Blood flow velocity in the extraocular vessels in chronic smokers

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Abstract

***Aims*—To determine blood flow velocity in the extraocular vessels in healthy, chronic smokers and to compare these blood flow velocities with those of healthy non-smokers.**

***Methods*—In 46 healthy chronic smokers and 189 healthy non-smokers, peak systolic velocity (PSV), end diastolic velocity (EDV), and the resistivity index (RI) were measured in the ophthalmic artery (OA), central retinal artery (CRA), lateral short posterior ciliary artery (LPCA), and medial short posterior ciliary artery (MPCA) by means of a colour Doppler device, Siemens Quantum 2000.The maximal (max) and minimal (min) velocities were measured in the central retinal vein (CRV). Only one eye was measured in each subject, and right and left eyes were chosen randomly. Blood flow velocities were compared with one way MANOVA and *t* tests. The influence of age, sex, systolic and diastolic blood pressure, as well as heart rate on blood flow velocity and RI were evaluated by an analysis of covariance. The potential differences of the influence of the covariables on blood flow variables in smokers and non-smokers were tested by calculating the interactions.**

***Results*—In the majority of measured vessels blood flow velocity was higher in smokers than in non-smokers. This difference was statistically significant in the OA, CRV, and LPCA. The RI indices were equal or slightly lower in smokers. Furthermore, smokers had significantly lower systolic and diastolic blood pressure. Heart rate was higher in smokers but this difference did not reach statistical significance.**

***Conclusions*—Colour Doppler measurements may differ significantly in smokers compared with non-smokers. Therefore, smoking habits should be considered when interpreting colour Doppler imaging results, and comparing different groups of diseased or healthy subjects.**

(*Br J Ophthalmol* 1997;**81**:133–135)

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Accepted for publication
4 November 1996

Cigarette smoking acutely increases catecholamine levels in the blood resulting in moderate tachycardia and elevation of systemic blood pressure.[1–3] During smoking free intervals, however, blood pressure has been found to be lower in chronic smokers than in non-smokers.[4–7] The effect of acute exposure to nicotine on vascular resistance, however, is controversial. There is some evidence that the change in vascular tone with cigarette smoking may be different in non-smokers than in chronic smokers.[8] It has been shown that during test smoking forearm vascular resistance increases significantly in healthy non-smokers,[9] whereas it remains unchanged in healthy, chronic smokers.[10]

Little is known about the haemodynamic effects of nicotine on the ocular circulation. Small doses of nicotine (Nicorette gum) increased blood flow velocities in the ophthalmic artery (OA) in 18 glaucoma patients and eight normal subjects measured with transcranial Doppler ultrasound, whereas it significantly decreased finger blood flow, measured with a laser Doppler flowmeter.[11] The authors, however, did not indicate whether the subjects were smokers or not. Williamson *et al* found that cigarette smoking was associated with lower ophthalmic artery velocities.[12] Morgado *et al* found decreased retinal blood flow in acute smoking using laser Doppler velocimetry.[13]

In the present study blood flow velocity in the extraocular vessels in healthy, chronic smokers was measured during a smoking free period and compared with those of healthy non-smokers with the help of colour Doppler imaging (CDI). CDI is an ultrasonic imaging method that provides a display of blood flow characteristics on a real time, grey scale, B-mode background, thus permitting the non-invasive assessment of blood flow velocity in blood vessels,[14–17] including those of the orbit.[18–23]

Subjects and methods

Visitors to a public fair ('Mustermesse' in Basel, Switzerland) were invited by an ophthalmologist of the university eye clinic to participate in this study on a volunteer basis without payment. Included were 46 chronic smokers who smoked more than five cigarettes daily at least for the past year and 189 subjects who did not smoke at all. Excluded were subjects under local or systemic medication, as well as subjects with a history of eye or general disease. None of the included subjects had any pathological findings in an ophthalmic examination, including funduscopy with a direct ophthalmoscope. Only one eye per subject was measured. Right and left eyes were chosen randomly. All the CDI measurements were performed by the same ophthalmologist (HJK). The interval

Table 1 Patient characteristics, blood pressure, and heart rate in healthy smokers and non-smokers

	Smoker	Non-smoker
Number	46	189
Sex (female/male)	21/25	86/103
Age (years):		
Mean (SD)	37.3 (13)	47.8 (18.2)
Range	16–70	7–78
Mean (SD) systolic blood pressure (mm Hg)	125 (13)	133 (19.4)
Mean (SD) diastolic blood pressure (mm Hg)	71.5 (10)	75.2 (11.7)
Mean (SD) heart rate (beats/min)	75 (10)	71 (9)

