Porphyrins in aluminium foundry workers exposed to hexachlorobenzene and octachlorostyrene

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Introduction

Cases of chronic hepatic porphyria (CHP), i.e. one of several metabolic disorders of heme biosynthesis, have been linked to exposure to some organochlorine compounds (1). Notably, hexachlorobenzene (HCB) caused some 4,000 cases of CHP in Turkey after undue consumption of fungicide treated wheat seeds (2). Industrial HCB exposure with secondary porphyria, however, is rarely seen. The application of hexachloroethane as a degassing agent, i.e. for hydrogen removal, in aluminium founding has recently been identified as an important source of HCB and octachlorostyrene (OCS), a compound with a toxicological profile similar to HCB (3). In this study, the porphyrin status of foundry workers historically exposed to HCB and OCS in the course of aluminium degassing with hexachloroethane was investigated.

Materials and methods

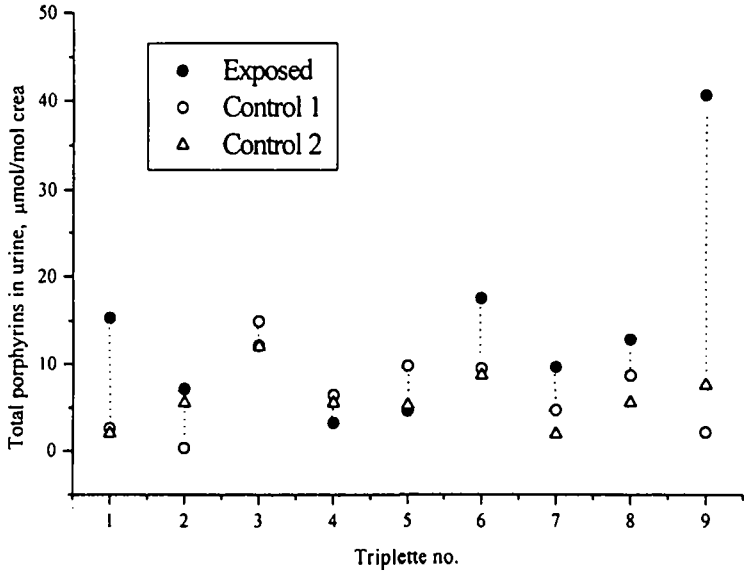
Nine male smelters (median age 50 y; range 26-64 y) from six foundries in central and southeast Sweden and 18 controls (two per case), matched for age, sex, residence and socioeconomic status, provided blood and urine specimen, which were analysed for HCB/-OCS (low resolution gas chromatography-mass spectrometry (4)) and porphyrins (reversed phase high performance liquid chromatography (5,6)). Erythrocyte uroporphyrinogen decarboxylase (E-URO-D) activity was analysed according to de Verneuil et al (7). The smelters had been exposed to the smoke and off-gases of hexachloroethane in the course of aluminium degassing for varying periods of time, but due to voluntary restrictions introduced by domestic industry less toxic degassing methods were substituted 2-4 years prior to the study.

Statistical analysis was conducted both with the matching retained (triplettes; analysis of variance (ANOVA)) and dissolved using logarithmic transformation of the porphyrin

measurements. Non-parametric methods were applied as an extra precaution in this small material. The relation of HCB/OCS with total porphyrins in urine was investigated with linear regression analysis. The study was approved by the appropriate human research ethics committee.

Results and Discussion

With one exception, the differences in the urinary levels of total porphyrins between the exposed workers and their matched controls were generally small. In six of the triplettes, however, the porphyrin levels were higher in the exposed subjects than in the corresponding controls, whereas in the remaining triplettes the level of porphyrins in the exposed individuals were equal to or lower than that of the controls (Figure; triplettes sorted according to duration of exposure for cases).



In the ANOVA model (matching retained) the level of total porphyrins was higher in the exposed group than in the control group ($p=0.03$). With regard to uroporphyrins, no difference was observed between exposed and controls, whereas the difference in coproporphyrins was statistically significant ($p<0.05$), mainly due to higher levels of the coproporphyrin III isomer. The results of the unmatched analysis were basically the same. Here, the level of total porphyrins in urine from exposed subjects was approximately twice that of the controls (13.6±11.1 (mean±SD) µmol/mol creatinine vs 6.2±3.8 µmol/mol creatinine). The E-URO-D activity was normal and similar in both groups indicating no influence of hereditary disturbances of porphyrin decarboxylation as well as no persistent damage to this function in the erythron of exposed subjects.

Details of the HCB and OCS analyses are available elsewhere (4). The correlations between the levels of plasma HCB and OCS adjusted for lipid content and the excretion of total porphyrins were of similar strength (r=0.78 and r=0.69, respectively). However, these results were strongly influenced by an exposed subject with extreme values of both the independent and the dependent variables. After logarithmic treansformation, correlations of about half the size were found for *ln* plasma HCB (r=0.40) and *ln* plasma OCS (r=0.32) versus *ln* total porphyrins in urine.

The material is rather small and the results must be interpreted with caution. However, the various statistical analyses were surprisingly concordant given the limited size of the study. Alcohol consumption and lead exposure are potential confounders and neither factor was directly measured. However, the response to a standardised questionnaire, the findings of a physical examination as well as liver enzyme analyses gave no indications of differential alcohol habits between the exposed group and the controls. With one exception, lead was not used in the foundries under investigation and there was also no history of differential lead exposure in the two groups.

In conclusion, the results of the present study indicate that the exposure to polychlorinated organic compounds occurring in aluminium degassing with hexachloroethane, notably HCB and OCS, may induce subtle changes in porphyrin metabolism of exposed subjects consistent with early CHP. It was noted that the findings were observed in subjects in whom the exposure had ceased some years prior to sampling, indicating that more pronounced effects could have been found if we had been able to study more recent exposure.

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