Intravitreal Dexamethasone Implant in the Treatment of Diabetic Macular Edema Focusing on the Role of Oct Biomarkers

Mudroch Tomáš[1,2], Hrevuš Michal[1,2], Karhanová Marta[1,2], Řehák Jiří[1,2], Marešová Klára[1,2]

[1]University Hospital Olomouc, Department of Ophthalmology, Czech Republic
[2]Palacký University in Olomouc, Faculty of Medicine and Dentistry, Department of Ophthalmology, Czech Republic

MUDr. Tomáš Mudroch

Correspondence address:
Oční klinika LF UP a FN Olomouc
Zdravotníků 248/7
77900 Olomouc
Česká republika
E-mail: tomas.mudroch@fnol.cz

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SUMMARY

Objective: The aim of this study was to evaluate the outcomes of Ozurdex® (DEX) implant in patients with diabetic macular edema (DME) in real-world clinical practice, and to determine the correlation between known OCT biomarkers and the effect of treatment.
Material and Methods: This retrospective study included 42 eyes of 33 patients (16 women, 17 men) treated with DEX at the Department of Ophthalmology, Faculty of Medicine and Dentistry of Palacký University and University Hospital Olomouc for DME indication between 2020 and 2023. Follow-up examinations were conducted at 1, 3, and 6 months after the first DEX application. The main assessed parameters were: best-corrected visual acuity (BCVA), intraocular pressure (IOP), central retinal thickness (CRT), OCT biomarkers. The results were subsequently statistically evaluated.
Results: At the first follow-up after DEX application, there was an average decrease in CRT of 186 ±146μm and a gain of 3 ±7 letters. Positive morphological and functional responses were observed in 39 eyes (92.9%) and 23 eyes (54.8%) respectively. The disorganization of retinal inner layers (DRIL) biomarker was initially present in 41 eyes (97.6%), with reduction or disappearance observed in 13 eyes (31%) post-application. Eyes with ellipsoid zone disruption (EZ disruption) had an average initial BCVA of 49.6 letters, compared to 57.8 letters in the group without this biomarker. The mean gain in BCVA was +8.7 letters in treatment-naive eyes and +2.1 letters in previously treated eyes. Chronic DME was less frequent in treatment-naive ($n = 1$, 14.3%) compared to previously treated eyes ($n = 28$, 84.8%). All these results were statistically significant ($p < 0.05$). An increase in IOP post-DEX application occurred in 9 patients (21.4%).
Conclusion: Our results confirm DEX as a safe and effective treatment option for DME. Treatment-naive patients achieved better functional outcomes. We confirmed ellipsoid zone disruption (EZ disruption) as a negative biomarker. Additionally, we demonstrated the capacity of DEX to reduce disorganization of the retinal inner layers (DRIL).
Key words: diabetic macular edema, OCT biomarkers, dexamethasone, Ozurdex

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INTRODUCTION

Diabetic macular edema (DME) occurs in approximately 7% of patients with diabetes mellitus (DM). Within the course of 10 years from the determination of a diagnosis of diabetes, DME develops in 20% of patients with type 1 DM and 25% of patients with type 2 DM [1]. Within two years, untreated DME leads to a deterioration of visual acuity (VA) by 2 or more rows in approximately 50% of patients [2]. With regard to the constantly increasing prevalence and increase in the number of complications, DM is becoming the main cause of severe loss of sight in the population of productive age [3]. In the Czech Republic one million patients were recorded with DM in 2017, and in the coming years an increase of 30% is expected [4].

The therapeutic options for DME include, among others, pharmacological intraocular intravitreal treatment (corticoids, anti-VEGF preparations). Of the group of corticoids, the pharmaceuticals currently used are molecules of triamcinolone acetonide, fluocinolone acetonide and dexamethasone. Dexamethasone is available as the intravitreal implant Ozurdex® (AbbVie Deutschland GmbH & Co.KG, Ludwigshafen, Germany), hereinafter referred to as DEX. This is a biodegradable drug with extended slow release and an effect lasting approximately 2–6 months. The implant contains 0.7 mg of dexamethasone [5].

At present, the gold standard in the treatment of DME is considered to be the application of anti-VEGF preparations, and corticoids are mostly administered as the drug

of second choice for patients with persistent chronic DME with an insufficient response to anti-VEGF treatment [6,7]. The aim of recent studies is the individualization of DME treatment and an endeavor to select suitable patients who would benefit from the application of DEX [1].

