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CLINICAL RESEARCH / KLİNİK ARAŞTIRMA

OCT Findings and Ocular Changes in Subclinical Hypothyroidism

Subklinik Hipotiroidizmde OKT Bulguları ve Oküler Değişiklikler

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Abstract

Objective: To evaluate the changes in intraocular pressure (IOP), central corneal thickness (CCT), retinal nerve fiber layer thickness (RNFLT), foveal thickness (FT) and choroid thickness (ChT) in patients with subclinical hypothyroidism.

Methods: Sixty eyes of 30 patients with subclinical hypothyroidism (study group) and 60 eyes of 30 healthy subjects (control group) were included in the study. A complete ocular examination including best corrected visual acuity (BCVA), IOP, anterior and posterior segment examination together with CCT, RNFLT, FT and ChT measurements were performed in each group. $p<0.05$ was accepted statistically significant.

Results: Global (G) RNFLT, nasal (N) RNFLT, nasal inferior (NI) RNFLT and ChT ($p=0.008$, $p=0.006$, $p=0.046$ and $p=<0.001$ respectively) values of the study group were statistically higher than the control group. There was a weak negative correlation between ChT and RNFLT temporal inferior (TI) and nasal (N) and global (G) quadrants in the study group ($r=-0.426$; $p=0.024$, $r=-0.403$; $p=0.034$ & $r=-0.410$; $p=0.030$ respectively). FT values of the control group were statistically higher than the study group ($p=0.026$).

Conclusions: Glucosaminoglycan accumulation in subclinical hypothyroid group may cause increase in RNFLT(G) and ChT. According to the SD-OCT (Spectral Domain - Optical Coherence Tomography) measurements of subclinical hypothyroid patients, negative correlation between ChT and RNFLT may be a guide in terms of progression to glaucoma. Besides, FT measurement follow-up, which may be inversely proportional with the level of hypothyroidism, may lead off about the level of visual acuity (VA). In addition to all these, the ChT may be a guide in following the treatment process. The results of our study should be supported by further studies.

Keywords: Choroid thickness, foveal thickness, intraocular pressure, retinal nerve fiber layer thickness, subclinical hypothyroidism

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Öz

Amaç: Subklinik hipotiroidisi olan hastalarda göz içi basıncı (GİB), santral kornea kalınlığı (SKK), retina sinir lifi tabakası kalınlığı (RSLTK), foveal kalınlık (FK) ve koroid kalınlığındaki (KK) değişiklikleri değerlendirmek.

Yöntem: Çalışmaya subklinik hipotiroidisi olan 30 hastanın 60 gözü (çalışma grubu) ile 30 sağlıklı olgunun 60 gözü (kontrol grubu) dahil edildi. Herbir grupta en iyi düzeltilmiş görme keskinliği (EİDGK), GİB, ön ve arka segment muayenesi ile birlikte SKK, RSLTK, FK ve KK ölçümlerini içeren tam bir oküler muayene yapıldı. p<0.05 istatistiksel olarak anlamlı kabul edildi.

Bulgular: Çalışma grubunun global (G) RSLTK, nazal (N) RSLTK, nazal inferior (Nİ) RSLTK ve KK değerleri kontrol grubuna göre istatistiksel olarak daha yüksekti (sırasıyla p=0.008, p=0.006, p=0.046 ve p=<0.001). Çalışma grubunda KK ile RSLTK temporal inferior (TI), nazal (N) ve global (G) kadranlar arasında zayıf bir negatif korelasyon vardı (sırasıyla r=-0.426; p=0.024, r=-0.403; p=0.034 & r=-0.410; p=0.030 r). Kontrol grubunun FK değerleri çalışma grubuna göre istatistiksel olarak daha yüksekti (p=0,026).

Sonuç: Subklinik hipotiroidisi olan grupta glukozaminoglikan birikimi RSLTK(G) ve KK'da artışa neden olabilir. Subklinik hipotiroidi hastalarının SD-OKT (Spectral Domain - Optik Koherens Tomografi) ölçümlerine göre KK ile RSLTK arasındaki negatif korelasyon, glokoma progresyon açısından yol gösterici olabilir. Ayrıca hipotiroidi düzeyi ile ters orantılı olabilen FK ölçüm takibi, görme keskinliği (GK) düzeyi hakkında fikir verebilir. Tüm bunlara ek olarak KK, tedavi sürecini takip etmemizde bize yol gösterebilir. Çalışmamızın sonuçları daha ileri çalışmalarla desteklenmelidir.

