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The relationship between exposure duration, carboxyhemoglobin, blood glucose, pyruvate and lactate and the severity of intoxication in 39 cases of acute carbon monoxide poisoning in man

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Abstract. The relationship between exposure duration, COHb, blood glucose, pyruvate and lactate and the severity of intoxication was investigated in a group of 39 cases of acute CO poisoning treated in the Clinical Toxicology Center in Łódź, Poland.

On the basis of clinical criteria the patients were classified into cases of mild, moderate, severe and very severe CO poisoning. COHb and carbohydrate metabolites were estimated in venous blood taken immediately after admission of the patient to hospital prior to treatment.

The severity of intoxication did not correlate with blood COHb; variation in exposure duration seems to be responsible for this phenomenon. Severe and very severe poisonings were associated with longer exposures and were accompanied by a markedly higher blood lactate level, compared to mild and moderate cases. Blood pyruvate depended less than lactate on the severity of intoxication. Blood glucose depended neither on exposure duration nor on the severity of intoxication.

Among the carbohydrate metabolic parameters studied, blood lactate determination can be helpful in the evaluation of the severity of CO poisoning in man.

Key words: Carbon monoxide – Acute poisoning – Severity of poisoning – Carboxyhemoglobin – Carbohydrate metabolites

Introduction

Acute carbon monoxide (CO) poisoning in man develops under various conditions of exposure, differing with duration of exposure and concentration of CO.

Clinical observations suggest that the blood carboxyhemoglobin (COHb) level is not sufficient as an indicator of the severity of poisoning (Roberts 1952; Burmeister and Neuhaus 1970; Bogusz et al. 1972) and that length of exposure constitutes an important factor in CO intoxication (Burmeister and Neuhaus 1970; Pach 1975). The reasons for these phenomena are not fully understood.

Biochemical effects of CO include increased levels of glucose, pyruvate and lactate in blood (e.g. Vitacca and Pagano 1955; Vyskocil 1957; Bogusz et al. 1972; Damm et al. 1972; Bogusz et al. 1975; Sokal 1975).

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The present study was undertaken to investigate the relationship between duration of exposure, COHb, blood glucose, pyruvate and lactate, and the severity of intoxication in a group of CO-intoxicated individuals.

Material and methods

The study was carried out in 39 cases of acute CO poisoning (18 men and 21 women), hospitalized in the Clinical Toxicology Center of the Institute of Occupational Medicine in Łódź. Twenty-five patients were intoxicated by household gas and 14 patients by coal-stove gas. The patients' ages ranged from 13 to 78 years.

The duration of exposure to CO varied between less than 1 and 14 h; it was established on the basis of an epidemiological review of the circumstances of poisoning. The severity of poisoning evaluated on admission to the hospital was graded according to the clinical criteria presented in Table 1. In seven patients complications developing during hospitalization covered mainly the central nervous and/or cardiovascular system. Treatment included administration of 100% oxygen by face mask and intravenous infusion of 40% glucose and 8.4% sodium bicarbonate.

The biochemical determinations (COHb, glucose, pyruvate and lactate) were carried out in samples of venous

Table 1. Classification of the severity of CO poisoning on the base of clinical symptoms

Clinical degree of intoxication	Specification of symptoms
I mild	Headache, vomiting, tachycardia; no disturbances of consciousness
II moderate	Disturbances or loss of consciousness without other neurological symptoms, tachycardia; nociceptive reflexes still intact
III severe	Loss of consciousness, intense muscular tonus, pathological neurological symptoms, tachycardia and tachypnoea; circulatory and respiratory disturbances not observed
IV very severe	Loss of consciousness, clinical signs of central nervous system damage, circulatory and respiratory disturbances

blood taken immediately after admission of the patient, before starting treatment. The blood COHb (in CO-poisoned patients) ranged from 5 to 53%.

Determinations of blood glucose, pyruvate and lactate were also performed in a control group of 12 healthy individuals (non-smokers).

COHb was measured spectrophotometrically according to Brückner and Desmond (1958). Pyruvate and lactate were determined spectrophotometrically using commercial enzymic tests (from Boehringer-Mannheim GmbH for lactate and from VEB Arzneimittelwerk Dresden for pyruvate). Blood glucose was estimated enzymatically with glucose oxidase and peroxidase, using a test kit from VEB Arzneimittelwerk Dresden.

