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ARAŞTIRMA / RESEARCH

Optic disc, macula and ganglion cell layer measurements obtained with optical coherence tomography in patients with thyroid disorder

Tiroid bozukluğu olan hastalarda optik koherens tomografi ile elde edilen optik disk, makula ve gangliyon hücre tabakası ölçümleri

Zeynep Kunt[1], Gamze Karataş[1], Egemen Karataş[1], Gülay Mart[2]

[1]Osmaniye Devlet Hastanesi, Göz hastalıkları Kliniği, [2]Dahiliye Kliniği, Osmaniye, Turkey

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Abstract

Purpose: The aim of this study was to compare retinal nerve layer thickness, central macula thickness and ganglion cell layer measurements using optical coherence tomography (OCT) between thyroid patients and age- and sex-matched healthy controls.

Materials and Methods: Eighty eyes of 80 patients in the thyroid patient group and 48 eyes of 48 patients in the control group were included in the study. After evaluating the exclusion criteria, visual acuity, anterior segment biomicroscopy, intraocular pressure, fundoscopy and spectral field optic coherence tomography (SF-OCT) imaging tests were performed on all patients included in the study. These data have been recorded. Central macular thickness (CMT), retinal nerve fiber layer (RNFL) and ganglion cell complex (GCC) measurements were evaluated by statistical methods for both groups.

Results: There was no statistically significant difference between the demographic data of the groups included in the study. IOP measurements were found to be statistically significantly higher in the patient group compared to the control group. CMT values were 258.2±16.1 μm in the patient group and 273.1±23.8 μm in the control group, and statistically significant differences were observed between the groups.

Conclusion: The findings supports that changes in the optic nerve and macula develop before vision loss in TO patients compared to the healthy control group. We can follow TO patients more objectively and reliably and make treatment planning more accurately by adding OCT, which is a noninvasive test, to our clinical practice, since structural changes develop before functional deterioration in TO patients.

Keywords:. Ganglion cell complex, thyroid disease, optical coherence tomography

Öz

Amaç: Bu çalışmanın amacı tiroid hastaları ile yaş ve cinsiyet uyumlu sağlıklı kontrol grubu arasında retina sinir tabakası kalınlıkları, santral makula kalınlığı ve gangliyon hücre tabakası ölçümlerini optik koherens tomografi (OKT) kullanarak karşılaştırmaktır.

Gereç ve Yöntem: Tiroid hasta grubuna 80 hastanın 80 gözü ve kontrol grubun 48 hastanın 48 gözü çalışmaya alındı. Dışlama kriterleri değerlendirildikten sonra çalışmaya alınan tüm hastalara görme keskinliği, ön segment biyomikroskopisi, göz içi basıncı, fundoskopi ve spectral field optik kohorens tomografi (SF-OKT) görüntüleme tetkikleri uygulandı. Bu veriler kaydedildi. Santral maküla kalınlığı (SMK), retina sinir lifi tabakası (RSLT) ve gangliyon hücre kompleksi (GHK) ölçümleri her iki grup için istatistiksel yöntemlerle değerlendirildi.

Bulgular: Çalışmaya dahil edilen grupların demografik verileri arasında istatistiksel olarak anlamlı fark saptanmadı. GİB ölçümleri hasta grubunda kontrol grubuna göre istatistiksel olarak anlamlı yüksek tespit edildi. SMK değerleri hasta grubunda 258,2±16,1 μm, kontrol grubunda 273,1±23,8 μm olarak saptandı ve gruplar arası istatistiksel olarak anlamlı fark gözlendi. GHK değerleri ve temporal kadran RSLT değerleri gruplar arasında istatistiksel olarak anlamlı fark gözlendi.

Sonuç: Bulgular TO hastalarında sağlıklı kontrol grubuna göre görme kayıplarından önce optik sinir ve makulada değişiklikler geliştiğini desteklemektedir. TO hastalarında fonksiyonel bozulmadan önce yapısal değişiklikler geliştiğinden noninvaziv bir test olan OKT yi klinik pratiğimize ekleyerek TO hastalarını daha objektif ve güvenilir bir şekilde takip edebilir ve tedavi planlamasını daha doğru yapabiliriz.

