SCIENTIFIC CORRESPONDENCE

Do sex and hormonal status influence choroidal circulation?

Marco Centofanti, Stefano Bonini, Gianluca Manni, Cesare Guinetti-Neuschüler, Massimo G Bucci, Alon Harris

Abstract

***Aims*—To investigate the relation between pulse amplitude (PA), pulsatile ocular blood flow (POBF), and sex and hormonal status.**

***Methods*—Measurements of POBF and PA were obtained by ocular blood flow tonography in 76 healthy subjects: 32 males and 44 females (age range 17–77 years). Females were divided into two age groups: group 1 (premenopausal) 17–42 years, and group 2 (post-menopausal) 55 years old and over. Two groups of age matched males served as controls.**

***Results*—Premenopausal females demonstrated a significantly higher rate of POBF and PA than age matched males and post-menopausal females.**

***Conclusion*—Sex and hormonal status were shown to influence choroidal circulation.**

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Cattedra di Clinica Oculistica, Università di Roma "Tor Vergata", Fondazione GB Bietti per l'Oftalmologia, Rome, Italy
M Centofanti
S Bonini
G Manni
C Guinetti-Neuschüler
M G Bucci

Department of Ophthalmology, Indiana University, Indianapolis, USA
A Harris

AFaR-CRCCS, Divisione Oculistica Ospedale Fatebenefratelli, Isola Tiberina, Rome, Italy
M Centofanti
C Guinetti-Neuschüler

Correspondence to: Marco Centofanti, MD, PhD, Via Bolzano 1, 00198 Rome, Italy
mcentofanti@lycosmail.com

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Choroidal circulation has an important role in ocular physiology[1] and may be affected in several ocular diseases such as glaucoma, retinitis pigmentosa, diabetic retinopathy, and myopia.[2 3] Various extraocular diseases seem to influence the choroidal circulation like Horton's temporal arteritis, systemic hypertension, carotid stenosis, and haematological diseases.[4] Almost 75% to 85% of total choroidal circulation follows cardiac output, with a pulsatile rather than linear flow.[5 6] One instrument currently used to measure pulsatile ocular blood flow (POBF), is the ocular blood flow tonograph. This instrument records the variation of the intraocular pressure (IOP) with the heart rate and allows the calculation of the pulse amplitude (PA) between systolic and diastolic intraocular pulse.[7] The change in pressure is related to an ocular volume difference induced by a bolus of arterial blood into the eye during systole.[8] A pneumatic probe recorded IOP variations, and computerised data analysis allowed us to have the mean value of the blood bolus. The POBF is then calculated using a mathematical formula which considered heart rate and scleral rigidity, expressed in µl/min.[9]

This variable may be affected by many physiological variables including blood pressure, heart rate, and IOP.[10 11] Other physiological variables have also been considered to modify the ocular circulation. For instance, it is well established that age related changes occur in ocular blood flow[12] and that the reduction in POBF and PA may be the consequence of increased vascular resistance. In contrast, although the hormonal status influences the circulation of several tissues according to the phase of woman's reproductive life,[13] no significant sex differences have been found in the ocular circulation.

In this paper, healthy subjects were evaluated to identify if sex and age related changes in hormonal status influence POBF.

Materials and methods

Seventy six healthy volunteers, 32 males and 44 females, aged 17–77 years, with no history of systemic or ocular diseases, and with a refractive error (when present) between −1 and +1 spherical equivalent,[14] were included in the study. None of the subjects used topical or systemic medication (hormone replacement therapy or systemic vasoactive drugs) at the time of the study. Informed consent was obtained from each volunteer according to the tenets of the Declaration of Helsinki. Each subject had a complete eye examination including visual acuity, slit lamp examination, intraocular pressure, and fundus oculi.

For each patient, the following systemic and ocular variables were considered: mean systemic blood pressure, heart rate, intraocular pressure, pulse amplitude, and pulsatile ocular blood flow.

