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Comparative analysis of ocular findings between surgical and natural menopause patients: A cross-sectional study

Rapid effect of surgical menopause on eye health

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Abstract

Aim: Menopause can play a role in changing eye findings. This study sought to examine early postsurgical menopause patients in comparison with natural menopause patients and premenopausal patients in terms of ocular findings.

Material and Methods: This cross-sectional study included data from 108 women (48 surgical, 30 natural menopausal and 30 perimenopausal women) attending the Gynaecology and Ophthalmology clinics. Data included age, women blood level of hormone, and eye findings at presentation.

Results: Women in surgical menopause differed in mean increase in bilateral intraocular pressure compared to women in natural menopause and perimenopause. Women in natural menopause had higher mean scores for bilateral intraocular pressure compared with women in perimenopause. Women in natural menopause had increased mean bilateral eye macular thickness compared to women in surgical menopause and perimenopause. Women in surgical menopause had significantly higher mean right and left eye macular thickness than women in perimenopause.

Bilateral eye central corneal thickness scores were significantly higher surgical menopause and natural menopause women than perimenopause women. Scores for bilateral eye grade were similar across the groups. Both surgical menopause and natural menopause were in significant associations with the intraocular pressure, macular thickness, and central corneal thickness of the right and left eye.

Discussion: Although there are no clear data on menopause and ocular symptoms in published studies, this study shows that menopause has significant adverse effects on intraocular pressure and macular thickness when pre-menopausal women are compared with menopausal women.

Keywords

Cornea, Glaucoma, Macular Thickness, Surgical Menopause

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This study was approved by the Ethics Committee of Batman Training and Research Hospital (Date:2020-07-20, No:2020/250)

Introduction

Sex hormones play an essential role in the development and function of the human cornea. The cornea is a gender-dependent and hormone-responsive tissue that expresses sex hormone receptors in at least three of the five corneal layers, including the corneal epithelium, stroma, and endothelium. The tissues that comprise the anterior segment, including the cornea, also express enzymes capable of endogenous sex hormone production. In addition to endogenous expression, the ocular tear film overlying the corneal surface allows hormones and other signalling molecules to reach the cornea by means of diffusion. Sex hormones produced or released from intraocular sources, including the retina and vitreous, may also access the cornea through direct diffusion or by means of the internal ocular circulation of aqueous fluid [1, 2]. The balance of sex hormones varies across a woman's life and has downstream effects on central corneal thickness (CCT), intraocular pressure (IOP), and the ocular tear film. The mechanisms by which sex hormones govern these corneal features and related physiologic processes remain under active investigation, but are likely related to a combination of direct effects on the tissues themselves, as well as indirect effects through their actions on neuroendocrine, immune, and vascular regulation [1, 2].

As far as we know, there have been no data on postsurgical menopause association with eye findings. This study sought to examine early postsurgical menopause patients in comparison with natural menopause patients and premenopausal patients in terms of ocular findings (macular thickness, corneal thickness, and intraocular pressure).

Material and Methods

Study design and participants

This cross-sectional study included data on 108 (48 for Surgical, 30 for natural menopause, and 30 for perimenopause women) consecutive women who had presented between January 1, 2020 and December 1, 2021 to the Department of Gynaecology and Ophthalmology clinics of the tertiary center of Turkey. A control group of 30 women, who presented to during same period was also included. Data included age, women blood level of hormone (FSH, LH, Estradiol), and eye findings (IOP, macular thickness, CCT) at presentation.

Inclusion criteria were age 35-57 years with healthy women for three groups. Those with the following conditions were excluded: Comorbid conditions (e.g., diabetes mellitus, cardiovascular disease, hypertension, obesity, thyroid disorders, kidney diseases, respiratory conditions, migraines, epilepsy, chronic medication use, cancer), history of a ocular or refractive surgery/trauma, dry eye, contact lens usage, topical medication usage, lenticular-corneal disorders, congenital or acquired eye diseases (strabismus, aphakia, and amblyopia), and receiving hormone replacement therapy (HRT).

Surgical Menopause Group with total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH-BSO) for benign indications before performing 3-6 months. Notably, these patients did not have preoperative menopausal symptoms but subsequently exhibited menopausal symptoms.

Natural Menopause Group

This group included patients who have transitioned into menopause and exhibit menopausal symptoms.

Perimenopause Group (Control)

Patients in this category did not have yet reached menopause but are displaying perimenopausal symptoms.