Anahtar kelimeler: Ganglion hücre kompleksi, tiroid hastalığı, optik koherens tomografi

Yazışma Adresi/Address for Correspondence: Dr. Zeynep Kunt, Osmaniye Devlet Hastanesi, Göz hastalıkları Kliniği, Osmaniye, Turkey E-mail: zynp.kunt@gmail.com
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INTRODUCTION

Thyroid ophthalmopathy (TO) is considered to be an autoimmune disease activated by the effect of environmental factors on an immunogenetic basis[1]. TO is generally seen bilaterally and often asymmetrically[2]. The signs and symptoms in TO are related to orbital connective tissue inflammation, fibrosis and inflammation of the extraocular muscles, and adipogenesis[3]. While clinically most of the TO patients have mild eye involvement, severe ophthalmopathy findings including increased chemosis, proptosis, ocular hypertension, and vision loss can be seen in 5% of cases[4,5,6]. The incidence of ocular hypertension in various studies is between 0.8% and 13.5%[7,8].

It is thought that the ocular hypertension and optic nerve damage seen into TO patients are caused by orbital mechanical compression by the extraocular muscles and soft tissue expansion[9]. Optic nerve involvement; It can cause different clinical findings such as decrease in visual acuity, narrowing of the visual field, deterioration in color vision, and change in optic disc configuration[10].

Previous studies have shown that optic disc function may be affected into TO patients without significant optic nerve involvement and extraocular muscle hypertrophy[11,12,13]. For this reason, various tests and parameters are used in order to prevent early diagnosis and possible vision loss.

Optical coherence tomography (OCT) is an alternative and non-invasive imaging modality to evaluate the macula and optic disc. OCT plays an important role in early diagnosis and follow-up in clinical practice. GCC mesaurement has shown to be a useful marker in the diagnosis and monitoring of multiple optic neuropathies and it is thought to be more sensitive than RNFL[14]. The thickness of macular retinal layer had shown to be thinner in TO patients which might be caused by the thinning of GCC[14].

In this study, we aimed to reveal the structural changes in the retinal nerve fiber layer (RNFL) and ganglion cell complex (GCC) of TO patients and age- and gender-matched control groups using OCT. Thus, we think that the combination of structural and functional measurements may provide more information about the condition of the optic nerve as subclinical optic neuropathy may progress even though there is no obvious visual abnormality in TO patients.

MATERIALS AND METHODS

This prospective and cross-sectional study was composed of patients who were followed up with the diagnosis of thyroid disease in the Department of Internal Medicine of Osmaniye State Hospital between August 2021 and February 2022 and ophthalmological examinations of all patients were performed in the eye department. Our study was carried out in accordance with the Declaration of Helsinki. SBU Adana City Training and Research Hospital Ethics Committee approval was obtained (Ethics committee decision no:1464). Consent was obtained from all patients before starting the study. Ophtalmological examination and OCT imaging of the patient and control groups were performed by the researchers.

Sample

Eighty of 110 patients with ophthalmopathy who were diagnosed as thyroid pathology by the Department of Internal Medicine, Osmaniye State Hospital, Osmaniye, Turkey, and were sent to ophthalmology clinic for eye involvement and 48 healthy volunteers who formed the control group were included in our study. Patients with early stage thyroid disease and low clinical activity score according to the European Graves Orbitopathy Study Group (EUGOGO) criteria were included in the patient group[15]. The control group had 20/20 vision (corrected or uncorrected), without any systemic disease and eye pathology The patients were selected among age and gender matched healthy volunteers. In both groups, those with another systemic disease, significant visual impairment, history of ocular surgery, high myopia (<-5D), high hyperopia (+3D), optic disc anomaly, vitreoretinal interface disease, vascular and degenerative retinal diseases, patients with corneal or lens opacity, glaucoma disease were excluded from the study. A random eye of the patients included in the patient and control groups were included in the study and statistical analysis was performed.

Procedure

A detailed ophthalmological examination was performed for all patients included in our study and the control group. The best corrected visual acuity (BCVA) was evaluated with the Snellen chart. Intraocular pressure was measured by Goldman aplanation tonometry. Anterior segment examination with slit lamp and posterior segment examination with 90D lens were performed.

