Effect Of The Inflammatory Bowel Diseases On Choroidal And Macular Thickness

İnflamatuar Bağırsak Hastalıklarının Koroidal ve Makular Kalınlık Üzerine Etkisi

* Fahrettin AKAY, MD, Associate Professor
** Halil GENÇ, MD
*** Yusuf Çağdaş KUMBUL, MD

* İzmir Katip Çelebi University Atatürk Training and Research Hospital, Department of Ophthalmology Gastroenterology, İzmir, Turkey

** İzmir Katip Çelebi University Atatürk Training and Research Hospital, Department of Gastroenterology, İzmir, Turkey

*** İzmir Katip Çelebi University Atatürk Training and Research Hospital, Department of Ear Nose Throat Head and Neck Surgery, İzmir, Turkey

Yazışma Adresi:

Fahrettin AKAY, MD, Associate Professor
İzmir Katip Çelebi University Atatürk Training and Research Hospital, Department of Ophthalmology, İzmir, Turkey

Email: drfakay@yahoo.com
GSM: +90 505 3829385

Öz

Amaç: Crohn hastalığı (CD) ve ülseratif kolit (ÜK) bir grup inflamatuar barsak hastalığıdır (IBD) .IBD'de oftalmik bozukluklar ortaya çıkabilir. En sık görülen bulgular episklerit ve üveittir. Çalışmanın amacı IBD'deki koroidal ve maküla kalınlığını (MT ve CT) değerlendirmek ve bunu hastalık aktivitesi ile kontrol etmektir. **Yöntem:** IBD grubu 50 hastanın 50 sağ gözünü içeriyorken, kontrol grubu ise 50 sağlıklı gönüllünün herhangi bir gözünden oluşmuştu. Tüm katılımcılar spectral domain optical coherence tomography (SD-OCT) ile test edildi. CT değerleri yedi farklı noktada elde edildi. **Bulgular:** IBD'nin ortalama süresi 3.9 ± 1.5 yıl idi. Foveal maküler kalınlık; çalışma grubunda 258.1 ± 14.2 µm, kontrol grubunda 262.7 ± 20.9 µm idi. Gruplar arasında anlamlı fark yoktu (P = 0,19). Subfoveal, temporal 500 µm, 1000 µm ve 1500 µm CT ölçümleri, çalışma grubunda sırasıyla istatistiksel olarak anlamlıydı (p <0.001). Çalışma grubunda ortalama BT 289.8 ± 25.6 µm, kontrol grubunda 273.9 ± 33.2 µm idi. Gruplar arasında anlamlı fark vardı (P = 0.008). Ortalama BT ve eritrosit sedimentasyon hızı, C-reaktif protein düzeyi ve diğer klinik parametreler arasında korelasyon yoktu (P = 0,05). **Sonuç:** Bağırsak iltihabı, koroidal vasküler yapıyı etkileyebilir.

Anahtar Kelimeler: Koroidal kalınlık, inflamatuar bağırsak hastalıkları, makuler kalınlık

Abstract

Objective: Crohn's disease (CD) and ulcerative colitis (UC) are a group of inflammatory bowel disease (IBD). Ophthalmic disorders might occur in IBD. The most common findings are episcleritis and uveitis.Then purpose of the study was to evaulate the choroidal and macular thickness (MT and CT) in the IBD and to check it with the disease activity. **Methods:** IBD group was including 50 patients and the control group consisted of 50 healty volunteers. All participants were tested with spectral domain optical coherence tomography (SD-OCT). The CT values were obtained at seven different points. **Results:** Mean duration of the IBD was 3.9 ±1.5 years. Foveal macular thickness was 258.1 ± 14.2 µm in study group and 262.7 ± 20.9 µm in the control group. There was not significant difference between groups(P=0,19). Subfoveal, temporal 500 µm, 1000 µm, and 1500 µm CT measurements were respectively statistically significant in the study group (p<0.001). Mean CT was

289.8 ± 25.6 µm in study group and 273.9 ± 33.2 µm in the control group. There was a significant difference between groups (P=0.008). There was no correlation between mean CT and erythrocyte sedimentation rate, C-reactive protein level and other clinical parameters (P> 0,05). **Conclusion:** Inflammation of the bowels might affect the choroidal vascular structure.