Hormone panel

Hormone panel values within the range of follicle stimulating hormone (FSH) 20-40 mIU/mL, Luteinising Hormone (LH) 20-40 mIU/mL, and Estradiol (E2) 20-40 mIU/mL (Venous blood samples taken in the morning on an empty stomach between 09.00 and 10.00 hours)

Ophthalmic Examination

Comprehensive eye examinations were conducted on the female participants, covering the following measurements: Visual Acuity, Intraocular Pressure, Corneal Thickness, Macular Thickness, Lens Opacity (Figure 1).

Eye Examination

The eye examination was performed by the same ophthalmologist. Each participant was performed a comprehensive ophthalmologic assessment, including auto-refraction (average of three values), intraocular pressure (IOP) in millimeters of mercury before cycloplegic

refraction (mmHg, Goldmann applanation tonometer), uncorrected visual acuity with cycloplegic refraction (with 0.5% cyclopentolate HCl) and slit-lamp biomicroscopy to check for corneal scarring or lenticular opacities (Figure 1).

Lens Opacity Status Evaluation

Lens opacity status was evaluated according to the Lens Opacities Classification System (LOCS) III grading guideline (12). Grade 1: the nucleus of the nuclear sclerosis (NS) is clearer than the anterior/posterior sections. Grade 2 : the nucleus of the NS is equal opacity throughout. Garde 3:The nucleus of the NS is denser than the anterior/posterior sections. Grade 4(cataract): The nucleus of the NS is completely opaque/brown.

Central Corneal Thickness Measurement (CCT)

Central corneal thickness measurement was done using the Sirius topography system (Costruzione Strumenti Oftalmici, Florence, Italy). The system includes a monochromatic 360°-rotating Scheimpflug camera and 22-ring Placido disc technology. This involved taking 25 corneal and anterior chamber radial sections, calculating tangential and axial curvature of the corneal surfaces, mapping corneal global refractive power and pachymetry, and conducting wave-front analysis. Measurements of the anterior corneal surface were obtained by combining Placido and Scheimpflug images, while central corneal thickness was measured using the Scheimpflug topography device.

Central Macular Thickness Measurement

For central macular thickness measurement, the Optovue RTVue spectral-domain OCT device (RT100 software version 6.3, Optovue Inc., Fremont, CA, USA) was used. All measurements were performed by an experienced researcher skilled in performing OCT. Reliable OCT image acquisition criteria included artifact-free, properly centered images with distinct retinal layers and a signal strength index greater than 50.

Data processing and analysis

For data collection, a structured format was used including all relevant clinical information. Data were processed using the Statistical Package for Social Sciences (SPSS) version 21 (IBM

Corp., Armonk, N.Y.; USA). Quantitative data were expressed as means, standard deviation (SD), median, minimum, and maximum, and qualitative data as frequencies and percentages. Multigroup comparisons, and numerical variables were compared using the one-way ANOVA test. Regression analysis was performed to determine the risk for eye findings in relation with menopause. $p < 0.05$ value is accepted as statistically significant. All variables were expressed with 95% confidence intervals (CI).

Ethical Approval

The study was approved by the Ethics Committee of Batman Training and Research Hospital (Date:2020-07-20, No:2020/250).

Results

During the study period, a total of 430 women with menopausal and perimenopausal presented to the gynaecology and eye outpatient clinics. As a result, 155 women were asked to participate in the study and 108 women gave consent and completed the physical examination.

Of 108 participating women, 30 had perimenopause, 30 had surgical menopause, and 48 had natural menopause. The mean age was 47.8±4.8 years (range 35-57). The mean FSH level was 36.5±0.7 mIU/ml (range 35–38 mIU/ml). The characteristics of the participants are summarised in Table 1.

Comparisons of the three groups with respect to age, hormone levels, intraocular pressure, macular thickness, and central corneal thickness measurements are presented in Table 2. Surgical menopause significantly differed from women in natural menopause and perimenopause with respect to increased mean levels of right and left eye IOP. Similarly, the natural menopause had significantly higher mean scores than the perimenopause women for right and left eye IOP. The natural menopause women had significantly increased mean levels of right and left eye macular thickness as compared with the surgical menopause and perimenopause women. Similarly, the surgical menopause had significantly higher mean scores than the perimenopause women for right and left eye macular thickness. Right and left eye CCT scores were significantly higher in surgical menopause and natural menopause women than perimenopause women($p<0.05$). Scores for right and left eye grades were similar across the groups ($p>0.05$) (Table 2). Results of the regression analysis are summarised in Table 3. Both surgical menopause and natural menopause were

