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THE USE OF FIBRONECTIN AND CHONDROITIN SULFATE RATHER THAN LIVER ENZYMES AS MARKERS FOR LIVER DAMAGE IN INDIVIDUALS EXPOSED TO CERTAIN OCCUPATIONAL HAZARDS

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ABSTRACT

Certain industrial works represent a major source of toxicity and environmental pollution either to workers or to their surrounders. Most toxicities here are chronic especially for those exposed mainly and directly to fumes of melten metals. Biochemical screening for them may deserve great importance and attention. Liver represents a major site for such biochemical abnormalities. Groups of male healthy workers were selected and recruited from certain industrial locations (melting units of different metals factories). Liver enzymes mainly (ALT, AST, ALP, AND ICDH), heavy metals (Cu, Fe, Pb), fibronectin and chondroitin sulphate were determined. Neither serum enzymes nor heavy metals levels recorded any changes. However, fibronectin and chondroitin sulphate demonstrated significant increase. This represents early signs that may lead to cirrhotic changes later on. Recent data collected from animal studies, and liver histopathology have confirmed the above clinical findings. Routine liver function tests may not be sufficient to reflect the extent of toxicity. Other biochemical markers must be included to guarantee the correct assessment.

INTRODUCTION

Industrial works represent a major source of environmental pollution and toxicity to workers and their surrounders. Lead, copper and iron are examples of heavy metals inducing such toxicity .

Most cases of toxicity are chromic and attributed mainly to direct exposure of those individuals to gases, fumes and finely divided dust particles.

Sources of lead pollution include leaded gasoline, tobacco , newspapers, lead industry and alloying [1].

Red blood cells can bind more than 95% of inhaled lead, the rest is directed to plasma proteins, lipids and lipoproteins in cell membrane .

This is represented through fromation of complexes with sulfhydryl groups especially compounds containing dithiol groups [2]. Concerning iron, liver is the main storage site for iron that exceeds the needs of the body , while the spleen represents another storage site for iron released from erythrocyte breakdown [3]. Fibrosis and hepatocellular damage are directly related to the iron contents of liver cells. The severity of fibrosis is maximal in peripheral areas encountered with deposited iron [4].

Iron plays also a principal role in lipid peroxidation through the generation of active oxygen species in hepatocytes accompanied by histopathological complications [5]. Regarding copper, exposure to copper fumes may arise through welding, grinding or alloying. Hepatomegaly, Jaundice, necrosis and cholestasis usually follow acute copper poisoning [6].

MATERIALS AND METHODS

Fourty eight male healthy workers were chosen from separate locations. All were of an overage age of 40 years (working for 10-20 years, each in his site). They were arranged in four groups each of 12 persons.

Group I: Iron – exposed workers, in iron melting unit, National Copper Co. Alexandira.

Group II: Copper – exposed workers, in copper melting unit, National Copper Co., Alexandria, Egypt.

Group III:Lead – exposed workers in lead melting unit, (Helwan factory of diesel Engineering, shobra El-khema – Egypt).

Group IV: Healthy persons chosen from regions free of metal pollution to a great extent, they were considered as normal control group.

The methods applied for the determination of the selected parameters were as follows: [7] for the aminotransferases ALT and AST, [8] as modified by [9] for alkaline phosphatase. [10] for the determination of isocitrate dehydrogenase activity.

Serum chondroitin sulphate was measured following the method of Gold [11].

Plasma fibronectin was evaluated using the radial immuno diffusion (R I D) procedure [12] and Fahey and Mckelvey [13].

Lead was determined following the modified method of De Silva [14] copper using that of Parker et al., [15].

Lastly iron according to the method of Dreux [16]

EXPERIMENTAL

Blood Sampling:

Fasting blood samples were collected, serum and plasma were prepared and fractionated for the determination of the following parameters: serum aminotransferases (ALT, AST), Alkaline phosphatase (ALP) isocitrate dehydrogenase (ICDH), chondroitin sulphate, plasma fibronectin and the heavy metals (Pb, Fe and Cu).

RESULTS

Table (1) shows a significant increase in the activity of alkaline phosphatase (A L P) in both iron and copper oven workers respectively. It shows also a significant increase in the activities of both ALT and AST in iron workers only.

