The Effect of Postmenopausal Hormone Replacement Therapy on Lens Opacities and Intraocular Pressure

POSTMENAPOZAL HORMON TEDAVİSİNİN LENS OPASİTELERİ VE İNTRAOKÜLER BASINÇ ÜZERİNE ETKİLERİ

Aysel PELİT, MD,[a] Ebru TARIM, MD,[b] Aykut PELİT, MD,[c] Yonca AYDIN AKOVA, MD[d]

Departments of [a]Ophthalmology, [b]Obstetrics and Gynecology, Başkent University, Faculty of Medicine, Adana Teaching and Medical Research Center,
[c]Department of Biophysics, Çukurova University, Faculty of Medicine, ADANA
[d]Department of Ophthalmology, Başkent University, Faculty of Medicine, ANKARA

Abstract

Objective: The aim of this study was to determine whether different postmenopausal hormone replacement therapies (HRT) reduced age-related cataract and influenced intraocular pressure (IOP).

Material and Methods: One hundred forty eight women on HRT for at least 4 years were included in this prospective study. Group 1 (n= 34) was on 2 mg of 17 beta estradiol, group 2 (n= 41) was on 2 mg of 17-beta estradiol and 1 mg of norethisterone acetate, and group 3 (n= 35) took 2.5 mg of tibolone. The control group (n= 38) did not take HRT. We investigated the association between postmenopausal HRT, lens opacities and IOP in different groups. Lens status was evaluated through a dilated pupil by means of a standardized grading system. The IOP was measured by a single examiner with standard Goldmann applanation tonometry. The tonometric value was considered the mean of three consecutive measurements.

Results: The mean ages in the control group, group 1, group 2, and group 3, were 52.44 ± 5.89, 50.87 ± 3.53, 52.05 ± 4.60, and 51.05 ± 3.07, respectively. There were no significant differences between the groups regarding age (p= 0.143) and among the 3 groups regarding HRT years (p= 0.176). We did not observe any significant difference between the groups with respect to the frequency of nuclear opacity (p= 0.361), cortical opacity (p= 0.960), and posterior subcapsular opacity (p= 0.856). In addition, there were no significant differences when we compared the IOP findings between the groups (p= 0.847).

Conclusion: These findings suggest that HRT for 4 years is not protective against lens opacity, and does not modify IOP.

Key Words: Cataract; hormone replacement therapy; menopause; intraocular pressure

Özet

Amaç: Bu çalışmada farklı postmenopozal hormon replasman tedavilerinin (HRT) yaşa bağlı katarakt ve göz içi basıncı (GİB) üzerine etkileri araştırılmıştır.

Gereç ve Yöntemler: En az 4 yıl boyunca HRT tedavisi alan 148 bayan hasta bu prospektif çalışmada değerlendirildi. Grup 1 (n= 34)'deki olgular 2 mg beta estradiol, grup 2 (n= 41)'deki olgular 2 mg 17-beta estradiol ve 1 mg noretisteron asetat ve grup 3 (n= 35)'teki olgular 2.5 mg tibilon tedavisi alan olgulardı. Kontrol grubu (n= 38) HRT almayan grubu oluşturdu. Farklı gruplarda postmenopozal HRT, lens opasiteleri ve GİB arasındaki ilişki araştırıldı. Lens dilate pupilden standardize edilen derecelendirme sistemi kullanılarak değerlendirildi. GİB bir klinisyen tarafından Goldmann aplanasyon tonometresi ile ölçüldü. Üç ölçümün ortalaması tonometrik değer olarak alındı.

Bulgular: Kontrol grubu, grup 1, grup 2, grup 3'ün yaş ortalamaları sırası ile 52.44 ± 5.89, 50.87 ± 3.53, 52.05 ± 4.60 ve 51.05 ± 3.07 idi. Gruplar arasında yaş karşılaştırıldığında anlamlı bir fark tespit edilmedi (p= 0.143). Üç grup arasında HRT yılları açısından anlamlı bir fark tespit edilmedi (p= 0.176). Gruplar arasında nükleer opasite (p= 0.361), kortikal opasite (p= 0.960) ve arka subkapsüler opasite (p= 0.856) ile ilgili anlamlı bir fark tespit edilmedi. Aynı zamanda gruplar arasında GİB karşılaştırıldığında anlamlı bir fark tespit edilmedi.

