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Original Article

Does Obesity Affect the Ocular Choroid Tissue in Children and Adolescents?

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ABSTRACT

Aim: Obesity may cause microangiopathic changes associated with the inflammatory process. The choroid tissue of the eye is one of the most highly vascularized tissues of body and supplies the outer 1/3 of the retina. Thinning in choroid tissue is an indicator of damage. Few studies have investigated obesity-induced choroid tissue damage in children, and their findings are inconsistent. The purpose of this study was to investigate changes in choroid tissue thickness in non-diabetic children and adolescents using optic coherence tomography (OCT) and the association with metabolic risk factors.

Materials and Methods: One hundred fifty-six eyes of 38 obese and 40 healthy children and adolescents aged 10-18 were included in the study. The bilateral choroidal thicknesses were measured. We then investigated correlations between choroidal thickness and age, body measurements, pubertal stages, systolic and diastolic blood pressures, homeostasis model assessment insulin resistance and lipid values.

Results: Mean choroidal thicknesses measured using OCT were 284.4±34.9 µm in the obese group and 316.3±39.7 µm in the control group (p=0.018). Choroidal thickness in the obese group decreased as body mass index (BMI) standard deviation scores (SDS) increased (r=-0.390, p=0.000).

Conclusion: Mean choroidal thickness was lower in obese children and adolescents in this study compared to the healthy controls and thinning in the choroid tissue was more pronounced as BMI-SDS values increased. Increased adipose tissue may result in a susceptibility to damage by thinning choroid tissue.

Keywords: Choroidal thickness, optical coherence tomography, pediatric obesity

Introduction

The prevalence of childhood obesity is growing. Obesity may cause microangiopathic changes associated with the inflammatory process (1,2). Microvascular changes caused by obesity may result in damage to the optic nerve, retinal nerve fiber layer (RNFL) and choroidal regions, and damage can be revealed in the early period with optic coherence tomography (OCT). The layers of the eye can be visualized in a painless, rapid and non-invasive way using OCT (3). The choroid is one of the most highly vascularized tissues of body and it supplies the outer 1/3 of the retina. The choroid also plays important anatomical and physiological roles, including ocular thermoregulation, the regulation of intraocular pressure and growth factor secretion. Thinning of choroid tissue is a damage indicator (4,5). Previous studies have investigated choroidal thickness in healthy children (6-9). However, few studies have investigated the effect on choroidal and retinal structure in obese children, and their results are inconsistent. The purpose of this study was to investigate changes in choroid tissue thickness in non-diabetic children and adolescents using OCT and the association with metabolic risk factors and pubertal stages.

Materials and Methods

Consent form was filled out by all participants. The study was approved by the İzmir Tepecik Training and

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Research Hospital Local Ethics Committee (approval number: 29.12.2014/20). All procedures were conducted in line with the ethical principles of the Declaration of Helsinki.

Inclusion criteria for study and control subjects:

- Age 10-18 years
- No neurological diseases
- No history of ocular disease or surgery
- Children and parents being compliant with examinations
- Subjects with spherical values between -0.50 D and +0.50 D were enrolled.

Exclusion criteria for study and control subjects:

- Presence of diabetes mellitus or any systemic disease
- Use of systemic corticosteroids
- Non-compliance with OCT measurement.
- History of ocular trauma and dense media opacities

Seventy-six eyes of 38 obese children and adolescents aged 10.1-17.2 years presenting to the İzmir Tepecik Training and Research Hospital Pediatric Endocrinology Clinic, Turkey, between January 2015 and May 2016, and 80 eyes of 40 healthy children and adolescents aged 10.2-18.0 years were included in the study. The demographic characteristics of the obese and control groups were recorded from their medical files. Body measurements, blood pressure values and pubertal stages were assessed by an experienced pediatric endocrinologist. Pubertal stages were classified based on Tanner's system (10). Height was measured to the nearest centimeter using a rigid stadiometer. Weight was measured to the nearest 0.1 kg using a calibrated balance scale with the subject unclothed. Body mass index (BMI) was determined using the formula weight (kg)/ height squared (m2). Established reference values for Turkish children were employed to calculate the standard deviation scores (SDS) for weight, height and BMI (11). Obesity was diagnosed on the basis of World Health Organization definitions (12). Blood pressure was measured in all cases following a period of rest. Measurements were taken at least three times at 10-minute intervals. Individuals with systolic and/or diastolic blood pressure values greater than the 95th percentile were considered hypertensive (13). Blood glucose, insulin and serum lipids in the case of obese subjects were measured using an automatic analyzer from fasting venous specimens collected on that day. Insulin resistance using the homeostasis model assessment insulin resistance (HOMA-IR) was calculated using the formula fasting insulin (μIU/mL) x fasting glucose (mg/dL)/405 (14). All cases underwent detailed eye examinations performed by the same ophthalmologist. Best corrected visual acuities were measured, detailed anterior segment examination was performed with a slit-lamp biomicroscope, intraocular pressure measurement using Goldman applanation tonometry, ocular motility evaluation and optic nerve and retinal examination with a 90 dioptric lens. For pupil dilation, 1% cyclopentolate hydrochloride (Sikloplejin R; Abdi İbrahim İlaç Sanayi, İstanbul) eye drops were applied twice at 5 min intervals, and the mean of three measurements performed 30 min after the final application using an autorefractometer (Canon RK-F1) was taken. Ocular biometry was measured by the LenStar biometer (Haag-Streit, Switzerland)