Table 1. Clinical characteristics

Parameters	Mean± SD
Age	47.8±4.8
Right ocular hypertention	12.1±2.34
Left ocular hypertention	12.16±2.49
Right eye grade	1.35±0.48
Left eye grade	1.37±0.48
Right eye macular thickness	233.85±30.23
Left eye macular thickness	238.79±22.39
Right eye CCT	527.92±25.58
Left eye CCT	527.2±24.26
FSH mIU/ml	36.5±0.7
LH mIU/ml	34.1±1.3
E_2 pg/ml	25.8±0.9

Table 2. Comparisons across groups with age, hormone levels, intraocular pressure, macular thickness, and central corneal thickness measurements

Parameters	Control group	Naturel menopouse	Surgical menopause	P
Mean	mean±SD	mean±SD	mean±SD	
Age	42.1±2.8	50.8±4.0	46.8±3	P: 0.0001
Right eye IOP	9.9±0.9	12.1±1.6	13.6±2.9	P: 0.0001
Left eye IOP	9.7±0.9	12.3±2.0	13.6±2.8	P: 0.0001
Right eye grade	1.2±0.4	1.4±0.5	1.4±0.5	P: 0.301
Left eye grade	1.3±0.4	1.3±0.5	1.5±0.5	P: 0.069
Right eye macular thickness	205.4±44.7	246.8±16.2	232±22.2	P: 0.0001
Left eye macular thickness	219.7±11.7	250±21.8	233.7±18.2	P: 0.0001
Right eye CCT	504.9±15.7	535.7±22.6	530.9±26.9	*P1: 0.0001 *P2: 0.0001 *P3: NS
Left eye CCT	505.7±19.3	533.6±20.5	531.3±25.3	P1: 0.0001 P2: 0.0001 P3: NS
FSH	37.1±0.2	36.3±0.7	36.4±0.9	P1: 0.0001 P2: 0.0001 P3: NS
LH	34.0±1.0	34.5±1.1	33.7±1.8	P3: 0.045 P1: NS P2: NS
E2	26.6±0.9	25.7±0.7	25.6±1.1	P1: 0.0001 P2: 0.0001 P3: NS

*P1:control- nature menopause, p2:control- surgery menopause, p3: nature menopause- surgery menopause

Table 3. Associations of natural menopause and surgical menopause with age, intraocular pressure, macular thickness, and central corneal thickness measurements

Parameters	Natural Menopause	Surgical Menopause	P value
Age	2.29 (1.64-3.21)	1.72 (1.26-2.35)	0.0001
Right eye IOP	3.25 (1.82-5.83)	4.45 (2.40-8.26)	0.0001
Left eye IOP	3.01 (1.69-5.53)	3.88 (2.10-7.18)	0.0001
Right eye grade	2.4 (0.69-8.31)	2.67 (0.71-9.95)	p1=0.167, p2=0.144
Left eye grade	1.36 (0.42-4.45)	3.43 (0.99-11.85)	p1=0.607, p2=0.052
Right eye Macular thickness	1.13 (1.07-1.19)	1.08 (1.03-1.13)	p1=0.0001, p2=0.002
Left eye Macular thickness	1.16 (1.09-1.23)	1.09 (1.03-1.16)	p1=0.0001, p2=0.003
Right eye CCT	1.07 (1.03-1.10)	1.06 (1.02-1.09)	0.0001
Left eye CCT	1.07 (1.03-1.10)	1.06 (1.02-1.1)	0.0001

*Reference Group: perimenopause

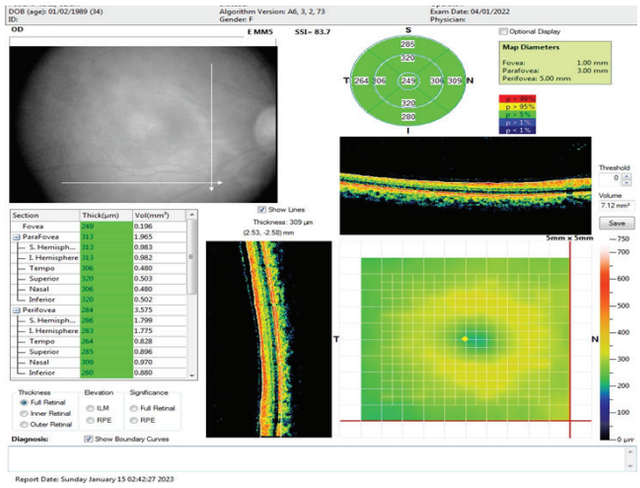

Figure 1. Macular thickness measurement

significantly associated with the IOP, macular thickness, and CCT of the right and left eye (p<0.05) (Table 3).

