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Does HRT change intraocular pressure in postmenopausal women?

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ABSTRACT

We aimed to investigate the changes of intraocular pressure in menopause patients with the use of hormone replacement therapy (HRT).
Totally 137 postmenopausal women were evaluated in the study. 61 of them were under the treatment of HRT due to the menopausal symptoms. 76 women did not receive treatment. Intraocular pressure (IOP) was measured with Goldmann tonometer both groups.
In the HRT treatment group (study group), mean values of IOP for 2 eyes in the first visits was 15.4±1.7 mmHg and 13.9 ± 1.4 mmHg after 6 months use of HRT, respectively ($p<0.05$). In the non-HRT group (control group) mean values of IOP for 2 eyes in the first visits was 14.4 ± 1.4 mmHg and 14.3 ± 1.4 mmHg after six months, respectively ($p>0.05$).
HRT use and regular measurement of IOP regularly seems to prevents to reduce the risk of glaucoma in these patients, unless there are strong evidence that glaucoma does not occur in women on HRT.

Key Words: Intraocular pressure, menopause, hormone replacement therapy, glaucoma, estrogen and progesterone

Introduction

Glaucoma is an important cause of blindness in the advanced age population. Risk factors for glaucoma consist of high intraocular pressure (IOP), advanced age, positive family history, systemic diseases and trauma. Optic nerve damage and glaucoma disease can be prevented by reducing IOP (1). The relationship between IOP and estrogen is known and has been reported previously in the literature (2). Estrogen and progesterone hormones decrease IOP by vasodilator influence. Additionally, estrogen receptors on retinal ganglion cells are available and oral estrogen intake has been shown to have a protective effect on retinal ganglion cells in rat models (3,4). In our study we aimed to investigate the changes of IOP in menopause patients with the use of hormone replacement therapy (HRT).

Material and Methods

Patients admitted to a tertiary hospital of southeast region of Turkey in 2015 were included in the study. The study was conducted in accordance with the principles in Declaration of Helsinki. Before starting study, ethics committee approval was obtained. All patients provided informed consent before enrollment in the study. The study was initiated with 150 patients. 13 patients were excluded from the study due to the systemic diseases. The presence of amenorrhea for 6 months and high serum levels of FSH (≥20 mIU/mL) has been recognized as menopause. Combined HRT (combine estrogen and progesterone therapy, 1 mg estradiol, 2 mg drospirenon) was given to patients with the indication of menopausal symptoms (Hot flushing, vaginal dryness, depressive mood, skin changes etc.). The study group was treated with HRT (n=61). HRT was not given to patients with no symptoms of menopause. Untreated group was considered as the control group. The control group is consisted of 76 patients. IOP of each group was measured at first admission, and again after 6 months. Whether there is a difference between the 2 measurements was investigated.

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Ophthalmoscopy was done to rule out any posterior segment disease. IOP was measured with the same Goldmann tonometer (Optilasa,S.L., Madrid, Spain). The device was calibrated prior to the study. Topical proparacaine 0.5% was administered into each eye of the subjects and fluorescein strip (Biotech, Gujarat, India) administered in inferior conjunctival sacs to measure the IOP of both eyes. The outcome measures were recorded. All measurements were performed in the morning between 8 to 10 am to avoid diurnal variation in IOP.

Statistical Analyses: The statistical package for the social sciences (SPSS) version 20.0 for Windows was used for all statistical analyses. The Shapiro-Wilk test was used to test distribution of normality. In the comparison of the groups we performed a non-parametric Wilcoxon test. A p value <0.05 was considered statistically significant. When we found a statistically significant difference, we performed a post-hoc analysis between all group pairs to determine the source of statistical significance.

Results

The mean age of the study group was 50.2 ± 3.4 years. The average age of the control group was 49.6 ± 2.8 years. The mean value of FSH was 21.8 ± 1.7 in the study group and 24. ± 2.9 in the control group. Descriptive statistics for each of the two groups is shown in Table 1.

In the study group (group using hormone replacement therapy), mean values of IOP for 2 eyes in the first visits was 15.4 ± 1.7 mmHg and 13.9 ± 1.4 mmHg after 6 months use of HRT, respectively ($p<0.05$). In the control group mean values of IOP for 2 eyes in the first visits was 14.4 ± 1.4 mmHg and 14.3 ± 1.4 mmHg after six months, respectively ($p>0.05$). Changes of 6 month follow-up IOP values in the 2 groups have been shown in Table 2 and 3.