Choroidal thickness was measured manually using OCT (Heidelberg Spectralis, Heidelberg Engineering, Heidelberg, Germany) in increased imaging depth mode in order to optimize choroidal resolution. Automatic real time eye tracking was performed. Choroidal thickness was measured between the outer border of the hyper-reflective retinal pigment epithelium and the inner border of the choroidal-scleral junction. Measurements were performed bilaterally by two independent masked observers. Choroidal thicknesses were measured using OCT, 500 μm nasal (N500) and 500 μm temporal (T500) from the foveal center (C). Mean choroidal thickness values were recorded. All OCT imaging

Table I. Clinical and laboratory characteristics of the study groups

Clinical or laboratory characteristics	**Control (n=40)**	**Obese (n=38)**	**p value[a]**	
Gender (male/female)	21/19	18/20	0.81b	
Age (years)	12.9±2.4	12.8±2.1	0.99	
Puberty stage (pre-pubertal/pubertal)	11/29	10/28	0.98b	
BMI-SDS	0.5±0.4	3.0±0.4	0.000	
Systolic BP (mmHg)	106.1±9.1	111.8± 9.4	0.19	
Diastolic BP (mmHg)	66.3±6.7	69.2±9.3	0.28	
Fasting glucose(mg/dL)	82.1±8.8	85.3±9.9	0.65	
Fasting Insuline (mIU/mL)	8.3±3.1	19.6±9.8	0.02	
HOMA-IR	1.9±0.7	4.7±2.7	0.01	
Triglycerides (mg/dL)	125.3±62.0	138.5±72.9	0.07	
LDL-cholesterol (mg/dL)	89.3±18.6	96.9±25.7	0.06	
HDL-cholesterol (mg/dL)		46.1±11.3	43.2±10.3	0.72

[a]Student's T test, [b]Chi-square test

BMI-SDS: Body mass index-standard deviation score, BP: Blood pressure, HDL: High density lipoprotein, HOMA-IR: Homeostasis model assessment of insulin resistance, LDL: Low density lipoprotein

was performed between 09.00 and 11.00 in order to avoid diurnal variation. Statistical analysis was performed using the choroidal thickness values measured and the mean thereof. Choroidal thicknesses were compared between the control and obese groups. We then investigated correlations between choroidal thickness and age, pubertal stages, body measurements, systolic and diastolic blood pressures, fasting insulin, HOMA-IR and lipid values.

Statistical Analysis

Statistical Package for Social Sciences (SPSS 20.0; IBM, USA) software was employed for statistical analyses. The Kolmogorov-Smirnov test was used to evaluate the normality of the sample distribution. Mean and standard deviation values are provided for all parameters. Pearson correlation analysis was used to assess relations for normally distributed variables. Spearman correlation analysis was applied to non-normally distributed variables. A value of $p<0.05$ was considered statistically significant.

