Contrast Sensitivity and Optical Coherence Tomography Examinations in Adolescent Patients with Diabetes Type I Preretinopathy (A Pilot Study)

ORIGINAL ARTICLE

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SUMMARY

Aim: To evaluate the development of retinal changes in adolescent patients with diabetes type I (T1DM) with disease's duration more than 10 years, which started before 5 years of age.
Methods: The development of the findings on the posterior pole was followed up. The retinal functions were established by means of contrast sensitivity in four space frequencies: 3 cycles/degree (c/deg) (perimacular area), 6 c/deg and 12 c/deg (macular area), and, finally, 18 c/deg (foveola). The central retinal thickness, average retinal thickness of the specified quadrant of macular area, the foveolar depth of its own, and the volume of the perimacular area (perimacular cube volume) were measured by means of optical coherent tomography (OCT).
Material: Altogether 20 patients with diabetes type I meeting the set criteria were examined, and their findings were compared with control group of healthy adolescent people. The values from the control group were used as our normative database.
Results: On the retina, there were found, during the disease's course lasting in average 13.3 years, changes of the macular area, especially tortuosity of macular final capillaries and pigmentation with disappearing of foveolar reflex, which, in 20 %, were followed by sporadic hard exsudates of the retina. Difference of the decreased values in adolescent patients, comparing to the control group, was recorded in contrast sensitivity in space frequencies of 3 c/deg (p 0.047) and 12 c/deg (p 0,0497), but statistically significant was the difference in space frequencies of 6 c/deg (p 0.0001) and 18 c/deg (p 0.0001). Using the OCT, no statistically significant difference was found in the central retinal thickness, but the values of foveolar depth in patients with diabetes type I were variable (p 0.0153); in four eyes it was much deeper, and in other four of them it was much shallower. Furthermore, there was higher the average thickness of the retina (p 0.0008) and the volume of the perimacular area (perimacular cube) (p 0,0001).
Conclusion: The findings in eight eyes out of five patients with T1DM were evaluated as diabetic preretinopathy – pre-stage of beginning stage of diabetic retinopathy in central area of the retina from the functional and structural point of view of current pathological changes of contrast sensitivity and OCT. The findings of other three patients were rated as diabetic preretinopathy according to sporadic hard exsudates of the retina and OCT changes, but. until now, without contrast sensitivity changes. The one-year profile of glycated hemoglobin (HbA1c) was higher in patients with diabetic preretinopathy than without the eye involvement, but it was not statistically significant (p 0,0314).

Key words: Contrast sensitivity (CS), Spectral Domain Optic Coherence Tomography (SD-OCT), diabetes mellitus type I (T1DM), diabetic preretinopathy (DpR), glycated hemoglobin (HbA1c)

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INTRODUCTION

The Liverpool declaration of EASDec (European Association for the Study of Diabetic Eye Complication) in 2005 set as its target a reduction of the risk of deterioration of vision as a consequence of diabetic retinopathy within 6 years, through the implementation of effective, systematic programmes of eye screening in patients with diabetes mellitus (31). Throughout Europe a total of 29 311 new patients with DM up to the age of 15 years were registered in the period of 1989-2003 in 17 countries, including the Czech Republic. The prevalence at this age presupposes an increase from 94 000 in 2005 to 160 000 in 2020 (9). The twenty year register of children with DM 1 in the Czech Republic over a period of twenty years (1989-2009) demonstrated a halting of the acceleration of the incidence of this metabolic disorder. Following a 15% increase in the period 1996-2001 there followed a stagnation in the number of newly diagnosed diabetic children in the period 2002-2009. A total of 5

155 new paediatric patients with DM were diagnosed over the course of the twenty year observation out of a child population of 1.76 million (3). In 2009 a total of 783 321 diabetic patients of both types of the disorder were registered in the Czech Republic, which represents approx. 8% of the population (26). From this there ensues a society-wide significance of the necessity of introducing screening programmes for prevention, as well as the availability of modern technologies in the treatment of diabetic retinopathy also within our region. The aim of our pilot study was to assess the functional and structural changes of the retina and to compare them with the finding on the ocular fundus, when visual acuity was within the norm also following applicable additional correction of the refractive error, at a time when no incipient changes of diabetic retinopathy were detected in the central region of the retina in the group of adolescent patients with DM 1.

