Cerebral Blood Flow and Cessation of Cigarette Smoking in Healthy Volunteers

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Abstract

Objective  The mechanisms by which cessation of cigarette smoking may improve regional cerebral blood flow (rCBF) and the details of the possible relationship remain unclear. Xenon-133 inhalation was used to determine rCBF in six smokers at baseline (during smoking) and again 6 and 9 years after they had quit smoking (quitter group). A control group of eight nonsmokers (nonsmokers group) underwent similar serial determinations.

Results  Regional CBF in quitters had decreased significantly after the 6 years, but improved significantly after 9 years, when abstinence had been maintained from 4 to 6 years. In the nonsmokers group rCBF did not change significantly over 9 years.

Conclusion  Cessation of cigarette smoking improves cerebral circulation, but this effect requires several years.

Key words: stroke, regression of atherosclerosis, blood pressure

Introduction

The number of smokers in Japan has been gradually decreasing. In October 1997, the percentage of smokers was 34.6% of the population over age 20; 56.1% of men and 14.5% of women were smokers. These percentages remain higher than in many other countries.

Cigarette smoking is the leading preventable cause of death. While coronary heart disease is considered one of the most important consequences of smoking, studies in some Western countries also have identified cigarette smoking as an important independent risk factor for both hemorrhagic and nonhemorrhagic stroke (1–3). However, this connection has not emerged in Japanese studies (4–7).

Long-term smoking habits are known to be significantly associated with reduction in regional cerebral blood flow (rCBF) (8–10), and smoking is known to accelerate cerebral atherosclerosis (8, 9). However, mechanisms relating cessation of cigarette smoking to improved rCBF remain unclear, and few reports have studied rCBF in the context of quitting cigarette smoking (11). In this study we examined the effects of quitting cigarette smoking on rCBF in normal adults.

Subjects and Methods

We initiated a brain health-screening program in 1982 at the Institute of Shimane Health Science with the goal of prevention of cerebrovascular diseases. The 67 normal men in this program were the subjects of a previous study (10). After the first examination, smokers were asked to quit smoking for their health. Among these individuals, 17 underwent three rCBF determinations, at baseline (during smoking), at 6 years, and at 9 years. Among the 17, 6 subjects (58.3±9.7 years; mean age first examination±SD, range, 47 to 74) quit smoking between the baseline and 6th-year determinations. A control group of 8 nonsmokers (57.8±8.4 years; range, 48 to 75) underwent the same three determinations. The remaining 3 subjects sometimes smoked, and thus were excluded from this study. Past histories included hypertension (2 quitters and 2 nonsmokers). The duration of smoking cessation among quitters was 5.3±2.4 years (4 to 6). At the first determination, the Brinkman’s smoking index of the quitters was at least 201 (years of smoking history×number of cigarettes per day). Neurological examinations revealed no abnormalities in any subject. Informed consent was obtained from each subject, in accordance with institutional guidelines.

Regional CBF was measured by the xenon-133 (133Xe) inhalation method as subjects rested with their eyes closed. This noninvasive method has been shown to be reliable and reproducible (12). Eight collimated probes were placed on the skull surface of each cerebral hemisphere. After a 5-min rest period during which background gamma activity was measured, subjects inhaled approximately 3 mCi/l of 133Xe gas and the activity of the isotope was monitored. End-tidal 133Xe activity was also measured to correct recirculation to the brain. The rCBF value (F1 value) was calculated by Fourier’s method, and the
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Mean rCBF was used in this study.

Mean arterial blood pressure, hematocrit and serum lipid concentrations (total cholesterol and HDL cholesterol) were determined on the same day as rCBF.

Data were analyzed by unpaired and paired t tests. A p value of <0.05 was considered as statistically significant.

Results

Figure 1 shows rCBF over 9 years in quitters and nonsmokers. Regional CBF in quitters significantly decreased from 60.3±10.1 ml/100 g/min at baseline to 46.5±6.5 ml/100 g/min at 6 years (p=0.016), but improved significantly to 62.3±7.4 ml/100 g/min at 9 years (vs rCBF at 6 years, p=0.008). On the other hand, rCBF in the nonsmoker group did not change over 9 years (72.3±9.6 ml/100 g/min at baseline; 69.0±9.9 at 6 years; and 70.4±14.6 at 9 years). Regional CBF in quitters was significantly lower than in nonsmokers at baseline (p=0.044) and at 6 years (p=0.001), but did not differ significantly from rCBF in nonsmokers at 9 years.