Results

Mean ages were 12.8±2.1 years in the obese group (n=38) and 12.9±2.4 in the control group (n=40). The difference between the two groups was not statistically significant (p=0.99). Also, no significant difference was determined between the two groups in terms of sex distributions, pubertal stages or mean systolic and diastolic blood pressures. BMI-SDS was 3.0±0.4 in the obese group compared to 0.5±0.4 in the control group (p<0.0001). Fasting blood glucose values were within normal limits in both groups (control group: 82.1±8.8 mg/dL, obese group: 85.3±9.9 mg/dL, p=0.65). As anticipated, morning fasting insulin and HOMA-IR values were statistically significantly higher in the obese individuals compared to the controls (obese group fasting insulin: 19.6±9.8, control group fasting insulin: 8.3±3.1 mIU/mL, p=0.02, obese group HOMA-IR: 4.7±2.7, control group HOMA-IR: 1.9±0.7, p=0.01). There was no difference between the two groups in terms of serum lipid levels. Clinical and laboratory characteristics of the obese and control groups are shown in Table I. Between the axial length measurement in study (22.7±0.6 mm) and control (22.8±0.5) groups, there was no statistically significant difference (p=0.211). No statistically significant difference was determined between sex and both eyes in terms of choroidal thickness values measured using OCT (p=0.81). When the central, nasal and temporal quadrants were assessed individually in terms of choroidal thicknesses, choroidal thinning was observed in all quadrants in the obese group compared to the controls, but the difference was not statistically significant. However, mean choroidal thickness values were 284.4±34.9 µm (range, 230-378 µm) in the obese group and 316.3±39.7 µm (range 293-348 µm) in the control group. This difference was statistically significant (p=0.018). Choroidal thickness values in the study groups are shown in Table II. The relations between clinical and laboratory variables and choroidal thickness were analysed. Age and pubertal stage were positively correlated with choroidal thickness, although no statistical significance was determined (p>0.05). No correlation was determined between choroidal thickness and blood pressure, serum fasting glucose, HOMA-IR or lipid levels. In the obese group, choroidal thickness decreased as BMI-SDS values increased (r=-0.390, p<0.0001). In the control group, although negative correlation was observed between increasing BMI and choroidal thickness, this correlation was not statistically significant (r=-0.112, p=0.079). Pearson correlation analysis results between choroidal thickness and clinical and laboratory data are shown in Table III.

Discussion

The choroid, one of the most highly vascularized tissues in the body, is particularly susceptible to diseases leading to microvascular complications. Like other ocular structures, choroidal thickness may vary throughout childhood. Examination of choroidal thickness provides important information in the diagnosis and management of various ocular and systemic diseases leading to chorioretinal inflammatory changes (4,15). Previous studies have shown choroidal thinning independent of stage of retinopathy in

Table II. Choroidal thickness in control and obese children

Choroidal thickness	Control (n=40)	Obese (n=38)	p value
Central (C) (µm)	320.5±40.0	288.5±35.0	0.112
Nasal (N500) (µm)	303.5±39.1	271.4±34.6	0.068
Temporal (T500) (µm)	325.1±40.0	293.4±35.1	0.082
Avarage (µm)	316.3±39.7	284.4±34.9	0.018

Table III. Correlation analysis of choroidal thickness with the clinical and laboratory parameters of the study groups

	Control		Obese	
Clinical or laboratory characteristics	r	p value	r	p value
Age	0.161	0.157	0.197	0.099
Puberty stage	0.142	0.214	0.156	0.116
BMI-SDS	-0.112	0.079	-0.390	0.000
Systolic BP	-0.159	0.164	-0.165	0.570
Diastolic BP	-0.145	0.209	-0.166	0.124
Fasting glucose	0.029	0.227	0.155	0.308
Fasting insulin	0.077	0.566	0.172	0.093
HOMA-IR	0.211	0.099	0.290	0.059
Triglycerides	0.014	0.731	0.189	0.231
LDL-cholesterol	0.073	0.632	-0.174	0.210
HDL-cholesterol	0.056	0.755	0.094	0.178

BMI-SDS: Body mass index-standard deviation score, BP: Blood pressure, HDL: High density lipoprotein, HOMA-IR: Homeostasis model assessment of insulin resistance, LDL: Low density lipoprotein