Spectral field optical coherence tomography imaging

Central macular thickness (CMT), retinal nerve fiber layer (RNFL), and ganglion cell complex (GCC) measurements were performed using spectral field OCT (SF-OCT) (Retina Scan RS-3000 Advance, NIDEK, Gamagori, Japan). GCC thickness obtained from peripapillary RNFL and macular map scanning was calculated automatically via the software of the device. Automated measurements in cup area, disc area, C/D horizontal, C/D vertical, superior, nasal, inferior and temporal quadrants were recorded as RNFL data. The superior and inferior GCC thickness values in the central 9 mm circle centered on the fovea determined by the OCT device were taken.

Statistical analysis

SPSS 22.0 (IBM Corp., Armonk, N.Y., USA) statistical package program was used for statistical analysis of the data of the study. In the descriptive statistics part of the data, categorical variables are given as numbers and percentages; continuous variables are presented with mean ± standard deviation and median (smallest - largest value). Conformity of continuous variables to normal distribution was evaluated using Kolmogorov-Smirnov or Shapiro-Wilk tests. For categorical variables, the difference in frequency between the groups was compared using the chi-square test. The Fischer test was used when the chi-square test conditions were not met. In the comparison of the data between all groups, Kruskall Wallis test would have been applied if the normal distribution conditions hadn't met. The Mann-Whitney U test was used in the analysis of the data that did not fit the normal distribution between the two groups. In statistical evaluations, a p value less than 0.05 ($p<0.05$) was considered significant.

RESULTS

In the study, 80 eyes of 80 patients aged 18-60 years with thyroid disease who applied to our clinic were included in the patient group, while 48 eyes of 48 healthy volunteers without thyroid disease were included in the control group.

The patient group included in the study consisted of 57 female (71.25%) patients and 23 male (28.75%) patients. The control group consisted of 36 female (75%) patients and 12 male (25%) patients.

While the mean age of the patient group was 42.1±7.8 years, the mean age of the control group was 37.2±15.0 years.

Intraocular pressure (IOP) measurements are; It was measured as 15.3±2.6 mmHg in the patient group and 12.1±1.8 mmHg in the control group.

While there was a statistically significant difference between the two groups in terms of age and IOP, no statistically significant difference was found in terms of gender and best corrected visual acuity (Table 1).

Table 1. Demographic and clinical findings of the patient group and control group

	Patient group	Control group	P value
Female	57 female (%71.25)	36 female (%75)	0.446
Male	23 male (%28.75)	12 male (%25)	0.446
Age (year)	42.1±7.8	37.2±15.0	0.008
IOP (mmHg)	15.3±2.6	12.1±1.8	0.000

IOP:İntraocular pressure

The CMT value was found to be 258.2 ± 16.1 μm in the patient group and 273.1 ± 23.8 μm in the control group, and a statistically significant difference was found between the groups ($p<0.05$) (Table 2). Superior quadrant GCC value was 98.5 ± 4.6 μm, inferior quadrant GCC value was 102.1 ± 5.4 μm in the patient group, superior quadrant GCC value was 100.9 ± 9.0 μm, inferior quadrant GCC value was 102.3 ± 8.4 μm in the control group. A statistically significant difference was found between the two ($p<0.05$) (Table 2.

Table 2: Comparison of CMT and GCC values between the patient group and the control group

	Patient group	Control group	P value
CMT	258.2±16.1	273±23.8	0.000
Superior GCC	98.5±4.6	100.9±9.0	0.000
İnferior GCC	102.1±5.4	102.3±8.4	0.001

Patient group Control group P value; CMT:Central macular thickness, GCC:Ganglion cell complex

In the patient group, superior quadrant RNFL thickness 132.8±11.9 μm, inferior quadrant RNFL thickness 140.6±13.7 μm, temporal quadrant RNFL thickness 76.3±10.3 μm, nasal quadrant RNFL thickness 79.7±10. In the control group, superior quadrant RNFL thickness was 132.6±18.3μm, inferior quadrant RNFL thickness was 138.0±20.7 μm, temporal quadrant RNFL thickness was 71.9±12.8μm, nasal quadrant RNFL thickness was 80.6±16.7 μm. Temporal quadrant RNFL values showed a statistically significant difference between the patient and control groups ($p< 0.05$). No statistically significant difference was observed between the superior, inferior and nasal quadrant RNFL thicknesses ($p=0.358$, $p=0.184$ and $p=0.864$, respectively).

