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Assessment of Central Corneal Thickness, Intraocular Pressure and Retinal Nerve Fiber Layer Thickness at Women with Polycystic Ovary Syndrome

ABSTRACT

Objective: To compare intraocular pressure, central cornea thickness, anterior chamber depth, axial length and thickness of retina nerve fiber layer between women with polycystic ovary syndrome and healthy at the same age segment.

Methods: Between August 2015-January 2016, 46 women who have polycystic ovary syndrome and 53 healthy women have been included to the study. After a complete ophthalmologic examination, intraocular pressure, central cornea thickness, anterior chamber depth, axial length and retinal nerve fiber layer thickness were investigated. In the statistical analysis of the data, Independent Samples t test was utilized to compare the groups.

Results: While mean age was 23.4 ± 4.5 (16-35) in the group with polycystic ovary syndrome, average age level was found as 24.0 ± 6.1 (18-54) among the controls ($P=0.549$). Intraocular pressure values were measured and determined as 17.7 ± 2.6 mmHg in the group with polycystic ovary syndrome, while the values were 15.2 ± 2.4 mmHg in the controls ($P < 0.001$). Although it was 79.4 ± 10.2 μ m in the group with polycystic ovary syndrome, retinal nerve fiber layer thickness in the nasal quadrant was found to be 73.8 ± 10.9 μ m among the controls ($P < 0.001$).

Conclusion: We found that the increased levels seen in intraocular pressure and retinal nerve fiber layer thickness in the nasal quadrants of the patients with polycystic ovary syndrome were statistically significance. Hence, we recommend that the patients with polycystic ovary syndrome should be specially analyzed as to eye assessment.

Keywords: Anterior Chamber Depth, Axial Length, Central Corneal Thickness, Intraocular Pressure, Polycystic Ovary Syndrome, Retina Nerve Fiber Layer Thickness.

Polikistik Over Sendromlu Kadınlarda Santral Kornea Kalınlığı, Göz İçi Basıncı ve Retinal Sinir Lifi Tabakası Kalınlığının Değerlendirilmesi

ÖZET

Amaç: Aynı yaş segmentinde polikistik over sendromlu ve sağlıklı kadınlar arasındaki göz içi basıncı, santral kornea kalınlığı, ön kamara derinliği, aksiyel uzunluk ve retina sinir lifi tabakası kalınlığını karşılaştırmak.

Yöntem: Ağustos 2015-Ocak 2016 tarihleri arasında 46 polikistik over sendromlu ve 53 sağlıklı olmak üzere toplam 99 kadın çalışmaya dahil edildi. Tam bir oftalmolojik muayeneden sonra göziçi basıncı, santral kornea kalınlığı, ön kamara derinliği, aksiyel uzunluk ve retina sinir lifi tabakası kalınlığı ölçümleri yapıldı. Verilerin istatistiksel olarak değerlendirilmesinde grupların karşılaştırılması amacıyla Independent Samples t test kullanıldı.

Bulgular: Polikistik over sendromlu grupta yaş ortalaması 23.4 ± 4.5 (16-35) iken, kontrol grubunda 24.0 ± 6.1 (18.54) olarak bulundu ($p = 0.549$). Polikistik over sendromlu grupta ortalama göz içi basıncı değeri 17.7 ± 2.6 mmHg ve kontrol grubunda 15.2 ± 2.4 mmHg olarak bulundu ($P < 0.001$). Nazal kadrandaki retina sinir lifi kalınlığı polikistik over sendromlu grupta 79.4 ± 10.2 mikron iken kontrol grubunda 73.8 ± 10.9 mikrondu ($P < 0.001$).

Sonuç: Polikistik over sendromlu hastaların nazal kadrandaki retina sinir lifi tabakası kalınlığı ve göz içi basıncında görülen artmış düzeylerin istatistiksel olarak anlamlı olduğu bulundu. Bu nedenle, polikistik over sendromlu hastaların göz muayenesi açısından yakından değerlendirilmesini önermekteyiz.

Anahtar Kelimeler: Ön Kamara Derinliği, Aksiyel Uzunluk, Santral Kornea Kalınlığı, Göz İçi Basıncı, Polikistik Over Sendromu, Retina Sinir Lifi Tabakası Kalınlığı

INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most frequently seen endocrinologic disorder in women of reproductive age and affects 6-8% of women (1). The syndrome is clinically characterized by oligo-amenore and hyperandrogenism. The etiopathogenesis and diagnosis of PCOS described first by Stein and Leventhal in 1935 remains controversial despite 80-year time (2). Clinicians mostly use the 2003 Rotterdam criteria although other criteria related to the diagnosis of PCOS have been described (3). Under the 2003 Rotterdam criteria, PCOS is diagnosed with at least two of the following criteria: oligo- or anovulation, the clinical and/or biochemical findings of hyperandrogenism, and the screening of polycystic ovaries through ultrasound (US).