Table 2 Blood flow velocities in the ophthalmic artery, central retinal artery, central retinal vein, lateral and medial posterior ciliary artery in 46 smokers and 189 non-smokers

	Smoker Mean (SD)	Non-smoker Mean (SD)	t Test p Value
Ophthalmic artery:			
PSV (cm/s)	41.7 (7.4)	39.3 (5.3)	0.009
EDV (cm/s)	10.4 (2.8)	9.1 (2.5)	0.001
RI	0.74 (0.05)	0.77 (0.05)	0.02
Central retinal artery:			
PSV (cm/s)	11.4 (1.6)	11.0 (1.7)	NS
EDV (cm/s)	3.2 (0.9)	3.3 (0.9)	NS
RI	0.71 (0.05)	0.71 (0.05)	NS
Central retinal vein:			
Max (cm/s)	4.7 (1.0)	4.5 (1.0)	NS
Min (cm/s)	3.6 (0.8)	3.3 (0.7)	0.01
Lateral posterior ciliary artery:			
PSV (cm/s)	12.1 (2.4)	11.2 (1.7)	0.005
EDV (cm/s)	4.1 (1.3)	3.7 (1.0)	0.03
RI	0.67 (0.06)	0.68 (0.06)	NS
Medial posterior ciliary artery:			
PSV (cm/s)	11.2 (1.9)	11.2 (1.7)	NS
EDV (cm/s)	3.7 (1.2)	3.6 (0.9)	NS
RI	0.68 (0.06)	0.68 (0.05)	NS

PSV = peak systolic velocity; EDV = end diastolic velocity; RI = resistivity index; NS = not significant.

between the time of the last cigarette smoked and the time of the CDI measurement was 30 to 60 minutes.

Blood flow velocity was measured by means of a Siemens Quantum 2000 (Siemens Albis AG, Zurich, Switzerland) using a 7.5 MHz linear phased array transducer. The transducer was applied gently to the closed eyelid using a coupling gel, and care was taken to avoid applying any pressure to the eye. During the examination, subjects were in the supine position, with the head tilted forward at about a 30° angle. The ophthalmic artery (OA), the central retinal artery (CRA) and vein (CRV), one lateral and one medial short posterior ciliary artery (LPCA and MPCA) were examined. If more than one PCA could be visualised, the velocity was measured in the larger one. The proximal and distal portions of the vessel were imaged to determine the Doppler flow angle. The ophthalmic artery can be traced nasally from the optic nerve after crossing it. Strong signals are routinely detectable at this side. When measuring the right OA, subjects are asked to look to the left, and vice versa. The CRA and the accompanying vein can be depicted within the anterior part of the optic nerve shadow, about 2–3 mm behind the surface of the disc. The CRV runs adjacent to the CRA and can be distinguished from the artery by the colour coding (flow away from the probe is encoded in blue) and by its Doppler spectrum with a continuous flow in systole and diastole. If the spectrum of the CRA is visualised, a simultaneous signal from the CRV is usually also displayed. Lateral and medial from the optic nerve shadow, the short posterior ciliary arteries can be depicted. Their locations are more variable than those of the other vessels. Because of their small size, it was not always possible to determine whether a coloured pixel on the image represents a single vessel. However, characteristic Doppler spectra can be obtained from the PCAs with higher diastolic flow velocities due to the low resistance in the choroid, which they supply. Peak systolic velocity (PSV), end diastolic velocity (EDV), and resistivity index (RI index) ((PSV − EDV)/PSV) were measured in the arteries. In the CRV the maximal (max) and minimal (min) blood flow velocities were measured. During the examination of about 20 minutes, systolic and diastolic blood pressure as well as heart rate were measured every 5 minutes.

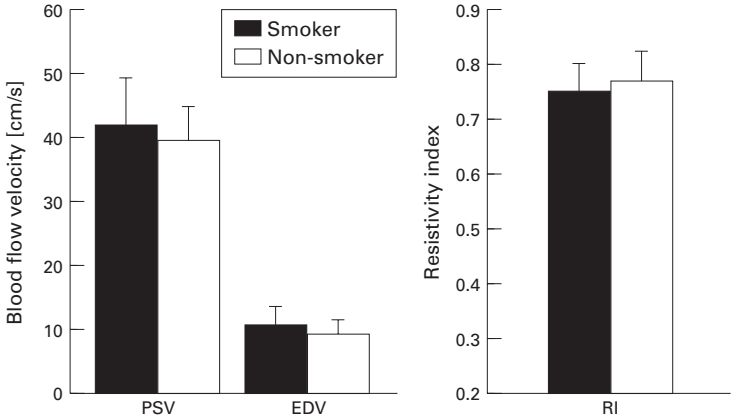

Figure 1 Mean (SD) of peak systolic (PSV), end diastolic (EDV) blood flow velocities and resistivity indices in the ophthalmic artery in smokers and non-smokers.

