear possibility of synergism of ketorolac and prednisolone in combined treatment of pseudophakic macular edema. Wittpenn et al. (7) reported that adding ketorolac drops to prednisolone significantly reduces the frequency of CME and retinal thickness post-surgery. Wolf et al. (31) proved that patients treated with topical prednisolone alone had a significantly higher incidence of CME after uneventful cataract surgery compared to patients treated with combined therapy of prednisolone and nepafenac.

Therefore, using the synergistic anti-inflammatory action of diclofenac paired with a steroid product is justified in reducing the postoperative inflammatory response and also in preventing and treating complications associated with cataract surgery.

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