METHOD OF FUNCTIONAL-STRUCTURAL EXAMINATION

Contrast sensitivity is a functional examination which is better at detecting the condition of the visual analyser than examination of visual acuity. It provides information about the quality of processing of the given optical stimulus within different spatial frequencies sent from the photoreceptor cells of the retina to the visual centre in the cerebral cortex. A total of 4 spatial frequencies were used: 3 cycles on one angular degree (c/deg) evaluating the perimacular region, also the macular region using 6 c/deg, 12 c/deg and finally a frequency of 18 c/deg, which corresponds to the foveola.

Optical coherence tomography is an analogy of a B-scan ultrasound examination, with the difference that instead of acoustic reflectivity, optical reflectivity is used. The principle is low-coherence interferometry, which measures the distance of various structures inside the tissue with high sensitivity to the light signal reflected from the structures of the eye. SD-OCT (spectral-domain optical coherence tomography) represents a method of three-dimensional evaluation of the structures of the retina and the choroid. The parameters measured by SD-OCT included central retinal thickness, average retinal thickness within a specified quadrant of the macular region with an edge of 6 mm, its difference as depth of the actual foveola and the cubic volume of the perimacular cube within a specified quadrant of 36 mm2.

Our own cohort

Within the framework of outpatient observation of patients at the 1st internal clinic and the Paediatric and Youth Clinic at the Královské Vinohrady University Hospital, as of 1 January 2013 we included a total of 172 patients with DM 1, with the duration of the disorder persisting for more than 10 years. Of this number there were 23 adolescents at the Paediatric and Youth Clinic aged up to 18 years who we had observed since the beginning of their metabolic disorder with regard to endocrinology and ophthalmology. Two patients were excluded from this number due to a primary ocular disease: unilateral microphthalmos and bilateral congenital nuclear cataract, together with a patient with a monogenic form of diabetes. Within the framework of the complex diagnostic approach, we first of all determined visual acuity with applicable optimal correction for an examination of contrast sensitivity using CSV 1000 (Vector Vision). In cycloplegia we evaluated the anterior segment of the eye on a slit lamp from the perspective of changes in the lenses. We conducted a stereoscopic examination of the ocular fundus by means of indirect ophthalmoscopy, using 90 and 66 D lenses, and supplemented this with an assessment of the macular region by means of a classic ophthalmoscope. For photo documentation of the central region we used an FF450 plus IR (Carl Zeiss) digital camera with sufficient resolution, e.g. of hard scattered deposits. Refraction was determined and spectral optical coherence tomography was conducted by means of Cirrus OCT (Carl Zeiss).

Our own examination of the group of 20 patients, which comprised 17 girls and 3 boys with DM 1, took place within the framework of regular checks over the period from November 2012 to July 2013, always in both eyes. The age of the patients at this complex examination ranged from 12.8 years to 18.4 years (median 16.4 years). DM 1 was diagnosed between the ages of 1.4 years to 4.7 years (median 3.1 years), thus before reaching the age of 5 years. The period of duration of DM 1 at the time of the ocular examination ranged from 10.1 years to 14.8 years (median 13.3 years). Theprecise time data about the individual patients, i.e. detection of the incidence of DM 1 and its duration, is presented in table 1. Of the metabolic parameters we observed the current value of HbA1c at the time of the complex ocular examination and its profile during the course of the last years of treatment of DM 1 before the ocular examination (table 1).

The control group comprised adolescents of the same sex representation and similar age composition from 13.2 to 18.1 years (median 16.8 years), who we examined as outpatients for non-ophthalmological diagnosis and whose general condition did not demonstrate any affliction in terms of metabolism, endocrinology or neurology (table 2). This concerned conditions of neurologically unexplained cephalea in 50% of cases and collapse or fainting in 40%. There was a secondary finding of asthenopic complaints (considered to constitute allergy due to lacrimation) and in some cases of headaches there was as yet uncorrected myopia in 20%. We examined visual acuity, the anterior segment of the eye and CS. In cycloplegia the examination was analogously supplemented with SD-OCT, determination of refraction and examination of the fundus with photo documentation. A condition for inclusion in the control group was visual acuity of 1.2 naturally or 1.0 with correction and physiological intraocular finding in the anterior and posterior segment of the eye.

RESULTS

From the beginning up to five years of observation of the ocular fundus, we observed isolated increased dilation and tortuosity of the end capillaries. Within the range from the 6th to the 10th year (within average thirteen year observation), capillary changes practically reached absolute values in 95% in almost half of the patients. Further ophthalmoscopic symptomatology included a change of the sketching of the actual foveolar and macular region after five years of duration of DM 1 in the form of increased irregular pigmentations. We detected a subsequent change of the sketching o the macula in the form of irregular foveolar reflex up to its disappearance, with relative thickening of the retina without manifest macular edema in 10% of patients. Another finding was hard scattered deposits of exudates in 20%, specified in detail in table 1.

