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Occupational exposure to low concentrations of carbon disulfide as a risk factor for hypercholesterolaemia

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Abstract Objective: The objective of this study was to investigate the effect of occupational exposure to carbon disulfide (CS$_2$) concentrations below threshold limit value (TLV)-time-weighted average (TWA) (31 mg/m$^3$) on total cholesterol, blood pressure and the prevalence of coronary heart disease (CHD). Methods: A cross-sectional study involving 141 viscose rayon workers (64 men), and 141 age- and gender-matched controls without occupational contact with noxious chemicals, was carried out. The probability for CHD was determined by means of the WHO questionnaire and was 12-lead electrocardiography-coded using Minnesota criteria. Blood pressure was measured by the standardized method of the WHO and blood was examined for total cholesterol. A cumulative exposure index (CS$_2$ index) was calculated for each worker by multiplying the number of years held in a particular job, by the CS$_2$ concentrations in that job-environment. According to the CS$_2$ index, the exposed workers were distributed into two groups: group 1 (CS$_2$ index <100) and group 2 (CS$_2$ index ≥100). Results: Depending on the job and specific work place the CS$_2$ concentrations were between 1 and 30 mg/m$^3$. Cholesterol levels were significantly higher in the exposed group (4.9 ± 0.7) compared with the controls (4.6 ± 0.7). Adjustment for age, smoking, body-mass index (BMI) and gender showed the significant effect of the CS$_2$ index on blood pressure and CHD prevalence was found. Conclusions: The results of our study show that occupational exposure to CS$_2$ concentrations below 31 mg/m$^3$ and a CS$_2$ index >100 may increase total cholesterol. Our results imply that even the CS$_2$ concentrations below TLV-TWA may produce morbidity changes, and suggest the mechanism of the effect of CS$_2$, leading to lipid metabolism disturbances and acceleration of atherosclerosis.

Key words: Carbon disulfide · Cholesterol · Blood pressure · Coronary heart disease · Occupational exposure

Introduction

It has become evident from epidemiological studies that occupational exposure to carbon disulfide (CS$_2$) increases the risk for coronary heart disease (CHD). Studies from the United Kingdom [18, 20], United States [9] Finland [10] and others [2, 13, 25] have demonstrated increased mortality from CHD in viscose rayon workers exposed for many years to high CS$_2$ concentrations. In contrast to these findings, a retrospective study in a Dutch viscose textile plant showed that prolonged exposure to relatively low CS$_2$ concentrations (average exposure of 22 mg/m$^3$) increased the risk for cardiovascular mortality, which did not decrease after cessation of exposure [17]. Increases in the prevalence of electrocardiographic (ECG) abnormalities [8], clinical coronary heart disease [11], high blood pressure [4, 21] and lipid metabolism disturbances [4, 21] in CS$_2$-exposed workers have been reported. However, in several studies, especially at low levels of exposure, no significant effects on blood pressure, impaired lipid metabolism and CHD prevalence were observed [3, 6, 12, 16]. Currently, one of the basic questions that can be asked is about the effect of low CS$_2$ concentrations on lipid metabolism, blood pressure and CHD. A statistical analysis of the NIOSH CS$_2$-exposure database was conducted for the purpose...
of establishing a benchmark concentration (BMC) for CS$_2$. A BMC in this analysis was the exposure concentration of CS$_2$ corresponding to an increase in cardiovascular endpoints relative to a background level. None of the CHD risk factors has a statistically significant relationship to exposure to CS$_2$ concentrations below 47.7 mg/m$^3$ (15.4 ppm) [14]. Based on the findings of the cardiovascular effects in workers exposed to CS$_2$, the American Conference of Governmental Industrial Hygienists (ACGIH) proposed as appropriate, a threshold limit value time-weighted average (TLV-TWA) of 31 mg/m$^3$ (10 ppm) [19].

Objective

The objective of this study was to investigate whether occupational exposure to CS$_2$ concentrations below TLV-TWA (31 mg/m$^3$) influences total cholesterol, blood pressure and the prevalence of CHD, and if so, to establish a non-observed adverse effect level.

Subjects and methods

Subjects

The study had a cross-sectional design. The exposed group consisted of 141 workers (64 men) aged between 20 and 60 years with a minimum of 1 year’s work in a viscoso rayon plant. The reference group was 141 age and gender-matched plastic industry workers without occupational contact with noxious chemicals. All workers were strongly recommended to participate in the study and the participation rate was 94.3% in exposed and 90.1% in non-exposed subjects.