Keywords : Choroidal thickness, Inflammatory Bowel Diseases, Macular Thickness

Introduction

Crohn's disease (CD) and ulcerative colitis (UC) are a group of inflammatory bowel disease (IBD) which characterized by relapses. They affect generally all gastrointestinal tractus especially the colon and small intestine primarily with unknown etiology. Intestinal inflammation is the main impairment in IBD but extraintestinal signs are observed in 5%-40% of patients. Extraintestinal signs may represent the first indication of disease in 10%-20% of all cases(1). Extraintestinal manifestations have undefined multifactorial pathogenesis(2). It is assumed that toxins and antigens leads to an antigen-antibody complex accumulation in different extraintestinal organs(2). Ophthalmic manifestations are categorized as primary, secondary, and coincidental(3). Primary signs are usually associated with IBD activations and secondaries are the complications that range cataracts to the visual impairments from 5-ASA, or blindness as a result the deficency of vitamins. Rare complications are ocular findings that occur as in the population. Ophthalmic disorders occur in 1.6%-5.4% among the ulcerative colitis and 3.5%-6.8% among the Crohn's disease(4). The most findings are episcleritis (2%-5%) and uveitis (0.5%- 3.5%). Ocular symptoms may be blurred vision, burning, or itchy eyes from the pain, photophobia, teary, red eyes, loss of visual acuity, and blindness(5).

Spectral domain optical coherence tomography (SD-OCT) is a subjective method for examining retina and choroidal structures in the globe. Detailed retinal and choroidal cross sectional images can be evaluated. Alterations in choroidal thickness have previously been reported in different autoimmune and inflammatory impairments(6-8). The goal of the study was to evaulate the choroidal and macular thickness alterations in the IBD and to check it with the disease activity.

Material and Methods

Our study is designed as prospective case-control clinical investigation. It was performed between January 2016 and February 2018 in Izmir Ataturk Training and Research Hospital, Izmir, Turkey. The IBD group included 50 patients who were referred from the gastroenterology department. These patients were underwent from the full ophthalmological examination to the ophthalmology department. The control group included 50 healthy volunteers. Only right eyes of the subjects was used for study. Signatured informed document was obtained from each participant. The principles of the Declaration of Helsinki were followed by the authors. It was allowed by the ethics committee. The diagnosis of IBD was dependent on the pathological biopsy results and clinical findings. OCT measurements were obtained during acute attacks. All patients were under the treatment and received nonsteroidal anti-inflammatory drugs. Age, sex, disease duration, white blood cell count (WBC), erythrocyte sedimentation rate(ESR) and C-reactive protein(CRP) levels were recorded. Arterial blood pressures were measured from the arm. All participants had been taken a rest for at least 10 minutes before measurements. Abnormal values of both groups were not included the study. The control group did not have a diagnosis of any disease. Ocular trauma, visual acuity under 20/32, uveitis, glaucoma, previous ocular surgery, lens-cornea opacities and systemic arterial hypertension, and spherical equivalent >±3.0 dpt. were excluded from the study. IOP was tested with Goldman applanation tonometry (Haag- Streit AG, Switzerland) and axial length (AL) was analysed with a biometer (OcuScan, Alcon, USA).

 SD-OCT (RS-3000, NIDEK, Japan) was used for macular and choroidal analysis after pupillary dilation. Scans were done between 9:00 and 10:00 a.m. Images were taken from patients and control subject. Signal strength (≥ 8 over 10) was chosen for best image. Macula line raster image was used for CT evaulations. The CT was ranged as the distance between the RPE line and the scleralborder drawn by examiner(-FA). The CT values were obtained at seven different points: starting at the subfoveal center and spaced at three points with the 500 µm intervals to the temporal and nasal retina(Figure 1).

All data were checkovered with using SPSS version 21.0 (SPSS Inc., USA). Results were expressed as

means ± standard deviation (SD). The normality of the values was analyzed using the Shapiro-Wilk test. The Student-t test or the Mann-Whitney U test was used according to the normality scores. $P < 0.05$ accepted as significant. Correlations between the variables were performed by the Pearson correlation coefficient test.
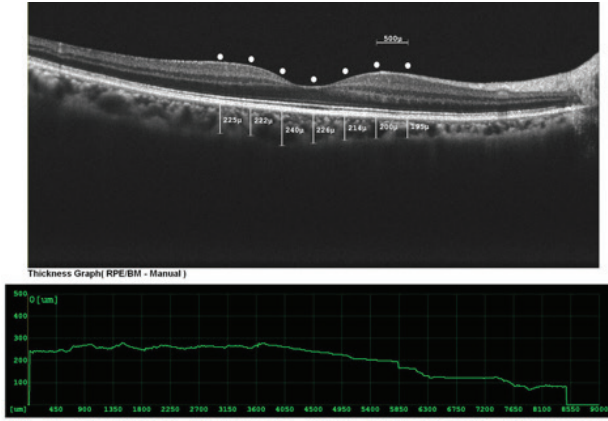
Figure 1:
Choroidal thickness measurements in IBD.