Spectral-domain optical coherence tomography (OCT) is used especially in the diagnosis and evaluation of DME. With the aid of OCT it is possible to assess specific markers which can be used as predictors of response to DEX treatment [1]. Correct evaluation and knowledge of these biomarkers may provide fundamental information for a suitable choice of treatment.

The aim of our observation was to evaluate the effect of treatment with an intravitreally applied DEX implant in patients with DME in actual clinical practice, and to determine the benefit of OCT biomarkers as potential prognostic predictors.

MATERIAL AND METHOD

Design of study and characteristics of cohort

The retrospective study includes patients with DME on whom treatment with the aid of DEX was commenced at the Department of Ophthalmology at the University Hospital Olomouc from September 2020 to July 2023. The observation of these patients continued until December 2023.

The inclusion criteria were as follows: DME, at least one application of DEX and length of observation of at least 3 months from the first application. The exclusion criteria were as follows: macular edema upon a background of another ocular pathology (age-related macular degeneration, retinal vein occlusion, uveitis, choroidal neovascular membrane), laser photocoagulation (LPC), intraocular surgery and treatment with another intravitreal preparation within the course of 3 months before the commencement of treatment with DEX, cataract surgery within a period of 6 months before the commencement of treatment. Treatment-naive patients were defined as patients who had not undergone any previous treatment with an intravitreal preparation. DME persisting for longer than 2 years was classified as chronic.

A total of 42 eyes of 33 patients (16 women, 17 men) aged between 53 and 87 years (median 71.5) were included in the observation. The mean baseline value of glycated hemoglobin (HbA1c) was 62.3 mmol/mol. The basic characteristics of the cohort are presented in Table 1. The cohort was predominantly composed of patients with type 2 DM, artephakic eyes and chronic DME. The majority of eyes (n = 35, 83.3%) had previously been treated with another intravitreal preparation (triamcinolone acetonide 26 eyes, ranibizumab 10 eyes, aflibercept 5 eyes).

Method

Before the commencement of treatment, the patients' detailed ocular and general medical history was recorded, as well as the current value of HbA1c. Follow-up examinations were conducted on the patients 1, 3 and 6 months after application. In the case of 5 patients, omission of the follow-up examination after 1 month was tolerated, and the first examination took place within 3 months of the commencement of treatment. The follow-up examination six months after application was conducted on 32 eyes (76%). At the follow-up examinations patients were examined for best corrected visual acuity (BCVA) on an ETDRS chart, a detailed ophthalmological examination was conducted in artificial mydriasis on a slit lamp, intraocular pressure (IOP) was measured using a noncontact tonometer (Canon TX-20P), and an OCT evaluation was conducted (Spectral Domain, Heidelberg Engineering, Germany).