Although the despite effects of PCOS on metabolic, endocrinologic, reproductive and cardiovascular systems are well-established, there are limited data concerning the effects on vision system (4-8).

PCOS was reported to lead to many alterations in the steroidogenesis of ovary/adrenal gland function (9). The existence of hormone receptors has recently been revealed in eye tissues, such as conjunctiva, cornea, meibomian glands, choroid, retina and lenses (10-11). The existence of these receptors suggests that PCOS may also lead to changes in ocular tissues.

In the present study, it was aimed that the effects of hyperandrogenism seen in women with PCOS on eye-related structures, such as central cornea thickness (CCT), anterior chamber depth (ACD), axial length (AL) and thickness of retina nerve fiber layer (RNFL) were compared with the values measured in healthy population at the same age segment.

MATERIAL AND METHODS

The study designed prospectively was performed after obtaining an approval from the Ethical Board of Medical School of Duzce University (registration number, 2015/161). Informed consent was also obtained from all participants. All procedures in the study were

performed in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Women admitted to the obstetrics and gynecology, and the ophthalmology departments of Medical School of Duzce University between August 2015-January 2016 were included and evaluated in the study. Right eyes of a total of 99 women, as 46 with PCOS and 53 healthy controls, were investigated. The diagnosis of PCOS was performed through a detailed gynecological examination and screening by an

obstetrician/gynecologist under the 2003 Rotterdam criteria for the diagnosis of PCOS. As a result, those with at least two of the following criteria including oligomenore-amenore and the clinical and/or biochemical findings of hyperandrogenism and polycystic ovaries assessed on US (existence of 12 or more follicles 2-9 mm in diameter in ovaries) were enrolled into the study. The control group was composed of healthy women inconsistent with the 2003 Rotterdam PCOS diagnostic criteria and with regular or normal menstrual cycle. Women in both groups with disorders, such as metabolic irregularity, pregnancy, taking psychiatric medication, addiction to smoking and alcohol, ophthalmologic disorders and traumas, and malignancy were excluded out of the criteria.

All patients were meticulously examined by a single ophthalmologist (KT). After performing refraction measurements, the best corrected visual acuity (BCVA) was tested in all cases through the Snellen chart. Intraocular pressure (IOP) was measured via the Goldman applanation tonometry (GAT) (Nikon, Japan). Biomicroscopic fundus examination after the dilatation with 1% cyclopentolate and following measurements of CCT, AL and ACD were conducted with the device of Echoscan US 500 (Nidek Co. Ltd, Aichi, Japan). For investigating the thickness of RNFL (superior, nasal, inferior, temporal and average) in detail, the optical coherence tomography (OCT) (Topcon 3D OCT-1000, Tokyo, Japan) was used. In the statistical analysis of the data, the Independent Samples t test was utilized in the comparison of groups. Statistical analyses were performed through SPSS v.22 package program, and the significance level was accepted as 0.05.

RESULTS

While mean age was 23.4 ± 4.5 (16-35) in the PCOS group, mean age level was found as 24.0 ± 6.1 (18-41) among the controls ($P=0.549$). The IOP values obtained via the GAT were measured as 17.7 ± 2.6 mmHg in the PCOS group, while the values were 15.2 ± 2.4 mmHg in the control group, and a statistically significant difference was observed between two groups ($P < 0.001$). The average central corneal thickness was 547.7 ± 45.4 μ m in the PCOS group and 544.0 ± 41.1 μ m in the control group. There was no statistically significant difference between them ($p = 0.67$). There was no significant difference between the two groups regarding axial length and anterior chamber depth in our study. Although it was 79.4 ± 10.2 μ m in the PCOS group, the thickness of RNFL in the nasal quadrant was found to be 73.8 ± 10.9 μ m among the controls, and the difference between the nasal quadrants of both groups was statistically significant ($P < 0.011$). No statistically significant difference was found between the other quadrant (Table 1).

Table 1. Mean values of best corrected visual acuity, intraocular pressure, central corneal thickness, axial length and anterior chamber depth, and of rNFL thickness measured in all quadrants measured in both groups.