Results

Characteristic of the IBD and study groups were shown in Table 1. There were no statistical difference between groups according to the age, sex, visual aquity and other parameters. In the study group 18 patients were Crohn's disease and 32 patients were ulserative colitis. Mean duration of the IBD was 3.9 ±1.5 years. Foveal macular thickness was 258.1 ± 14.2 µm in study group and 262.7 ± 20.9 µm in the control group. There was not significant difference between groups(P=0,19). Subfoveal, temporal 500 µm, 1000 µm, and 1500 µm CT measurements were respectively statistically significant in the study group(p<0.001). Mean CT was 289.8 ± 25.6 µm in study group and 273.9 ± 33.2 µm in the control group. There was significant difference between goups(P=0.008)

Correlations between mean CT and clinical or laboratory parameters were evaluated with Pearson's correlation coefficient. There was no correlation between mean CT and erythrocyte sedimentation rate, C-reactive protein level and other clinical parameters (P> 0,05).

Table 1	Characteristics and laboratory findings of the IBD patients and control groups		
Characteristics and Laboratory Findings	**Study group** n= 50	**Control group** n= 50	**P value**
Age, years	25.5 ± 3.5	24.1 ± 2.6	0.07*
Males, Females	38/12	35/15	0.10*
BCVA, logMAR	-0.007 ± 0.01	-0.008 ± 0.03	0.72*
IOP, mmHg	15.9 ± 2.5	15.1 ± 2.6	0.12**
Axial length, mm	22.7 ± 0.9	22.6 ± 0.7	0.40**
Spherical equivalent, dioptres	-0.48 ± 0.9	-0.25 ± 0.6	0.09*
BMI	24.5 ± 1.7	24.1 ± 1.6	0.69**
MBP, mmHg	89.2 ± 3.2	87.3 ± 4.1	0.53**
Crohn's disease/Ulcerative colitis,n	18/32	N/A	-
Disease duration, years	3.9 ± 1.5	N/A	-
Serum C-reactive protein level, mg/L	13.5 ± 6.9	-	-
Eryhtrocyte sedimentation rate, mm/hr	18.9 ± 5.9	-	-

BCVA = best- corrected visual acuity**, logMAR =** logarithm of the minimum angle of resolution,
IOP= intraocular pressure, **BMI =** Body mass index**, MBP =** mean blood pressure, **N/A =** not applicable
*Mann-Whitney U test, **Independent samples t-test,

Table 2	Correlation of the choroidal and macular thickness between groups

Choroidal and macular thickness measurement location	Study group n= 50	Control group n= 50	P value
Subfoveal, µm	298.9 ± 26.9	279.1 ± 34.3	**P=0,02**
Temporal, 500 µm	300.8 ± 28.3	279.5 ± 35.2	**p<0.001**
Temporal, 1,000 µm	304.7 ± 29.3	277.9 ± 34.1	**p<0.001**
Temporal, 1,500 µm	302.3 ± 31.1	272.1 ± 33.2	**p<0.001**
Nasal, 500 µm	289.6 ± 27.7	277.1 ± 34.7	P=0,65
Nasal, 1,000 µm	273.9 ± 32.1	270.9 ± 34.6	p=0.75
Nasal, 1,500 µm	258.5 ± 35.5	260.7 ± 35.5	p=0.20
Mean CT, µm	289.8 ± 25.6	273.9 ± 33.2	**P=0.008**
Foveal macular Thickness, µm	258.1 ± 14.2	262.7 ± 20.9	p=0.19

* Independent samples t-test.

Discussion

Inflammatory bowel diseases are a group of disorders which effect the multiple organs including the ocular tissues. For that reason it is very important to understand the ocular manifestations of the IBD. It may be helpful for preventing the visual morbidity. Pathophysiology which leads the ocular complications of the IBD is still unclear. In this study we aimed to evaluate the choroidal and macular thickness changes compared with the healthy controls. Posterior portion of the uveal tract continues with choroidal vascular structure in the globe. It is divided in to the three layers: Haller layer that includes large vessels, Sattler layer with medium vessels with choroidal stroma and the innermost layer of choriocapillaris(9). It provides up to 85% of the ocular blood flow and supply the outer two thirds of the retina(9).