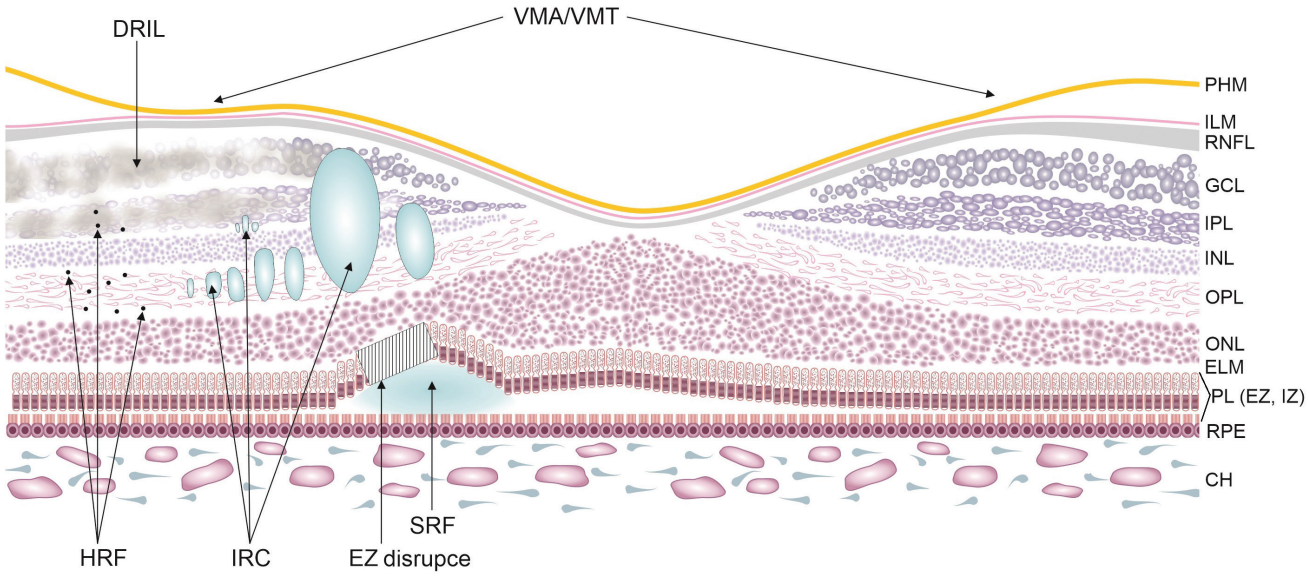


Figure 1. Scheme of OCT biomarkers in diabetic macular edema
Biomarkers: *DRIL – disorganization of retinal inner layers; HRF – hyperreflective foci; IRC – intraretinal cysts; EZ disrupce – disruption of ellipsoid zone continuity; SRF – subretinal fluid; VMA / VMT – vitreomacular adhesion / vitreomacular traction*
Retinal layers: *PHM – posterior hyaloid membrane; ILM – inner limiting membrane; RNFL – retinal nerve fiber layer; GCL – ganglion cell layer; IPL – inner plexiform layer; INL – inner nuclear layer; OPL – outer plexiform layer; ONL – outer nuclear layer; ELM – external limiting membrane; PL (EZ, IZ) – ellipsoid zone, outer segments and interdigitation zone; RPE – retinal pigment epithelium; CH – choroid*

OCT analysis (Evaluation of OCT scans adjusted according to Vujosevic et al. [8])
Evaluation of the OCT scans was performed by a single ophthalmologist. Central retinal thickness (CRT) was measured in µm with the aid of an automatic analysis of the instrument software. In the case of other OCT biomarkers, the ophthalmologist evaluated their presence and change manually, always before the commencement of treatment and at the first follow-up examination after the application (Fig. 1, 2).

Large intraretinal cysts (IRC) were measured manually by a caliper of the OCT instrument software within an area of 3 mm centered on the fovea, in which the criterion was a diameter of the cyst of ≥ 250 µm. Disorganization of retinal inner layers (DRIL) was evaluated as an absence of a distinguishable border between the layer of ganglion cells and the inner plexiform layer within an area of 1 mm centered on the fovea. The presence of hyperreflective foci (HRF) was observed within an area of the scope of 3 mm centered on the fovea. This concerns sharply bordered small dotted lesions of an intensity analogous to the retinal pigment epithelium (RPE). Subretinal fluid (SRF) was evaluated as the presence of fluid between the RPE and the retina within an area of 1 mm centered on the fovea. Defect of the continuity of the ellipsoid zone (EZ disruption) was evaluated within an area of 1 mm centered on the fovea. The condition of the vitreoretinal interface was also observed: posterior vitreous detachment (PVD), vitreomacular adhesion (VMA) and vitreomacular traction (VMT).

The patients were divided into two subgroups – treatment-naive and previously treated. A positive morphological response was stipulated as a reduction of CRT by ≥ 10%. A positive functional response was stipulated as an improvement of BCVA by ≥ 5 letters within 3 months of the first application. In the opposite case the patient was evaluated as a "non-responder".

Intravitreal applications were conducted under aseptic conditions according to the current standards of health care of the center (Fig. 3, 4). All patients signed an informed consent form before application. The study protocol adhered to the principles of the Declaration of Helsinki.

