Methylene chloride exposure and carboxyhemoglobin levels in cabinetmakers

Abstract

Methylene chloride (MeCl₂) is a clear colorless volatile sweet smelling lipophilic solvent used as a constituent of wood vanishes and paints. Human exposure is mainly due to inhalation and its biotransformation by the hepatic mixed function oxidases (MFO) leads to formation of carbon monoxide (CO). Simultaneous exposure to MeCl₂ and increased ambient CO results in undesirably increased carboxyhemoglobin (COHb) formation, which predisposes to carboxyhemoglobinemia with the central nervous system as the primary target organ of toxicity. In this study, ambient CO levels were determined using a CO personal monitor in different parts of Ibadan Nigeria and work place microenvironment of 50 Cabinet makers (test group) and 50 volunteer (control) in non-furniture making occupations. Mann Whitney U and Kruskal Wallis were the statistical methods of analysis used. Questionnaires were administered to both groups carboxyhaemoglobin levels were determined in venous blood drawn from individuals in the two groups by differential spectrophotometric method. Ambient CO levels in Ibadan were observed to be between 4 and 52 ppm with a mean of 20 ppm. Work environment CO levels were significantly higher in test subjects than controls at 5.2 ± 1.08 ppm and 2.08 ± 0.91 ppm respectively (P<0.001). COHb in cabinetmakers with mean working hours of 9.48 ± 2.9 per day was 3.95 ± 1.35 (‰) while that of controls with mean working hours of 8.0 ± 0.8 per day was 2.08 ± 0.91 ppm (P<0.001). Smoking however did not significantly affect the COHb levels within the two groups (P>0.05).

It is therefore imperative to substitute MeCl₂ for safer chemicals in wood vanish and paints and the use of protective gas masks and adequate ventilation should be mandatory whenever MeCl₂ is used.

Key words: Carbon monoxide, carboxyhaemoglobin, methylene chloride

INTRODUCTION

Methylene chloride (MeCl₂), also known as dichloromethane (DCM), methylene dichloride, methylene bichloride (CH₂Cl₂) is a chlorinated hydrocarbon of relatively low flash point, widely used in modern industry as a solvent for cellulose esters, fats, oils, resins and rubber. It forms a large proportion of certain proprietary paint removers and has also been used in the paint trade to raise the flash points of lacquers.[4]

MeCl₂ is a volatile, clear, colorless, hypophilic solvent. It has a mild sweet odor with an olfactory threshold of 100 - 300 ppm.[2]

It is also an anesthetic with a pleasant chloroform-like smell, slightly more toxic and irritant them chloroform.[2]

The liver is the primary site of metabolism, where significant amount are bio-transformed to carbon monoxide (CO).[3]

The primary target organ of methylene chloride toxicity is the central nervous system (CNS).[4,5]

These effect results from both direct solvent related narcosis and endogenous promotion of CO with subsequent carboxyhemoglobin (COHb) formation.[6-8]

Human subjects exposed to concentration of 550 ppm or less for one hour (1 hr.) have COHb levels of 1-4%. These levels increased to an average of 10% saturation within one hour after exposure to 1000 ppm for two hours.[9] COHb in excess of 10% was reported following exposure to 250 ppm of CO for 7.5 hours. [10]

If CO is inhaled from either the environment or from tobacco smoke; this exogenous CO exposure leads to additional COHb formation in additive fashion.[10] The most serious manifestations of MeCl₂ poisoning are headache and nausea in the
healthy and sufficient cardiovascular stress in the patient with coronary heart disease to cause cardiac ischemia and unconsciousness, which could be fatal.[9,11]

Level of COHb in the blood following exposure to MeCl₂ are both dose and times-dependent.

Human exposure to MeCl₂ is mainly due to inhalation and it is usually occupational in nature.[12] MeCl₂ has a wide variety of application and these include; cleaning, degreasing, paint and vanish thinning, manufacturing of synthetic fibers and plastic, uses as aerosol propellant, blowing agent for food and spices uses as grain fumigant low pressure refrigerant uses in certain inks, adhesives, pharmaceuticals and photographic films. It has been estimated that more than a million people are at risk of occupational exposure.

