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Health evaluation of employees occupationally exposed to methylene chloride: twenty-four hour electrocardiographic monitoring

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Health evaluation of employees occupationally exposed to methylene chloride

Twenty-four hour electrocardiographic monitoring

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OTT MG, SKORY LK, HOLDER BB, BRONSON JM, WILLIAMS PR. Health evaluation of employees occupationally exposed to methylene chloride: Twenty-four hour electrocardiographic monitoring. *Scand j work environ health* 9 (1983): suppl 1, 26–30. Reports concerning the potential of methylene chloride and related chemicals to increase cardiac sensitivity to epinephrine and concerns stemming from the metabolism of methylene chloride to form carboxyhemoglobin prompted interest in the electrocardiographic monitoring of men with methylene chloride exposure. Fifty employees of two fiber production plants were selected for study, 24 of whom were occupationally exposed to methylene chloride. All the participants were white males between the ages of 37 and 63 years. Eleven of the men had reported a history of heart disease. Under the conditions of this study, neither an increase in ventricular or supraventricular ectopic activity nor episodic ST-segment depression was associated with exposure to methylene chloride that ranged from a time-weighted average of 60 ppm to a time-weighted-average of approximately 475 ppm.

Key terms: holter monitoring, carboxyhemoglobin.

This is the fourth in a series of health surveillance reports on fiber production employees exposed to solvents in two separate plants. In one of the plants, methylene chloride ($MeCl_2$) was a major component of the solvent system used to dissolve cellulose triacetate. In this paper, we present the results of 24-h electrocardiographic monitoring of 50 white male employees from the two plants.

A number of commonly used industrial solvents, including both unsubstituted and halogenated hydrocarbons, have been shown to increase cardiac sensitivity to epinephrine (3, 12). Other solvents, such as ethyl ether, ethyl alcohol, and acetone have shown comparatively little, if any, activity in increasing the electric irritability of cardiac muscle (7). In regard to methylene chloride, cardiac sensitization was observed in one dog study at concentrations of 2.4 % in air but was not seen in a second study at concentrations of about 2 % (4, 12).

An additional concern stems from the presence of increased blood carboxyhemoglobin from methylene chloride metabolism. In monkeys, increased vulnerability to induced fibrillation has been demonstrated with carbon monoxide exposures sufficient to produce 5 to 10 % carboxyhemoglobin saturations (6). Similar effects may extend to man (14). Knelsen reported abnormal electrocardiograms in 7 of 26 men, aged 41 to 60 years, upon exposure to 100 ppm of carbon monoxide (5–9 % carboxyhemoglobin) (8). Arrhythmias were observed in two of these men, but not in 12

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men under the age of 40. Furthermore, two experimental studies have been reported in which low levels of carboxyhemoglobin (2 to 5 %) derived from direct carbon monoxide exposure were associated with decreased time to onset and increased duration of angina during exercise (1, 2). ST-segment depression was also frequently observed in connection with the onset of angina. It should be noted that all the patients participating in these studies had suffered from stable angina pectoris.

The occurrence of a fatal acute myocardial infarction associated with paint stripping has also been reported for a 66-year-old man. (13). The formulation used to remove the paint was labeled as containing 80 % methylene chloride; however no data were given from which to estimate exposure.

The objective of this study was to determine whether occupational exposure to methylene chloride in the present work setting resulted in increased ventricular or supraventricular ectopic activity or ST-segment depression.

Methods

The 24-hour electrocardiographic monitoring was conducted with two Avionics mini holter recorders, model 445. The men (24 from a plant with methylene chloride exposure and 26 from a reference plant) were a subset of the 51 exposed white men and the 114 white referents who were 35 or more years of age and who had participated in a prior health evaluation (11). Preference was given to selecting older individuals and those with a history of heart disease under the presumption that these individuals would be the most likely to demonstrate positive findings.