Table 1. Baseline characteristics

	n	Percentage
Total	42	100.0%
Phakic	12	28.6%
Naive	7	16.7%
Diabetes		
Type 1	6	14.3%
Type 2	36	85.7%
PDR	7	16.7%
Chronic DME	29	74.4%
MLP	15	35.7
PPV	9	21.4 %
IOP elevation	9	21.4%

n – number of eyes; phakic – eyes with their own lens; naive – eyes that have not yet undergone any treatment with intravitreal medication; PDR – proliferative diabetic retinopathy; DME – diabetic macular edema; MLP – eyes that have previously undergone laser photocoagulation of the macula; PPV – eyes after pars plana vitrectomy; IOP –intraocular pressure

Statistical analysis

The statistical software IBM SPSS Statistics version 23 (Armonk, NY: IBM Corp.) was used for the analysis of the

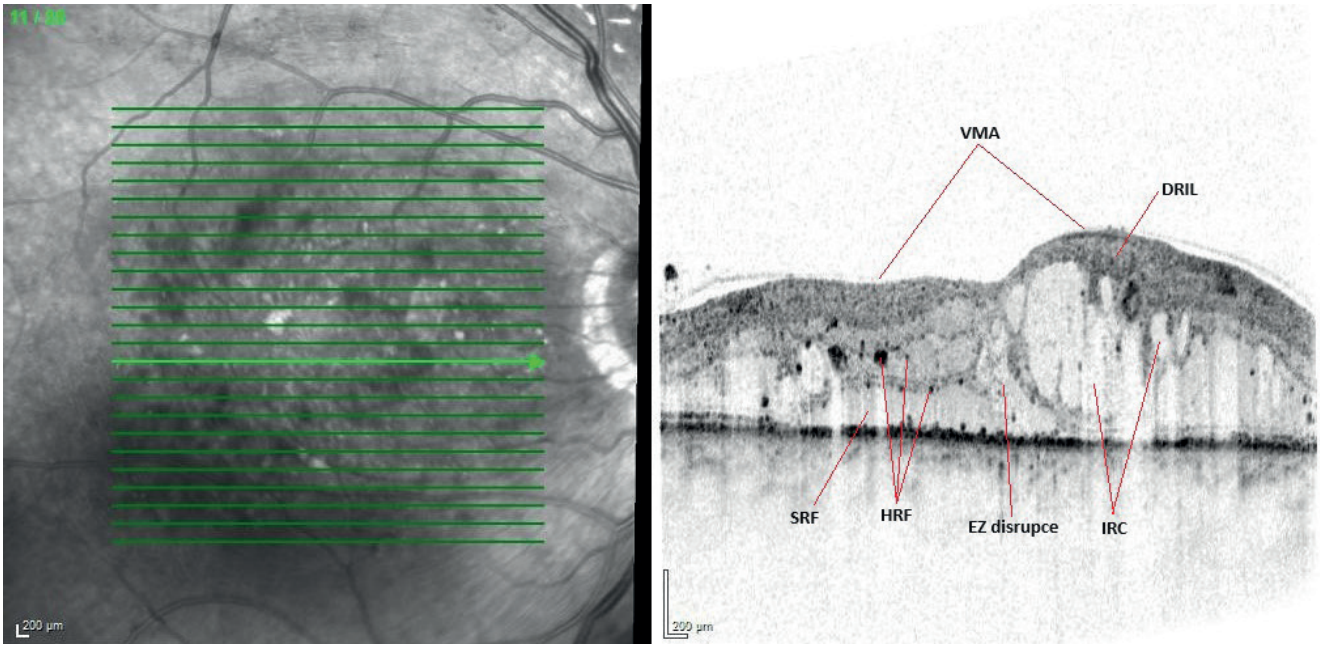


Figure 2. Chronic diabetic macular edema (Heidelberg Spectralis OCT)
DRIL – disorganization of retinal inner layers; HRF – hyperreflective foci; IRC – intraretinal cysts; EZ disrupce – disruption of ellipsoid zone continuity; SRF – subretinal fluid; VMA – vitreomacular adhesion

data. A Wilcoxon paired test was used for assessment of the change of CRT and change of BCVA 3 months after application. The significance of the change of OCT biomarkers was analyzed with the aid of a McNemar's test. The correlation between CRT, BCVA and the level of HbA1c, or age was assessed with the age of a Spearman's rank correlation coefficient. A Fisher's exact test was used for a comparison of the group with positive and negative functional response in the qualitative parameters. A Mann-Whitney U test was used for a comparison of the subgroups according to PVD or EZ disruption in the quantitative parameters. The normality of the quantitative parameters was assessed with the aid of a Shapiro-Wilk test. All the tests were performed on a level of significance of 0.05.