Physical exercise performed during exposure to MeCl₂ will produce higher blood - carboxyhaemoglobin levels than those found in sedentary workers.[13,14] Under a moderate workload, an exposure to 10 ppm for 7.5 hours may cause a COHb saturation of about 5% at the end of the exposure period.[14] Other factors, including smoking and exposure to combustion and automobile exhaust is expected to increase COHb levels. Symptoms of CO toxicity and poisoning include: loss of consciousness, neurological abnormalities, myocardial ischemia, pulmonary edema, metabolic acidosis, headache, nausea and delayed neuropsychological features [Figure 1].[15]

This study was to assess the extent of risk of the use of MeCl₂ coupled with the ambient CO level in the environment.

MATERIALS AND METHODS

Chemicals and instrument
Ammonia solution, sodium dithonite (Na₂S₂O₄) reagent grade, formic acid (HCOOH) and conc sulphuric acid (H₂SO₄) were obtained from BDH, CO personal monitor was obtained from Crowncon U.K. and UV-Visible spectrophotometer from Unipath.

Subjects
Fifty cabinetmakers were recruited for the study and the benefits and the importance of the study were duly explained to them in English and Yoruba (Local) languages.

Fifty age-matched individuals who were students and workers within the University College Hospital, Ibadan, Nigeria were recruited as controls.

Smokers were not included in the study to reduce confounding factors.

Questionnaire
Semi-structured interviewer administered questionnaire were completed by the 50 cabinet workers and 50 control subjects. The questionnaire was designed to address demographic features, common health problems. Social habits, work history and work habits.

Blood sample
Blood samples were collected by venepunctive from both the subjects under study and the controls. 5 ml of blood was collected into a lithium heparin anti-coagulated bottles and immediately tightly covered to prevent interference of atmospheric oxygen with the carboxyhemoglobin to be estimated. The samples were estimated for carboxyhemoglobin within two hours of sample collection.

Determination of carboxyhaemoglobin levels
Carboxyhaemoglobin levels in the blood samples were determined by the differential spectrophotometric method of Zijlstrar and Van Kampen.[16]

Preparation of calibration curve

- 0.1 ml of blood from a control subject was mixed with 20 ml of 0.1% ammonia solution and divided into two equal lots.
- To each lot, 20 mg Na₂S₂O₄ was added to achieve 100% Hb saturation.
- Through one of the lots pure CO formed by heating HCOH (formic acid and H₂SO₄) allowed to bubble slowly for 2 minutes to give 100% HbCO solutions.
- Both samples were then measured at wavelength of 538 and 578, using 1.00 cm Cuvettes and a slit width of 0.02 mm spectrophotometer.
- The reading was carried out within 10 mm of the addition of Na₂S₂O₄.
- Calibration curve of absorbance ratio. A₅₃₈/A₅₇₈ against percentage of COHb saturation was plotted on the graph.

Procedure for COHb estimation
0.1 ml blood was mixed with 20 ml of 0.1% ammonia solution. 20 mg of sodium dithionite (Na2S2O4) was added to convert HbO2 to Hb. The absorbance was recorded at a wavelength of 538 and 578 nm (isobestic wavelength) using a spectrophotometer. The measurements were carried out within 10 minutes of the addition of Na2S2O4. The percentage COHb saturation was determined from the calibration curve.

Ambient carbon monoxide estimation

Ambient carbon monoxide levels were determined on weekly basis for six weeks in six different areas of Ibadan metropolis selected by quota sampling. These include Molete in South-west (SW) local government, Dugbe, in the North-west (NW) local government, Eleyele in the North-west (NWII) local government, Eleta in South-East (SE) local government, University College Hospital Compound, Mokola and Ojoo expressway all in the Ibadan North (NI, NII, NIII) local government area of Oyo State, Nigeria.