Discussion

The rates of oophorectomy in women who have undergone hysterectomy have decreased over time, but they remain high. While discussing menopause, healthcare providers typically discuss hot flashes, cardiovascular problems, sleep disturbances, and sexual health issues in detail with patients [3, 4]. During natural menopause, there is a gradual decline in ovarian estrogen production, while serum testosterone levels remain relatively stable [4]. In surgical menopause, however, ovarian hormone production ceases abruptly. However, the effects of menopause on the eye are not often discussed in clinical practice. Additionally, there is limited information about the effects of surgical menopause, which is a more rapid transition than natural menopause.

In present study, we evaluated intraocular pressure, macular thickness, and central corneal thickness measurements of natural menopause and surgical menopause women in comparison with perimenopausal women. Our findings were that bilateral eyes IOP and CCT were significantly higher in natural menopause and surgical menopause women.

Studies on the impact of menopause have mainly compared eye findings among women with and without menopause To our knowledge, premenopause and natural-surgery menopause comparisons among the same sample have not been reported. The current comparative study represents the first to provide insight into the eye findings of natural-surgery menopause.

There have been discrepant reports concerning the association between menopause and eye findings. Birgul et al. no association was found between menopause and eye findings such as bilateral eye horizontal keratometry, eye vertical keratometry, eye axial, and eye central corneal thickness [5]. In another study menopause was found a significant association with decreased CCT of both eyes, but no association with intraocular pressure [6]. Other studies found similar results. Keskin et al found CCT differences between women in the premenopausal and postmenopausal period and found significantly decreased CCT in postmenopausal women [7]. Sharma et al. compared the CCT in post-menopausal women compared with the women in the reproductive age group and showed that postmenopausal women have significantly thinner CCT when comparing women in the reproductive age [8].

In a study of animals, sudden hormone reduction was achieved by surgical menopause, and menopause itself was found to be a risk factor for glaucoma. The main factor thought to be responsible for the change in intraocular pressure (IOP) is the change in aqueous humor flow [9]. In a comparison between age-matched women, between menopausal and premenopausal women, 1-3 mmHg higher levels are observed in menopausal women [10].

The Rotterdam study is a population-based study that looked at the association between age at menopause and glaucoma in women over the age of 55. The study found that women who went through menopause before the age of 45 had a 2.6-fold increased risk of glaucoma than women who went through menopause after the age of 50 [10, 11]. Similar to the Rotterdam study and the Blue Mountain Eye Study reported that a shorter lifetime exposure to endogenous estrogen increases the risk of developing glaucoma [12]. The findings of two population-based studies suggest that estrogen may play a protective role against glaucoma. In a study by Vajaranant and colleagues, women who underwent bilateral oophorectomy before age 43 had an increased risk of developing glaucoma, but estrogen treatment did not appear to reduce this risk [13].

Estrogens' antioxidant and anti-inflammatory properties may help prevent the development of age-related macular degeneration (AMD)(14). In addition, In the retinal environment, estrogen can have a down-regulating effect on the genetic expression of YKL-40, a known inflammatory marker that influences angiogenesis [15].

A study by Snow et al. found that women with age-related macular degeneration who had used postmenopausal estrogen therapy in the past had significantly lower odds of advanced AMD than nonusers [16]. This finding is consistent with the results of a study by Feskanich et al. which showed that women receiving postmenopausal hormone therapy (HRT) had a lower risk of neovascular AMD. These findings suggest that estrogen may play a role in protecting against AMD [17]. Some tissue factors can also alter macular thickness through the oxidative stress pathway [18]. Estrogen acts through the ESR1 receptor in

the retina [19]. These hormones regulate smooth muscle tone, decrease vascular resistance, and increase endothelial-based nitric oxide synthase (NOS3) activity [20], thereby reducing vascular resistance in large ocular vessels, playing a protective role in eye health, and regulating blood flow in the retina and choroid.

In the present study, the findings were also at the expense of the natural menopause and surgical menopause women with decreased right and left eye macular thickness. It is not surprising that menopause would be associated with decreased eye macular thickness. This is because the expression of estrogen and progesterone receptors in the eye is responsible for their ocular effects [21].

Strengths and Limitation

The limitations of the study are that it was relatively small, with only 108 participants, and it was conducted over a relatively short period, 3-6 months. This may limit the power of the study to detect significant differences between groups and to capture all potential changes in ocular health associated with surgical menopause. Additionally, the study did not include pre-surgical measurements, which makes it difficult to determine whether the observed differences between groups were caused by surgical menopause or by other factors.

Conclusion

Our findings suggest that menopause women experience considerable eye IOP and macular thickness adverse effects as compared with their perimenopause counterparts. More studies are needed to address the eye findings issues of menopause women, particularly surgical menopause.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or compareable ethical standards.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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