RESULTS

Morphological response

The anatomical result of treatment is presented in Table 2 and Graph 1. The most pronounced reduction of CRT was recorded at the first follow-up examination after the application of DEX, by an average of 186 µm ($p < 0.0001$). Subsequently CRT increased again, but the effect of treatment persisted even six months after application ($p < 0.05$). A positive morphological response was recorded in 39 eyes (92.9%). A negative weak to medium correlation was demonstrated between change of CRT after application and the age of the patients. In younger patients the reduction of CRT was greater at the first follow-up examination (r = -0.382).

Functional response

The functional effect of treatment is summarized in Table 3 and Graph 2. At the first follow-up examination after application there was a significant gain by an average of +3 letters ($p = 0.001$). A positive functional response was recorded in 23 eyes (54.8 %). In the group with a positive response to treatment there were significantly more treatment-naive eyes (n = 7, 30.4%) than in the group of non-responders (0 %, $p = 0.01$).

OCT biomarkers

IRCs were present at baseline in 42 eyes (100%), after application a complete disappearance was recorded in 11 eyes (26.2%), and a reduction was recorded in 26 eyes (62%). DRIL was present at baseline in 41 eyes (97.6%), after application a statistically significant reduction to disappearance was recorded in 12 eyes (28.6%, $p = 0.0005$). HRFs were present at baseline in 42 eyes (100%), after application a reduction was recorded in 8 eyes (19%). EZ disruption was present at baseline in 30 eyes (71.4%), after application complete disappearance was recorded in 1 eye (2.4%), reduction was recorded in 3 eyes (7.1%). PVD was present at baseline in 29 eyes (69%), VMA in 9 eyes (21.4%), after application PVD and disappearance of VMA was recorded in 2 eyes (4.8%). In one case it was not possible to evaluate possible PVD after application. VMT was present before application in 3 eyes (7.1%), after application it developed in 1 eye, and was therefore present in 4 eyes (9.5%). SRF was present at baseline in 3 eyes, complete disappearance was recorded in 2 eyes, reduction was recorded in one eye.

In the group of eyes with the present biomarker of EZ disruption, baseline BCVA was significantly lower in comparison with the group without this biomarker (Table 4). Other than a significant reduction of DRIL, no significant difference was recorded in the incidence of OCT biomarkers before the commencement of treatment and at the first follow-up examination after the application of DEX. We did not succeed in demonstrating a correlation between OCT biomarkers and functional or morphological response to treatment.

Subgroups

The subgroups of treatment-naive (n = 7) and previously treated patients (n = 35) were subsequently compared. Average baseline CRT was higher in the group of previously treated eyes, and these eyes also recorded a more pronounced change of CRT after application. Nevertheless, these results

Figure 3. Instrumentation for Ozurdex® application
From left to right: eyelid speculum, caliper, forceps, implant in applicator, cotton swab

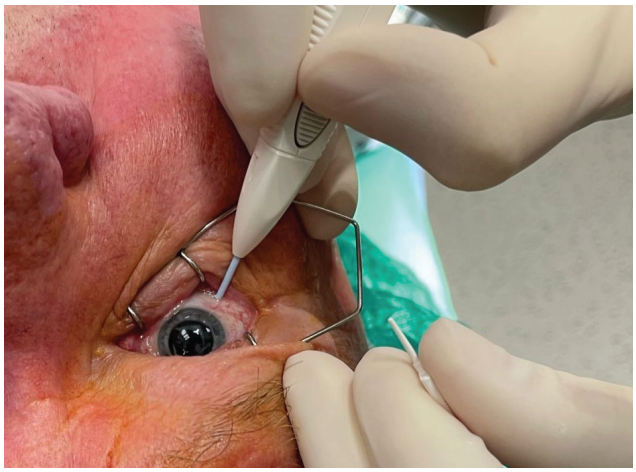


Figure 4. Ozurdex® application in the operating room

were not statistically significant (Table 5). Treatment-naive eyes recorded a statistically more significant improvement of BCVA ($p = 0.025$) after application of DEX, and manifested a significantly less frequent incidence of chronic DME (n = 1, $p = 0.002$). In other characteristics the subgroups did not differ statistically. No significant difference was demonstrated between the groups in terms of the incidence of OCT biomarkers before and after treatment.