Discussion

HRT seems to affect the ocular system and its outcomes are conflicting. Estrogen, progesterone and androgen receptors may have a role on the effects of HRT on the ocular system but it is unclear how these receptors are affected. It is well documented that estrogen has a neuroprotective effect on the optic nerve in clinical, epidemiological, and basic science studies. Estrogen loss in menopause may result with a damage in optic nerve through several mechanisms. First, the mechanical theory suggests that mechanical stress from increased IOP may damage the optic nerve (5). IOP may be regulated by estrogens which influence the aqueous production and outflow systems (6). The postmenopausal level of IOP is higher than premenopausal women of the same age, and there is a reduction of 1–4 mmHg in response to postmenopausal HRT in women with and without primary open angle glaucoma (POAG) (2,7,8). Second, the vascular theory suggests that optic nerve degeneration caused by decreased perfusion or vascular dysregulation (5,9,10).

Table 1. Clinical Features of the Groups

	N	Minimum	Maximum	Mean	Std. Deviation
Age (HRT treatment group)	61	45.00	56.00	50.24	3.46
FSH (HRT treatment group)	61	20.00	30.00	21.83	1.79
Age (Control group)	76	45.00	55.00	49.67	2.84
FSH (Control group)	76	20.00	28.00	24.01	2.90

Table 2. IOP Changes in the HRT Group

Study Group	N	Minimum	Maximum	Mean	Std. Deviation	p
IOP before HRT treatment	61	10.50	22.50	15.41	1.76	<0.005
IOP after HRT treatment	61	11.00	18.00	13.9344	1.47	<0.005

Table 3. IOP Changes in the Control Group

Control Group	N	Minimum	Maximum	Mean	Std. Deviation	p
IOP in First Visit	76	9.00	19.00	14.44	1.45	0.250
IOP 6 Months Later	76	12.00	20.00	14.35	1.40	0.250

Estradiol hormone (E2) modulates smooth muscle tone and vascular resistance. And also endothelial-based nitric oxide syntheses (eNOS3) activity enhanced by E2 (11,12). Additionally, animal models and clinical studies have shown that the perfusion of the optic nerve, retinal ganglion cells, and their supporting structures are increased by estradiol (13-15). Finally, estradiol has neuroprotective effect which appears to be mediated at least in part through estrogen receptors in the retinal ganglion cells in glaucoma animal models (4,13). These findings suggest that estradiol has optic nerve protective effect and that it prevents glaucoma.

The anti-glucocorticoid properties of progesterone may have role in the reduction of IOP. Endogen corticosteroids have ocular hypertensive effect and progesterone blocks this effect (16). In a previous study of Lang Y et al, HRT has been shown to reduce the intraocular pressure (17). It was shown that the use of HRT reduce both ophthalmic artery and central retinal artery vascular resistance (8). In a study with 263 participants done with Tint NL et al, the mean IOP was measured to be less in the HRT group. There is a 1.41 mmHg decline in the value of the IOP in HRT group ($p<0.001$) (3). In another study in which patients were followed up 6-months done by Coksuer and colleagues, 2 mg drospirenone + 1 mg estradiol treatment has been shown to reduce the mean IOP (18). Studies have been reported that HRT use in postmenopausal women alters IOP (19,20). Again in another study there is a decline in IOP by 12 months only estrogen treatment in postmenopausal women (in this study mean IOP value was 14.6 mmHg before treatment, and 12.6 mmHg after 12 months estrogen treatment). However, in this study, mean IOP has not changed in the group receiving combined hormone replacement therapy (estrogen plus progesterone) (21).

In this study, we aimed to show the effects of HRT treatment on IOP in postmenopausal women. We wanted to see 6 months effect of HRT regimens. We showed that 6 months use of HRT has a decreasing effect on IOP in postmenopausal population concordance as shown previously in the literature.

Primary open-angle glaucoma is an age-dependent disease which can be defined as aging of the optic nerve related with IOP (22). Identification of modifiable risk factors is important in preventing glaucoma. The most important preventable risk factor for glaucoma progression is to take control of high IOP (23). Therefore postmenopausal population of patients are at-risk groups for glaucoma regarding advanced age, so HRT use and regular measurement of IOP seems to prevent the development of glaucoma in these patients. Over all, these findings, along with results of other population-based studies suggest that HRT use may generally affect women's' risk for glaucoma. Although these findings emphasize the importance of changeable risk factors in the prevention of glaucoma, a long-term cohort study is necessary to confirm the hypothesis.

In conclusions, primary open-angle glaucoma is an age-dependent disease which can be defined as aging of the optic nerve related with IOP. Identification of modifiable risk factors is important in preventing glaucoma. The most important preventable risk factor for glaucoma progression is to take control of high IOP. Therefore postmenopausal population of patients are at-risk groups for glaucoma regarding advanced age so HRT use and regular measurement of IOP seems to prevent the development of glaucoma in these patients.

Conflict of interests: The authors report that no conflicts of interest.

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