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Effect of hormone replacement therapy on ocular hemodynamics in postmenopausal women

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PURPOSE. *To evaluate the effect of hormone replacement therapy on ocular hemodynamics in postmenopausal women.*
METHODS. *Ocular Doppler ultrasonography was performed in 20 postmenopausal women on hormone replacement therapy (HRT) and in 20 women without treatment, as the control group. Central retinal artery (CRA), posterior ciliary artery (PCA) and ophthalmic artery (OA) flow velocities and vascular resistances were measured prospectively by a radiologist blinded to the therapy. There were no associated systemic or ocular diseases or any medication history.*
RESULTS. *The mean age of the patients on HRT was 50.05 ± 4.5 yrs (range 44 - 62). The mean age of the control group was 52.8 ± 4.09 yrs (range 46 - 65). The mean duration of HRT was 1.6 ± 1.4 yrs (range 3 months - 5 years). There were no differences between the groups in terms of flow velocities, vascular resistivities or pulsatility indices of OA, CRA and PCA ($p>0.05$).*
CONCLUSIONS. *HRT is essential in postmenopausal women for relief of vasomotor symptoms, cardioprotection and prevention of osteoporosis. Even though vaso-occlusive complications of hormone preparations have been reported, we did not observe any changes in ocular hemodynamics detectable with Doppler ultrasonography. (Eur J Ophthalmol 2001; 11: 277-80)*

KEY WORDS. *Color Doppler ultrasonography, Hormone replacement therapy, Ocular blood flow*

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INTRODUCTION

Menopause and the postmenopausal period is an important time of a woman's life. With increasing life expectancy, modern menopause treatment aims to reduce the unwanted effects of menopause with hormonal support while keeping the side effects and complications at a minimum level. Hormone replacement therapy (HRT) has become popular in this aspect, but studies related to its side effects are still going on. The cardiovascular system as well as blood coagulation elements and lipid profile undergo changes after the menopause. Clinical studies have shown that HRT has a 25-50% preventive and protective role in coronary heart disease in women (1, 2). This cardioprotective effect is also related to the effects on lipid profile and lipoproteins. Animal studies found positive effects of HRT on vessel walls, and estrogen therapy prevented vasoconstriction in coronary vessels of monkeys (3). On the other hand, there are some risks for HRT such as an increased incidence of endometrial and breast cancer, cholelithiasis, hypertension, glucose intolerance and thromboembolic events. Ocular hemodynamic changes such as age-related loss

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of the ophthalmic arterial blood flow velocity (4) were reported in the elderly population, but the effects of menopause and HRT have not been studied.

Color Doppler ultrasonography (CDU) is a non-invasive, reproducible, two-dimensional vascular imaging technique that has been used for the diagnosis or follow-up of intraocular tumors and their vascularisation, arteriovenous malformations, varices, retinal detachment and vascular disease such as artery occlusions, Takayasu disease, diabetic retinopathies and uveitis (5-8). In this study, we measured blood flow velocities in the ophthalmic artery (OA), central retinal artery (CRA), and posterior ciliary artery (PCA) using CDU in postmenopausal women on HRT and compared them with age-matched postmenopausal women not taking any medication.

MATERIALS AND METHODS

Twenty postmenopausal women that were on HRT and 20 women at the age of menopause without HRT were included in the study, after detailed information was given and informed consent forms were signed. All women had normal ophthalmologic findings except for minor refractive errors and presbyopia, and were otherwise healthy.