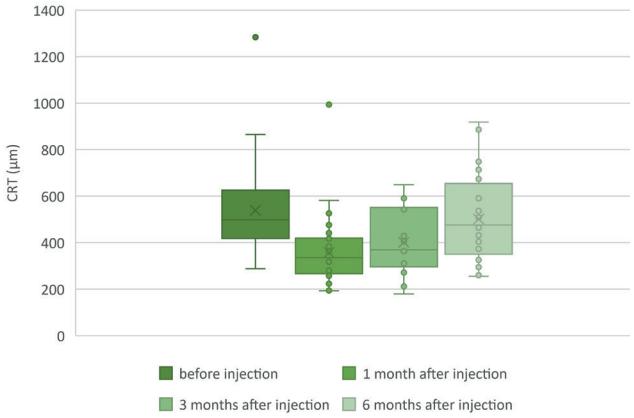
Safety analysis

Elevation of IOP during the course of DEX treatment occurred in 9 patients (21.4%), in all cases temporary administration of local antiglaucoma agents was sufficient in order to ensure normalization. No serious complications of treatment were recorded during the course of the follow-up observation period.

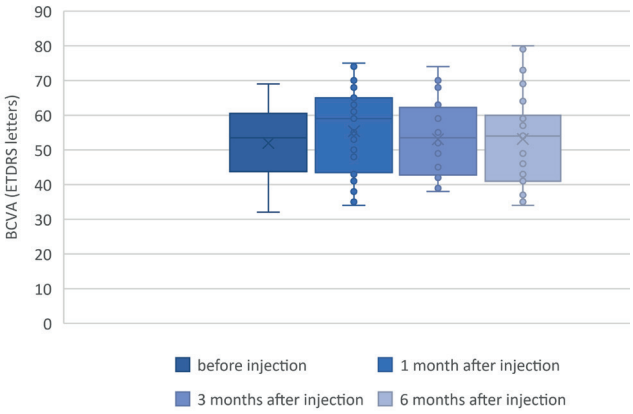
DISCUSSION

Effect of DME treatment

The results of our study confirm DEX as an effective and safe treatment for DME. At the first follow-up examination after application we recorded a statistically significant reduction of CRT and improvement of BCVA. The gain of letters after application was significantly higher in the group of treatment-naive patients. These results are in accordance with



Graph 1. Central retinal thickness during treatment
CRT – Central retinal thickness



Graph 2. Best-corrected visual acuity during treatment
BCVA – Best-corrected visual acuity

Table 2. Morphological response

CRT (µm)	Mean	SD	Median	Minimum	Maximum	p-value
Before injection	539	184	498	288	1284	
1 month after injection	353	137	332	193	994	
Change at 1 month	186	146	137	15	545	< 0.0001[1]
3 months after injection	402	139	369	180	649	
Change at 3 months	167	237	97	-128	837	0.012[1]
6 months after injection	502	177	476	255	919	
Change at 6 months	48	154	49	-388	428	0.013[1]

CRT – central retinal thickness; SD – standard deviation; 1 – statistically significant (Wilcoxon paired test p-value < 0.05)

Table 3. Functional response

BCVA (letters)	Mean	SD	Median	Minimum	Maximum	p-value
Before injection	52	11	54	32	69	
1 month after injection	55	12	57	34	75	
Change at 1 month	3	7	5	-26	17	0.006[1]
3 months after injection	53	11	54	38	74	
Change at 3 months	1	6	3	-18	11	0.53
6 months after injection	53	13	54	34	80	
Change at 6 months	1	12	0	-28	45	1

BCVA – best corrected visual acuity; SD – standard deviation; 1 – statistically significant (Wilcoxon paired test p-value < 0.01)

previously published studies [9,10]. The study conducted by the authors Neves et al. [10] also confirms a different functional response between the groups of treatment-naive and previously treated patients. This indicates the benefit of using DEX in treatment-naive patients in the early phases of DME.