Concerning serum chondroitim sulphate and plasma fibronectin levels, a significant increase in the level of both of them was observed in all groups of oven workers exposed to vapours of the three different metals (Table 1). An insignificant increase in serum level of lead, iron and copper was seen in all groups (Table 2)

Table (1): Serum activities of ALP, ICDH, ALT and AST in iron, copper and lead oven workers compared to control. Values are expressed as mean ± S.E. (n=12):

Subject	ALP	ICDH	ALT	AST
	U/L	U/L	U/L	U/L
Control	26.4 ± 0.3	9.8 ± 0.4	8.0 ± 0.4	9.2 ± 0.4
Iron workers	29.0 ±0.7**	10.0 ± 0.6	8.9 ± 0.6	11.6 ± 0.5**
Copper workers	29.9 ± 0.34***	9.9 ± 0.3	9.3 ± 0.7	10.4 ± 0.5
Lead workers	26.4 ± 0.8	9.7 ± 0.4	9.0 ± 0.4	8.7 ± 0.5

** Significantly different from control at P < 0.01
*** Significantly different from control at P < 0.001

Table (2): Plasma levels of fibronectin and chondroitin sulphate in iron, copper and lead oven workers compared to control. Values are expressed as mean ± S.E. (n=12):

Subject	Fibronectin	Chondroitin sulphate
	mg/L	µg / mL
Control	240 ± 4.0	281.7 ± 2.0
Iron workers	344.2 ± 1.0***	558.3 ± 4.0***
Copper workers	321.3 ± 4.0**	473.3 ± 3.0***
Lead workers	259.6 ± 5.0***	585.6 ± 1.89***

** Significantly different from control at P < 0.01
*** Significantly different from control at P < 0.001

Table (3): Serum iron, copper and lead levels in metal oven workers compared to control. Values are Expressed as mean ± S.E

Iron (mg/L)		Copper (mg/L)		Lead (mg/L)	
Control	Workers	Control	Workers	Control	Workers
1.6 ± 0.1	1.8 ± 0.1	2.15 ± 0.04	2.17 ± 0.004	0.77 ± 0.006	0.78 ± 0.006

DISCUSSION

This study revealed that, the fluctuation in serum level of lead, iron and copper was unpronounced subsequent to chronic exposure to vapours of the same metals.

Concerning liver enzymes, iron workers showed a significant increase in the activities of both ALP and AST. This was in agreement with the work of Modenova et al., [17], and was attributed to the deposition of iron in liver cells.

Oven workers exposed to copper showed elevated ALP activity. Similar results were registered by Ganter et al., [18] and Abu – Damir et al., [19]. Chronic inhalation of lead vapours affected the transaminases (AST and ALT) only. This agreed with the work of Stowe et al., [20] and Singh et al., [21].

Concerning fibronectin which is a glycoprotein having high molecular weight, located considerably in plasma and other body fluids. It is related to the connective tissue matrices and cell surfaces [22].

Results of metal workers showed a significant increase in plasma fibronectin level, the same was reported by Liao et al., [23]. It has been stated before that,cirrhotic patients exhibited higher plasma fibronectin level without any obvious clinical symptoms of ascites [24]. As regard to chondroitin sulphates it is aglycosaminoglycan synthesized from glucose by different tissues in the body and is essential for extracellular matrix morphology and cell adhesion [25]. It is involved also in liver regeneration as well as liver fibrosis [26]. Serum chondroitin sulphate for metal workers demonstrated higher values. This result was supported by the work of [27], who stated that lead can stimulate chondroitin sulphate synthesis in isolated human plan chondrocytes.

The above mentioned results revealed the ability of the insignificant increase of serum metals level in metal workers to stimulate the biosynthesis of both fibronectin and chondroitin sulphate. This observation may be considered a marker indicating the extent of liver tissue damage.

In conclusion it can be stated that it is necessary to replace the routine liver function tests which are as longer sufficient to assess the degree of hepatotoxicity induced by heavy metals by both fibronectin and chondroitin sulphate measurments which should be carried on periodically for metal workers.

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