Sonuç: Bu bulgular 4 yıl boyunca HRT kullanımının lens opasitelerine etkisinin olmadığını ve GİB'sinde değişiklik yapmadığını göstermektedir.

Anahtar Kelimeler: Katarakt; hormon replasman tedavisi; menapoz; göz içi basıncı

Turkiye Klinikleri J Med Sci 2007, 27:811-815

Geliş Tarihi/*Received:* 15.12.2006 **Kabul Tarihi/*Accepted:*** 19.06.2007

Presented in part at the European Society of Cataract and Refractive Surgeons Meeting, Munich, Germany, September 6-10, 2003.

Yazışma Adresi/*Correspondence:* Aysel PELİT, MD
Başkent University Faculty of Medicine
Adana Teaching and Medical Research Center,
Department of Ophthalmology, ADANA
aypelit@yahoo.com

Factors that may predispose to cataract formation include aging, diabetes mellitus, smoking, elevated body mass index, UV light, alcohol use, and perhaps a history of systemic hypertension.[1-4] Protective roles of micronutrients in the development of cataract have recently

intrigued researchers, but studies up to date have been inconclusive. Previous studies demonstrated that men and premenopausal women had a similar prevalence of cataract; however, in postmenopausal women the prevalence of cataract is higher, compared to men of the same age group. The increased prevalence of cataract in postmenopausal women suggests a possible role for estrogen in retarding cataract formation.[5,6] Another important point is the relationship between IOP and HRT. The incidence of glaucoma is much higher in men than in women under 50 years of age. This difference between the sexes becomes less pronounced after this age, which suggests a relationship between IOP and estrogen.[7]

In this study we aimed to determine the effects of estradiol, estradiol/norethisterone acetate (NETA) and tibolone regimens on cataracts (cortical, nuclear, and posterior subcapsular) and IOP in postmenopausal women.

Material and Methods

One hundred forty eight women, who attended to the Menopause Outpatient Clinic of Başkent University Faculty of Medicine, were included in this study. After informed consent was obtained, a complete medical history, physical examination, and laboratory tests were performed to exclude diabetes, cardiovascular, cerebrovascular or thromboembolic disorders, untreated hypertension, endocrine, liver or renal disorders, and chronic usage of medication that may affect the eye (oral or topical corticosteroids, sex hormones, vitamins). The reproductive history included questions about the age of menstrual onset and end, the number of pregnancies and the number of children. The questionnaire also included questions on smoking history, the frequency of alcohol consumption, and educational status. The cases on HRT for at least 4 years were included in the study group.

The control group included 76 eyes of 38 age-matched subjects who did not take HRT. HRT patients were divided into 3 groups. Group 1 comprised 68 eyes of 34 patients who were on 2 mg of 17 beta estradiol in one tablet daily (Estrafem; Novo Nordisk). Group 2 included 82 eyes of 41 patients who were on 2 mg of 17-beta estradiol and 1 mg of NETA in one tablet daily (Kliogest; Novo Nordisk). Group 3 included 70 eyes of 35 patients who took tibolone (Livial; Organon).

The lens opacities were graded with slit-lamp by a single examiner (AP).

Lens Opacity Classification

The observer (AP) was blinded to treatment. Lens status was evaluated at the slit lamp using 16X magnification through a dilated pupil by means of a standardized grading system described by Taylor and West.[8] The photographs of each eye were obtained by using a Haag-Streit photo-slit lamp 900 P-BQ (Haag-Streit AG, Switzerland). The slit-lamp was modified with the illuminating beam fixed at an angle of 45^0 to the observation system.