Anahtar Kelimeler: Koroid kalınlığı, foveal kalınlık, göz içi basıncı, retina sinir lifi tabakası kalınlığı, subklinik hipotiroidi

Introduction

Subclinical hypothyroidism is a disorder related with a raised concentration of thyroid stimulating hormone (TSH) but a normal free thyroxine (FT4) and free tri-iodothyronine (FT3) levels. It is a frequent disorder, approximately 10% of women more than 55 years of age are affected and autoimmunity is the most frequent reason. Every year approximately 2.5% of patients with subclinical hypothyroidism develop overt hypothyroidism.

Hydrophilic mucopolysaccharides accumulate in the dermis and other tissues which lead to myxoedema in hypothyroid patients[1]. Some authors pointed out that the relationship between hypothyroidism and glaucoma was collection of glycosaminoglycan in trabecular meshwork resulting in the aqueous humor flow blockage, therefore as a result might cause glaucoma[1-4].

There have been some studies supporting the higher prevalence of primary open angle glaucoma (POAG) among hypothyroid individuals; however there are some others which could not[2,4-7]. Centanni et al.[3] showed reversibly increased intraocular pressure (IOP) even in subclinical hypothyroidism and this result brought to mind whether some microscopic findings might lead to macroscopic findings in hypothyroidism. Ozturk et al.[8] reported that both hypothyroidism, and its replacement therapy did not cause any variation in IOP, central corneal thickness (CCT), anterior chamber parameters, retinal nerve fiber layer thickness (RNFLT), retinal thickness (RT) and cup to disc ratio (C/D). The prevalence of POAG, increases with age as hypothyroidism[5,9].

However, there is no existing data when these diseases are together in their subclinical stage. Therefore, it is important to assign the presence of early ocular variations in the early stage of thyroid hormone insufficiency which is not apparent yet. That's why in this study, our purpose was to investigate the variations in IOP, CCT, and Spectral Domain- Optic Coherence Tomography (SD-OCT) findings in patients with subclinical hypothyroidism in order to determine if variations in these parameters might show the relationship between subclinical hypothyroidism and progression to glaucoma and be a guide for follow-up and treatment of both diseases.

Materials and Methods

This retrospective clinical trial was directed at the Department of Ophthalmology with the association of the Department of Endocrinology of a Education and Research Hospital. The study was built in compliance with the principles of the statements of Helsinki and the protocol was confirmed by Health Sciences University, İzmir Tepecik Education and Research Hospital ethics committee (No:2019/13-6; Date:11.09.2019). Informed consent was provided from all the patients. Sixty eyes of 30 patients with newly diagnosed subclinical hypothyroidism (study group) referred from Endocrinology outpatient clinic and 60 eyes of healthy subjects (control group) were enrolled in the study. The diagnosis of subclinical hypothyroidism was determined according to the laboratory findings with elevated basal TSH (mean 13.5±5µ/1; range 5.8-32.4 µ/l), normal serum free triiodothyronine (FT3) (3.60± 1.24 pmol/l) and serum free thyroxine (FT4) (12.83±2.38pmol/1) levels. The presence of

anti-thyroid peroxidase antibodies (anti-TPO Ab)>120 mg/dL supported the autoimmune origin of hypothyroidism. The first ocular examination was performed in newly diagnosed subclinical hypothyroid patients to eliminate any evidence of an ophthalmological disturbance. Ocular examination including best corrected visual acuity (BCVA), IOP, anterior and posterior segment examination was performed. Patients with orbitopathy, corneal pathology, retinal vascular disease, maculopathy, optic neuropathy, glaucoma and any history of ocular surgery were eliminated from the study. BCVA was evaluated with Snellen chart and IOP was evaluated with Goldmann applanation tonometry. CCT measurement was performed with non-contact infrared method (Topcon CT-1P, Japan). C/D, RNFLT, foveal and choroid thickness (FT, ChT) measurements were performed with SD-OCT (Heidelberg Engineering, Germany). Fast optic disc and fast RNFL scans (with quadrant distribution), automated FT and sub-foveal choroid thickness (SFCT) measurements with enhanced depth imaging (EDI) mode using the Heidelberg SD-OCT caliper were performed. SFCT scanning was performed at sub-foveal region using SD-OCT, EDI mode with software version 6.9. The horizontal division passing straight ahead the center of the fovea was used for the measurement of SFCT. SFCT in the enhanced images was measured as the perpendicular distance between the outer portion of the hyper-reflective line matching to the retina pigment epithelium (RPE) to hyporeflective line matching to the chorio-scleral junction. The measurement of SFCT was made manually by a single qualified doctor. C/D ratios were enrolled after optic disc analyses were achieved. Thyroid hormone level measurements consisting TSH, free T3, free T4, and anti-TPO levels were recorded. To refrain the influence of diurnal and personal changes, all the patients were examined and all of the SD-OCT measurements were acquired at the same time in the morning by the same doctor. For intraobserver reproducibility, SD-OCT measurements were performed for 3 times by the same doctor. SD-OCT scans were acquired without pupil dilation and only images with an imaging quality score of >20 were studied.

