54) EFFECT OF SMOKING ON CHOLESTEROL METABOLISM IN SPONTANEOUSLY HYPERTENSIVE RATS (SHR). Nobuyuki Utagawa, Masahiro Kihara, Masayuki Mano, Yasuo Nara, Ryoichi Horie, and Yukio Yamori. Department of Pathology, Shimane Medical University, Izumo 693, Japan.

Introduction

A body of evidence from clinical or epidemiological studies has been strongly suggestive of the causal relationship between cigarette smoking and the development of atheromatous diseases. Although arterial wall hypoxia due to the elevated level of carboxyhemoglobin (CO-Hb), altered lipoprotein profile, increased platelet aggregation and some hematological changes have been so far proposed as possible mechanisms involved, the definite mechanisms linking smoking to such diseases are still unclear especially because experimental evidence from studies on the effect of chronic smoking has been rather scarce due to the practical difficulty in conducting chronic smoking exposure to experimental animals. We have therefore tried to make a suitable system for a long-term smoking exposure to rats.

In the present study, spontaneously hypertensive rats (SHR) and Wistar-Kyoto rats (WKY) were subjected to chronic smoking exposure using the new system that we recently developed in an attempt to examine the effect of smoking on cholesterol metabolism and its possible modification by some genetic-predisposition.

Materials and Methods

Fifteen male SHR and 15 WKY at the age of 2 months were studied. Rats from each strain were equally divided into the following three groups: (1) normal diet (ND) without smoking, (2) high-fat-cholesterol diet (HFCD: 20% suet, 5% cholesterol and 2% bile acid) and (3) HFCD with smoking. ND was fed ad libitum but HFCD was given 14g per day for each rat. Tap water containing 1% NaCl was given freely to all groups to facilitate cholesterol absorption from the intestine. Rats were exposed to smoking by using a modified Humberg II type smoking machine a cigarette per rat at one time, every 2 hours from 9:00 a.m. and six times in total everyday. On the 9th day, all rats were sacrificed by decapitation after over night fasting and blood was analyzed for total cholesterol (TC), HDL-cholesterol (HDL-C) and atherogenic index (AI: TC-HDL-C/HDL-C).

Results

(1) There was no difference in TC between SHR and WKY fed ND. TC was elevated equally by about 33 mg/dl in SHR and WKY fed HFCD compared to their counterparts on ND. Smoking aggravated the lipidemia in SHR (96.4 ± 20.7 mg/dl, $M \pm SD$) but attenuated in WKY (57.2 ± 15.3). The difference was statistically significant ($p < 0.01$). (2) AI showed similar change. Smoking enhanced the pre-existing difference in AI between SHR and WKY on HFCD. (3) HDL-C level was consistently higher in SHR groups than in WKY groups and showed neither significant change by HFCD nor by smoking.

Discussion

The present study showed a contrasting difference between SHR and WKY in the response of cholesterol metabolism to smoking. Since HDL-C was unaffected by smoking, such a difference should be due to the difference in the change of VLDL and/or LDL fraction of the lipoprotein profile. Although the mechanism is unknown, the present result suggests that the effect of smoking on lipid metabolism may be different by some genetic predisposition related to hypertension.

(This study was supported by a grant from Japan Tobacco & Salt Public Corporation.)