Grading of the slit-lamp photographs was accomplished by comparing each subject's photographs with the four standard photographs for opalescence of the nucleus. The grades for the level of severity were as follows: grade 0, no opacity; grade 1, as clear as or clearer than standard 1; grade 2, not as clear as standard 1 but as clear as or clearer than standard 2; grade 3, not as clear as standard 2 but as clear as or clearer than standard 3; grade 4, not as clear as standard 3 but as clear as or clearer than standard 4. Cortical opacities were graded by estimating the cumulative number of one-eight wedges of the retroilluminated lens affected by cortical opacities. A cortical opacity was judged to be present if the opacity affected at least one-eighth the area of the lens cortex. Posterior subcapsular opacity was present when either the vertical or horizontal width of a posterior subcapsular opacity seen on retroillumination was at least 1 mm.

The IOP was measured by a single examiner (AP) with standard Goldmann applanation tonometry. The measurements were always taken between 10:00 AM and 11:00 AM. The tonometric value was considered the mean of three consecutive measurements.

To minimize systematic bias, only one eye of each patient was included in the study. We did not compare both eyes for individual patients.

The values of age, menarche age, hormone replacement therapy years, IOP were normally distributed. One-way Anova test (Post hoc Tukey) was used to determine differences between the groups regarding age, menarche age, hormone replacement therapy years, IOP. Chi-square test was used to determine differences between the groups regarding education, smoking, alcohol consumption, number of births, and lens opacity.

Results

The age of the subjects ranged from 46 to 57 years. The mean ages in the control group, group 1, group 2, and group 3 were 52.44 ± 5.89, 50.87 ± 3.53, 52.05 ± 4.60, and 51.05 ± 3.07, respectively (mean ± SE). There were no significant differences between the 4 groups regarding age (p= 0.143).

The mean menarche age in the control group, group 1, group 2, and group 3 were 13.05 ± 0.91, 13.55 ± 0.85, 13.35 ± 0.98, and 13.35 ± 1.00, respectively (mean ± SE). We did not observe significant difference in the groups regarding menarche age (p= 0.274). In the control group, the mean menopausal year was 4.2 ± 1.1 years. The mean HRT years in group 1, group 2, and group 3 were 4.7 ± 1.7, 4.5 ± 1.6, and 5.3 ± 1.0 years, respectively (mean ± SE). There were no significant differences between the three groups with respect to years of HRT (p= 0.176).

There were also no significant differences between the groups when we compared the educational status (p= 0.437), alcohol consumption (p= 0.998), smoking (p= 1.0) and number of births (p= 0.08) (Table 1).

We did not observe any significant differences between the groups regarding nuclear opacity (p= 0.361), cortical opacity (p= 0.960), and posterior subcapsular opacity (p= 0.856).

No significant difference was observed in the cross comparison of the IOP findings between the HRT groups (p= 0.780). There were no significant differences between the HRT groups and the con-

Table 1. Characteristics of postmenopausal subjects of this study.

Characteristic	Group 1 (n= 34)	Group 2 (n= 41)	Group 3 (n= 35)	Control group (n= 38)	p value
Education					
No education	10	12	11	11	
Elementary school	9	10	10	10	0.437
High school	8	10	8	9	
University	7	9	6	8	
Alcohol consumption (drinks/week)					
No alcohol	30	34	30	31	0.998
<7	3	5	4	5	
>7	1	2	1	2	
Smoking					
Never smoked	17	19	16	18	
Ex-smoker	7	9	8	8	1.0
Current	10	13	11	12	
Number of births					
0	5	6	5	5	
1	4	6	5	5	
2	7	7	7	8	
3	6	8	6	7	0.08
4	4	5	3	4	
5	3	4	4	4	
6	5	5	5	5	

Table 2. IOP results in the control group and in group 1, 2, and 3.

	Group 1 Mean ± STD	Group 2 Mean ± STD	Group 3 Mean ± STD	Control group Mean ± STD	p value
IOP	14.87 ± 2.44	13.97 ± 2.08	14.16 ± 1.87	13.94 ± 2.17	0.847

IOP: Intraocular pressure.

trol group when we compared the IOP findings. (p= 0. 847) (Table 2).