Statistical analyses were conducted according to Remington and Schork (1970) Differences in means were evaluated according to Student's *t*-test. Frequency data were compared using the Chi-square test. The relationship between exposure duration, COHb and blood lactate was also evaluated by calculating correlation coefficients.

Results

On the basis of clinical criteria (Table 1) 16 cases were classified as the first degree ("mild") of CO poisoning, 12 patients as the second degree ("moderate"), eight patients as the third degree ("severe") and four patients as fourth degree ("very severe") of poisoning. For statistical analysis the mild and moderate cases were pooled into one group and the severe and very severe cases into another.

The frequencies of severe and very severe poisoning and of cases with complications, in relation to exposure duration and blood COHb level, are presented in Table 2. Higher incidences of severe and very severe poisoning and of cases with complications were observed following CO exposures equal to or longer than 8 h, compared to exposures below 8 h. All very severe intoxications developed after CO exposure longer than 8 h. Severe and very severe poisoning and cases with complications also tended to be more frequent in groups with higher blood COHb levels, but the differences were not statistically significant.

Table 3 shows the duration of exposure and the results of biochemical determinations in relation to the clinical severity of CO poisoning.

Mean blood COHb levels in the group of severe and very severe poisonings were slightly higher than those in the mild and moderate group, but this difference was also not statistically significant. On the other hand, the average duration of exposure which then induced severe or very severe poisonings was about twice as long as that associated with mild or moderate poisonings.

CO poisoning results in a marked increase in blood lactate level. This increase was about twice as high in the group of severe and very severe cases, as compared to the mild and moderate cases. An increase in blood pyruvate was less pronounced.

The average levels of blood glucose in patients intoxicated with CO were higher than those in the controls, but this difference was statistically significant only for the group of mild and moderate cases.

Very severe cases, associated with the longest exposure, were accompanied by the highest concentrations of blood lactate, but not of pyruvate and glucose. It is important to note that blood COHb levels in very severe poisoning were similar to those found in less severe intoxication.

In the analysis of the whole group of CO poisoning cases, a weak but still statistically significant ($0.05 > p > 0.01$) correlation was detected between exposure duration and blood lactate as well as between blood

Table 2. Frequency of severe CO poisoning (3rd or 4th degree according to Table 1) and cases with complications in relation to exposure duration and COHb level [a]

Exposure duration and blood COHb	Total number of cases	Number of severe or very severe cases	Number of cases with complications
Exposure duration			
< 8 h	25	3	2
$\geqslant 8$ h	14	9	5
		$Chi^2 = 11.26$	$Chi^2 = 4.68$
		$p < 0.001$	$p < 0.05$
COHb [b]			
$< 20\%$	10	2	1
$\geqslant 20\%$	28	9	5
		$Chi^2 = 0.53$	$Chi^2 = 0.34$
		$p > 0.05$	$p > 0.05$
$< 30\%$	19	3	2
$\geqslant 30\%$	19	8	4
		$Chi^2 = 3.19$	$Chi^2 = 0.79$
		$p > 0.05$	$p > 0.05$
$< 40\%$	27	6	3
$\geqslant 40\%$	11	5	3
		$Chi^2 = 2.05$	$Chi^2 = 1.54$
		$p > 0.05$	$p > 0.05$

[a] For criteria of the severity of poisoning, see Table 1

[b] One patient was excluded from this analysis because of the long time period elapsing from the cessation of exposure to blood sampling

Table 3. COHb, exposure duration and blood levels of glucose, pyruvate and lactate in relation to the severity of CO poisoning[a]

	Severity of CO poisoning[b]			Control
	Mild and moderate	Severe and very severe	Very severe[g]	
COHb %	27 ± 12 (27)	34 ± 13 (11)	31 ± 14 (3)	n.d.[h]
Exposure duration h	4.6 ± 3.3 (27)	9.1 ± 3.5[f] (12)	10.3 ± 1.3 (4)	–
Blood levels of:				
glucose mg%	129 ± 68[c] (27)	146 ± 106 (11)	100 ± 54 (3)	80 ± 14 (12)
pyruvate μmol/ml	0.20 ± 0.8[d] (19)	0.27 ± 0.08 (9)[d,e]	0.27 ± 0.01 (3)	0.09 ± 0.04 (12)
lactate μmol/ml	4.1 ± 3.6[d] (27)	8.8 ± 3.1 (11)[d,f]	11.0 ± 2.2 (3)	1.4 ± 0.3 (12)

