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EFFECT OF OBSTRUCTIVE SLEEP APNEA SYNDROME ON RETINAL NERVE FIBER LAYER AND GANGLION CELL COMPLEX

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ABSTRACT

In this study, we aimed to identify the effect of oxygen desaturation due to comparing ganglion cell complex (GCC), retinal nerve fiber layer (RNFL) between patients with obstructive sleep apnea syndrome (OSAS), simple snoring and healthy individuals. Patients (n=2440 people) who applied to Bursa Yüksek Ihtisas Training and Research Hospital Sleep Policlinic between 2016-2018 constituted the universe of the study, which is a case control type. At the time of the study, 132 (264 eyes) patients and 88 (136 eyes) healthy volunteers who were diagnosed and applied to the study were selected by sampling. The patients were grouped according to the Apnea Hypopnea Index (AHI). Healthy volunteers and the patients with simple snoring (the AHI index value lower than 5) were grouped as respectively Group 1 (G1) and Group 2 (G2). Groups 3 to 5 were separated according to the AHI index as mild OSAS (Group 3 (G3); AHI=5-15), moderate OSAS (Group 4 (G4); AHI=16-30) and severe OSAS (Group 5 (G5); AHI>30). All study participants underwent an examination of both eyes including corrected visual acuity, intraocular pressure measurement, dilated-pupil fundus examination, with RNFL and GCC thickness which were measured with optical coherence tomography (OCT). Of the 132 patients included in the study, 29 had simple snoring, 22 mild, 22 moderate and 57 severe OSAS. When bilateral mean, superior, inferior, temporal and nasal RNFL thickness and mean, superior and inferior GCC values were compared among the study groups; no statistically significant difference was found (p>0.005). No significant difference was evaluated between mean RNFL thickness, four quadrants RNFL thicknesses, mean GCC thickness, two quadrants GCC thickness with OCT in the study patients. Patients diagnosed with OSAS may be at risk of developing glaucoma, so they may be advised to have regular eye exams.

Keywords: Sleep Apnea, Retinal Nerve Fiber Layer, Ganglion Cell Complex, Optical Coherence Tomography

1.INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is characterized by repetitive respiratory arrest episodes occurring during sleep due to the repeating obstructions in the upper respiratory tract and as a result of sleep fragmentation, excessive daytime sleepiness and oxygen desaturation (Partinen, Jamieson, Guilleminault 1988; Young, Skatrud, Peppard 2004). An epidemiologic study published in 1993 by Young, reported that the incidence is like 4% in men and 2% in women (Young et al.,1993).

The retina consists of 3 layers named as the ganglion cell complex (GCC) that can be investigated using optical coherence tomography. The first layer is Retinal Nerve Fiber Layer (RNFL) consisting of cell axons, the second one is the Ganglion Cell Layer (GCL) including cell body and the third one is the inner plexiform layer (IPL) consisting of cellular dendrites (GUYTON AND Hall, 1996).

Primarily cerebral hypercapnia increased intracranial pressure and then secondarily increased mean blood pressure due to hypoxia during apnea periods and reducing the response of the vascular endothelial system to vasodilator mediators (Xin, Wang, Zhang, Wang, Peng 2014). The blood supply to the outer layer of the retina is through the choroidal vessels that are innervated by sympathetic nerve fibers with rapid blood flow. In contrast, the retinal vessels supply the inner layer of the retina that has slow blood flow and large oxygen intake to maintain metabolic demands, therefore the layer is more sensitive to the hypoxia than other parts of the retina (Papst, Demant, Niemeyer 1982). Patients with OSAS could develop nocturnal hypertension as a result of especially the retinal nerve fiber layer may be affected by endothelial dysfunction secondary to chronic or intermittent hypoxia (Adam et al. 2013). The hypoxia could damage the ganglion cells in the retina which leads to thinning in RNFL. In addition to this, the researches reported that the increased post-systolic and end-diastolic velocity were measured in ophthalmic artery, central retinal artery and posterior ciliary artery by color doppler ultrasonography in the patients with OSAS (Erdem et al., 2003).

Primary open-angle glaucoma and normal tension glaucoma are frequently seen in patients with OSAS (Mojon, Goldblum, Fleischhauer 1999). Changed ocular perfusion pressure and hypoxia that occur in OSAS stimulate the oxidative stress and the inflammation on ganglion cell damage resulting from glaucomatous damage in OSAS.