Statistical Analysis

All data were evaluated with IBM SPSS Statistics Standard Concurrent User version 25 (IBM Corp., Armonk, New York, USA) statistics package software. Definitive statistics were given as number (n), percentage (%), mean ± standard deviation ($\bar{x}$±SD), median (M), minimum (min) and maximum (max) values. Range of Anti-TPO variable was very large so descriptive statistics were evaluated by using geometric mean and within 95% confidence limit. Normality of numerical data distributions was evaluated by Shapiro-Wilk normality test and Q–Q plots. Homogenity of variances were evaluated by Levene test. Age values were normally distributed, so comparisons between the groups were made by using independent-two samples t test. Visual acuities were not normally distributed so compared by using Mann-Whitney U test. Comparisons between the groups in terms of gender were made by using Fisher exact test.

While generalized linear mixed models were used to compare the differences between the RNFLT, IOP, CCT, FT, ChT and C/D ratio values of the groups, general linear models were used for thyroid functions. Age and gender-adjusted partial correlation analysis was used to examine the associations between numeric variables. For all tests, $p<0.05$ was accepted as statistically significant.

Results

The study covered 60 eyes of 30 (50%) subclinical hypothyroid (study group) patients and 60 eyes of 30 (50%) healthy subjects (control group). Of the study group 26 (86.7%) were women, 4 13.3(%) were men and of the control group 18 (60.0%) were women, 12 (40.0%) were men. In the study group female gender was statistically higher than the control group (χ^2=5.455; p=0.039). The mean age of the patients was 42.00±12.28 years in the study group and 38.16±11.17 years in the control group. Distribution of age between the groups was statistically similar (t=1.264; p=0.211). Since the significance value of the comparisons of the groups according to age and gender was p<0.25, the comparisons were adjusted according to age and gender.

BCVA levels of study and control groups were statistically similar in women, men and the whole group (Table 1).

Groups were compared according to RNFLT, IOP, CCT, FT, ChT, C/D ratio and thyroid functions. The RNFLT nasal (N), RNFLT nasal inferior (NI), RNFLT global (G), and ChT values of the study group were statistically higher than the control group (p=0.008, p=0.006, p=0.046 and p=<0.001 respectively). However, FT values of the control group were statistically higher than the study group (p=0.026). FT3 and FT4 values were not statistically significant between the groups (p=0.170 and p=0.945 respectively). However, TSH and anti-TPO Ab values of the study group were statistically higher than the control group (p<0,001 and p=0,003 respectively). (Table 2).

There was a statistically negative correlation between FT and RNFLT N in the whole group (r= -0.364; p=0.005).

Table 1. Comparison of visual acuity according to gender and all group

	Groups		Test statistics	
	Subclinical hypothyroidism	Control		
	M (min-max)	M (min-max)	z	p
BCVA of women	1.00 (0.05-1.00)	1.00 (1.00-1.00)	1.190	0.234
BCVA of men	1.00 (0.16-1.00)	1.00 (1.00-1.00)	1.732	0.521
BCVA of all group	1.00 (0.05-1.00)	1.00 (1.00-1.00)	1.761	0.078

z: Mann-Whitney U test, BCVA: Best corrected visual acuity

Table 2. Comparison of groups according to RNFLT, IOP, CCT, FT, ChT, C/D ratio and thyroid functions

