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SHORT COMMUNICATION

Comparison of visual function and ocular hemodynamics between pre- and post-menopausal women

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PURPOSE. *The incidence of eye disease increases with age and can often be linked to worsening cardiovascular function and increasing intraocular pressure. Estrogen is known to have vasodilatory effects in the systemic circulation. Decreased estrogen levels during menopause may therefore complicate or contribute to ocular pathologies as estrogen receptors are found in both retinal and choroidal tissue. The purpose of this investigation was to determine the effects of menopause on visual function and cardiovascular and ocular hemodynamics.*

METHODS. *Twelve premenopausal and 24 postmenopausal women were evaluated at the Indiana University School of Medicine during a single study visit. Vision screening and ocular blood flow evaluations were performed, including blood pressure, heart rate, visual acuity, contrast sensitivity, intraocular pressure, and retinal capillary and retrobulbar blood flow imaging. Vision and ocular hemodynamics were compared using unpaired Student t-tests with $p<0.05$ regarded as statistically significant.*

RESULTS. *The premenopausal group had significantly lower heart rate (–16.1 b/m, p=0.0001) and systolic blood pressure (–17.7 mmHg, p=0.003) than postmenopausal subjects. Contrast sensitivity was significantly higher (measured in log units) in premenopausal women in both the right (0.25, p=0.039; 0.16, p=0.039) and left (0.45, p=0.001; 0.27, p=0.032) eyes at 9 and 18 cycles per degree, respectively. Premenopausal women also had significantly lower intraocular pressure in both the right (–2.19 mmHg, p=0.024) and left (–1.74 mmHg, p=0.035) eyes. Total ocular perfusion was not significantly different between groups.*

CONCLUSIONS. *This pilot work suggests that postmenopausal women have lower contrast sensitivity detection and elevated intraocular pressures compared to premenopausal women. Premenopausal women have lower cardiovascular risk factors, while total ocular circulation was similar to postmenopausal women. (Eur J Ophthalmol 2008; 18: 320-3)*

KEY WORDS. *Blood flow, Hormone, Menopause, Vision*

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INTRODUCTION

As a population ages, diseases such as glaucoma, age-related macular degeneration, and diabetic retinopathy increase in prevalence. In the elderly, reduced cardiovascular function and a lack of ocular perfusion may contribute to these disease processes (1). For women in their postmenopausal years, the additional reduction in endogenous estrogen may further alter vascular reactivity. Estrogen's vasodilatory effects are linked to increased nitric

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oxide synthase activity, the blockage of calcium channels in endothelial cells, changes in lipid profiles, and alterations in the renin-angiotensin system (2). Since estrogen receptors exist within retinal and choroidal tissues (3), menopause may significantly impact the ocular vasculature and ultimately affect visual function thereby reducing the quality of a postmenopausal woman's life. This study investigated systemic cardiovascular, retinal, and retrobulbar hemodynamics as well as visual function in pre- and postmenopausal women.

MATERIALS AND METHODS

This study adheres to the Declaration of Helsinki and was approved by the Institutional Review Board of Indiana University. Subjects signed informed consent to procedures reviewed and approved by the institutional review board.

Visual function and cardiovascular and ocular perfusion parameters were examined during a single visit in 36 female participants: 12 premenopausal women and 24 postmenopausal women. Postmenopausal women were at least 50 years old and 2 years postmenopausal. Exclusion criteria for both groups included use of vasoactive medications, prior or current use of hormone replacement therapy (HRT) and ocular or vascular disease. Subjects were also excluded if they used caffeine or tobacco and/or had exercised within 4 hours of their visit.

Measurements were taken in the same order for each patient at the same time of day: blood pressure (BP), heart rate, visual function in both eyes as measured by ETDRS LogMAR and contrast sensitivity CSV-1000 charts, slit lamp examination, intraocular pressure (IOP) using Goldmann applanation tonometry, pupil dilation, and fundus examination. Ocular blood flow was assessed in a randomly selected study eye using confocal scanning laser Doppler flowmetry for retinal perfusion and color Doppler imaging of retrobulbar blood flow. Additionally, ocular perfusion pressures were evaluated (OPP = 2/3 mean arterial pressure–IOP).

Confocal scanning laser Doppler flowmetry

Confocal scanning laser Doppler flowmetry (Heidelberg Retinal Flowmeter, Heidelberg Engineering, Heidelberg, Germany) was used to measure perfusion within peripapillary retinal capillary beds of the superior and inferior temporal fields. Flow was measured as number of zero flow pixels and number of pixels falling into the 10th, 25th, 50th, 75th, and 90th percentiles of total flow thereby describing the total vascularity of the fundus. The technique has been described in detail previously (4).

Color Doppler imaging

A Siemens Quantum 2000 color Doppler imaging system (CDI, Siemens Quantum, Issaquah, WA) with a 7.5 MHz linear probe was utilized. Blood flow velocities and resistive indices were measured in the ophthalmic, central retinal, and nasal and temporal short posterior ciliary arteries.