[a] Mean values ± SD of (n) subjects
[b] For criteria of severity of poisoning, see Table 1
[c,d] Statistically significant difference in relation to the control group at $0.01 > p > 0.001$ and $p < 0.001$, respectively
[e,f] Statistically significant difference in relation to the CO group of first and second degree (see Table 1), at $0.05 > p > 0.01$ and $p < 0.001$, respectively
[g] This group was not statistically compared with the other groups
[h] n.d. – not determined. Using gas chromatographic methods we estimated in the blood of non-smokers living in Łódź 0.77 ± 0.23 and 0.73 ± 0.23% COHb for males and females, respectively (Majka et al. 1981)

COHb and blood lactate (r values amounted to 0.37 and 0.34, respectively). When 19 patients with COHb values equal or higher than 30% were considered, the correlation between exposure duration and blood lactate was higher ($r=0.60$; $0.001<p<0.01$) and the correlation between COHb and blood lactate was not observed. A similar correlation between blood lactate and COHbx exposure duration (r values amounting to 0.54, $p<0.001$ and 0.60, $0.001<p<0.01$, respectively) was found in both groups of CO patients.

Discussion

Despite extensive literature on clinical and biochemical effects of CO, the relationships between exposure duration, COHb, severity of intoxication and disturbances in carbohydrate metabolism in cases of acute CO poisoning in man have not been satisfactorily recognized.

Burmeister and Neuhaus (1970) observed no relationship between blood COHb and the clinical severity of CO poisoning. Severe CO intoxication, however, was accompanied by metabolic acidosis. In 47 patients poisoned by coal-stove gas for different time periods (Bogusz et al. 1975) blood lactate tended to be higher only following longer exposures, but was significantly higher in patients with higher COHb levels. A significant relationship was observed between clinical symptoms of intoxication and blood lactate. Similar tendencies were also observed by the same authors in a group of 47 patients poisoned by household gas (Bogusz et al. 1972). In the CO-poisoned patients observed in our present study, blood COHb ranged from 5 to 53%, and the duration of exposure to CO varied between less than 1 and 14 h.

The results show that the severity of CO poisoning depends more on the duration of exposure than on the COHb level alone (Tables 2 and 3); variations in exposure duration seem to be the most important factor responsible for the discrepancies between the severity of poisoning and blood COHb level. Other factors, e.g. variation in time elapsing from the cessation of exposure until admission to hospital (Bogusz et al. 1972) or individual susceptibilities to CO hypoxemia, may also be of significance.

The question why prolonged CO exposures can be particularly harmful may be related to more profound tissue hypoxia under such conditions, even if blood COHb is not yet drastically increased. Severe CO poisoning associated with longer exposure is therefore accompanied by high blood lactate and pyruvate levels (Table 3).

In rats intoxicated with CO (long exposures) the cerebral high-energy phosphates were not depleted (Sokal 1982); similar apparently paradoxical phenomena were observed in animal studies under conditions of nitrogen hypoxia and hypoxia due to ischemia (Sokal 1982; Myers and Yamaguchi 1976; Rehncrona et al. 1980). The detrimental effect of excessive cellular acidosis may be regarded as a possible factor to explain these findings (Myers and Yamaguchi 1976; Siesjö et al. 1977; Rehncrona et al. 1980; Kalimo et al. 1982; Drake-Holland 1982).

The importance of cellular acidosis for the clinical severity of acute CO poisoning is also stressed by the relationship between blood lactate (or metabolic acidosis measured gasometrically) and the severity of CO poisoning in man (Burmeister and Neuhaus 1970; Bogusz et al. 1975) and by the effectiveness of alkalization therapy (Burmeister and Neuhaus 1970).

The results obtained in the present study support the clinical value of a quantitation of metabolic acidosis in CO poisoning, either by blood lactate determination or by blood gasometric analysis.

Blood pyruvate seems to be less valid as a biochemical criterion of CO poisoning, since the relationship between this parameter and the severity of poisoning is not as clear as for blood lactate.

Blood glucose, in our study groups, exhibited large individual variations and a lack of dependence on the severity of poisoning; therefore its diagnostic value is very limited.

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