In this study, we aimed to evaluate intraocular pressure (IOP), RNFL and GCC thicknesses in patients who admitted to the sleep outpatient clinic and were diagnosed with OSAS and simple snoring to investigate whether disease severity was correlated with ocular measurements and compare with healthy volunteers.

2.METHODS

2.1.Patients and Study Design

Patients (n=2440 people) who applied to Bursa Yüksek Ihtisas Training and research Hospital Sleep Policlinic between 2016-2018 constituted the universe of the study, which is a case control type. At the time of the study, 132 (264 eyes) patients and 88 (136 eyes) healthy volunteers who were diagnosed and applied to the study were selected by sampling.

The study patients were evaluated by polysomnography to identify the AHI index to diagnose severe, moderate, mild OSAS and simple snoring patients. And the study included 88 age and gender-matched healthy volunteers who admitted to the ophthalmic outpatient clinic with symptoms of refractory defects without any pathologic ophtalmotalogic examination in both eyes and having a systemic disease. N20 Ethics committee approval was received from Bursa Yüksek İhtisas Training and Research Hospital Clinical Research Ethics Committe, dated 2015/22-12 and numbered 2011KAEK-25.

The eligibility criteria included briefly; patients of both sexes aged between 18-65 years, diagnosed with OSAS and simple snoring and having intraocular pressure (IOP) lower than 22 mmHg. Patients with diabetes mellitus, arterial hypertension, cardiovascular disease, chronic airway diseases, and chronic lung parenchymal disease in addition to OSAS, those with systemic medication use, having an IOP >22 mmHg, patients undergone any eye trauma and surgery, having >±5D refractive defect, anterior segment pathology that would prevent optic measurement, those with retina or optic nerve disease and patients with alcohol and tobacco use were excluded from the study. The inclusion and exclusion criteria for the healthy volunteers were similar to the patient groups except for being diagnosed with OSAS.

The data obtained were statistically analyzed using IBM SPSS version 22.0 package software. In the evaluation of the data, Pearson's Chi-square and Yates tests were used in the comparisons of descriptive statistics (frequency, percentage, mean and standard deviation) and categorical variables. Normal distribution of the data was tested with Shapiro-Wilk method and the data were found to be normally distributed. One-way ANOVA test was used for comparisons between the groups. When statistical significance was found with the one-way ANOVA analysis, Tukey test was applied to determine the group which caused the difference. Independent sample t test was used in comparisons paired groups. Pearson's correlation test was used in the correlation analyses. $p<0.05$ values were considered statistically significant.

2.2.Polysomnography

Patients were followed up all night long with 58-channel polysomnography device (Compumedics, E Series, Australia) including 6-channel electroencephalography (EEG), chin-leg electromyography (EMG), electrocardiography (ECG), electrooculography (EOG), oximeter monitor, airflow monitor, abdomen and chest breathing effort bands and snoring microphone recorders and video and sleep recorders that were taken notes for at least 6 hours. The polysomnogram records were scored and assesed by a certified sleep specialist who was using the 2007 AASM criteria. Apnea was defined as ≥ 10 seconds interruption in the oronasal airflow and hypopnea was defined as a 3% decrease in oxygen saturation prolonged 10 seconds or higher durations or at least a 50% decrease in the airflow together with brief arousal. Apnea-Hypopnea Index was defined as the number of apneas and hypopneas per hour of sleep. The patients with an AHI score lower than were diagnosed as simple snoring and grouped control group (G2), while patients with an AHI score ≥5 were accepted to have OSAS. OSAS in the patients was categorized as mild (AHI 5-15, Group3 (G3)), moderate (AHI 15-30, Group 4 (G4)) and severe (AHI ≥ 30, Group5 (G5)). Group 1 (G1) as a control group consisted of healthy volunteers.