Table 1 Relationship of CS and SD-OCT to incidence and duration of DM 1 (ocular finding: T – tortuosity of capillaries, M – Macula: increased pigmentation of macula, F – Foveola: loss of reflex, HE (Hard Exudates) – hard scattered deposits, values of HbA1c (mmol/mol according to IFCC).

Order	**CS** (c/deg) Number of targets				**SD-OCT** (µm)				Ophthalmological changes			Solution of refraction (vision)	Note incidence of DM1 duration	HBA1c -current -annual
	3	6	12	18	Central thickness	Average thickness	Depth of foveola	Volume (mm3)	Lenses	fundus	refraction			
1	6	7	7	7	238	298	60	10.7	Clear	M	0-75=0.25	Sine	From 3.8 years	66
F	6	7	7	6	237	297	60	10.7			0.25		i.e. 11.2 years	60.7
2	6	6	7	6	235	305	70	11	1st degree	M, T	1=1.25	With corr. 1.2	From 1.4 years	64
M	6	6	7	7	224	293	69	10.6			0.25	Sine	i.e. 11.4 years	64.3
3	7	7	7	7	240	287	47	10.1	1st degree	M, T	-0.75	Sine	From 2.7 years	85
F	7	7	7	7	238	283	45	10.2			-0.25		i.e. 13.9 years	76.5
4	6	6	5	6	234	272	38	9.8	Y-suture	M, T	.-4=0.75	With corr. bil.	From 3.3 years	60
F	6	5	7	6	236	276	40	10			-4	1.2	i.e. 13.8 years	73
5	6	7	7	7	242	283	39	10.2	Y-suture	M, T	-0.75	With corr. bil.	From 3.2 years	55
M	6	6	7	7	244	279	35	10			-0.75	1.2	i.e. 14 years	55.5
6	6	7	7	6	277	298	22	10.7	1st degree	M, T Isolated	.-1/170	With corr. bil.	From 2.4 years	67
F	6	7	7	6	282	306	24	11		HE bilat.	.-0.5/175	1.2	i.e. 11.2 years	66.4
7	6	6	7	7	262	298	36	10.7	1st degree	T, F+M	0.5	Sine	From 3.5 years	88
M	6	6	7	7	256	296	40	10.7			0.5		i.e. 14.8 years	82
8	6	7	6	7	253	295	42	10.6	Y-suture	M, T	-0.75	Sine	From 4 years	83
F	6	6	7	6	257	294	37	10.6	1st degree		-0.75		i.e. 10.7 years	95.4
9	6	7	7	6	247	282	35	10.2	1st degree	M, T	-0.75	Sine	From 4.1 years	88
F	6	7	7	7	247	284	37	10.2			-0.5		i.e. 14.3 years	79.2
10	6	7	7	7	249	289	40	10.4	(1st degree)	M, T, drusis	-0.75	Sine	From 2.5 years	82
F	6	7	6	7	250	288	38	10.4		dx.	-0.25		i.e. 12.1 years	74.2
11	6	7	7	7	264	280	24	9.7	Clear	M, T	0.5=0.5	Sine	From 4.7 years	92
F	6	7	7	7	263	281	24	9.7			0.75=0.25		i.e. 10.9 years	88.8
12	6	6	7	7	255	289	34	10.4	Y-suture	T, F+M	0	Sine	From 2.5 years	125
F	6	7	6	6	258	295	37	10.6			0.25		i.e. 13.4 years	114.7
13	6	7	7	7	265	309	44	11.1	(2nd degree)	M, T,	-0.25	Sine	From 3.2 years	86
F	6	7	8	7	261	303	42	10.9		HE bil.	0.25		i.e. 10.4 years	76.3
14	5	7	6	5	265	297	33	10.7	(2nd degree)	M, T	0.5	With corr. bil.	From 1.9 years	67
F	6	6	7	6	261	299	38	10.8			0.25=0.5	1.0	i.e. 13 years	66.5
15	6	7	6	6	273	299	26	10.8	1st degree	M, T	.-3.0=0.5	With corr. bil.	From 4.4 years	69
M	7	7	7	7	273	295	22	10.6			-2	1.2	i.e. 10.1 years	70.4
16	6	7	7	6	233	280	47	10.1	1st degree	M, T	0.5	Sine	From 1.8 years	66
F	6	7	7	7	239	280	41	10.1			0.25		i.e. 13.5 years	72.8
17	6	6	7	6	268	305	37	11	1st degree	M, T	-1	With corr. bil.	From 2.9 years	100
F	6	7	7	7	270	307	37	11.1		HE bil.	-1	1.2	i.e. 14.2 years	98.4
18	7	7	7	7	226	269	43	9.7	1st degree	M, T	.-0.5=-0.5	With corr. bil.	From 2.8 years	86
F	6	7	7	7	228	267	39	9.6			-1	1.2	i.e. 13.7 years	75
19	6	7	7	7	230	263	33	9.5	1st degree	M, (T)	-0.5	Sine	From 3 years	78
F	6	7	7	7	229	263	34	9.5			-0.5		i.e. 13.7 years	73.8
20	6	6	7	7	233	295	32	10.6	1st degree	M, T	0.25	Sine		66
F	6	6	7	6	233	295	32	10.6		HE bil.	0			68.8