Right Eye	Patients (n=46)	Controls (n=53)	P
BCVA (Snellen)	0.9 ± 0.0	1	0.323
IOP mmHg	17.7 ± 2.6	15.2 ± 2.4	<0.001
CCT µm	547.7 ± 45.4	544 ± 41.1	0.67
AL mm	22.7 ± 0.8	23.1 ± 1.3	0.082
ACD mm	3.3 ± 0.3	3.3 ± 0.4	0.811
RNFL (I) µm	119.8 ± 12.3	117.5 ± 12.9	0.378
RNFL (S) µm	114.0 ± 20.8	133.9 ± 138.2	0.336
RNFL (N) µm	79.4 ± 10.2	73.8 ± 10.9	0.011
RNFL (T) µm	68.2 ± 9.5	69 ± 8.9	0.678
RSLT (G) µm	95.8 ± 8.1	93.3 ± 5.9	0.085

BCVA: Best corrected visual acuity, IOP: Intraocular pressure, CCT: Central corneal thickness, AL: Axial length, ACD: Anterior chamber depth, RNFL: Retina nerve fiber layer, RNFL (I): Retina nerve fiber layer inferior, RNFL (S): Retina nerve fiber layer superior, RNFL (N): Retina nerve fiber layer nasal, RNFL (T): Retina nerve fiber layer temporal, RNFL (G): Retina nerve fiber layer global

DISCUSSION

Although the number of the studies investigating the association between PCOS and IOP is limited, it was detected in a study that IOP also increased due to the elevation seen in serum testosterone level (12). Enzyme estradiol aromatase mediates many actions of testosterone by converting it to estradiol after binding to the estrogen receptors (13), but testosterone is also convertible to dihydrotestosterone (DHT), its potent metabolite, by the enzyme five α reductase and function directly on androgen receptors (14). Hence, testosterone may function like estradiol to increase nitric oxide (NO) synthase in some regions of the body where aromatase is available, whereas it would decrease NO synthase in other regions where five α reductase is available. Because of that androgen receptor protein and five α reductase mRNAs exist in a variety of ocular tissues (15,16), Taking reductase of androgen receptor protein and five α into account, mRNAs exist in many parts of ocular tissues. It might be speculated that testosterone, by acting through androgen receptors may negatively regulate the NO synthase activity in the outflow pathway and ciliary muscle, and thus may induce an increase in IOP. Also, while the thickness of RNFL in the nasal quadrant was found to be $79.41 \pm 10.28 \mu\text{m}$ in the PCOS group, it was found as $73.83 \pm 10.98 \mu\text{m}$ among the controls, and the difference between both groups was observed to be statistically significant ($P < 0.011$). We consider that such a difference could arise from neurotrophic effects of androgenic hormones increasing in those with PCOS. In RNFL of other retinal quadrants, however, no significant difference was observed. In a study performed by Acmaz et al., RNFL was reported to be significantly thicker in the nasal and global quadrants of patients with PCOS, compared with the controls (17). In the study performed by Demir et al., it was statistically showed that RNFL was significantly thicker in the nasal and

superotemporal quadrants of patients with PCOS than those of the controls (18). In another study, however, Ulas et al. demonstrated RNFL in the PCOS group was thinner in all quadrants, although the finding was statistically insignificant, and suggested that the insignificance could have been due to circulatory disorder and subclinical cardiovascular disorder (19). PCOS is characterized by the overproduction of androgenic steroids and relatively higher amount of serum oestrogen levels. The presence of sexual steroid hormone receptors in several eye tissues may be effective on ocular physiology, functions and structures (20,21). For this reason, as different from other studies, we compared the results of ACD measurements between the PCOS and control groups, but the findings were not statistically significant.

No significant difference was found between both groups in terms of the mean values of CCT. Despite similar findings in some previous studies to those in our study (18,19). There are also studies indicating controversial results. In the study by Kebapcilar et al., CCT values of the patients with PCOS were found to be significantly thicker, compared to those of the controls. In the same study, it was also determined that insulin-like growth factor-1 (IGF-1) levels and homeostasis model assessment of insulin resistance values of the women with PCOS were significantly higher than those of the controls, and there was a positive correlation between CCT and IGF-1, and so testosterone levels were positively and independently associated with CCT in both left and right eyes (22).

One of the important limitations in our study is the small sample size of study participants. It is considered that the statistical significance rate of the findings obtained in our study may be different from that of other studies with larger spectrum. In addition, more comprehensive and long-term

studies are required to determine how PCOS will be effective on patients from different age segments.

In our study, the measurements of mean BCVA, CCT, AL, ACD and the thickness of RNFL in all other quadrants, except for the nasal quadrant, were found to be similar in both the PCOS and

control groups. IOP measurements assessed via the GAT were observed to be statistically significantly higher in the PCOS group, compared with the controls. Hence, we think that more extensive research is needed in terms of eye examination findings in patients with polycystic over syndrome.