Medical examinations

Medical and job history were documented using a standardized questionnaire, directly administered by the interviewer on the day of the screening visit. Physical examination of the heart and blood vessels, and routine 12-lead ECGs at rest were performed. Blood pressure was measured with the subject in a sitting position after 5 min rest, by one physician using a random zero aneroid sphygmomanometer. Average values from the three measurements at intervals of 5 min were used for the analysis. The degree of arterial hypertension was determined according to the classification of the American Heart Association (JNC VI, 1997). Arterial hypertension was defined as systolic blood pressure (SBP) ≥140 mmHg and/or diastolic blood pressure (DBP) ≥90 mmHg or as the subject taking antihypertensive medication [7]. Fasting, morning venous blood samples were collected and analyzed for total cholesterol. The “elevated cholesterol” was defined as total cholesterol >5.17 mmol/l. Body weight and height were measured with the subject wearing light indoor clothes without shoes, and body-mass index (BMI) was calculated as $\text{weight (kg)} / \text{height (m)}^2$. The probability for CHD was determined by means of the WHO standardized cardiovascular questionnaire and the electrocardiograms coded on the basis of the Minnesota code [15]. All tracings were coded separately by two trained physicians with no knowledge of exposure status of the subject. The differences were discussed and a consensus reached, or a third supervisor adjudicated the differences. Codes I1-3 (abnormal Q/ QS waves), IV1-3 (S-T junction and segment depression), VI1-3 (abnormal T-wave) and VII1 (complete left bundle branch block) were considered as possible signs of ischaemia. CHD was considered possibly to be present when either angina or infarction were recorded in the questionnaire, or/and signs of possible ischaemia were seen on the ECG. Subjects with symptomatic hypertension (two of the exposed and one of the non-exposed) and diabetes (one of the exposed and three of the non-exposed) were excluded from the study.

Exposure assessment

In this study, CS$_2$ was the only chemical present in the working environment that was considered to be important to the investigated cardiovascular outcomes. Concentrations of CS$_2$ were assessed using stationary measurements and personal sampling methods. Personal breathing zone samples from some workers within each job category were collected with NIOSH type 100/50 mg charcoal absorption tubes at a flow rate of up to 50 ml/min using calibrated Gillian low-flow sampling pumps. Charcoal samples were desorbed with toluene and analyzed by gas chromatography according to NIOSH method 1600 [5].

The personal CS$_2$ exposure was assessed in three ways:

1. As binary (exposed persons vs. non-exposed persons)
2. As cumulative exposure index (CS$_2$ index), in order to model exposure as a continuous variable; it was calculated for each worker by multiplying the number of years at a particular job in the viscoso factory by the average CS$_2$ concentrations for that job
3. As different exposure groups: according to the degree of personal exposure, the exposed workers were allocated to two groups: group 1 (CS$_2$ index <100) and group 2 (CS$_2$ index ≥100).

Statistical analysis

The equality of distributions of baseline characteristics and cardiovascular outcomes between the exposed and the controls were evaluated using the non-parametric Kruskal–Wallis or Mann–Whitney tests for continuous variables and $\chi^2$ analysis, or Fisher’s exact test for proportions. In order to eliminate possible confounding factors, we carried out multiple linear and multiple logistic regression. Potential confounders for the investigated cardiovascular parameters were age, smoking-status (pack-years), gender and BMI. Multiple linear regression models were fitted to assess the effect of the CS$_2$ index on the quantitative cardiovascular parameters (SBP, DBP and cholesterol). Logistic regression was applied to evaluate the relationship between the risk of hypercholesterolaemia, hypertension and CHD (dependent variables) and CS$_2$ exposure (independent variable). Blood pressure and total cholesterol are major risk factors for CHD and were not considered as determinants in the statistical analysis, because they may represent mechanisms through which CS$_2$ causes CHD. The level of significance was accepted to be at 0.05. All calculations were carried out with SPSS 7.5 for Windows statistical software.

Results

The results showed that the current personal exposure for the different job categories ranged from 1 to 30 mg/m$^3$. A total of 70 subjects was in group 1 (CS$_2$ index <100), while 71 subjects were in group 2 (CS$_2$ index ≥100).

Some personal characteristics of the population are shown in Table 1. No significant differences were found between exposed and controls in relation to their BMI and smoking habits. A total of 45.4% of the exposed and the controls was male. The mean age was 42.6 (±7.3) years in the exposed and 42.8 (±8.4) in the controls. A total of 44.7% of the exposed and 48.9% of the non-exposed were smokers.