Table 2 Norm of CS and SD-OCT values.

Order	Age	**CS** (c/deg) Number of targets				**SD-OCT** (µm)				Refraction	Ophthalmological changes (correction)	Note incidence of DM1 duration
		3	6	12	18	Central thickness	Average thickness	Depth of foveola	Volume (mm3)			
1	17.8	6	7	8	7	260	271	11	9.8	0.5	Sine	Cephalea
F		7	7	7	8	262	272	10	9.8	0.5=0.75		
2	16.7	7	8	7	8	226	269	43	9.7	-0.25	Sine	Orthostatic fainting
F		6	7	7	7	226	269	43	9.7	-0.25		
3	17	7	7	8	7	249	284	35	10.1	0.75/90	Conjunctivas - no patho-	v.s. ocular allergy
F		6	7	7	8	251	289	38	10.3	o.5=0.25	logy	
4	16.5	6	7	7	7	238	283	45	10.1	.-0.25=0.5	Sine	"School" cephalea
F		6	7	7	7	236	291	57	10.4	.-0.25=0.75		
5	16.7	7	7	7	7	276	298	22	10.6	0.25	Sine	Cephalea
F		6	7	7	7	273	291	18	10.4	-0.5		
6	15.2	6	7	6	7	249	266	27	9.5	1.25=0.5	Sine	Orthostatic fainting
M		6	7	7	7	249	263	24	9.4	1.0=0.25		
7	12.2	6	7	7	6	257	268	11	9.6	-3.5	Sine	Cephalea myopia
F		6	7	6	7	263	274	11	9.7	-3.5	(rp. glasses)	
8	17.8	6	7	7	7	240	283	43	10.1	.-1.0=0.75	Sine	Cephalea myopia
F		6	7	7	8	244	280	36	10	.-1.0=1.00	(rp. glasses)	
9	15.5	6	7	6	8	263	300	37	10.7	0.25/80	Sine	"School" cephalea
M		7	7	8	8	252	298	46	10.6	0.50/115		
10	13.4	6	7	7	7	267	277	10	9.9	-2	Sine	v.s. ocular allergy
F		6	7	7	7	264	275	11	9.9	.-1.75=0.5	(rp. glasses)	
11	18	6	7	7	7	237	267	30	9.5	0.5	Sine	Orthostatic fainting
F		6	7	7	7	240	274	34	9.8	0.25=0.5		
12	17.8	6	7	7	6	273	262	9	9.3	-2.5	Sine	Collapse state
F		6	7	7	6	273	264	11	9.4	-0.25		
13	16.7	6	7	7	6	253	279	26	9.9	.-2.5=0.25	Sine	Collapse state
F		6	7	7	7	258	284	26	10.1	.-2.0=0.25	(rp. glasses)	
14	15.4	6	7	7	8	234	267	33	9.5	.-1.75=-0.25	Sine	Orthostatic fainting
F		6	7	6	7	229	264	35	9.4	.-0.75=-0.75	(rp. glasses)	
15	14.5	7	7	7	7	215	261	49	9.3	-2.25	Sine	Orthostatic fainting
F		7	7	7	7	212	263	51	9.4	.-2.0=0.25	(rp. glasses)	
16	17.8	7	8	8	8	255	293	38	10.4	.0.25=-0.25	Sine	Cephalea
F		7	8	7	8	255	290	35	10.4	Emmetropia		
17	18.1	6	7	8	7	232	279	47	10	-1.25	Sine	Cephalea myopia
F		7	7	7	7	237	279	42	10	.-0.75=-0.5	(rp. glasses)	
18	16.7	7	7	8	8	267	300	33	10.7	0.25=0.5	Sine	Cephalea
F		6	8	8	8	266	300	34	10.7	0.75=0.25		
19	15.6	7	7	7	7	261	292	31	10.4	.-0.25=-0.75	Sine	Collapse state
F		6	7	7	7	265	292	27	10.4	.-0.5=-0.25		
20	13.2	7	7	7	7	238	293	55	10.5	1.25	Sine	Cephalea
M		7	7	7	7	237	288	51	10.3	1.75=0.5		