	Groups				Test statistics*	
	Subclinical hypothyroidism		Control			
	$\bar{x}$	sh	$\bar{x}$	sh	F	p
IOP (mmHg)	17.22	0.55	17.73	0.53	1.917	0.172
CCT (µm)	521.85	7.24	525.31	6.99	0.006	0.938
RNFLT (T) (µm)	69.91	1.91	67.96	1.84	0.047	0.828
RNFLT (Tİ) (µm)	150.67	3.83	147.45	3.70	0.304	0.584
RNFLT (TS) (µm)	145.76	3.56	137.16	3.44	1.636	0.206
RNFLT (N) (µm)	86.04	2.21	76.90	2.21	8.128	**0.006**
RNFLT (NS) (µm)	120.00	3.65	109.89	3.53	1.868	0.177
RNFLT (Nİ) (µm)	123.86	4.72	109.92	4.72	4.154	**0.046**
RNFLT (G) (µm)	107.07	1.92	99.46	1.92	7.493	**0.008**
Foveal thickness (FT) (µm)	218.12	2.57	226.64	2.57	5.232	**0.026**
Choroid thickness (ChT) (µm)	340.34	5.99	286.44	5.95	38.880	**<0.001**
C/D	0.327	0.023	0.371	0.023	1.768	0.189
FT3 (n_{sk}=26; n_{nor}=29) (pmol/1)	3.134	0.124	3.344	0.086	1.942	0.170
FT4 (n_{sk}=26; n_{nor}=29) (pmol/1)	0.885	0.045	0.889	0.031	0.005	0.945
TSH (n_{sk}=27; n_{nor}=30) (µ)	8.462	0.514	1.578	0.313	130.884	**<0.001**
Anti-TPO Ab (n_{sk}=27; n_{nor}=30) GO (%95 LCL-HCL) (mg/dL)	57.992 (19.457-172.848)		1.991 (1.012-3.915)		10.212	0.003**

*Values corrected according to gender, **Logarithmic values were compared, GO: Geometric mean, LCL: Lower Confidence Limit, HCL: Higher Confidence Limit, IOP: Intraocular Pressure CCT: Central Corneal Thickness, RNFLT: Retinal Nerve Fiber Layer Thickness, T: Temporal quadrant, TS: Temporal Superior quadrant, TI: Temporal Inferior quadrant, N: Nasal quadrant, NS: Nasal Superior quadrant, NI: Nasal Inferior quadrant, G: Global, C/D: Cup Disc ratio

There was a statistically negative correlation between ChT and RNFLT TI, RNFLT N and RNFLT G in the study group (r=-0.426; p=0.024, r=-0.403; p=0.034 & r=-0.410; p=0.030, respectively). There was a statistically positive correlation between ChT and RNFLT NI in the control group (r=0.381; p=0.046) (Table 3).

There was a positive correlation between ChT and TSH and anti-TPO Ab values (r=0.652; p=<0,001, r=0,332; p=0,026 respectively) in the whole group. There was a statistically negative correlation between RNFLT G and TSH (r= -0.469; p=0.043), and a statistically positive correlation between RNFLT G and FT3 (r=0.465; p=0.045) in the study group. There was a statistically positive correlation between CCT and anti-TPO Ab values in the control group (r=0.405; p=0.049) (Table 4).

Intraclass correlation coefficient (ICC) values for subfoveal ChT measurements ranged from 0.901 to 0.999 and were statistically significant

Discussion

Thyroid hormone has an important mission in the neural restructuring of the eye particularly for normally

Table 3. Relationships between RNFLT, ChT and FT

	All group		Subclinical hypothyroid group		Control group	
	ChT	Foveal T	ChT	Foveal T	ChT	Foveal T
ChT (µm) r p	-	-0.160 0.231	-	0.373 0.051	-	
RNFLT T (µm) r p	-0.046 0.733	-0.064 0.631	-0.152 0.440	-0.006 0.977	-0.014 0.945	-0.132 0.503
RNFLT TS (µm) r p	-0.009 0.947	-0.049 0.716	-0.274 0.158	-0.090 0.649	0.128 0.517	0.093 0.638
RNFLT Tİ (µm) r p	-0.167 0.210	-0.034 0.802	**-0.426** **0.024**	0.097 0.623	0.137 0.486	-0.080 0.685
RNFLT N (µm) r p	0.080 0.550	**-0.364** **0.005**	**-0.403** **0.034**	-0.346 0.071	0.332 0.084	-0.322 0.095
RNFLT NS (µm) r p	0.114 0.393	-0.073 0.585	-0.155 0.432	-0.371 0.052	0.172 0.382	0.267 0.169
RNFLT Nİ (µm) r p	0.143 0.283	-0.124 0.352	-0.179 0.361	-0.161 0.412	**0.381** **0.046**	0.036 0.856
RNFLT G (µm) r p	0.058 0.666	-0.202 0.129	**-0.410** **0.030**	-0.229 0.241	0.347 0.070	-0.062 0.752