TABLE I - PRE- VS POSTMENOPAUSAL RESULTS

Variable	Premenopause, mean ± SD	Postmenopause, mean ± SD	t-Test p value
Age	22.2±2.9	54.6±3.8	<0.0001
Heart rate (beats/min)	70.8±7.5	86.9±11.6	<0.0001
Systolic blood pressure (mmHg)	119.5±11.0	137.2±18.0	0.003
Contrast sensitivity R 9 (cpd)	1.62±0.25	1.37±0.40	0.039
Contrast sensitivity R 18 (cpd)	1.18±0.17	1.02±0.26	0.039
Contrast sensitivity L 9 (cpd)	1.69±0.26	1.24±0.35	0.001
Contrast sensitivity L 18 (cpd)	1.21±0.27	0.94±0.32	0.032
IOP R (mmHg)	12.7±2.5	14.89±2.0	0.024
IOP L (mmHg)	13.2±2.0	14.94±2.0	0.035
Nasal PCA systolic (cm/s)	5.64±0.79	6.78±1.52	0.015
Nasal PCA diastolic (cm/s)	1.69±0.18	2.13±0.80	0.034
Infranasal flow, 90th % (arbitrary units)	550.0±132.1	700.7±129.3	0.015

Statistically significant differences in measured parameters between premenopausal and postmenopausal women as demonstrated by Student t-test.
cpd = Cycles per degree with values expressed in log units; IOP = Intraocular pressure; PCA = Posterior ciliary artery

In each vessel, peak systolic velocity (PSV), end-diastolic velocity (EDV), and Pourcelot's resistive index were determined. The technique has been described in detail previously (5). The same experienced ultrasound technician was utilized for all patient examinations in a controlled repeatable fashion with the patient resting in the supine position for 5 minutes before examination.

Statistical analysis

Premenopausal women were compared to postmenopausal women using an unpaired Student *t*-test with $p<0.05$ regarded as statistically significant. A 95% confidence interval for the mean difference between the two groups was estimated. Previous studies of populations and test/retest variability of the color Doppler measurement of retrobulbar blood flow velocities show that a sample size of 12 individuals (smallest n in study) provides ~90% power to detect a 20% difference in peak systolic and end-diastolic velocity and an 8% difference in resistance index, between glaucoma treatment groups.

RESULTS

Table I presents the demographics and statistically significant differences between the pre- and postmenopausal subjects. Premenopausal women had significantly lower heart rate, systolic BP, IOP, and higher contrast sensitivity detection than postmenopausal women. The premenopausal women had a significantly lower 90th percentile retinal blood flow value of the inferior peripapillary field with no other significant differences in the 25th, 50th, 75th, or 90th percentiles of total retinal blood flow. The premenopausal women had significantly lower nasal posterior ciliary artery blood flow velocities than the postmenopausal women. No significant differences in ophthalmic or central retinal artery blood flow velocities were found between study groups.

DISCUSSION

Maintaining ocular perfusion is crucial in the prevention of disease states such as glaucoma and macular degeneration. Both endogenous estrogen and HRT have been shown to improve systemic blood flow (3). The effect of menopause on visual function and ocular blood flow, however, is not well established. Previously, decreased IOP and increased ocular perfusion has been reported during increased systemic estrogen in pregnant women and postmenopausal women on HRT (6). This investigation examines menopause's effects on visual function and total ocular perfusion in otherwise healthy individuals.

Decreased contrast sensitivity and increased IOP were found in postmenopausal women. Increased IOP and decreased visual function are both known effects of aging and possibly decreased estrogen (7). Therefore, loss of visual function with age may be exacerbated in women who experience concomitant decreases in vasoprotective estrogen. Our investigation found BP and heart rate were increased in the postmenopausal group. Total ocular blood flow, however, was not found to be significantly different between pre- and postmenopausal women. We were surprised that the differences seen in systemic cardiovascular variables and IOP did not translate into lower ocular blood flow values for the postmenopausal group. In fact, a decreased 90th percentile retina flow value and decreased nasal posterior ciliary artery velocities were found in the premenopausal group. These results are mitigated, however, as premenopausal women maintained a statistically similar vascular resistance to postmenopausal women. Previously, studies have shown menopause to increase resistance to flow and decrease end diastolic velocity in the ophthalmic and/or central retinal arteries (6, 8, 9). In our investigation, we did not find ophthalmic or central retinal artery blood flow parameters to be affected by menopause. These differing findings are likely due to the differing patient populations, methodologies, or statistics utilized in these investigations. It is also important to note that differentiating between the effects of aging and a reduction in estrogen via menopause remains difficult in these preliminary studies. Only a longitudinal comprehensive assessment of ocular hemodynamics between age-matched pre- and postmenopausal women may reveal what long-term effects menopause may have on the ocular vasculature.

Our pilot study was limited by factors innate to its design. We were not able to obtain a group of age-matched nonmenopausal women not on HRT which would have been ideal for this comparison. Since menopause is almost always associated with advanced age, it is difficult to discriminate whether changes in visual function and blood flow were due to age or decreased estrogen. As mentioned above, a comprehensive longitudinal study utilizing a larger sample size and closely age-matched subjects is strongly suggested.

In conclusion, increased BP, heart rate, and IOP are evident with the onset of menopause. Menopause is also accompanied by reduced contrast sensitivity detection. Total ocular blood flow, however, appears not to be affected by menopause itself. These results suggest that changes in systemic cardiovascular function during aging, including loss of vascular compliance and narrowing of the arteries, may play a greater role than the loss of estrogen itself in the ocular vasculature.

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