POBF and PA were measured at the slit lamp, with the OBF System (Labs UK, Ltd). Subjects were in the sitting position and under topical ocular anaesthesia. Women were divided into two groups, pre- and post-menopausal: group 1, 17–42 years of age (n=23); and group 2, 55 years of age or more (n=16). Two groups of age matched males were also evaluated: (group 1: n=15, group 2: n=12). Ten subjects (five males, five females), aged 43–54 years, were excluded from the statistical evaluation to avoid overlapping between the two groups of women[15 16] (Table 1).

Non-parametric statistical analysis (Mann–Whitney U test) was performed using SYSTAT 5.2 (Macintosh, Tolentino, USA). A p value

Table 1 Results (mean (SEM)) obtained for pulsatile ocular blood flow (POBF), pulse amplitude (PA), intraocular pressure (IOP), heart rate (HR), and blood pressure (BP) in the four groups tested with patient number and mean age noted

	No	Mean age	POBF (μl/min)	PA (mm Hg)	IOP (mm Hg)	HR (min)	Mean BP (mm Hg)
Female <42 years	23	28.05 (7.4)	1178.2 (50.5)	4.1 (0.8)	16 (2.7)	75 (11)	96 (8)
Female >55 years	16	70.7 (7.4)	994.6 (94.4)	2.7 (0.7)	17 (2.9)	74 (11)	105 (4)
Male <42 years	15	25.4 (5.7)	989.7 (80.9)	3.4 (1.0)	16.5 (2)	72 (12)	98 (9)
Male >55 years	12	65.4 (5.9)	898.4 (116.7)	3.2 (0.7)	17.5 (1.8)	77 (15)	106 (7)

of 0.05 or less was considered statistically significant.

Results

We evaluated the difference variables in the two groups for each sex and we observed that (a) premenopausal females had significantly higher rates of POBF ($p = 0.002$) and PA ($p = 0.005$) when compared with age matched males. In contrast, no statistical differences in POBF and PA were observed in post-menopausal females compared with their age matched males. (b) Premenopausal women were also shown to have a significantly higher POBF ($p = 0.002$) and PA ($p = 0.0006$) than post-menopausal females, while no age related differences were observed in males. We observed no statistical differences between the groups for the other variables evaluated—IOP, HR, and BP.

Discussion

In this study we observed that ocular circulation is influenced by sex and probably these changes are related to hormonal status. It is known that POBF and PA values may have an high individual variability as a result of several physiological conditions which may interfere with the ocular circulation.[9 17 18]

Possibly other unknown ocular or systemic variables may influence the individual variability observed in ocular circulation. Although in our study we confirmed the age related ocular blood flow changes, we founded that premenopausal females had a significantly higher rate of blood flow than age matched males—a sex difference which was not significant in male and female subjects over 55 years of age. The possible influence of female sex hormones on ocular blood flow was further demonstrated by the significantly higher rate of POBF and PA observed in premenopausal compared with post-menopausal females. These differences were not evident in the two male age groups.

Previous study do not report significant differences between sexes.[12] These conflicting data are probably the consequence of grouping the patients into decades of age, thus nullifying the major hormonal changes occurring in a woman's life.

Sex is known to influence the occurrence and outcome of several vascular diseases, probably because of the vascular effects of oestrogens and progestins.[19] Female hormones exert a protective effect on coronary heart disease and oestrogen replacement therapy is effective in the reduction of the vasomotor symptoms of menopause and the prevention of cardiovascular disease.[20] At present, the effect of oestrogen replacement therapy on the ocular blood flow has not been studied. Indeed, physiological changes in sex hormone levels can improve the course of some diseases in which the choroidal circulation has a major role; for example, the course of glaucoma is impaired during pregnancy.[21] In conclusion, sex and the changes in female hormonal status provoked by the menopause were shown to influence choroidal circulation in healthy subjects. Oestrogens may be responsible for these changes, and it is suggested that these hormones may modify the course of some ocular diseases. While the present study only evaluated the effect of sex on ocular blood flow, without defining the mechanisms, studies elaborating these findings are in progress, the objectives of which are to identify exactly the role of oestrogens in modulating choroidal blood flow.

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