* Corrected values according to age and gender, **ChT: Choroid Thickness RNFLT: Retinal Nerve Fiber Layer Thickness T: Temporal quadrant TS: Temporal Superior quadrant, TI: Temporal Inferior quadrant, N: Nasal quadrant, NS: Nasal Superior quadrant, NI: Nasal Inferior quadrant, G: Global

restructuring of the retina and accession of color vision. It arranges internal mechanisms for managing stratification of retina[10]. The study of Gamborino et al.[11] supports this information, they verified that, in a rat model the photoreceptor and ganglion cell layer thickness were lower in congenital neonatal hypothyroidism.

It is clearly identified that an elevation in IOP in Graves' thyroid orbitopathy may arise according to variable situations consisting contraction of extraocular muscles, elevated episcleral venous pressure secondary to orbital stuffiness, secondary angle closure, and enhanced mucopolysaccharide deposition within the aqueous outflow pathways[12]. Nevertheless, the impacts of subclinical and clinical hypothyroidism on IOP have not been completely determined. In hypothyroidic phase, hyaluronic acid collects in connective tissues due to the reduced dissolvement of hyaluronic acid crosschecked with its formation. It has been proved that the collection of hyaluronic acid in variable tissues decrease with medical therapy[12].

The initial statements concerning the IOP elevation in hypothyroidism extend to1897 and glaucoma has been related with thyrotoxicosis and myxoedema together with a genetic tendency to both situations[13-15]. Smith et al.[6] noticed a decline in outflow ability in hypothyroidic phase and connected IOP rise to mucopolysaccharide collection in the trabecular meshwork and/or external outflow pathways. They defined a considerable improvement in the aqueous outflow with therapy and recommended that glaucoma would improve with the therapy of hypothyroidism.

There are some conflicting statements in the literature that assign the rate of hypothyroidism among POAG patients to state if following of thyroid hormones are effective for POAG

Table 4. Relationships between IOP, CCT, ChT, FT, RNFLT G, TSH, Anti-TPO Ab, FT3 and FT4

	All group				Subclinical hypothyroidism group				Control group			
	TSH	Anti-TPO	FT3	FT4	TSH	Anti-TPO	FT3	FT4	TSH	Anti-TPO	FT3	FT4
CCT (µm)												
r	-0.074	0.156	0.035	-0.052	-0.446	0.001	0.210	-0.315	0.329	**0.405**	-0.041	0.038
p	0.627	0.307	0.820	0.735	0.056	0.998	0.387	0.189	0.116	**0.049**	0.849	0.859
IOP (mmHg)												
r	-0.133	0.119	0.187	0.064	-0.181	0.379	0.219	0.161	0.261	0.125	0.116	-0.032
p	0.384	0.438	0.220	0.678	0.458	0.110	0.367	0.510	0.219	0.560	0.590	0.881
Ch T (µm)												
r	**0.652**	**0.332**	-0.258	0.009	0.420	-0.212	-0.405	0.231	0.225	0.115	-0.083	-0.016
p	<0.001	**0.026**	0.087	0.955	0.073	0.383	0.085	0.342	0.291	0.591	0.701	0.940
FT (µm)												
r	-0.280	-0.106	0.092	-0.232	0.252	-0.020	0.094	0.035	-0.156	0.096	0.012	-0.382
p	0.062	0.489	0.548	0.126	0.297	0.935	0.702	0.888	0.467	0.654	0.954	0.066
RNFLT G (µm)												
r	0.062	0.098	0.223	0.088	**-0.469**	0.139	**0.465**	0.037	0.101	-0.128	0.102	0.127
p	0.686	0.521	0.141	0.567	**0.043**	0.571	**0.045**	0.881	0.639	0.552	0.637	0.554

*Corrected values according to age and gender, **CCT: Central corneal thickness, IOP: Intraocular pressure, FT:Foveal thickness, RNFLT G: Retinal nerve fiber layer thickness global

patients or not[2,5,16]. Some of these previous studies noticed a relationship between hypothyroidism and OAG, however some others could not[2-6,13,16].