Earlier reported environmental surveys (11) indicated that one individual was employed in a work area in which typical methylene chloride exposure was an 8-h time-weighted average (TWA) of 60 ppm, ten men were employed in areas in which typical exposure was a TWA of 140 ppm, four men were employed in work areas in which typical exposure was a TWA of 280 ppm, and nine men were employed in work areas in which typical exposure was a TWA of 475 ppm.

The procedure for carrying out the monitoring consisted of attaching and testing the recorder in the Medical Department, after having instructed the employee in the purposes and procedures of the study. The recorder was calibrated prior to each use with an Avionics 1-millivolt calibrator, model 356B. Each volunteer was asked to keep a diary of his activities during the 24-h period and record any pain, shortness of breath, or other discomfort experienced during the day. In two of three instances in which tapes did not record properly, a second monitoring session was scheduled and acceptable tapes were obtained. The 24-h tape and diary were sent to Cardio-Bionic-Scanning-Inc for computer analysis of the tape, visual scanning by a technician, and interpretation by a cardiologist. Copies of the subsequent reports provided the basic information for our analyses. Ventricular ectopic activity was classified according to the Lown grading system: no ventricular ectopic activity; occasional, isolated ventricular premature beats (VPB); frequent VPB; multiform VPB; and repetitive VPB (9). Supraventricular ectopic activity was classified as to the presence or absence of atrial premature beats, atrial couplets and atrial tachycardia. ST-T wave changes were classified as ischemic if there was a $\geq$ 1-mm horizontal or down-sloping ST-segment depression for $\geq$ 0.08 s in at least three consecutive beats (5). Analysis of the hourly rate of ventricular ectopic activity in relation to solvent exposure was also performed. In essence, the individual was his own control and ventricular ectopic activity was compared during work hours versus nonwork hours.

Characteristics of the population

Characteristics of the white male participants from both plants under study are summarized in table 1. Although the age range of the participants was nearly the same for the two plants, there was a four-year difference in average age, referents being older. There were also more men from the reference plant with either a positive smoking history or a reported history of heart disease. There were no statistical differences between the height/weight distribution, blood pressure, alcohol history, or cholesterol level of the two populations.

Table 1. Characteristics of the participants, all of whom were white and male.

Characteristics	Exposed employees	Referents
Number of men	24	26
Age (years)		
Mean	51.5	55.4
Range	37–62	38–63
Smoking history		
Never smoked	5	1
Past smoker	9	10
Current smoker		
< 1 pack/d	1	1
≥ 1 pack/d	9	14
Diastolic blood pressure > 100 mm Hg[a]	4	4
Reported history of heart disease	3	8
Under medication for cardiovascular disease or hypertension	5	6

[a] 1 mm Hg = 133.3 Pa.

Results

For the combined group of 50 participants, the percentage of men with ventricular ectopic activity increased with age and history of heart disease. Under the age of 45, 33 % (2 of 6) of the men experienced ventricular ectopic activity, whereas over the age of 44, 77 % (34 of 44) of the men experienced this symptom. All 11 men with a history of heart disease were found to have ventricular ectopic activity. These men also had a greater likelihood of being classified as having multiform or repetitive ventricular premature beats (4 of 11 vs 4 of 39 among men not reporting a history of heart disease). A comparison of ventricular ectopic activity by plant indicated a similar distribution for the total groups, as well as for the subgroups of those persons not reporting a history of heart disease (table 2).

A comparison of supraventricular ectopic activity did not reveal differences between the two plants either. Of the 50 men studied, only four referents and two exposed employees did not show at least one isolated supraventricular ectopic beat during the monitoring period. Supraventricular couplets were observed among 6 of the 26 referents and 6 of the 24 exposed employees. Supraventricular tachycardia, including junctional tachycardia, was observed in four exposed employees and six referents.

Table 3 summarizes the distribution of ventricular ectopic activity per hour during work, sleep, and nonwork awake hours for the two groups combined and separately. The three time periods were a duration of approximately 8 h each. A Wilcoxon Rank Sum test was used to compare the ventricular ectopic activity (work minus nonwork awake hours and work minus sleep hours) between the two plants, each man thus serving as his own control. In neither comparison was the relative difference between the two groups statistically different from zero ($p > 0.1$, two-sided test).