We did not record an occurrence of ophthalmoscopic evident haemorrhages or microaneurysms in any of the patients. Table 1 also presents the findings in the lenses (presence of accentuated posterior "Y" suture, posterior subcapsular dissociation evaluated as 1st degree of changes, in the case of simultaneously present anterior and posterior dissociation as 2nd degree of changes), and the relationship of refraction to vision of the patients. A fundamental observation was the records of the results of the individual patients within the area of CS and SD-OCT examination (table 1). Table 2 presents the results of the CS and SD-OCT measurements on the control group. Finally table 2 presents the summary average values of the individual CS and SD-OCT measurements of both group with standard deviations and a mutual relationship of the results of both groups with the level of significance, which was calculated using a two-sample T-test.
In the CS examination we determined a borderline significant difference between the control group and the group of patients with DM 1 for 3 c/deg (p 0.047) and 12 c/deg (p 0.0497). In the other two measured quantities, the values differed by a decline of detected sensitivity on a fundamental level of significance (p 0.0001), in both 6 c/deg and 18 c/deg.
In the SD-OCT examination we did not determine a significant difference between the groups in terms of central retinal thickness (p 0.9614), the other values differed with varying statistical significance, least in depth of foveola (p 0.0153), more fundamentally in average retinal thickness (p 0.0008). We demonstrated a pronounced statistical difference in the volume of the central part of the retina on a surface of 36 mm2 (p 0.0001).
On the basis of these results, we determined pathological values for both examinations. For CS this was a decline in the ability to detect by one less target than the average value in the control group, at least in three frequencies in one eye with simultaneous decline of two frequencies also in the other eye (essentially this always concerned frequency of 3 c/deg). We recorded this finding in 6 patients. For SD-OCT an increase in the content of the examined volume above the average value of the control group, with allowance for the standard deviation always counted as a pathological value. This finding was detected in 21 eyes. At the same time they were accompanied by increased values of average retinal thickness in 20 eyes. These values were manifested in a relative deepening of the foveola (fig. 2) in 4 eyes (patients no. 1, 2), or conversely its softening (fig. 3) also in 4 eyes (patients no. 6, 15). Altogether we recorded the above-stated pathological changes on CS and SD-OCT in 8 eyes (20%) of

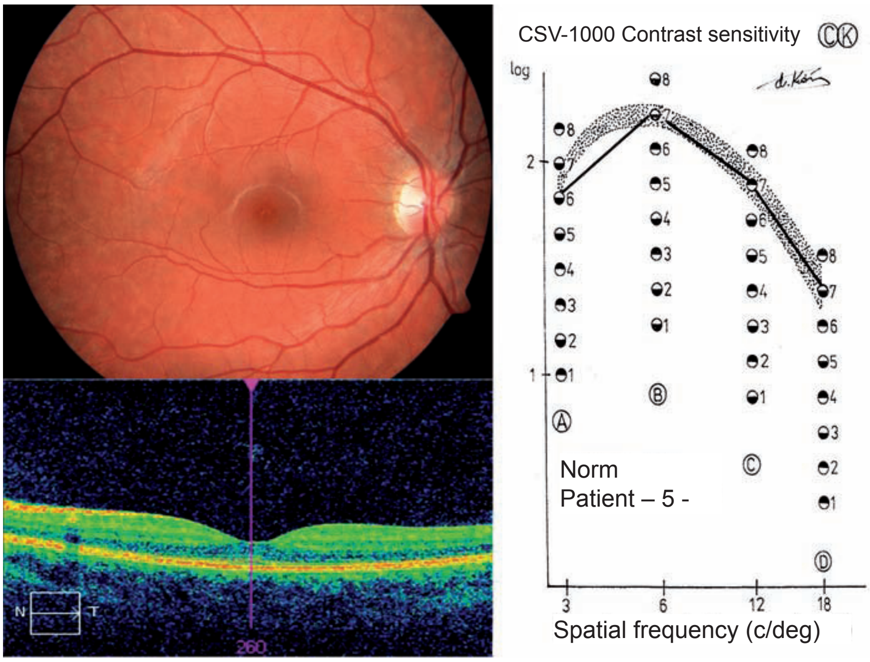

Fig. 1 Patient no. 5. Photo of fundus in right eye, CS: reduction 3 c/deg, SD-OCT: depth of foveola and volume of perimacular cube within norm.