The determinations were done using a digital battery operated personal CO monitor.

The zero knob was depressed to erase any previous reading and to activate its use. It was then placed in the desired environment for between one and three min at which the readings were stabilized. The stable reading, which was direct CO concentration value was recorded.

This same monitor was used for ambient air, the cabinetmaker’s workshops and the offices microenvironment’s CO concentrations.

Data analysis

A coding device was developed for the questionnaire after comprehensive review of responses manually. The coded responses were fed into a computer. The Statistical Package for Social Sciences (SPSS) Software programme was employed to produce frequency tables and statistical test. Mann Whitney u and Kruskaal Wallis were the statistical methods of analysis utilized in this study.

RESULTS

Ambient CO levels in Ibadan city ranged between 4.0-55.0 pp with a mean rate and standard deviate of 20.18 ppm [Table 1].

The cabinetmakers were averagely exposed to a significantly higher carbon monoxide levels (P < 0.001) compared to the control group [Table 2].

COHb in cabinet makers with mean working hours of 9.48 ± 2.9 per day was (3.95 ± 1.35%) while that of controls with mean working hours of 8.0 ± 0.8 per day was 2.08 ± 0.91% (P < 0.001) [Table 2].

The COhb was significantly raised in both smoking and non-smoking cabinetmakers: P < 0.01 [Table 2].

There was no significant difference between the COHb levels in smoking and non-smoking cabinetmakers (P = 0.008) [Table 3].

DISCUSSION

In humans, COHb occurs naturally at low concentration as an endogenous pigment derived from the breakdown of red cells.[17]

Ambient concentration of COHb have been reported in various studies.[8] These concentrations are influenced largely by environmental factors and practices associated with incomplete combust of carbonaceous fuels constituting CO among others. The majority of the population is invariably exposed to varied ambient background CO levels.

The resting level of COHb observed in the control subjects were high compared to 1.5% COHb recommendation of the American Clean Air Acts Quality Standards of 1971, the cabinet workers on the other hand had a still higher value of carboxy hemoglobin [Table 2]. This is no doubt due to increased background CO level coupled with exposure to methylene chloride, which is bio-transformed to carbon monoxide.

<table>
<thead>
<tr>
<th>Site</th>
<th>1st week</th>
<th>2nd week</th>
<th>3rd week</th>
<th>4th week</th>
<th>5th week</th>
<th>6th week</th>
<th>Mean</th>
<th>Std Dev.</th>
</tr>
</thead>
<tbody>
<tr>
<td>S.E</td>
<td>16.0</td>
<td>18.0</td>
<td>15.0</td>
<td>17.0</td>
<td>14.0</td>
<td>16.0</td>
<td>16.0</td>
<td>0.89</td>
</tr>
<tr>
<td>NW I</td>
<td>17.0</td>
<td>16.0</td>
<td>18.0</td>
<td>14.0</td>
<td>13.0</td>
<td>15.0</td>
<td>15.0</td>
<td>1.00</td>
</tr>
<tr>
<td>NW II</td>
<td>11.0</td>
<td>12.0</td>
<td>10.0</td>
<td>11.0</td>
<td>12.0</td>
<td>10.0</td>
<td>11.0</td>
<td>1.34</td>
</tr>
<tr>
<td>N I</td>
<td>24.0</td>
<td>23.0</td>
<td>25.0</td>
<td>21.0</td>
<td>21.0</td>
<td>24.0</td>
<td>22.0</td>
<td>0.63</td>
</tr>
<tr>
<td>N II</td>
<td>55.0</td>
<td>49.0</td>
<td>49.0</td>
<td>49.0</td>
<td>51.0</td>
<td>54.0</td>
<td>52.0</td>
<td>2.53</td>
</tr>
<tr>
<td>N III</td>
<td>5.0</td>
<td>4.0</td>
<td>4.0</td>
<td>4.0</td>
<td>4.0</td>
<td>4.0</td>
<td>4.0</td>
<td>1.79</td>
</tr>
</tbody>
</table>

Range 4.0-55.0 ppm, Mean 20 ± 8.08 ppm

Table 1: Ambient carbon monoxide levels in selected areas of Ibadan - City, A six weeks study
Cabinet workers with undiagnosed or diagnosed cardiovascular disease may be at risk of myocardial ischemia due to increased exposure to work place CO and combined increased COHb from ambient CO exposure and bio-transformed MeCl₂.\(^{[21]}\) Such workers also have low tolerance to simple exercise like climbing of staircases and walking long distances.