For three of the 50 individuals, positive ST-T changes were reported. Of these positives, which were suggestive of ischemic heart disease, two occurred in referents and one in an exposed employee. The exposed individual with ST-segment depression had had no ventricular ectopic activity. The ST-segment depression occurred during a period of sinus tachycardia, while the person was riding a bicycle. For one of the two referents with ST-segment depression, the events occurred during periods of sinus tachycardia, once with chest pain reported after walking up steps. During a second episode, no symptoms were reported. The second referent experienced ST-T wave changes throughout a period of supraventricular tachycardia.

Discussion

The rationale for choosing continuous ambulatory monitoring was that it might detect electrocardiographic changes associated with particular exposures whenever they occur, however short-term. However, the use of this method is not without limitations. For example, marked variability in ventricular premature depolarizations between days for the same individual and between individuals may decrease the sensitivity of the procedure (10). Thus there were sample size limitations to the study, both in terms of the number of men monitored and in terms of the number of monitoring sessions per individual.

Given these limitations, neither increased ventricular or supraventricular ectopic activity nor increased episodic ST-segment depression was found to be

associated with methylene chloride exposure. This lack of positive findings is consistent with cardiac sensitization studies in that the present methylene chloride exposures were much lower than those shown experimentally to sensitize the myocardium (4, 12).

The present study did not apparently have the resolving power of investigations conducted with angina patients subjected to controlled exercise regimens. In at least two such studies, low-level carbon monoxide exposure led to electrocardiographic abnormalities, an earlier onset of angina, and ST-segment depression (1, 2). For many employees, the carboxyhemoglobin saturations, derived from methylene chloride exposure in the present work environment, were comparable to or greater than those associated with electrocardiographic changes in the controlled studies (1, 2), even when the carbon monoxide derived

Table 2. Summary of the ventricular ectopic activity by study group.

Grading system	Exposed employees		Referents	
	N	%	N	%
Including men with a history of heart disease				
No ventricular ectopic activity	8	33	6	23
< 30 [maximum ventricular premature beats (VPB) within any 1 h]	11	46	14	54
≥ 30 (maximum VPB within any 1 h)	–	0	1	4
Multiform VPB	4	17	4	15
Repetitive VPB	1	4	1	4
Excluding men with a history of heart disease				
No ventricular ectopic activity	8	38	6	33
< 30 (maximum VPB within any 1 h)	10	48	9	50
≥ 30 (maximum VPB within any 1 h)	–	0	1	6
Multiform VPB	2	10	2	11
Repetitive VPB	1	5	–	0

Table 3. Distribution of ventricular ectopic beats by daily activity (work, nonwork awake, sleep).

Ventricular ectopic beats (number/h)	Activity					
	Work		Nonwork awake		Sleep	
	N	%	N	%	N	%
Exposed group						
0	11	46	11	46	14	58
< 1	5	21	6	25	4	17
1–9	5	21	4	17	3	13
10–19	–	0	–	0	2	4
≥ 20	3	13	3	13	1	4
Reference group						
0	10	38	6	23	13	50
< 1	8	31	9	35	7	27
1–9	3	12	8	31	4	15
10–19	2	8	–	0	–	0
≥ 20	3	12	3	12	2	8
Exposed and reference groups combined						
0	21	42	17	34	27	54
< 1	13	26	15	30	11	22
1–9	8	16	12	24	7	14
10–19	2	4	–	0	2	4
≥ 20	6	12	6	12	3	6

from cigarette smoke is not taken into consideration. However, in our study no attempt was made to control the exercise level or to exclude employees without known ischemic heart disease. It appears then that the critical factors in obtaining positive responses are the choice of subjects (ie, inclusion of patients with coronary disease), the exercise regimen, and the tighter controls possible with laboratory studies.

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