Discussion

Age-related lens opacities are more common in women than in men of the same age.[6] The increased prevalence of cataract in postmenopausal women suggests a possible role for estrogen in retarding cataract formation. A report from the Beaver Dam Eye Study suggested that estrogen replacement therapy might reduce the risk of some cataract types.[9] Observational epidemiological studies report that estrogen replacement therapy reduces the risk of ischemic heart disease and hip fractures, and increases the risk of endometrial and breast cancer. In recent studies, continuous combined HRT was suggested to last for a maximum of 5 years to avoid the above mentioned risks.[10]

Longer duration of estrogen use was reported to be associated with a decreased prevalence of nuclear opacities in the Salisbury Eye Evaluation Project and the Framingham Eye Study Cohort.[11,12] The mechanism by which estrogen replacement therapy may protect against lens opacities is unclear. In an animal model of age-related cataract, estrogen reduced the incidence of methylnitrosourea-induced cataract in rats subject to ovariectomy.[13] Other investigators suggested that estrogen might confer protection against cataract via negative effect on transforming growth factor β, which was demonstrated in the eye, and is capable of inducing opacities in cultured rat lenses. Lenses from rats subject to ovariectomy are sensitive to the damaging effects of transforming growth factor β, but in vivo or in vitro estrogen replacement restores resistance. Finally, the reported antioxidant activity of estrogen was suggested to have a beneficial effect on cataractogenesis.[14]

McCarty CA and colleagues reported no association between HRT and cataract.[15] Blue Mountains Eye Study demonstrated an association between cortical opacity and HRT while no relationship with nuclear opacity.[16] In contrast, the Beaver Dam Eye Study found that users of HRT had a lower prevalence of nuclear cataract. The study found no association between HRT and cortical cataract, and no findings were reported for posterior subcapsular cataract. The Beaver Dam Eye Study reported little evidence on the association of hormone exposures with incident age related cataract in women who have been on HRT for 5 years.[17]

The Framingham Eye Study Cohort showed that women who had taken estrogen for 10 years or longer had a 60% reduction in risk compared to nonusers. Posterior subcapsular opacities were also less common in estrogen users, but this finding was at a borderline level of significance. No association was noted for cortical lens opacities.[12]

In this study, we aimed to determine the effects of different HRT regimens on lens opacities and IOP in postmenopausal women. We wanted to see the long-term effect of HRT regimens. Group 1 was on estradiol, group 2 was on estradiol/norethisterone and group 3 was on tibolone treatment. Tibolone has estrogenic, progesteronic, and androgenic effects.[18] We did not find any differences between the control, estradiol, estradiol/NETA and tibolone regiments regarding cataract. Thus, we were unable to support the hypothesis that HRT is protective against lens opacity. Our results are consistent with the findings of Uncu and colleagues. They reported that conjugated equine estrogen and medroxyprogesterone acetate, tibolone, and estradiol regimens did not affect lens opacity after 12 months of treatment.[19]

Lang Y and coworkers suggested that HRT might decrease the intraocular pressure[20] Reports in the literature indicated that HRT reduced vascular resistance in either the central retinal artery or the ophthalmic artery or both.[21] Guaschino S and coworkers evaluated the average IOP in the HRT and control groups at baseline and 1 year later.[22] They found that there were no significant differences between HRT and control groups at baseline (15.1 mmHg, 14.7 mmHg, respectively) and one year after (14.8 mm Hg, 14.9 mmHg, respectively). Similarly, there were no significant differences between the HRT groups and the control group when we compared the IOP findings the IOP.

Data on the effects of HRT on the ocular system are scarce and results are contradictory. The presence of estrogen, progesterone and androgen receptors in the ocular system may suggest a positive effect of HRT, but the role of these receptors is unclear. More observational studies on such relations, particularly longitudinal studies involving incident cataract and IOP are certainly warranted. Basic biologic research is also needed.