2.3.Ophthalmologic Examination

All patients underwent a detailed ophthalmologic examination including corrected visual aquity, intraocular pressure measurement, and dilated-pupil fundus examination. RNFL and GCC thicknesses were measured with spectral domain optical coherence tomography (SD-OCT). RTVue XR Avanti (Optovue, Frement, CA, USA) was used as the SD-OCT device. This system runs with 840 nm wavelength, and has 70.000 axial scanning rate per second and 5µm resolution. It is possible to distinguish 3 inner layers (nerve fiber layer (NFL), ganglion cell layer (GCL) and inner plexiform layer (IPL) of the retina in the retinal layer with the GCC screening protocol. Standard 3.45 mm diameter circular section was used to measure of RNFL thickness. Measurements of mean nerve thickness, inferior, superior, nasal and temporal quadrants were taken as microns. The mean GCC, inferior and superior quadrant measurement were also taken in microns. All measurements were taken from the dilated pupils by the same physicians and those with a signal quality ≥ 50 were used for the analysis.

3.RESULTS AND DISCUSSION

Of the 132 patients included in the study, 29 had simple snoring, 22 mild OSAS, 24 moderate OSAS and 57 severe OSAS (Table 1). There was a statistically significant difference in favour of the patients in the simple snoring group in terms of age ($p<0.001$). Patients in the simple snoring group were younger than those in the other groups. Forty-four of 88 healthy volunteers, 10/29 of the patients in the simple snoring group, 9/22 of the patients in the mild OSAS group, 7/24 of those in the moderate OSAS group, and 19/57 of the patients in the severe OSAS group were female. No significant difference was found between the groups in terms of gender ($p>0.05$) (Table 1).

Whereas there was a statistically significant difference between G1 and G4 groups in terms of mean left eye GCC values ($p=0.042$) (it was thinner in G1 group), no statistically significant difference was found among the other groups ($p>0.05$). Again, no statistically significant difference was observed among the groups in terms of the other values (gender; rihgt and left IOP; right and left mean, inferior, superior, temporal, nasal RNFL; right inferior, superior, mean GCC; left inferior, superior GCC) ($p>0.05$) (Table 1).

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Table 1. Caracteristics and ophthalmic findings of the healthy, simple snoring and OSAS groups

	Healthy=G1 (n=88)	**Simple snoring=G2 (n=29)**	**Mild OSAS=G3 (n=22)**	**Moderate OSAS=G4 (n=24)**	**Severe OSAS=G5 (n=57)**	**p**
Age	49.49±10.37	40.24±11.52	49.55±11.50	49.08±10.34	49.60±8.06	***<0.001***
Gender (Female/%)	44 (%50)	10 (%34.5)	9 (%40.9)	7 (%29.2)	19 (%33.3)	0.184
IOP R	17.25±2.37	16.11±2.39	16.82±2.11	16.13±2.44	16.49±2.19	0.112
IOP L	17.27±2.50	16.42±2.56	17.31±2.06	16.00±2.17	16.96±1.90	0.125
Mean RNFL R	102.17±9.36	100.79±9.78	100.95±8.19	103.21±9.69	103.33±8.67	0.693
RNFL inferior R	125.81±12.97	125.45±16.96	125.68±10.94	125.46±14.60	125.75±17.23	N/A
RNFL superior R	120.52±13.10	115.69±15.54	118.18±16.87	120.67±11.91	120.98±15.04	0.494
RNFL nasal R	84.92±16.97	83.86±14.88	85.27±13.64	83.67±10.28	83.37±14.47	0.971
RNFL temporal R	75.97±9.32	78.31±10.86	77.64±11.78	76.88±8.91	78.11±13.11	0.757
Mean GCC R	98.44±6.60	98.78±5.46	98.58±5.27	98.19±7.14	99.92±6.55	0.692
GCC superior R	97.43±6.87	98.02±6.21	111.14±64.73	98.02±7.41	98.99±6.93	0.114
GCC inferior R	98.43±11.73	99.79±5.60	99.50±5.55	94.62±21.36	100.64±6.73	0.254
Mean RNFL L	101.32±8.93	101.59±11.45	102.41±6.79	101.75±10.22	102.56±10.39	0.959
RNFL inferior L	121.57±14.94	118.15±21.15	123.45±11.73	121.79±15.56	123.42±17.64	0.715
RNFL superior L	124.98±13.50	121.48±12.30	124.36±14.56	122.71±14.18	125.49±14.76	0.733
RNFL nasal L	81.20±13.79	81.81±16.31	82.77±15.12	79.50±10.89	80.00±10.29	0.887
RNFL temporal L	78.59±16.42	76.48±10.45	76.09±10.50	75.83±10.71	76.35±14.43	0.843
Mean GCC L	97.74±6.26	100.96±8.99	99.09±6.10	103.59±15.20	99.67±6.76	***0.042***
GCC superior L	97.32±6.43	100.80±13.71	111.33±64.81	102.98±14.35	99.23±7.04	0.152
GCC inferior L	98.40±6.25	101.05±7.52	100.32±6.22	100.52±26.46	116.43±114.97	0.525