There are some studies which evaluated the prevalence of OAG in acquired hypothyroid patients, which could not describe an association between the two diseases, except Tahat et al.[7-8,17] Centanni and friends determined an important rise of IOP in subclinical hypothyroid patients checked with age matched healthy controls[3]. These results were consistent with the study of Smith et al.[6] in patients with obvious hypothyroidism and they defined a high prevalence (23%) of hypothyroidism in patients with POAG. In Centanni's study, no patient had glaucoma, but 38% had IOP values above 18 mmHg[3]. In our study there was no significant IOP difference between the groups, 33.3% of both study and control group had IOP levels above 18 mmHg, but not above 21 mm Hg and no patient had evidence of glaucoma as well. This might be due to the young age distribution of both studies.

Studies investigating the incidence of hypothyrodism among patients with glaucoma have usually older age ranges, conversely studies planned to assign the rate of glaucoma among hypothyroidic patients had younger subjects which may clarify the lower glaucoma rates detected in these studies including our study as well[9].

Evaluating the prevalence of glaucoma alone, may lead to miss the real influence of hypothyroidism on IOP as alterations under 21 mmHg would not be regarded; therefore, Özturk et al.[8] evaluated the association of IOP with the variation of TSH, but did not detect any reduction in IOP with therapy and the mean CCT did not change significantly either. Bahçeci et al.[7] detected a crucial reduction in IOP with therapy, which was not parallel with the change in the thyroid hormone level and stated a meaningful decrease in CCT after therapy. They reported that these changes might be correlated with mucopolysaccharide accumulation in corneal stroma. Ulaş et al.[18] found that healthy subjects and euthyroid patients receiving levothyroxine treatment had lower IOP than patients with subclinical hypothyroidism and overt hypothyroidism in their study. On the contrary of Ulaş and friends study, we could not find any difference in terms of IOP and CCT between the groups like Ozturk and friends. We found no correlation with IOP change and TSH levels as well.

A few studies have proposed that IOP might be overestimated in thick and underestimated in thin corneas[19-21]. The mechanism by which, hypothyroidism causes IOP rise is not known so far. However, immunologic response cannot be eliminated as the association between OAG and immune processes has already been proved[10]. In Centanni et.al study, the elevations in IOP were only present in patients with autoimmune hypothyroidism and they provided IOP decrease by using L-T4[3]. Unfortunately, the blood levels of anti-TPO Ab were not parallel with IOP levels, therefore it was not possible to support an immunological pathogenesis. In our study we found no relation between IOP and anti-TPO Ab levels either.

The studies of both Bahçeci and Özturk covered recently diagnosed hypothyroid patients, on the other hand the duration of hypothyroidism was not known and the methods used for CCT evaluation were different[7-8]. Bahçeci et al.[7] performed CCT measurement with ultrasonic pachymetry, whereas it was performed with Scheimpflug camera by Ozturk et al.[8] These might be the reasons for the contradictory outcomes. In our study, the patients were newly detected and subclinical; therefore the effect of hypothyroidism on CCT and IOP might not be detected yet. However, the procedure for CCT measurement we used was different from the other two studies which was non-contact infrared method.

To our knowledge, Bahçeci et al.[7] study is the first study in which hypothyroid individuals were investigated in terms of CCT and RNFLT. After L-thyroxine therapy there was no meaningful alteration in RNFLT parameters evaluated with Scanning Laser Ophthalmoscope (SLO). The parameter, which is a significant indicator of glaucomatous damage in Scanning Laser Polarimeter (NFA-GDx), was also found within normal limits. Higher IOP values in hypothyroid patients seemed to be non-glaucomatous IOP elevations, which might be a pseudohypertension due to increased CCT caused by hypothyroidism. The normal values of RNFLT and visual fields in all cases also supported this proposal. Ozturk and friends also evaluated the variations in RNFLT, C/D ratio and RT, and they found all these parameters constant during the follow-up period[8]. In the literature, RNFLT of hypothyroid patients was only acquired in the studies of Bahçeci and Özturk, and they did not find any difference in RNFLT values between pre and post-treatment measurements[7-8]. Unlike their study, the RNFLT N, RNFLT NI, RNFLT G values of the subclinical hypothyroid patients were statistically higher than the healthy subjects in our study.