Inflammation of the eye effects the choroidal vascular structure. Some authors reported reported many ocular inflammatory diseases that effect the choroidal tissue. Voght-Koyonagi Harada (VKH), sarcoidosis, Behçet's disease, familial mediterranean fewer(FMF), IBD and posterior scleritis have been reported beforely(6-8, 10, 11). Kim et al. enounced that increased blood flow, vascular resistance, and exudates may effect the choroidal thickening. They found the increased CT during the active phase of Behcet's posterior uveitis. Also they showed the degree of decrease in CT was significantly correlated with improvement in vascular leakage(12). With a similar mechanism, IBD may also affect the choroidal vascular system with inflammatory mediators.

Episcleritis and uveitis are the most common ocular findings in IBD. Low-grade recurrent acute anterior uveitis is common in IBD. In our study there was no uveitis in study group. Posterior uveitis with chorioretinitis have been reported in a study(13). But subclinical inflammation in uveal tissue may have a role in increased mean CT in IBD group. Cloche at al. reported that low rate ocular inflammation may have a role ocular symptoms of IBD in a large cohort study(14). Önal at al. declared a similar study which CT was increased in IBD with ileal involment(8). Similarly we find out increased CT in both Crohn and UC patients in our study.

In conclusion SD-OCT is a new and current method for the visualization of the CT. Inflammation of the any part of the body can effect the choroidal vascular structure. The exact influence of IBD on choroid is still unclear. Further studies will reveal the pathogenesis of these disorders in the future.

References

1. Bernstein CN. Extraintestinal manifestations of inflammatory bowel disease. Current gastroenterology reports. 2001;3(6):477-83.

2. Goudet P, Dozois RR, Kelly KA, Ilstrup DM, Phillips SF. Characteristics and evolution of extraintestinal manifestations associated with ulcerative colitis after proctocolectomy. Digestive surgery. 2001;18(1):51-5.

3. Mady R, Grover W, Butrus S. Ocular Complications of Inflammatory Bowel Disease. The Scientific World Journal. 2015;2015:1-5.

4. Troncoso LL, Biancardi AL, de Moraes HV, Jr., Zaltman C. Ophthalmic manifestations in patients with inflammatory bowel disease: A review. World J Gastroenterol. 2017;23(32):5836-48.

5. Felekis T, Katsanos K, Kitsanou M, Trakos N, Theopistos V, Christodoulou D, et al. Spectrum and frequency of ophthalmologic manifestations in patients with inflammatory bowel disease: a prospective single-center study. Inflamm Bowel Dis. 2009;15(1):29-34.

6. Ishikawa S, Taguchi M, Muraoka T, Sakurai Y, Kanda T, Takeuchi M. Changes in subfoveal choroidal thickness associated with uveitis activity in patients with Behcet's disease. The British journal of ophthalmology. 2014;98(11):1508-13.

7. Fong AH, Li KK, Wong D. Choroidal evaluation using enhanced depth imaging spectral-domain optical coherence tomography in Vogt-Koyanagi-Harada disease. Retina (Philadelphia, Pa). 2011;31(3):502-9.

8. Onal IK, Yuksel E, Bayrakceken K, Demir MM, Karaca EE, Ibis M, et al. Measurement and clinical implications of choroidal thickness in patients with inflammatory bowel disease. Arquivos brasileiros de oftalmologia. 2015;78(5):278-82.

9. Nickla DL, Wallman J. The multifunctional choroid. Progress in Retinal and Eye Research. 2010;29(2):144-68.

10. Baltmr A, Lightman S, Tomkins-Netzer O. Examining the choroid in ocular inflammation: a focus on enhanced depth imaging. Journal of ophthalmology. 2014;2014:459136.

11. Gundogan FC, Akay F, Uzun S, Ozge G, Toyran S, Genç H. Choroidal thickness changes in the acute attack period in patients with familial Mediterranean fever. Ophthalmologica Journal international d'ophtalmologie International journal of ophthalmology Zeitschrift fur Augenheilkunde. 2015;235(2):72-7.

12. Kim M, Kim H, Kwon HJ, Kim SS, Koh HJ, Lee SC. Choroidal thickness in Behcet's uveitis: an enhanced depth imaging-optical coherence tomography and its association with angiographic changes. Investigative ophthalmology & visual science. 2013;54(9):6033-9.

13. Banares A, Jover JA, Fernandez-Gutierrez B, Benitez del Castillo JM, Garcia J, Vargas E, et al. Patterns of uveitis as a guide in making rheumatologic and immunologic diagnoses. Arthritis and rheumatism. 1997;40(2):358-70.

14. Cloche V, Buisson A, Trechot F, Batta B, Locatelli A, Favel C, et al. Ocular symptoms are not predictive of ophthalmologic inflammation in inflammatory bowel disease. Dig Liver Dis. 2013;45(3):195-9.