STATISTICAL ANALYSIS

Mean values and standard deviations were calculated for PSV, EDV, and the RI index in the arteries, and for max and min in the CRV. Blood flow velocity and RI index of smokers and non-smokers were compared by means of one way MANOVA (multivariable analysis of variance) and *t* tests.[24] The influence of sex, systolic blood pressure, diastolic blood pressure, and heart rate on the 14 variables were analysed by an analysis of covariance. The potential differences of the influence of the covariables on blood flow variables in smokers and non-smokers were tested by calculating the interactions.

Results

Forty six smokers and 189 non-smokers were included in this study. The patient characteristics are listed in Table 1. In the group of smokers the mean number of cigarettes smoked per day was 20 (SD 10) with a range of 5 to 50. The blood pressure was lower in smokers than in non-smokers. This difference was statistically significant both for the systolic ($p = 0.003$) and diastolic values ($p = 0.05$). Heart rate was slightly but not statistically significantly higher in smokers (Table 1).

The majority of mean values of PSV and EDV were higher in smokers than in non-smokers (Table 2). This difference was statistically significant in the OA (Fig 1) and LPCA.

Furthermore, the average minimal velocity in the CRV was significantly higher in smokers. The RI indices were the same or slightly lower in smokers. This difference was only statistically significant in the OA. *t* Tests confirmed the significance of the differences found with testing by a one way MANOVA. In smokers no statistically significant correlation was found among blood flow variables and age, blood pressure, and heart rate, nor had sex an influence. Similar results were obtained earlier in non-smokers.[25] No significant differences of the influence of the covariables on blood flow variables in smokers and non-smokers were revealed by calculating the interactions.

Discussion

Blood flow velocities tended to be higher in smokers. The effect of smoking was most pronounced in the OA. The differences were significant in the OA, LPCA, and CRV. The RI indices, a measure of vascular resistance, however, were not increased. In some vessels the RI indices were even lower in smokers than in non-smokers. How can we explain these observations? The smoke of a cigarette contains, among many other components, 2%–6% carbon monoxide. Smoking leads to an increase in carboxyhaemoglobin levels up to 5%–15% in smokers compared with 0.5% in non-smokers.[26] The elevated level of carboxyhaemoglobin has two consequences. Firstly, it reduces the available oxyhaemoglobin and, secondly, it changes the dissociation curve of oxyhaemoglobin, resulting in a reduction in oxygen transport into the tissues.[26] It is, therefore, conceivable that a relative oxygen deficit provokes regulatory effects, leading to downstream vasodilatation and an increase in blood flow velocity at the measuring site.

Smokers were considerably younger in this study. No significant correlation was found between blood flow variables and age in the smokers and non-smokers. When age correction was performed the statistically significant differences between the two groups did not change.

Smokers also had significantly lower blood pressure in the smoking free interval than did non-smokers under the same conditions during examination. These data may appear to be paradoxical because cigarette smoking elicits an increase in sympathoadrenergic tone, resulting in elevation of systemic blood pressure. It has been shown, however, that healthy cigarette smokers have an increased sensitivity to endogenous endothelium dependent and endothelium independent vasodilators.[27] Assuming that the repeated increase in adrenergic tone appearing with each cigarette smoked is counteracted by an augmented sensitivity to endogenous vasodilator stimuli, the lower blood pressure is reasonably explained. When comparing different groups of diseased or healthy subjects, future study designs should, therefore, take into account the differences between smokers and non-smokers.

The results of the present study show that chronic smoking increases blood flow velocities in the extraocular vessels. Therefore, smoking habits should be considered when interpreting results of CDI of the orbital vessels. It is also essential that the interval between measurements and the most recent cigarette is noted, because the acute effect of cigarette smoking persists for about 30 minutes.[9]

We thank Phillip Hendrickson, PhD, for correcting the manuscript.

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Br J Ophthalmol 1997 81: 133-135
doi: 10.1136/bjo.81.2.133