Transorbital color Doppler examinations were done using Toshiba SSA-270A and 380 PowerVision Doppler systems by the same examiner who was blinded to the treatment. Color Doppler linear transducers of 7.5 and 10 MHz were used in the low PRF level to image the vessels optimally without artifacts. In view of the small size of the vessels, the smallest (1 mm) sample volume size was used. So as not to damage the eye, examinations were done at lower acoustic output levels (mechanical index: 0.6). The women lay supine with the tested eye looking downward and medially. The Doppler transducer was carefully placed over the upper eyelid without pressure and methyl cellulose was applied as a coupling gel. Depending on the direction of flow with respect to the transducer, the flow data were displayed in either red or blue, red depicting flow towards the transducer (arterial) and blue flow away (venous flow). Arteries had a positive signal on pulsed Doppler curves and veins had a negative signal. For ophthalmic artery measurements, the probe was most often placed superotemporally at an angle of 15-30 degrees from the midline towards the orbital apex. The subjects were asked to look medially or laterally to increase the visibility of ciliary vessels.

Both eyes were examined and three readings were recorded from each eye. Peak systolic (PSV) and end-diastolic flow velocities (EDV) were recorded in cm/sec. Flow volumes (FV) of the ophthalmic arteries were calculated in ml/sec by the software of the equipment. Resistivity indices (RI - Pourcelot index) [(Vmax-Vmin)/Vmax] and pulsatility indices (PI) [(Vmax-Vmin)/mean] were calculated with the measured velocities. Statistical analysis was done with the t-test for independent samples.

RESULTS

Twenty postmenopausal women with a mean (±SD) age of 50.1 ± 4.5 years (range 44 to 62 years) with no ocular and systemic disease were investigated to evaluate the effects of HRT on ocular hemodynamics. As a control group, 20 postmenopausal women with a mean age of 52.8 ± 4.1 years (range 46 to 65 years) were included. All the patients had non-surgical menopause. Thirteen women were taking estrogen and progesteron combinations and seven were taking only natural estrogen preparations as HRT. Mean duration of menopause was 3.1 ± 2.1 years (range 1-9 years) in the HRT group and 5.1 ± 3.4 years (range 1-15) in the control group. Mean duration of HRT was 1.6 ± 1.4 years (range 3 months - 5 years).

The flow velocities and resistivity indices for the OA, PCA and CRA and the flow volume for OA are shown in Table I. Peak systolic velocities in OA ranged from 24 to 58 cm/sec with a mean (± SD) of 37.17 ± 7.85 cm/sec in the HRT group and 37.32 ± 9.66 cm/sec (range 20 - 57 cm/sec) in the control group. The mean peak systolic velocity in the CRA was 19.85 ± 3.86 cm/sec (range 13 - 28 cm/sec) in the HRT group and 21.20 ± 5.49 cm/sec (range 14 - 38 cm/sec) in the controls. The mean peak systolic velocity in the PCA was 11.70 cm/sec ± 2.65 (range 8 - 18 cm/sec) in the HRT group and 11.53 ± 1.96 cm/sec (range 9 - 16 cm/sec) in the controls (Tab. I). No significant differences were found between the systolic and end-diastolic velocities. In consideration of sample power estimates, power was found to be 94% when the effect size was 0.80*SD, ∞=0.05 and N=40.

DISCUSSION

HRT seems to be protective against cardiovascular diseases. It has beneficial effects on the lipoprotein metabolism, reducing total and low-density lipoprotein cholesterol and increasing high-density lipoprotein cholesterol. Estrogen directly affects estrogen receptors on vessel walls and increases prostacycline synthesis reducing thromboxane synthesis. Prostacyclines act as vasodilators and platelet antiaggregants and thromboxane acts as a vasoconstrictor and platelet aggregant, so estrogens increase blood flow and prevent blood clotting. Estrogens themselves may however have an adverse effect on blood coagulation, notably on fibrinogen, factor VIIc and antithrombin (9). Oral contraceptives may increase the risk of retinal vein occlusion, but HRT does not appear to be associated with any excess risk of retinal vein occlusion (9).

Observational epidemiological studies suggest that estrogen replacement therapy reduces the risk of ischemic heart disease and hip fractures but increases the risk of endometrial and breast cancers. In a large cross-sectional study in Australia, it was suggested that long-term users of HRT might be protected against cortical cataract but might be at a higher risk of posterior subcapsular cataract (10). The Beaver Eye Study showed that users of HRT had a lower prevalence of nuclear cataract (11).

