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Macular Ganglion Cell Layer Thickness in Patients using Oral Isotretinoin

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Abstract

Objective: Determining the effects on macular ganglion cell layer thickness in patients using isotretinoin by utilization of optical coherence tomography.

Material and Methods: Sixty eyes of 30 patients using isotretinoin and 60 eyes of 30 control group patients in the same age range were included in this study. The average age of the patients using isotretinoin was; 21.2 ± 3.62 years, whereas the average age of the patients in the control group was 22.7 ± 3.7 years. The thickness of the macular ganglion cell layer (GCL), the retinal nerve fiber layer (RNFL) and subfoveal macular thickness of all patients were measured with optical coherence tomography (OCT).

Results: The macular ganglion cell layer thickness in the OCT of the patients using isotretinoin was measured as 61.6±4.6 µm, 62.4±4.4µm, for the right and left eye respectively, whereas the thickness in the control group was measured as 60.6±4.1µm, 61.2±4.9µm respectively. The retinal nerve fiber layer thickness in the OCT of the patients using isotretinoin was measured as 74.8±11.3µm, 76.2±12.3µm, for the right and left eye respectively, whereas the thickness in the control group was measured as 72.2±10.5µm, 74.1±1.9µm, respectively.

Conclusions: No statistically significant difference was observed in the macular ganglion cell layer thickness, retinal nerve fiber layer thickness and macular thickness in terms of both the right and left eyes between the control group and patients using isotretinoin.

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Introduction :

Isotretinoin is a synthetic retinoid used for various dermatological diseases such as severe nodular cystic acne, acne vulgaris, stubborn psoriasis and is frequently used for various types of cancers.[1] Isotretinoin has many known systemic and ocular side effects. The ocular side effects of isotretinoin are; meibomian gland atrophy, impaired meibomian gland secretion, blepharoconjunctivitis, dry eye, keratitis, myopia, decreased dark adaptation, decreased color vision, permanent dark adaptation, optic neuritis, diplopia, optic disc edema and intracranial hypertension.[2,3] Retinal ganglion cells contain melanopsin. Melanopsin is very similar to other opsin photopigments and is a retinaldehyde chromophore. Isotretinoin has an inhibiting effect on the chromophore regeneration of retinal ganglion cells.[4] In this study, the effects on retinal ganglion cell layer thickness in patients using oral isotretinoin was investigated.

Methods:

This prospective study was performed Department of Ophthalmology, Faculty of Medicine, Ahi Evran University, Kirsehir, Turkey. Patients diagnosed with nodular acne,whom were using systemic isotretinoin (1mg/kg/day) were referred to the dermatology clinic. Informed consent forms were signed by all patients. Following the description of the Helsinki Declaration, the approval of the ethics committee was obtained. All patients underwent a complete ophthalmic examination, including best visual acuity and intraocular pressure measurements as well as biomicroscopy and fundoscopy examinations. Patients with over ± 3 diopters of refractive error, glaucoma, previous eye surgery, optic nerve diseases, macular disease and systemic diseases such as diabetes and hypertension were excluded from the study. The macular ganglion cell layer, retinal nerve fiber layer thickness, and subfoveal macular thickness were measured with Heildelberg OCT. The macular ganglion cell layer was measured at the thickest part of the macula, whereas the retinal nerve fiber layer thickness was measured from the temporal peripapillary area.

Statistical Analysis:

The statistical analysis were performed using the Statistical Package for the Social Sciences (SPSS) software version 23.0. The variables were investigated using visual (histograms, probability plots) and analytical methods (Kolmogorov-Smirnov / Shapiro-Wilk test) to determine whether or not they are normally distributed. Descriptive analysis was presented using means and standard deviations for normally distributed variables. The t-test was used to compare parameters betweenthe two groups. In cases where the age and the period of dru use beingnot normally distributed, the Mann-Whitney U test was used. While investigating the association between non-normally distributed variables, the correlation coefficients and their significance were calculated using the Spearman test. A p-value of less than 0.05 was considered to show a statistically significant result.

Results:

The mean duration of the isotretinoin treatment was 3.5±2.1 months. The average age of the patients using isotretinoin was; 21.2 ± 3.62 years, whereas the average age of the patients in the control group was 22.7 ± 3.7 years. Demographic data study group in table 1. No statistically significant difference related to age was observed in the macular ganglion cell layer thickness in between the control group and the patients using isotretinoin in Table 2($p>0.05$). No statistically significant difference was observed in the thickness of the macular ganglion cell layer, the retinal nerve fiber layer and macular thickness of the left or right eye between the control group and the patients using isotretinoin($p>0.05$).