OCT Biomarkers

The most significant prognostic OCT biomarkers in DME include DRIL and the integrity of the outer layers of the retina. EZ disruption negatively influences the functional outcome of treatment. Damage to the photoreceptor layer is the result of chronicity of DME and macular ischemia [1]. In our cohort, EZ disruption was linked with significantly lower BCVA upon commencement of treatment (p = 0.034). In eyes with preserved continuity of EZ we recorded better baseline VA, and it is therefore possible also to presume a better functional outcome of treatment. During the course of DEX treatment, the integrity of the outer retinal layers may be restored, and patients using anti-VEGF therapy with persistent EZ disruption may benefit from a change of treatment to DEX [11,12]. In our cohort we recorded a partial reparation of EZ in 4 eyes (9.5%); nevertheless, this result was not statistically significant (p = 0.125). The presence of DRIL is also placed in correlation with a chronic course of DME and probably concerns a manifestation of dysfunction of the Müller cells [13]. Zur et al. [14] demonstrated a negative influence of the presence of DRIL on resulting VA in patients treated with DEX. At the same time, this concerns the first study in which a significant reduction of this biomarker was achieved following the application of DEX. This trend is confirmed also by our observation, in which we recorded a statistically significant reduction of DRIL in 12 eyes (28.6%, p = 0.0005). This reduction may be associated with the anti-inflammatory activity of DEX and its action on the Müller cells [13]. In our observation the biomarker of EZ disruption was linked with a higher average baseline CRT, a more pronounced reduction of CRT and a lower average gain of ETDRS letters following the application of DEX than in the group without this biomarker. Nevertheless, the aforementioned correlation was not statistically significant.

Another evaluated biomarker was IRCs. Cystic changes are a characteristic feature of DME, and in our cohort macrocysts of ≥ 250 µm were represented at baseline in all eyes. Their pathogenesis and significance differ according to the localization of their incidence and according to size. Large cysts of more

Table 4. Relationship between BCVA and CRT based on EZ disruption biomarker

		EZ disruption		p-value
		0	1	
CRT before injection (µm)	Median	481	517	0.271
	Mean	479	563	
	Minimum	288	304	
	Maximum	699	1284	
BCVA before injection (letters)	Median	57.5	49.5	**0.034** [1]
	Mean	57.8	49.6	
	Minimum	45.0	32.0	
	Maximum	69.0	65.0	
CRT change	Median	137	137	0.813
	Mean	168	193	
	Minimum	29	15	
	Maximum	437	545	
BCVA change	Median	5.0	5.0	0.758
	Mean	4.3	2.8	
	Minimum	-4.0	-26.0	
	Maximum	17.0	15.0	

EZ disruption 0 – eyes with preserved ellipsoid zone continuity; CRT – central retinal thickness; BCVA – best corrected visual acuity; 1 – statistically significant result < 0.05

Table 5. Subgroup analysis of treatment-naive and previously treated eyes

Morphological response (µm)		Naive		Mann-Whitney U test p-value
		0	1	
CRT before injection	Median	521	443	0.516
	Mean	554.3	462.6	
	Minimum	288	373	
	Maximum	1284	583	
CRT 1 month after injection	Median	331	333	**1**
	Mean	357.3	334.3	
	Minimum	193	224	
	Maximum	994	462	
CRT change	Median	146	82	0.343
	Mean	197	128.3	
	Minimum	15	29	
	Maximum	545	312	
Functional response (letters)				
BCVA before injection	Median	52	58	0.181
	Mean	50.7	58.1	
	Minimum	32	43	
	Maximum	65	69	
BCVA 1 month after injection	Median	54	70	**0.008**[1]
	Mean	52.9	66.9	
	Minimum	34	49	
	Maximum	70	75	
BCVA change	Median	4	8	**0.025**[1]
	Mean	2.1	8.7	
	Minimum	-26	5	
	Maximum	15	17	

Naive 0 – previously treated patients; CRT – central retinal thickness; BCVA – best corrected visual acuity; 1 – statistically significant result (Mann-Whitney U test, < 0.05)

than 250 μm are generally present in more advanced stages of the pathology, and are associated with a chronic course of DME. They usually respond better to DEX treatment than anti-VEGF therapy, and their presence may be used in the choice of therapy [1,15]. We recorded a reduction or disappearance of IRCs after the application of DEX in our cohort in 37 eyes (88.1%). Nevertheless, a statistical evaluation of IRCs as a predictor of treatment was not possible due to the 100% prevalence.