Tuntinalli et al.\(^{[22]}\) listed CO as a cause of rhabdomyolysis and myoglobinuria. It is therefore imperative for regulatory public health authorities to enforce the use of facemasks during spray-painting and such places of work should be well ventilated.

There is also the need for enlightenment and health education on the use of such chemicals. Effort should also be made by manufacturers to eliminate the use of methylene chloride while replacing it with a less toxic base.

**ACKNOWLEDGEMENT**

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**REFERENCES**

14. Astrand I, Ovrum P, Carlsson A. Exposure to methylene chloride its concentration in alveolar air and blood during rest and exercise and its

**Table 2: Working environment carbon monoxide and carboxyhemoglobin levels in control, smoking and non-smoking cabinetmakers**

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Smoking</th>
<th>Non smoking</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambient working environment</td>
<td>2.08±0.91</td>
<td>5.20±1.08</td>
<td>5.20±1.08</td>
</tr>
<tr>
<td>COHb</td>
<td>1.88±0.77</td>
<td>3.95±1.35</td>
<td>3.82±1.22</td>
</tr>
<tr>
<td>Working hours per day</td>
<td>8.0±0.8</td>
<td>9.40±1.29</td>
<td>9.40±1.29</td>
</tr>
</tbody>
</table>

**Table 3: Table of comparison of smoking and non-smoking cabinetmakers**

<table>
<thead>
<tr>
<th></th>
<th>Smoking cabinet makers</th>
<th>Non smoking cabinet makers</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microenvironment CO</td>
<td>5.20±1.08</td>
<td>5.20±1.08</td>
<td>-</td>
</tr>
<tr>
<td>Carboxyhemoglobin</td>
<td>3.85±1.35</td>
<td>3.82±1.22</td>
<td>P = 0.008</td>
</tr>
<tr>
<td>Working hours/day</td>
<td>9.48±1.29</td>
<td>9.48±1.29</td>
<td>-</td>
</tr>
</tbody>
</table>

Similar results were obtained previously by other investigators in a furniture worker exposed to methylene chloride.\(^{[19]}\)

The detrimental effect of CO is consequent on the fact that inhaled CO readily combines with hemoglobin (with an affinity of over 200 times) to form COHb.

Therefore a low concentration of CO can result in a clinically significant reduction in the oxygen carrying capacity of the blood.

In addition, the presence of COHb shifts the oxyhemoglobin dissociation curve to the left so that tissue oxygen tension must fall to lower levels before the remaining oxyhemoglobin can give up its oxygen. Following CO exposure, the resultant decrease in oxygen carrying capacity of the blood together with the unpaired release of oxygen to the tissues lead to a large tissue oxygen deficiency (tissue hypoxia). The resultant effect is that exercise tolerance is reduced.

It was however observed that there was no significant difference in the COHb levels of smoking and non-smoking cabinet worker. This could be attributed to physiological adaptation to a constantly raised COHb.

Further, in experimental animals, common air pollutants, such as ozone and nitrogen dioxide have been shown to cause shifts in the thymocyte and spleen T-lymphocyte subpopulation at ambient level of exposure.\(^{[19]}\)

There was a delay in the deoxyribonucleic acid (DNA) turn over in the lymphocytes of these animals. Suggesting there could be immune compromisation due to air pollution.

MeCl₂ exposure up to toxic level had been reported to result in rhabdomyolysis.\(^{[20]}\)

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