Table 3 Statistical values of CS, SD-OCT and also HbA1c (mmol/mol according to IFCC).

	Patients with DM 1		**Control group**		**T-test**	**Result**
	Average value	Standard deviation	Average value	Standard deviation	Two-sample	Value
CS (number of targets)						
3 c/deg	6.1	0.3	6.4	0.4	p 0.047	**(differs)**
6 c/deg	6.7	0.5	7.1	0.3	p 0.0001	**differs**
12 c/deg	6.9	0.5	7.1	0.5	p 0.0497	**(differs)**
18 c/deg	6.6	0.5	7.2	0.6	p 0.0001	**differs**
SD-OCT (μm)						
Central thickness	249.4	15.7	249.5	16.2	p 0.9614	**does not differ**
Average thickness	289.4	12.1	279.8	12.2	p 0.0008	**differs**
Depth of foveola	38.8	10.8	31.9	13.7	p 0.0153	**differs**
Volume of retina (mm3)	10.4	0.5	9.9	0.4	p 0.0001	**differs**
HbA1c	**Patients with DpR**		**Patients without DpR**			
	Average value	Standard deviation	Average value	Standard deviation		
Current value	82.25	20.1	76.3	11.9	p 0.4908	**does not differ**
Year-round value	81.35	17.7	73.5	8.4	p 0.3014	**does not differ**

five patients, as functional and structural changes conditioning the diagnosis of preretinopathy (DpR) DM 1, in contrast with physiological findings (fig. 1) upon examination by CS and SD-OCT in 12 eyes (30%). In half of the examined eyes we demonstrated certain non-specific changes, but also more serious findings, primarily the incidence of hard scattered exudates (patients 6, 13, 17, 20). Pathological changes were also found on SD-OCT in the first three patients of this sub-group, whereas at the time of examination CS was within the norm. It was also possible to classify this finding into the group of DpR without functional changes. We classified the last stated patient (no. 20) amongst preretinopathy on the basis of pathological values of CS.
At the time of current examination, the value of HbA1c in the patients we observed with DM 1 was within the range from 55 to 125 mmol/mol (7.2% to 13.6% according to DCCT), and the average one year profile curve showed values between 55.5 and 114.7 mmol/mol (7.2% to 12.6% according to DCCT). The values of the individual patients are presented in table 1. We conducted a comparison of the HbA1c values in the patients with signs of functional-structural DpR and an accompanying finding of hard scattered deposits, i.e. in eight of the above patients together with twelve observed without symptoms of DpR. Both values (current examination and year-round profile) were higher in the patients with DpR in comparison with the group of patients without these symptoms. Nevertheless, the average values and standard deviations were without any statistically significant difference (table 3).

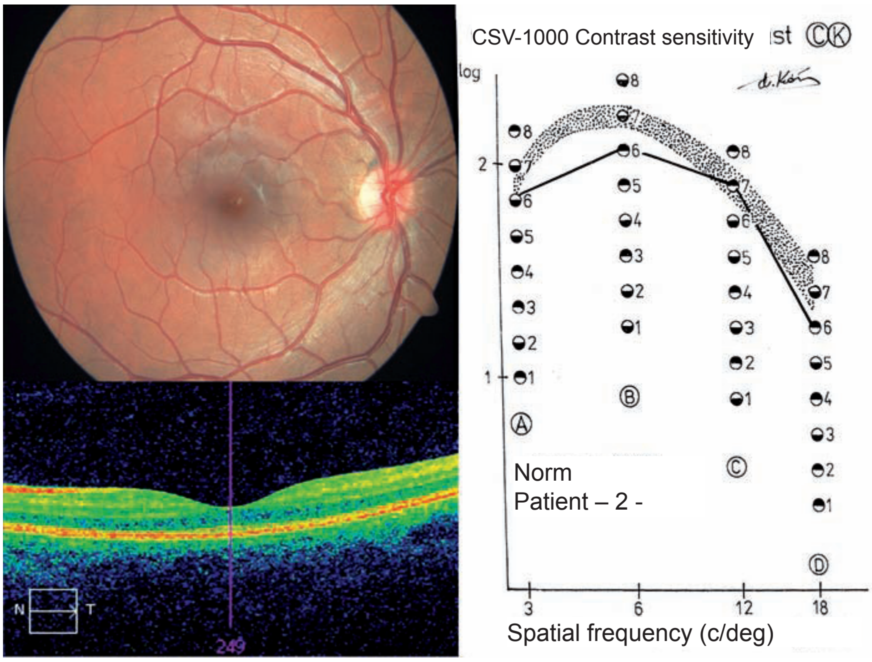

Fig. 2 Patient no. 2. Photo of fundus in right eye, CS: reduction 3, 6, 18 c/deg, SD-OCT: deepening of foveola and volume of perimacular cube increased.