Notes. All results are expressed as mean ± standard deviation. OSAS: Obstructive sleep apnea syndrome, **BMI:** Body mass index, **IOP:** Intraocular pressure, **RNFL:** Retinal Nerve Fiber Layer,**GCC:** Ganglion Cell Complex**, Normal:** Healthy volunteer, **G1:** Group 1, **G2:** Group 2, **G3:** Group 3, **G4:** Group 4, **G5:** Group 5, **R:** Right, **L:** Left. RNFL thickness was measured in µm.

When RNFL and GCC values were compared between the right and left eye according to OSAS levels, no statistically significant difference was observed among the groups (p>0.05) (Tables 2-3).

Table 2. Comparison of RNFL thickness between the Mild, Moderate and Severe OSAS groups

	Mild OSAS=G3 (n=22)	Moderate OSAS=G4 (n=24)	Severe OSAS=G5 (n=57)	p
Mean RNFL R	100.95±8.19	103.21±9.69	103.33±8.67	0.544
RNFL inferior R	125.68±10.94	125.46±14.60	125.75±17.23	0.997
RNFL superior R	118.18±16.87	120.67±11.91	120.98±15.04	0.747
RNFL nasal R	85.27±13.64	83.67±10.28	83.37±14.47	0.851
RNFL temporal R	77.64±11.78	76.88±8.91	78.11±13.11	0.914
Mean RNFL L	102.41±6.79	101.75±10.22	102.56±10.39	0.942
RNFL inferior L	123.45±11.73	121.79±15.56	123.42±17.64	0.909
RNFL superior L	124.36±14.56	122.71±14.18	125.49±14.76	0.736
RNFL nasal L	82.77±15.12	79.50±10.89	80.00±10.29	0.573
RNFL temporal L	76.09±10.50	75.83±10.71	76.35±14.43	0.986

Notes. All results are expressed as mean ± standard deviation. OSAS: Obstructive sleep apnea syndrome**, RNFL:** Retinal Nerve Fiber Layer, **G3:** Group 3, **G4:** Group 4, **G5:** Group 5, **R:** Right, **L:** Left. RNFL thickness was measured in µm.

Table 3. Comparison of GCC measurements between the Mild, Moderate and Severe OSAS groups

	Mild OSAS=G3 (n=22)	Moderate OSAS = G4 (n=24)	Severe OSAS=G5 (n=57)	p
Mean GCC R	98.58±5.27	98.19±7.14	99.92±6.55	0.475
GCC superior R	111.14±64.73	98.02±7.41	98.99±6.93	0.236
GCC inferior R	99.50±5.55	94.62±21.36	100.64±6.73	0.109
Mean GCC L	99.09±6.10	103.59±15.20	99.67±6.76	0.190
GCC superior L	111.33±64.81	102.98±14.35	99.23±7.04	0.340
GCC inferior L	100.32±6.22	100.52±26.46	116.43±114.97	0.652

Notes. All results are expressed as mean ± standard deviation. OSAS: Obstructive sleep apnea syndrome**, GCC:** Ganglion Cell Complex, **G3:** Group 3, **G4:** Group 4, **G5:** Group 5, **R:** Right, **L:** Left. RNFL thickness was measured in µm.