Type II diabetes (16). Lower choroidal thickness has also been observed compared to healthy controls in several diseases, such as hypertension, rheumatoid arthritis, systemic lupus erythematosus, and obstructive sleep apnoea (17-20). Chronic microvascular systemic inflammation is implicated in the development of all these diseases. Obesity and severe obesity have become an increasingly severe public health problem in children in recent years (21,22). Obesity can lead to systemic and ocular complications. The RNFL and the thickness of choroid tissue can be affected by obesity. Previous studies have shown that obesity causes a thinning in RNFL thickness in children (23,24). Low level systemic inflammation is known to occur in obesity (25-27). For may also have the potential to affect the choroid layer. Previous studies have reported normative data concerning choroidal thicknesses in healthy children and adolescents. Read et al. (6) reported a mean subfoveal choroidal thickness of 330±65 µm (range, 189-538 µm) in 194 healthy children aged 4-12. In addition, they determined normal choroidal thicknesses of 312±62 µm at age 4-6, 337±65 µm at age 7-9, and 341±61 µm at age 10-12. Based on these findings, they reported that choroidal thickness increases from early childhood. We also determined a positive correlation, although not at a statistically significant level, between age and pubertal stage and choroidal thickness. In The Copenhagen Child Cohort 2000 Eye Study of 1323 children aged 11-12, Li et al. (7) determined a mean subfoveal choroidal thickness of 369±81 µm, but determined no relation between choroidal thickness and sex. We also observed no significant difference between the sexes in terms of choroidal thickness values ($p>0.05$). Bidaut-Garnier et al. (8) measured a mean subfoveal choroidal thickness of 341.96±74.7 µm and reported that the choroid was thinner in the nasal region than in the temporal region. In their study of healthy children under 18, Lee et al. (9) determined greater choroidal thicknesses in the macular region in all quadrants investigated compared to adults. They also emphasized that pediatric subfoveal choroidal thickness is disposed to thinning with age and refractive error. Subjects with refractive error were excluded from our study. The mean choroidal thickness measured with OCT in the healthy children and adolescents we enrolled as the control group was 316.3±39.7 µm. These values are in agreement with previous studies. Few studies have investigated choroidal thickness in obese children, and their findings are inconsistent. In their study of obese children aged 5-15, Erşan et al. (28) determined a mean choroidal thickness of 301.95±56.72 m in the control group and of 270.20±56.13 µm in the obese group ($p=0.014$). They reported that this thinning might be due to microvascular complication. In contrast to that study, Bulus et al. (29) reported a mean choroidal thickness of 348.43±73.21 µm in the control group and of 385.77±6.09 µm in obese children. Choroidal thickness increased in the obese group ($p=0.017$). The authors suggested that choroidal thickening might be attributed to obesity-related vascular changes and increased adipocyte tissue. We observed thinning of choroidal thickness in all the measured quadrants in obese children compared to the healthy controls. Mean choroidal thicknesses were 316.3±39.7 µm (range 293-378 µm) in the control group and 284.4±34.9 (range, 230-360 µm) in the obese group. This difference in choroidal thicknesses was statistically significant ($p=0.018$). Thinning in choroidal thickness in obese cases may be associated with chronic systemic inflammation and microvascular disturbance (25-27). Oxidative stress and hypoxia may occur in obesity. In addition, changes in leptin and adipokines levels, adipose tissue dysfunction and insulin resistance may also occur. The production of inflammatory cytokines and reactive oxygen species increases due to the oxidative stress. Apoptosis and tissue necrosis are then triggered as a result. Studies have shown that oxidative stress may be a significant factor in cell death (30-33). Vascular endothelial damage, oxidative stress and chronic inflammation may impair the permeability and nutrition of microvascular structures. This may then give rise to thinning of choroid tissue. Choroidal thickness measurement may be affected by diurnal variation. We performed our measurements at the same time interval, between 09.00 and 11.00, in order to avoid diurnal fluctuation. The border of the chorioscleral junction was measured manually. Choroid OCT images were taken by two independent masked observers. Studies concerning the reliability and repeatability of this manual measurement method have reported powerful correlation between measurements and the individuals performing them (34-36). There are a number of limitations to this study. Plasma levels of inflammatory mediators such as adiponectin, leptin and interleukin-6 could not be measured. However, the metabolic and vascular effects of these mediators were evaluated indirectly by measuring insulin, lipid and glucose levels. No studies have shown whether changes in choroidal thickness values will occur through weight loss in obese individuals. Prospective observational studies involving weight control are needed in order to reveal more clearly the effect of obesity, and therefore the chronic inflammatory process, on choroidal tissue. In conclusion, this study shows a lower mean choroidal tissue thickness in obese children and adolescents compared to healthy controls. In addition, the decrease in choroidal tissue thickness becomes more marked as BMI-SDS values increase. An increase in adipose tissue may result in a susceptibility to retinal damage. Long-term observational studies are now needed in order to confirm the findings of this cross-sectional study.

Ethics

Ethics Committee Approval: The study was approved by the İzmir Tepecik Training and Research Hospital Local Ethics Committee (approval number: 29.12.2014/20).

Informed Consent: Consent form was filled out by all participants.

Authorship Contributions

Surgical and Medical Practices: B.Ö., H.Ö, Concept: B.Ö., H.Ö, G.Ç., Design: B.Ö., H.Ö, G.Ç., Data Collection or Processing: B.Ö., H.Ö, G.Ç., Analysis or Interpretation:

B.Ö., H.Ö, G.Ç., B.D., Literature Search: B.Ö., H.Ö, G.Ç., B.D., Writing: B.Ö., H.Ö, G.Ç.

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