Analogously, a frequent marker in DME is the presence of HRFs. The incidence of HRFs is associated with inflammatory activity, a more advanced degree of diabetic retinopathy and more frequent recurrence of DME [1]. According to histopathological analysis, it is assumed that HRFs are extravasations of lipoproteins in the incipient stages of a breach of the blood-retinal barrier. Nevertheless, the role and origin of HRFs are not entirely clear, and the results of the studies published so far have varied [1]. Vujosevic et al. [8] consider the incidence of HRFs as a positive biomarker associated with a better therapeutic response to DEX than to anti-VEGF treatment. By contrast, Zur et al. [16] and Chatziralli et al. [9] link the presence of HRFs with a worse effect of DEX treatment. A possible explanation of these differing conclusions is that the prognostic significance of HRFs is probably dependent upon the size of the HRFs and their incidence within a specific layer of the retina [17]. In our observation no quantitative evaluation was conducted, neither was any emphasis placed on the anatomical localization of HRFs, and we did not succeed in demonstrating the significance of this biomarker. Clarification of the predicative value of this marker shall require more detailed study.

Also linked with inflammatory changes in DME is the presence of SRF. According to Huang et al. [13], SRF is associated with a higher level of Interleukin-6 in the vitreous cavity, and with a more pronounced reduction of CRT following DEX treatment. In a multicentric study conducted by the authors Zur et al. [16], the presence of SRF before treatment was a predictor of a better result of BCVA 4 months after implantation of DEX. This effect is explained by the anti-inflammatory activity of DEX [13]. In our cohort it was not possible to conduct a statistical evaluation due to the low incidence of SRF (n = 3).

The last monitored OCT biomarker was the condition of the vitreomacular interface. There is insufficient evidence about the influence of this parameter on the result of treatment of DME with the aid of DEX, and in our observation also we did not succeed in demonstrating the influence of VMT, VMA or PVD on the outcome of treatment. The majority of studies focusing on this subject published to date have been conducted on patients treated with anti-VEGF preparations. A negative influence of VMA and VMT is presumed, whereas by contrast PVD is thought to have a positive functional and morphological effect on the outcome of treatment [1]. However, with reference to the inconsistent results of studies, further evidence is required in the case of this biomarker.

In our study there was a perceptible correlation between patient age and morphological response to the application of DEX. In younger patients the reduction of CRT was statistically more significant (r = -0.382). The relationship between patient age and the effect of DEX treatment for DME is also described in a study by Chatziralli et al. [9], in which final BCVA was worse in older patients. The influence of age on the functional effect of treatment was not demonstrated in our cohort. This may have been caused by the higher representation of chronic DME, in which the reduction of CRT is not necessary accompanied by an improvement of vision as a consequence of dystrophic changes.

The safety analysis of DEX is consistent with previously published studies [7,18]. During the course of treatment, monitoring of IOP is recommended due to the potential incidence of elevation. Another adverse effect of DEX may be the development and progression of cataract. At the same time, progressive cataract may entirely certainly influence the functional outcomes of treatment. Nevertheless, in our cohort artephakic eyes predominated (n = 30, 71.4%), and patients who had undergone cataract surgery during the course of treatment were excluded from the study.

We consider the weaknesses of our study to include especially its observational character. DEX was used as the drug of second choice, which was manifested in a higher representation of eyes with advanced and chronic DME at the commencement of treatment (n = 29, 74.4%) and only a small cohort of treatment-naive eyes (n = 7, 16.7%). Another limitation is the fact that a considerable proportion of the eyes had previously been treated with LFC of the macula (n = 15, 35.7%), which may lead to a more difficult evaluation of the OCT biomarkers. It was not possible to conduct a statistical evaluation of certain OCT biomarkers (HRF, IRC, DRIL) as predictors of treatment as a consequence of their high prevalence in the cohort.

By contrast, the strengths of our study include the relatively large cohort of patients and the strict inclusion criteria. A total of 30 eyes were excluded due to failure to meet these criteria.

CONCLUSION

In our study we confirmed that DEX is a safe and effective option for treatment of DME in real clinical practice. A significant morphological and functional response was recorded in the observed patients. The effect of treatment was present also in patients with advanced chronic edema and in patients who had not responded satisfactorily to previous treatment using other intravitreal preparations. OCT biomarkers may assist in the choice of suitable treatment for DME. Our study confirmed EZ disruption as a negative biomarker. At the same time, we demonstrated the capacity of DEX to suppress inflammatory processes of DME and restore correct retinal segmentation through the reduction of DRIL. Treatment-naive patients attained better functional results, which indicates the potential benefit of using DEX in the first line of treatment of DME..

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