The ophthalmic artery perfuses all ocular tissues and 65-85% of this blood flow supplies the choroid. Therefore, the RI, an index of vascular resistance of the ophthalmic artery, presumably mainly reflects the vascular resistance in the choroid. There is no autoregulation in the choroidal circulation so changes in either mean arterial blood pressure or intraocular pressure produce a linear response in ocular blood flow. However, there is autoregulation in the retinal blood flow and the flow velocities are lower (12-14). The optic disc head is richly supplied by the ciliary vascular system (ciliary arteries). The retrolaminar portion of the disc and the layers of superficial nerve fibers are perfused mainly by the retinal vascular system (central retinal artery) (5).

There is an age-related decline in ophthalmic arterial blood flow velocity (4). In systemic diseases such as diabetes mellitus, ocular blood flow was reportedly decreased due to the increase in vascular re-

TABLE I - PEAK SYSTOLIC VELOCITY (PSV), END-DIASTOLIC VELOCITY (EDV), PULSATILITY INDICES (PI) AND RESISTIVITY INDICES (RI) FOR OPHTHALMIC ARTERY (OA), POSTERIOR CILIARY ARTERY (PCA) AND CENTRAL RETINAL ARTERY (CRA) AND FLOW VOLUME (FVol) FOR OA

	HRT Group (40 eyes)	Control Group (40 eyes)	
OA PSV*	37.17 ± 7.85	37.32 ± 9.66	p>0.05
OA EDV*	11.15 ± 4.46	11.65 ± 4.19	p>0.05
OA PI	1.26 ± 0.23	1.20 ± 0.22	p>0.05
OA RI	0.70 ± 0.06	0.69 ± 0.06	p>0.05
OA FVol**	59.72 ± 14.49	57.75 ± 17.17	p>0.05
CRA PSV	19.85 ± 3.86	21.20 ± 5.49	p>0.05
CRA EDV	6.28 ± 1.83	6.53 ± 1.95	p>0.05
CRA PI	1.17 ± 0.19	1.17 ± 0.15	p>0.05
CRA RI	0.68 ± 0.06	0.68 ± 0.05	p>0.05
PCA PSV	11.7 ± 2.65	11.53 ± 1.96	p>0.05
PCA EDV	4.0 ± 1.09	3.8 ± 0.85	p>0.05
PCA PI	1.1 ± 0.2	1.1 ± 0.18	p>0.05
PCA RI	0.66 ± 0.07	0.66 ± 0.06	p>0.05

* Flow velocities in cm/sec

** FVol in ml/sec

sistance (14). In ocular diseases such as uveitis and vasculitic retinal diseases, vascular hemodynamic changes can be recorded with CDU (15). The increasing use of CDU is introducing significant changes in the diagnostic imaging of the vascular system, as it provides a reproducible, non-invasive means of obtaining high-resolution anatomical information, combined with useful quantitative velocity data (5). CDU has been used in the diagnosis of ocular and orbital vascular diseases (carotido-cavernous fistula, arterio-venous malformations, varices, retinal or ophthalmic artery occlusion, cranial arteritis), intraorbital or choroidal vascular tumors, retinal detachment and vitreous membranes (5-8, 16). There is no report in the literature of CDU in the study of HRT in postmenopausal women.

The beneficial effects of HRT are greater than its adverse effects as regards protection from osteoporosis, cardiovascular, genito-urinary and vasomotor symptoms. HRT can be started after an evaluation of relative and absolute contraindications. We observed no adverse effects of HRT on ocular blood flow, and no change in resistivity or pulsatility indices in the HRT group that could be taken as a sign of occlusion. Long-term follow-ups of the women now taking HRT are needed to observe any changes in ocular hemodynamics that could result in ischemic optic neuropathies or vein occlusions. However, other diseases that can affect vascular structures such as hypertension and diabetes must be considered as well.

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