When correlation analysis was performed between the right eye RNFL and GCC values; a positive significant statistical correlation was found among right mean RNFL; and right mean GCC (p<0.001, r=0.566) and right sperior GCC (p=0.007, r=0.263) and right inferior GCC p=0.008, r=0.259) and left mean GCC ($p<0.001$, r=0.415) and left superior GCC (p= 0.014, r=0.251) values. There were statistically significant positive correlations between right inferior RNFL; and right mean GCC ($p<0.001$, r=0.347) and left mean GCC ($p<0.001$, r=0.365). Again there were statistically significant positive correlations between the right RNFL superior; right mean GCC ($p<0.001$, r=0.382) and left mean GCC (p=0.007, r=0.274) values. There were statistically significant positive correlations between the right RNFL nasal; right mean GCC (p=0.007, r=0.263) and left mean GCC (p=0.018, r=0.243) values. A positive significant statistical correlation was found among right temporal RNFL; and right mean GCC ($p<0.001$, r=0.507) and right superior GCC ($p<0.001$, r=0.363) and right inferior GCC $p<0.001$, r=0.345) and left mean GCC (p=0.002, r=0.314) and left superior GCC (p= 0.001, r=0.341) values. A positive significant statistical correlation was found among left mean RNFL; and right mean GCC ($p<0.001$, r=0.532) and right sperior GCC (p=0.016, r=0.239) and right inferior GCC p=0.005, r=0.277) and left mean GCC ($p<0.001$, r=0.370) and left superior GCC (p= 0.023, r=0.233) values. There were statistically significant positive correlations between left inferior RNFL; and right mean GCC ($p<0.001$, r=0.368) and left mean GCC (p=0.004, r=0.296). Again there were statistically significant positive correlations between the left RNFL superior; right mean GCC (p=0.001, r=0.318) and left mean GCC (p=0.005, r=0.287) values. There were statistically significant positive correlations between the left RNFL nasal; right mean GCC (p=0.007, r=0.267) values. A positive significant statistical correlation was found among left temporal RNFL; and right mean GCC (p=0.001, r=0.445) and right superior GCC (p=0.002, r=0.304) and right inferior GCC p=0.002, r=0.298) and left mean GCC (p=0.003, r=0.306) and left superior GCC (p= 0.004, r=0.288) values (Table 4).

Table 4. Correlation between the right and left eye RNFL measurements and both eyes GCC values

	Mean GCC R	GCC superior R	GCC inferior R	Mean GCC L	GCC superior L	GCC inferior L
Mean RNFL R r	0.566	0.263	0.259	0.415	0.251	0.024
p	***<0.001***	***0.007***	***0.008***	***<0.001***	***0.014***	0.819
RNFL inferior R r	0.347	0.149	0.078	0.365	0.166	-0.008
p	***<0.001***	0.133	0.433	***<0.001***	0.106	0.937
RNFL superior R r	0.382	0.153	0.138	0.274	0.143	0.075
p	***<0.001***	0.124	0.166	***0.007***	0.165	0.466
RNFL nasal R r	0.263	0.089	0.100	0.243	0.090	0.021
p	***0.007***	0.374	0.316	***0.018***	0.381	0.836
RNFL temporal R r	0.507	0.363	0.345	0.314	0.341	0.016
p	***<0.001***	***<0.001***	***<0.001***	***0.002***	***0.001***	0.879
Mean RNFL L r	0.532	0.239	0.277	0.370	0.233	-0.005
p	***<0.001***	***0.016***	***0.005***	***<0.001***	***0.023***	0.959
RNFL inferior L r	0.368	0.162	0.131	0.296	0.141	0.015
p	***<0.001***	0.106	0.191	***0.004***	0.169	0.888
RNFL superior L r	0.318	0.152	0.102	0.287	0.163	0.005
p	***0.001***	0.129	0.310	***0.005***	0.112	0.961
RNFL nasal L r	0.267	0.077	0.142	0.176	0.069	0.066
p	***0.007***	0.445	0.157	0.087	0.506	0.522
RNFL temporal L r	0.445	0.304	0.298	0.306	0.288	-0.051
p	***<0.001***	***0.002***	***0.002***	***0.003***	***0.004***	0.619

Notes. RNFL: Retinal Nerve Fiber Layer, **GCC:** Ganglion Cell Complex**, R:** Right, **L:** Left. GCC and RNFL thickness was measured in µm.

When mild-moderate OSAS patients were evaluated as a single group and compared with the severe OSAS group in terms of RNFL and GCC thicknesses; no statistically significant difference was found among the groups in all values (p>0.05) (Table 5).