REFERENCES

1. West SK, Valmadrid CT. Epidemiology of risk factors for age-related cataract. Surv Ophthalmol 1995;39:323-34.
2. Hodge WG, Whitcher JP, Satariano W. Risk factors for age-related cataracts. Epidemiol Rev 1995;17:336-46.
3. Glynn RJ, Christen WG, Manson JE, Bernheimer J, Hennekens CH. Body mass index. An independent predictor of cataract. Arch Ophthalmol 1995;113:1131-7
4. Solberg Y, Rosner M, Belkin M. The association between cigarette smoking and ocular diseases. Surv Ophthalmol 1998;42:535-47.
5. Sperduto RD, Hiller R. The prevalence of nuclear, cortical, and posterior subcapsular lens opacities in a general population sample. Ophthalmol 1984;91:815-8.
6. Mitchell P, Cumming RG, Attebo K, Panchapakesan J. Prevalence of cataract in Australia: The Blue Mountains eye study. Ophthalmol 1997;104:581-8
7. Qureshi IA. Intraocular pressure: A comparative analysis in two sexes. Clin Physiol 1997;17:247-55.
8. Taylor HR, West SK. The clinical grading of lens opacities. Aust N Z J Ophthalmol 1989;17:81-6.
9. Klein BE, Klein R, Ritter LL. Is there evidence of an estrogen effect on age-related lens opacities? The Beaver Dam Eye Study. Arch Ophthalmol 1994;112:85-91.
10. Rossouw JE, Anderson GL, Prentice RL, LaCroix AZ, Kooperberg C, Stefanick ML, et al Risks and benefits of estrogen plus progestin in healthy postmenopausal women: Principal results From the Women's Health Initiative randomized controlled trial. JAMA 2002;288:321-33
11. Freeman EE, Munoz B, Schein OD, West SK. Hormone replacement therapy and lens opacities: The Salisbury Eye Evaluation project. Arch Ophthalmol 2001;119:1687-92.
12. Worzala K, Hiller R, Sperduto RD, Mutalik K, Murabito JM, Moskowitz M, et al. Postmenopausal estrogen use, type of menopause, and lens opacities: The Framingham studies. Arch Intern Med 2001;161:1448-54.
13. Bigsby RM, Cardenas H, Caperell-Grant A, Grubbs CJ. Protective effects of estrogen in a rat model of age-related cataracts. Proc Natl Acad Sci USA 1999;96:9328-32.
14. Niki E, Nakano M. Estrogens as antioxidants. Methods Enzymol 1990;186:330-3.
15. McCarty CA, Mukesh BN, Fu CL, Taylor HR. The epidemiology of cataract in Australia. Am J Ophthalmol 1999;128:446-65.
16. Cumming RG, Mitchell P. Hormone replacement therapy, reproductive factors, and cataract. The Blue Mountains Eye Study. Am J Epidemiol 1997;145:242-9.
17. Klein BE, Klein R, Lee KE. Reproductive exposures, incident age-related cataracts, and age-related maculopathy in women: The beaver dam eye study. Am J Ophthalmol 2000;130:322-6.
18. Gupta PD, Johar K Sr, Nagpal K, Vasavada AR. Sex hormone receptors in the human eye. Surv Ophthalmol 2005;50:274-84.
19. Uncu G, Avci R, Uncu Y, Kaymaz C, Develioğlu O. The effects of different hormone replacement therapy regimens on tear function, intraocular pressure and lens opacity. Gynecol Endocrinol 2006;22:501-5.
20. Lang Y, Lang N, Ben-Ami M, Garzozi H. The effects of hormone replacement therapy (HRT) on the human eye. Harefuah 2002;141:287-91, 313, 312.
21. Toker E, Yenice O, Akpinar I, Aribal E, Kazokoglu H. The influence of sex hormones on ocular blood flow in women. Acta Ophthalmol Scand 2003;81:617-24
22. Guaschino S, Grimaldi E, Sartore A, Mugittu R, Mangino F, Bortoli P, et al. Visual function in menopause: The role of hormone replacement therapy. Menopause 2003;10:53-7.