Table 1 shows differences in blood pressure, hematocrit, total cholesterol, and HDL cholesterol between the two groups. Mean arterial blood pressure in quitters decreased significantly over 9 years. In nonsmokers, mean arterial blood pressure did not show any significant changes over 9 years.

Discussion

Although some investigators (13–15) have reported that rCBF is increased by smoking, Wechsler (16) concluded that rCBF is not affected by smoking. On the other hand, studies by Rogers et al (8) and Kubota et al (9) as well as our previous study (10) found rCBF in long-term cigarette smokers to be significantly lower than in nonsmokers. Rogers et al (8) measured rCBF using 133Xe inhalation, and revealed that long-term cigarette smokers show less cerebral vasomotor reactivity to either 100% oxygen or 5% CO2 inhalation than controls. They surmised that long-term cigarette smoking enhances cerebral atherogenesis. Kubota et al (9) found significantly higher total cholesterol and significantly lower HDL cholesterol concentrations in smokers than nonsmokers. They also speculated that decreased CBF in smokers most likely results from advanced cerebrovascular atherosclerosis. Although no consensus has been reached on cerebral arteriosclerosis in relation to cigarette smoking, some studies have provided highly convincing evidence of a relationship. For example, Whisnant et al (17)
reported that in patients undergoing carotid arteriography at or before 60 years of age, the likelihood of severe carotid atherosclerosis was approximately 3.5 times higher for a person who had smoked for 40 years than in subjects who had never smoked.

Clinical trials to assess the effect of the cessation of smoking on the risk of stroke have been hampered by methodologic problems. Although there is no conclusive evidence from such trials, observational studies comparing former and current smokers suggest that quitting is highly beneficial.

The rapid reduction in the risk of stroke after quitting is not consistent with the notion that cigarette smoking acts chiefly to promote atherosclerosis (2). This may occur by increasing fibrinogen levels in the blood and by adversely affecting hemorheologic factors that promote thrombus formation. This may be one of the reasons why decreasing fibrinogen levels in the blood after quitting causes rCBF to increase. In contrast, Rogers et al (11) demonstrated a significant linear increase in rCBF over 1 year as a relationship between rCBF and cessation of cigarette smoking. Such gradual changes suggest that structural alterations are responsible for increases in rCBF, since pharmacologic effects would be expected to occur within a much shorter period (11). The follow-up period in the present study was considerably longer than that in the study of Rogers et al (11), and rCBF of quitters was lower than that of non-smokers. Continued cessation may result in beneficial changes in arterial smooth muscle or even regression of atherosclerosis in the circle of Willis and its main branches. The present study suggests that recovery of rCBF may require a long period to become apparent after cessation of cigarette smoking. This is the reason why it took a long time to recover rCBF in smokers who continued smoking for over twenty years in this study. In our study, it was suggested that cerebral artery phenomena preceded an increase or recovery of rCBF.

In an autopsy study of atherosclerosis in the circle of Willis and its major branches (18) atherosclerosis in large arteries was found to be consistently related to age, diastolic blood pressure, and serum cholesterol, and inversely to height. Weak trends toward association were also found for increased serum glucose concentration, increasing cigarette consumption, and decreasing alcohol intake. In small arteries, atherosclerosis was associated with increasing diastolic blood pressure and serum triglyceride concentration. In a prospective study in the town of Hisayama (19), arteriosclerosis in the circle of Willis and its main branches was significantly associated with increased systolic and diastolic blood pressure. Since the present study showed a significant decrease in blood pressure with abstention from cigarette smoking, this change might be responsible for eventual improvement of rCBF.

A meta-analysis of smaller studies has estimated the relative risk of stroke associated with cigarette smoking to be 1.5 (3). A 7-year program that reduces smoking prevalence by 1% per year should result in a total of 34,261±9,133 fewer strokes (20). Another report showed that smoking cessation causes the risk of stroke to decrease rapidly, becoming that of a nonsmoker between 2 to 5 years after cessation (2). Aids to stop smoking, such as counseling, nicotine chewing gum, or skin patches, may be necessary. In conclusion, cessation of cigarette smoking has a beneficial long-term effect on blood pressure and rCBF, and may help to prevent stroke.

References