Table 5. Comparison of both eyes RNFL and GCC values between Mild+Moderate OSAS Group and Severe OSAS Group

	Mild+Moderate OSAS=G3+G4 (n=46)	**Severe OSAS=G5 (n=57)**	**p**
Mean RNFL R	102.13±8.98	103.33±8.67	0.492
RNFL inferior R	125.57±12.84	125.75±17.23	0.951
RNFL superior R	119.48±14.38	120.98±15.04	0.608
RNFL nasal R	84.43±11.90	83.37±14.47	0.689
RNFL temporal R	77.24±10.27	78.11±13.11	0.715
mean GCC R	98.38±6.25	99.92±6.55	0.228
GCC superior R	104.29±45.03	98.99±6.93	0.382
GCC inferior R	96.95±15.93	100.64±6.73	0.116
Mean RNFL L	102.07±8.66	102.56±10.39	0.796
RNFL inferior L	122.59±13.73	123.42±17.64	0.795
RNFL superior L	123.50±14.23	125.49±14.76	0.494
RNFL nasal L	81.07±13.04	80.00±10.29	0.647
RNFL temporal L	75.96±10.49	76.35±14.43	0.879
Mean GCC L	101.39±11.77	99.67±6.76	0.377
GCC superior L	106.97±45.64	99.23±7.04	0.239
GCC inferior L	100.42±19.39	116.43±114.97	0.354

Notes.All results are expressed as mean ± standard deviation. OSAS: Obstructive sleep apnea syndrome**, RNFL:** Retinal Nerve Fiber Layer, **GCC:** Ganglion Cell Complex**,G3:** Group 3, **G4:** Group 4, **G5:** Group 5, **R:** Right, **L:** Left.

Table 6. Comparison of both eyes RNFL and GCC values between the healthy group and simple snoring group

	Healthy=G1 (n=88)	Simple snoring=G2 (n=29)	p
Mean RNFL R	102.17±9.36	100.79±9.78	0.498
RNFL inferior R	125.81±12.97	125.45±16.96	0.905
RNFL superior R	120.52±13.10	115.69±15.54	0.103
RNFL nasal R	84.92±16.97	83.86±14.88	0.765
RNFL temporal R	75.97±9.32	78.31±10.86	0.262
Mean GCC R	98.44±6.60	98.78±5.46	0.806
GCC superior R	97.43±6.87	98.02±6.21	0.680
GCC inferior R	98.43±11.73	99.79±5.60	0.547
Mean RNFL L	101.32±8.93	101.59±11.45	0.900
RNFL inferior L	121.57±14.94	118.15±21.15	0.360
RNFL superior L	124.98±13.50	121.48±12.30	0.238
RNFL nasal L	81.20±13.79	81.81±16.31	0.850
RNFL temporal L	78.59±16.42	76.48±10.45	0.533
Mean GCC L	97.74±6.26	100.96±8.99	0.042
GCC superior L	97.32±6.43	100.80±13.71	0.081
GCC inferior L	98.40±6.25	101.05±7.52	0.072

Notes. All results are expressed as mean ± standard deviation. OSAS: Obstructive sleep apnea syndrome**, RNFL:** Retinal Nerve Fiber Layer, **GCC:** Ganglion Cell Complex**,G1:** Group 1, **G2:** Group 2, **R:** Right, **L:** Left.

When patients in the G1 and G5 groups were compared in terms of RNFL and GCC thicknesses, no statistically significant difference was found among the groups in all values (p>0.05) (Table 7).

Table 7. Comparison of both eyes RNFL and GCC values between the healthy group and Severe OSAS group

	Healthy=G1 (n=87)	Severe OSAS=G5 (n=57)	p
Mean RNFL R	102.17±9.36	103.33±8.67	0.453
RNFL inferior R	125.81±12.97	125.75±17.23	0.983
RNFL superior R	120.52±13.10	120.98±15.04	0.846
RNFL nasal R	84.92±16.97	83.37±14.47	0.570
RNFL temporal R	75.97±9.32	78.11±13.11	0.253
Mean GCC R	98.44±6.60	99.92±6.55	0.192
GCC superior R	97.43±6.87	98.99±6.93	0.189
GCC inferior R	98.43±11.73	100.64±6.73	0.199
Mean RNFL L	101.32±8.93	102.56±10.39	0.461
RNFL inferior L	121.57±14.94	123.42±17.64	0.514
RNFL superior L	124.98±13.50	125.49±14.76	0.835
RNFL nasal L	81.20±13.79	80.00±10.29	0.584
RNFL temporal L	78.59±16.42	76.35±14.43	0.414
Mean GCC L	97.74±6.26	99.67±6.76	0.104
GCC superior L	97.32±6.43	99.23±7.04	0.118
GCC inferior L	98.40±6.25	116.43±114.97	0.171

Notes. All results are expressed as mean ± standard deviation. OSAS: Obstructive sleep apnea syndrome**, RNFL:** Retinal Nerve Fiber Layer, **GCC:** Ganglion Cell Complex**, G1:** Group 1, **G5:** Group 5, **R:** Right, **L:** Left.