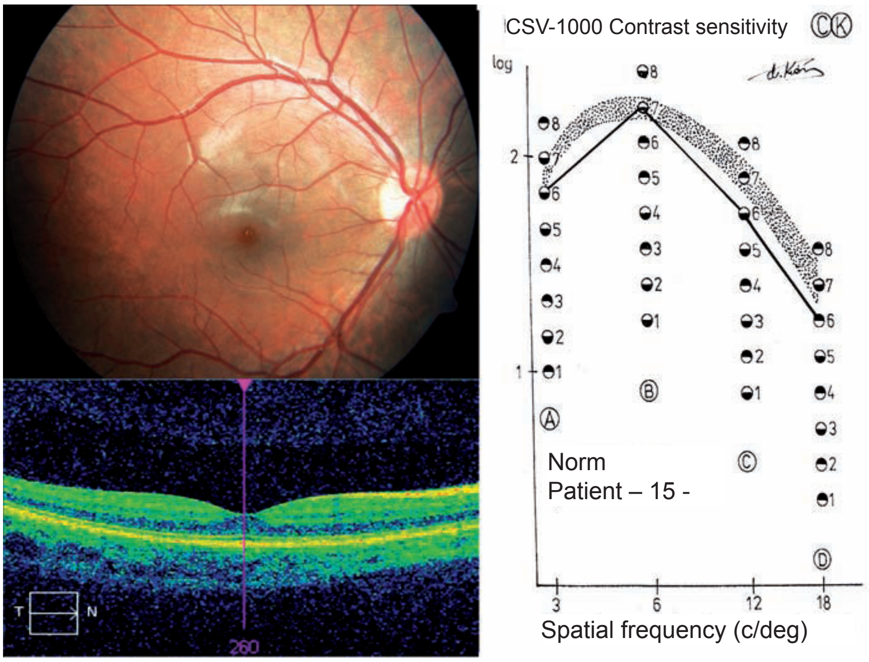

Fig. 3 Patient no. 15. Photo of fundus in right eye, CS: reduction 3, 12, 18 c/deg, SD-OCT: softening of foveola and volume of perimacular cube increased.

DISCUSSION

Upon detection of incipient changes, the basis used is the pathophysiology of diabetic changes. The first demonstrable sign of diabetic retinopathy is a breakdown of the hemato-ocular barrier, which can be assessed e.g. by fluorophotometry. This theory refers to an oxidation stress accompanying hyperglycaemia, in which the resulting pseudohypoxia may breach the cellular membrane of the vascular endothelium, or refers to damage to the pericytes due to a paradoxical glucose deficiency, which leads to their apoptosis (30).
Our group of patients was designated if possible by the lowest age of the onset of the metabolic disorder, maximally up to the age when spatial vision is still becoming fixed and the development of sight is still malleable. The period of duration was set at above ten years, in which incipient changes of the sketch of the retina in the central region had already been regularly detected (18, 20). The first functional abnormalities included defective function of the amacrine and bipolar cells of the photoreceptors, which precedes the onset of diabetic retinopathy (31). A basis forms for a pathological response upon electro-physiological examinations, as well as a reduction of CS. In diabetics without diabetic retinopathy, a decrease in the amplitude of visually evoked potentials was recorded, together with a reduction of CS (23) or abnormalities before the onset of retinopathy with normal visual acuity (24). CS has been used for screening changes for a quarter of a century (10, 29). A reduction of CS has been recorded in the case of DM 1 without manifestations of diabetic retinopathy only in certain spa-

tial frequencies (10, 14, 18, 20, 29, 33, 35, 36), whereas in the case of diabetic retinopathy changes of CS have been markedly abnormal. A significant dependency of the decrease of CS on an increase of HbA1c has been found (18, 20, 29, 36), though this fact has not been confirmed by other authors (10, 35). We took observation of the decrease in the ability to detect individual targets for previous studies of IGA as the basis of our evaluation of CS (22). The value of the decrease in sensitivity by at least two targets attested to DpR, whereas a decrease of four targets or more was more typical of DR (20, 22). We have already demonstrated previously that incipient changes in the transparency of lenses in the anterior and posterior subcapsular layer, detectable using a Schemipflug camera (Pentacam) have no fundamental influence on CS (21).