Cup area 0.6±0.2 μm, disc area 2.3±0.3 μm, C/D horizontal value 0.5±0.1 μm, C/D vertical value 0.5±0.1 in the patient group. In the control group, the cup area value was 0.7±0.4 μm, the disc area value was 2.4±0.5 μm, the horizontal C/D value was 0.6±0.2 μm, the C/D vertical value was 0.5±0.1 μm. C/D horizontal and vertical values showed a statistically significant difference between the patient and control groups ($p<0.005$). No statistically significant difference was observed between cup area and disc area values ($p=0.465$ and $p=0.584$, respectively).

RNFL thickness values, cup area, disc area, C/D horizontal and vertical values between groups are shown in Table 3.

Table 3. Comparison of optic disc and RNFL values of the patient group and the control group

	Patient group	Control group	P value
Cup area	0.6±0.2	0.7± 0.4	0.465
Disc area	2.3±0.3	2.4±0.5	0.584
C/D Horizontal	0.5±0.1	0.6±0.2	0.001
C/D Vertikal	0.5±0.1	0.5±0.1	0.017
Superior RNFL	132.8±11.9	132.6±18.3	0.358
İnferior RNFL	140.6±13.7	138.0±20.7	0.184
Temporal RNFL	76.3±10.3	71.9±12.8	0.000
Nasal RNFL	79.7±10.5	80.6±16.7	0.864

RNFL: Retinal nerve fiber layer

DISCUSSION

TO is a progressive and autoimmune disease. Severe ophthalmopathy findings including chemosis, proptosis, ocular hypertension, obstructive optic neuropathy, and vision loss can be observed due to the increase in the volume and inflammation in the extraocular muscle mass, intraorbital fat and connective tissue[4,5,6]. There are many studies showing a relationship between thyroid patients and high IOP. It is thought that increased IOP values are due to increased fat, muscle and connective tissue volume in the intraorbital area and increased episcleral venous pressure[2,7,8,16,17]. Previous studies have shown that patients with TO have higher IOP measurements compared to the control group[18]. In the study performed by Şen et al., IOP values were found to be higher in patients with Graves' disease compared to the healthy control group[19]. In our study, IOP measurements were found to be statistically higher in the patient group compared to the control group, which was consistent with the literature. The results of the Advanced Glaucoma Intervention Study (AGIS) showed that an increase

in IOP to 26 mmHg or more increases the risk of glaucoma twelve times in long-term follow-up[19]. Thus, intraocular pressure must be carefully monitored in patients with thyroid orbitopathy during all phases and stages of the disease[21].

In recent years, OCT has emerged as a more reliable and reproducible tool to evaluate nerve anatomy and CMT value[22,23,24,25]. It has been proven that RNFL thickness decreases in TO patients who do not have clinical signs of optic neuropathy, which indicates that structural damage may occur earlier than functional deterioration[19,26]. In addition, there are different results related to RNFL thickness in the literature[9,19,25]. The existence of different results in the literature is attributed to the fact that different RNFL measurements were taken at different stages of TO patients included in the study[9,27]. However, we think that our results are more reliable since we included stable patients according to the EUGOGO criteria in our study. In the study of Meirovitch et al. in which 21 TO patients and 41 healthy controls were compared, thickening of the RNFL and thinning of the CMT were found in the patient group[9]. In the study conducted by Şen et al., it was observed that RNFL thinning was observed in patients with Graves' disease compared to the healthy control group[19]. In the study by Forte et al., it was shown that there was a decrease in RNFL values in the patient group with TO compared to the control group and there was a correlation between this change and the visual level[28]. While no significant difference was observed in terms of GCC values, a statistically significant thinning was observed compared to the control group[25].

In our study, it was found that CMT, GCC and temporal RNFL values were thinner in the patient group compared to the control group. According to our results, the changes in CMT, GCC and RNFL values seen in TO patients are a direct indicator of optic nerve pathologies. Therefore, it may be recommended to use OCT more widely in the evaluation and follow-up of TO patients.

Thinning can be seen in RNFL and GCC values with advancing age. A statistically significant age difference between the patient and control groups in our study is a limitation of our study as it may affect GCC and RNFL measurements.

In conclusion, we can follow TO patients more objectively and reliably and make treatment planning more accurately by adding OCT, which is a noninvasive test, to our clinical practice, since structural changes develop before functional deterioration in TO patients. Thus, we think that anatomical changes that may develop in TO patients can be prevented without causing functional vision loss. Our data are preliminary and a larger study population is needed to confirm our findings.

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