REFERENCES

1. Azziz R, Woods KS, Reyna R, et al. The prevalence and features of the polycystic ovary syndrome in an unselected population. *J Clin Endocrinol Metab* 2004;89(6):2745-9.
2. Stein IF, Leventhal ML. Amenorrhea associated with bilateral polycystic ovaries. *Am J Obstet Gynecol* 1935;29(2):181-91.
3. Rotterdam ESHRE/ASRM-Sponsored PCOS consensus workshop group. Revised 2003 consensus on diagnostic criteria and long-term risks related to polycystic ovary syndrome (PCOS). *Hum Reprod* 2004;19(1): 41-7.
4. Dunaif A, Segal KR, Futterweit W, et al. Profound peripheral insulin resistance, independent of obesity, in polycystic ovary syndrome. *Diabetes* 1989;38(9):1165-74.
5. Apridonidze T, Essah PA, Iuorno MJ, et al. Prevalence and characteristics of the metabolic syndrome in women with polycystic ovary syndrome. *J Clin Endocrinol Metab* 2005;90(4):1929-35.
6. Ehrmann DA, Barnes RB, Rosenfield RL, et al. Prevalence of impaired glucose tolerance and diabetes in women with polycystic ovary syndrome. *Diabetes Care* 1999;22(1):141-6.
7. Conway GS, Agrawal R, Betteridge DJ, et al. Risk factors for coronary artery disease in lean and obese women with the polycystic ovary syndrome. *Clin Endocrinol (Oxf)* 1992;37(2):19-25.
8. Brent H, Johnstone E, Dorais J, et al. Female infertility, infertility-associated diagnoses, and comorbidities: a review. *J Assist Reprod Genet* 2017;34(2):167-77.
9. Gilling-Smith C, Willis DS, Beard RW, et al. Hypersecretion of androstenedione by isolated thecal cells from polycystic ovaries. *J Clin Endocrinol Metab* 1994;79(4):1158-65.
10. Fuchsjaeger-Mayrl G, Nepp J, Schneeberger C, et al. Identification of estrogen and progesterone receptor mRNA expression in the conjunctiva of premenopausal women. *Invest Ophthalmol Vis Sci* 2002;43(9):2841-4.
11. Esmali B, Harvey JT, Hewlett B. Immunohistochemical evidence for estrogen receptors in meibomian glands. *Ophthalmology* 2000;107(1):180-4.
12. Toker E, Yenice Ö, Temel A. Influence of Serum Levels of Sex Hormones on Intraocular Pressure in Menopausal Women. *J Glaucoma* 2003;12(5):436-40.
13. Balthazart J, Foidart A. Brain aromatase and the control of male sexual behaviour. *J Steroid Biochem Mol Biol.* 1993;44:521-540.
14. Celotti F, Melcagni RC, Martini L. The 5 alpha-reductase in the brain: molecular aspects and relation to brain function. *Front Neuroendocrinol.* 1992;13:163-215.
15. Wickham LA, Jianping G, Toda I, et al. Identification androgen, estrogen and progesterone receptor mRNAs in the eye. *Acta Ophthalmol Scand.* 2000;78:146-153.
16. Rocha EM, Wickham LA, da Silveira LA, et al. Identification of androgen receptor protein and 5alpha-reductase mRNA in human ocular tissues. *Br J Ophthalmol.* 2000;84:76-84.
17. Açmaz G, Atas M, Gülhan A, et al. Evaluation of the Macula, Retinal Nerve Fiber Layer, and Choroid Thickness in Women With Polycystic Ovary Syndrome Using Spectral-Domain Optical Coherence Tomography. *Reprod Sci.* 2014;21(8):1044-9.
18. Demir M, Güven D, Koç A, et al. Retinal Nerve Fiber Layer Thickness in Women with Polycystic Ovary Syndrome. *J Ophthalmol* 2013; 2013: 752186.
19. Ulaş F, Doğan Ü, Duran B, et al. Evaluation of Polycystic Ovary Syndrome Patients Using Optical Coherence Tomography Türkiye Klinikleri *J Ophthalmol* 2015;24(2):76-83.
20. Siesky BA, Harris A, Patel C, et al. Comparison of visual function and ocular hemodynamics between pre- and post-menopausal women. *Eur J Ophthalmol* 2008;18(2):320-3.
21. Lang Y, Lang N, Ben-Ami M, et al. The effects of hormone replacement therapy (HRT) on the human eye. *Harefuah* 2002;141(3):287-91.
22. Kebapçılar AG, Tatar MG, Ipekci, et al. Cornea in PCOS patients as a possible target of IGF-1 action and insülin resistance. *Archives of Gynecology and Obstetrics* 2014;290(6):1255-63.