Ulaş et al.[18] stated that all subgroups of hypothyroid patients had thicker ChT compared to healthy subjects in their study. As it is known from the other studies that, choroidal thickness is affected by diurnal variation,, we evaluated the choroidal thickness values of the groups in the morning in our study and the result of our study was consistent with Ulaş and friends study[18,22-24]. As in their study we also found that the choroid thickness was higher in the subclinical hypothyroid group compared with the healthy control group.

The increase in RNFLT and ChT might be caused by the accumulation of glycosaminoglycan, however FT values of the study group were statistically lower than the control group, this might be due to the mean age of the study group which was 42.00±12.28 years, whereas it was 38.16±11.17 years in the control group. Choroidal vasculature is responsible for feeding the outer 1/3 of the retina. A disorder in the choroid vasculature, as which is due to the accumulation of glycosaminoglycan in choroid tissue in our study, may impair retinal blood supply and lead to a decrease in FT. This hypothesis may also explain the negative correlation between ChT and RNFLT G, RNFLT TI and RNFLT N in the study group. However, thyroid hormone plays an important role in the development and maintenance of the neural structure of the retina, its deficiency may cause atrophy of the layers of retina and decrease in FT as well, which may affect vision negatively in advanced deficiencies.

As far as we investigated the literature, our study is the first study, which evaluated RNFLT, FT and ChT altogether with SD-OCT in subclinical hypothyroid patients. Both Bahçeci and Ozturk also evaluated RNFLT with two different devices, SLO and OCT respectively[7-8]. However, study populations of both Bahçeci and Ozturk were hypothyroid patients whereas our population was subclinical hypothyroid patients. Besides, Ozturk evaluated RT with OCT and Ulaş evaluated ChT with SD-OCT. Nevertheless, the difference of our study from other studies[7-8,18] is that; our study group is different from other studies since our study group consists of patients with subclinic hypothyroidism, and we could evaluate FT, RNFLT and ChT altogether in one study by SD-OCT.

Study Limitations

The gender distribution of the study group was not equal and the duration of the disease was unknown. Besides, patients with subclinical hypothyroidism were not separated according to etiology.

Conclusion

In the light of our study and previously published studies, it can be possible to state that thyroid hormones may not have a direct effect on CCT and IOP. The younger mean age and lack of orbitopathy, unknown duration of the disease might be responsible for the contradictory outcomes, as well as tendency to autoimmunity such as hypothyroidism and glaucoma. Further studies investigating the subclinical hypothyroid patients due to the etiology separately, may enlighten this dilemma.

As far as we know from the previously published studies, RNFLT parameters independent of the measured device; SLO or OCT do not seem to be affected by hypothyroidism, but according to our study RNFLT and ChT measurements of the study group were statistically higher than the control group. As we mentioned previously, increase in RNFLT and ChTs in the study group might be caused by accumulation of glycosaminoglycan. Besides, with the development of sophisticated devices and techniques over the years, SD-OCT might offer the opportunity to make more reliable and improved measurements. Positive correlation between ChT and both TSH and anti-TPO Ab levels may give an opinion about the progression of subclinical hypothyroidism to clinically apparent hypothyroidism by using the SD-OCT. According to the SD-OCT evaluations of subclinical hypothyroid patients, negative correlation between ChT and RNFLT may be a guide in terms of progression to glaucoma. Besides, FT follow-up with SD-OCT, which may be inversely proportional with the level of hypothyroidism, may lead off about the visual prognosis. In addition to all these, the ChT may be a guide in following the treatment process of hypothyroidism. Our results should be supported by further studies.

Ethics

Ethics Committee Approval: The study were approved by the University of Health Sciences Turkey, İzmir Tepecik Education and Research Hospital of Local Ethics Committee (protocol number: 2019/13-6, date: 11.09.2019).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: E.K., H.Y.Y., Concept: E.K., H.Y.Y., Design: E.K., H.Y.Y., Data Collection or Processing: E.K., H.Y.Y., Analysis or Interpretation: E.K., Literature Search: E.K., Writing: E.K.

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