In Table 3, no statistically significant difference was observed between the right or left eye regarding the thickness of the macular ganglion cell layer, the retinal nerve fiber layer and macular thickness in the group using isotretinoin ($p>0.05$). No statistically significant difference was observed between the right or left eye regarding the thickness of the macular ganglion cell layer, the retinal nerve fiber layer and macular thickness in the control group($p>0.05$). In Table 4, a statistically significant, moderate degree, negative

Table1: Demographic data of the study group

	Isotretinoin	Control
Age(y)	21.2±3.62	22.7±3.7
Gender (n)		
(Woman/Man)	22/8	24/6
uration(m)	3.5±2.1	

Y: year, M: month

Table 2. Evaluation of age, ganglion cell layer, retinal nerve fiber layer and macula layer between control group and isotretinoin group

		Isotretinoin Mean±SD	Control Mean±SD	Statistic pvalue	95% CI	
AGE*		21.2±3.62	22.7±3.7	0.079	0.072	0.083
GCL**(µ)	R	61.6±4.6	60.6±4.1	0.412	-1.326	3.193
	L	62.4±4.4	61.2±4.9	0.348	-1.264	3.531
RNFL**(µ)	R	74.8±11.3	72.2±10.5	0.348	-2.974	8.307
	L	76.2±12.3	74.1±10.9	0.487	-3.911	8.111
MACL**(µ)	R	218.3±22.1	213.7±13.4	0.334	-4.846	14.046
	L	216.6±20.7	215.2±11.6	0.736	-7.19	10.123

*Mann-WhitneyU

**IndependentsamplesT Testi

GCL: Ganglion cell layer. RNFL: Retinal nerve fiber layer. MACL: Macula layer. R: Right. L: Left µ: Micron

correlation related to age and the thickness of the ganglion cell layer of the left eye was observed in the group using isotretinoin(r=-0.483 p=0.007). No relationship related to the thickness of the macular ganglion cell layer of the right eye and the age was observed(p>0.05). No relationship related to the thickness of the retinal nerve fiber of the right and left eye and the age was observed(p>0.05). No statistically significant difference was observed between the duration of the isotretinoin administration and the thickness of the macular ganglion cell layer, the retinal nerve fiber layer and macular thickness of the right and left eye in the group using isotretinoin (p>0.05). A statistically significant, moderate degree, negative correlation related to age and the thickness of the ganglion cell layer of the right eye was observed in the control group (r=-0.52 p=0.003). No relationship related to the thickness of the macular ganglion cell layer of the left eye and the age was observed (p>0.05). No relationship related to the thickness of the retinal nerve fiber of the right and left eye and the age was observed (p>0.05).

Discussion:

It is considered that retinoids play a vital role in the function, replacement,and growth of the nerve tissue. Electrophysiological and clinical findings indicate a causal relationship between central nervous system neurotoxicity or neuropathy acquired with oral retinoids.[5-7] Decrease in visual acuity, various visual field defects, pseudotumor cerebri, optic neuritis and decreased color vision are the most common ocular nervous system side effects in patients receiving oral isotretinoin.[3,8] Central

Table 3. Comparison of ganglion cell layer, retinal nerve fiber layer and macular layer thickness between control group and isotretinoin group for both eyes

Groups		Eye	Statistic		
			P value	95% CI	
Isotretinoin	GCL	R	0.493	-3.1	1.5
		L			
	RNFL	R	0.664	-7.4	4.8
		L			
	MACL	R	0.764	-9.4	12.7
		L			
Control	GCL	R	0.609	-2.9	1.7
		L			
	RNFL	R	0.495	-7.4	3.6
		L			
	MACL	R	0.652	-7.9	5.0

Independentsamples T Testi

Table 4. Correlation between GCL, RNFL, MACL development with age and isotretinoin usage period

*CORRELATION	Statistic			
	AGE	EYE	r	p
Isotretinoin	GCL	R	-0.034	0.86
		L	-0.483	0.007
	RNFL	R	-0.299	0.108
		L	-0.096	0.613
	MACL	R	0.14	0.462
		L	0.171	0.365
	AGE			
Control	GCL	R	-0.52	0.003
		L	0.095	0.616
	RNFL	R	-0.079	0.678
		L	-0.096	0.615
	MACL	R	0.01	0.96
		L	-0.078	0.682
	TIME			
Isotretinoin	GCL	R	-0.18	0.33
		L	-0.35	0.055
	RNFL	R	0.25	0.178
		L	0.19	0.309
	MACL	R	-0.18	0.33
		L	-0.14	0.461

*Spearman Testi

field of vision defects due to optic neuropathy and / or psodotumorcerebri are more common.[9] Several studies have reported the importance of determining the RNFL thickness for the management and early diagnosis of glaucoma, optic nerve diseases and optic nerve disorders containing optic neuritis. [10] OCT defines the changes in the RNFL thickness before the emergence of defects of the visual field.[11] Dinc et al [12] reported cases of decreased RNFL thickness and bilateral optical disc atrophy related to isotretinoin administration for the treatment of acne vulgaris. Ucak et al.[13] reported the possible toxic effects of isotretinoinon RNFL, especially in the temporal layer. In the study conducted by Kapti et al.[14] It is reported that isotretinoin has no effect on RNFL thickness We did not find a statistically significant difference in RNFL thickness in our study. Sari et al.[9] investigated the optical nerve function, both clinically and in vision field test in patients treated with oral tretinoin and have not observed any differences in the same findings during 5.5 months. Sekeryapan et al. [15] did not find any difference in the thickness of GCL in patients using systemic isotretinoin in their study. We were unable to find any statistically significant difference in the GCL thickness in our study as well. Demirok et al. [16]found no significant effect on macular ganglion cell layer thickness in patients who used systemic isotretinoin for 1 year.

As a result, even though oral isotretinoin has different ocular side effects, no effects related to the thickness of the retinal nerve fiber and the ganglion cell layer could be observed.

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