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TOXIC PORPHYRINURIA AND CHRONIC HEPATIC PORPHYRIA AFTER VINYL CHLORIDE EXPOSURE IN HUMANS

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SUMMARY

Urinary porphyrin and porphyrin precursors excretion were studied in workers from a PVC (polyvinyl chloride) producing and processing plant. Secondary coproporphyrinuria and partial transition to chronic hepatic porphyria were found consistently in workers with vinyl chloride induced toxic liver damage. The pathobiochemical mechanism for the development of coproporphyrinuria and chronic hepatic porphyria Type A is probably based on a toxic disturbance of hepatic coproporphyrinogen oxidase and uroporphyrinogen decarboxylase by vinyl chloride. In medical supervision of VC (vinyl chloride) exposed workers the determination of urinary porphyrins is a diagnostic and preventive parameter, which indicates toxic injury at an early stage.

INTRODUCTION

Due to the complexity and all-pervasive cultural, biological, and medical significance of the interactions between the environment and porphyrin metabolism, it is not surprising that systematic experimental and ecological studies have been done in widely scattered often isolated fields. Any global solution to the problems involved will require interdisciplinary cooperation in the fields of pharmacology and toxicology, agriculture, biology, pathology, pharmacy, industrial medicine and hygiene, clinical medicine, veterinary medicine, clinical chemistry and biochemistry. Common problems and methods from these varied disciplines have given impetus to a new specialty, environmental health sciences; it is to be hoped that this field will provide a suitable context for continued systematic work on the topic of porphyria and the environment, with emphasis on lead and polyhalogenated aromatic compounds[1]. Finally, vinyl chloride disease[2] should be mentioned: this industrial disease involves chronic liver damage, scleroderma-like cutaneous changes, thrombocytopenia,

coproporphyrinuria and chronic hepatic porphyria[3].

In workers of the polyvinyl chloride (PVC) producing and processing industry a complex syndrome was observed involving skin, vessels, bones and inner organs (table 1) and which was designated "vinyl chloride disease"[2]. Hepatic lesions are the most significant disturbances in this disease[3].

TABLE 1

SYMPTOMS AND SIGNS OF VINYL CHLORIDE DISEASE[2,3]

Scleroderma-like skin changes
Raynaud's Syndrome
Clubbing of terminal phalanges
Acroosteolyses
Liver damage
Biochemical findings:
serum values of GOT, GPT, AA activities normal or slightly increased
BSP-test pathological
secondary coproporphyrinuria
chronic hepatic porphyria Type A
Histological findings:
mild hepatocellular alterations
intralobular, perisinusoidal,
portal and capsular fibrosis
Hemangioendotheliosarcoma of the liver
Esophageal varices
Splenomegaly
Thrombocytopenia
Reticulocytosis

MATERIAL AND METHODS

In order to find biochemical parameters indicating toxic effects at an early stage, we have determined porphyrin precursors and porphyrins in the urine of 40 patients from a PVC producing and processing plant. Each patient examined showed one or several of the following symptoms[3]: scleroderma-like skin changes, Raynaud's syndrome, clubbing of terminal phalanges, acroosteolyses, pathological BSP test, esophageal varices, splenomegaly, thrombocytopenia, reticulocytosis. None of the patients from the PVC processing plant showed Raynaud's syndrome, scleroderma-like skin schanges, acroosteolyses or esophageal

varices. Time of exposition in the group of PVC producing workers ranged from 1.75 to 20 years, in the group of PVC processing workers from 1 to 13 years. At the time of examination 12 of the patients from the PVC production plant had had no vinyl chloride contact for a time ranging from 3 to 43 months. Alcoholism could be excluded as cause for the porphyrinopathies.

RESULTS

The results of urinary porphyrin studies are given in table 2. Nineteen patients exhibited a mild secondary coproporphyrinuria, and in eight patients a moderate secondary coproporphyrinuria was found. Excretion of δ-aminolevulinic acid was elevated in four cases with mild coproporphyrinuria. In ten patients with coproporphyrinuria, excretion of pentacarboxylicporpnyrin was found to be in the upper range. In a few cases critical amounts of tricarboxylicporphyrin were found. The characteristic porphyrin pattern of chronic hepatic porphyria Type A was observed in three cases (table 2).

DISCUSSION

The most frequent symptom amongst the patients examined is the elevated coproporphyrin excretion, apart from thrombocytopenia, which can be related in this connection to toxic effects by vinyl chloride. There is no correlation between the amount of urinary porphyrin excretion and the activities of "liver enzymes" in the serum.

A better correlation is seen between the BSP test and coproporphyrinuria. In patients who showed the symptoms thrombocytopenia, splenomegaly, pathological BSP test and on whom liver biopsis were performed so far, histological examination revealed no changes which indicated toxic influence by alcohol[3].

The investigations show clearly that the majority of the patients of the PVC producing and processing plants, whose biochemical and scintigraphic findings indicated liver damage, developed secondary coproporphyrinuria sometimes with slight δ-aminolevulinic aciduria. This disturbance of porphyrin metabolism led in some cases, which present an elevated excretion of uroporphyrin and heptacarboxylicporphyrin, to chroric hepatic porphyria Type A (table 2). It can be suggested that by some toxic processes vinyl chloride diminisnes the activity of hepatic coproporphyrinogen oxidase and in some (susceptible?) persons also the activity of hepatic uroporphyrinogen decarboxylase. It can not be excluded that the uroporphyrinogen decarboxylase defect is purely toxic in these workers, depending upon dose and time factors of exposure. The results allow the conclusion that the determination of urinary porphyrins might become an important

TABLE 2

URINARY PORPHYRIN AND PORPHYRIN PRECURSORS EXCRETION IN 40 PATIENTS WITH VINYL CHLORIDE DISEASE IN A PVC PRODUCING AND PROCESSING PLANT;

Groups: I no disturbance in porphyrin metabolism, II mild secondary coproporphyrinuria, III moderate secondary coproporphyrinuria, IV chronic hepatic porphyria type A. For groups I, II and III mean values are given.

Group	VC exposure (years)	ALA	PBG	Total Porphyrins	Uro	Hepta	Hexa	Penta	Copro	Tri	Proto
		µmol/24 h ($\bar{x}\pm s$)		nmol/24 h ($\bar{x}\pm s$)	(%)						
I (n=10)	1-21	25 ± 9	3.6 ± 2.1	108 ± 26	13	3	1	3	79	1	-
II (n=19)	2-18	35 ± 17	5.4 ± 2.7	186 ± 26	14	3	1	4	77	1	-
III (n= 8)	3-18	26 ± 9	5.9 ± 2.5	263 ± 53	12	2	1	4	80	2	-
IV : Patients CHP A											
1. G.K.(61)	13	28	3.5	603	18	10	1	3	67	1	<1
2. W.S.(46)	7	19	4.4	340	17	12	2	5	63	1	<1
3. K.H.(26)	3	12	2.6	382	21	9	1	4	64	1	<1
Upper normal limit		49	7.5	130							

parameter in medical monitoring and protection of vinyl chloride exposed workers.

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