Glaucoma is an optic neuropathy characterized by a progressive and irreversible damage of the retinal ganglion cells, that can represent with progressive loss of vision, resulting in irreversible blindness. The loss of retinal nerve fiber layer occurs by the time early optic head nerve changes and the loss of vision (Drance, 1998). Quigley et al have shown that about 40% of the optic nerve fibers should be lost for the occurrence of significant visual field defects (Quigley, 1992).

The retina needs regular oxygen support to maintain its structural and functional integrity. Kergoat et al. investigated the effects of hypoxia on the retina with electrophysiological studies and demonstrated that retinal ganglion cells are particularly susceptible to the decreases in normal perfusion and oxygen saturation (Kergoat, 2006). In addition, they showed improvements in electrophysiologic parameters at the advancing stages of the test, despite the continuing hypoxia. In a study (Aydın, 2018) with 45 OSAS patients, superior and nasal RNFL thicknesses were found to be significantly lower compared to the control group. No significant correlation could be found between oxygen saturation, the lowest oxygen saturation and AHI severity obtained during polysomnography and RNFL. In our study also no significant correlation could be found between RNFL and AHI severity. Otherwise, Kargu et al. suggested that RNFL thickness was found to decrease in correlation with OSAS severity in 33 OSAS patients (Kargi, 2005). Whereas in our study, RNFL and GCC thicknesses were not significantly different in the simple snoring and OSAS groups compared to the control group. The lack of difference between the groups might be resulted from that the OSAS patients were newly diagnosed in our study. We only demostrated a positive correlation between RNFL and GCC measurements (except for several quadrants) as expected. Similar to our study, Geyer et al. also found no significant difference between the 228 OSAS patients and control groups in terms of RNFL thickness.

In the current study, no significant difference was found between all patient groups (G5-G4-G3-G2) and the control group (G1) in terms of the intraocular pressure. Studies have shown that glaucomatous visual field defects occur only after about 50% of retinal ganglion cells and axons have damaged (Quigley, 1989; Quigley, 1992). Lack of a significant difference between the patients and healthy participants might result from the measurements were made immediately after the patients were diagnosed as OSAS. The patients with OSAS must be evaluated for progressive RNLF thickness at follow up. It should be remembered that a long time may be required for the development of damage in the retina caused by oxygen saturation during sleep. Lack of difference between the patient and control group in terms of RNFL and GCC thicknesses might have probably resulted from early exposure to chronic hypoxia during sleep. Therefore further studies with a group of older patients and longer follow up of the same patient group are needed to enlighten this issue.

4.CONCLUSION

In our study, no significant difference was found between the OSAS and control groups in terms of the mean RNFL thickness and four quadrants RNFL thicknesses and the mean two quadrants GCC thickness. Although our study was a case-control study, the patient group consisted of newly diagnosed patients. It was not possible to know exactly how long these patients were exposed to hypoxia. Even in the patients who spent all the sleep duration under normal saturation, RNFL and GCC values were not different from those of the control group, suggesting that duration of hypoxia rather than its severity may be important. Therefore, because patients with the diagnosis of OSAS have a risk of developing glaucoma, it would be appropriate for these patients to have a regular optic examination.

Conflict of Interest: All of Author declare that he/she has no conflict of interest.

Informed consent: Informed consent was obtained from all individual participants included in the study.

Ethical approval:

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (Bursa Yuksek Ihtisas Education and Research Hospital's Clinic Research Ethical Committee- 2011 KAEK-25 2015/22-12) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

The name of the ethics committee and the reference number where appropriate: Bursa Yuksek Ihtisas Education and Research Hospital's Clinic Research Ethical Committee- 2011 KAEK-25 2015/22-12

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