OCT has been used regularly for over ten years in order to assess the thickness of the macular region in the case of cystoids macular edema for evaluation of the frequency of changes (17) and also for correlation of therapy (13). Assessment of the actual thickness of the foveola has demonstrated a significant difference between the healthy population and patients with proliferative and non-proliferative form of retinopathy using a Zeiss-Humphrey instrument (28). Further research in recent years has not demonstrated differences of central thickness in the region of the foveola between the healthy population and patients with diabetes without signs of diabetic retinopathy (7, 11, 14), but a difference between a control group without DM 1 and non-proliferative form of retinopathy has been repeatedly confirmed (17, 24).

In our own observation we did not find a significant difference in the central thickness of the retina between the control group and the group of patients with DM1. We included a further parameter in the evaluation, namely the actual depth of the foveola, which ensues from the difference between central thickness and average thickness of the retina in the observed perimacular cube, and this helped specify their mutual relationship. This value appeared in an evaluation of the foveolar region in achromatopsia, where deepening of the foveola occurred on a basis of degeneration of the photoreceptors with a progressive character (34), which could also be manifested within the framework of further neuro-degenerations. Modern SD-OCT instruments working on the principle of three-dimensional patterns have enabled better detection of the construction of the actual retina and its individual layers, which has led to the consideration that this represents neuro-degenerative changes in the early stages of diabetes (1, 6, 37, 38). A thinning of the internal retinal layers has been recorded (37, 38), as well as a thickening of the plexiform and nuclear layer, whilst at the same time specific changes have been described in the layer of the ganglion cells (38). In our study we did not conduct an evaluation of the individual layers of the retina, because we did not have special software available. There are differences in the results in the evaluation of the thickness of the retinal layers between contemporary modern instruments, which upon an incorrect correlation may lead to an erroneous interpretation (2). For each study it is necessary to use the same instrument, stipulate own norms within the ratio to the healthy population, and the examination should not be conducted by more than one person.

Another diagnostic procedure in the evaluation of the development of retinopathy and other changes is fluorescence angiography, which assists in the indication of applicable laser treatment (30). In our group of adolescent patients we did not perform this, since the clinical picture of the vascular preretinopathic changes did not constitute a reason for a complex examination. We had already demonstrated clear ophthalmoscopic dilation and tortuosity of the end capillaries, including this contrast examination (19) in the last study using a digital camera. The previous procedure of examination using a mechanically controlled camera with a 15 degree visual field and coarse grain RS2 X-ray films was capable of demonstrating also the fine proportionate content of the capillaries, e.g. the heads of the optic nerve (12), which is difficult for the method of digital technology.

An analysis of the metabolic observation using HbA1c, primarily in its one-year profile, demonstrated higher values in the case of DpR than in individuals with DM 1 even without these functional-structural changes. In our entire study cohort, decompensation of DM 1 had an influence on higher values of HbA1c from the average in two patients during the course of the last year of observation. On the other hand, both patients had a pronounced ophthalmoscopic finding as against the physiological interface, which was a manifestation also of their year-round profile of pathological values of HbA1c. Compensation of diabetes evaluated by the level of HbA1c can be considered optimal at a value of up to 58 mmol/mol (7.5% according to DCCT), suboptimal up to 75 mmol/mol (9% according to DCCT), and higher values are highly risk-laden (27). This relationship is in accordance with the assertion that the long-term pathological values of HbA1c have an influence on the development not only of diabetic retinopathy, but also of diabetic macular edema (15, 16). With regard to compensation of DM 1, puberty represents a significant risk factor. A role in this is played by both biological factors (increase of insulin resistance) and psycho-social factors (worsened compliance with treatment) (4, 25). As a result, compensation of metabolic disorder is of fundamental importance in the prevention of the development of DR (32), which is substantiated also by the last DCCT (Diabetes Control and Complications Trial) (5) and EDIC (Epidemiology of Diabetes Intervention and Complications) (8) studies.

CONCLUSION

Using a complex diagnostic procedure, which combined a functional examination of the retina using CS and an evaluation of the structural changes of the retina using SD-OCT, we defined preretinopathy in the central region in five observed adolescents with type 1 diabetes. Another three patients were included in the group of DpR on the basis of pathological SD-OCT values with the presence of isolated hard scattered deposits. This pilot study was originally intended as the initial communication of the research project IGA NT/14490, which was not accepted. In future, in order to confirm our theory of preretinopathic changes it shall be necessary to extend the study cohort with further patients in other age groups, to retrospectively supplement the period of evaluation of HbA1c and include further parameters of metabolic observation. It is necessary to define the structural changes in more detail, with manifestations in the individual retinal layers, also with regard to the possible development of diabetic macular edema.

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