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Styrene exposure and the liver

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HÄRKÖNEN H, LEHTNIEMI A, AITIO A. Styrene exposure and the liver. *Scand j work environ health* 10 (1984) 59—61. The liver functions, as reflected by the serum enzyme activities of aspartate aminotransferase, alanine aminotransferase, and gamma glutamyl transferase and by the concentrations of cholic acid and deoxycholic acid, of 34 styrene-exposed and 34 reference female workers were followed prospectively for a year. The mean age of the exposed workers was 34.2 years, and the mean duration of past exposure 5.1 years. The mean age of the referents was 30.7 years. During the follow-up period blood samples were collected three times for the determinations. The history of possible liver disease and alcohol consumption was ascertained by questionnaire. Altogether 87 samples of both groups were analyzed. The styrene-exposed group did not have higher values for any measurement when compared with those of the referents. Two persons in both groups had one sample with transaminase activities exceeding laboratory reference values. The abnormal values were associated with the use of drugs or alcohol. Cholic acid and chenodeoxycholic acid concentrations were of the same magnitude in both groups.

Key terms: cholic acid, deoxycholic acid, hepatotoxicity, solvents, transaminases.

Styrene is a commercially important chemical used in the production of polymers, copolymers, and reinforced plastics. The exposure of workers to styrene is considered to be highest in the production of plastics reinforced with glass fibers.

The hepatotoxic effects of styrene have been demonstrated in animal studies. For example, styrene (6 g/kg) caused a strong elevation of alanine aminotransferase activity in the serum of hamsters (9). In addition, histological liver alterations consisting of parenchymal hydropic degenerations, steatosis, and congestion have been found in rats after six weeks of inhalation exposure to 300 ppm of styrene (11).

Some clinical reports have described styrene-exposed workers with abnormal liver function as reflected by some enzyme activities. Lorimer et al (8) found significantly elevated gamma glutamyl transferase activity in workers exposed to about 5—20 ppm of styrene. In addition elevated aminotransferase values have been found among styrene-exposed workers, but the etiology has been considered unclear (1). However other studies have been negative in this respect (2, 10). Bile acid determinations, especially of chenodeoxycholic acid, have been considered sensitive indicators of possible hepatoxicity, and, among styrene-exposed workers, a high frequency of abnormal values has been found (5, 12).

In previous reports the importance of studies on the effects of industrial agents on the liver has been emphasized, particularly the importance of an unbiased study design and the inclusion of a comparable reference group, without which the conclusions drawn about causal relationships may be irrelevant (7).

In order to evaluate the liver toxicity of styrene in long-term exposure, we have followed a group of 34 hand-laminators of polyester plastic products for one year prospectively.

Subjects and methods

The exposed subjects comprised all of the 34 female workers occupationally exposed to styrene in one plant. Their mean age was 34.2 (SD 8.9) years, and the mean duration of past styrene exposure was 5.14 (SD 8.9) years.

The reference group was composed of 34 female bank clerks, shop assistants, and textile workers, none of whom had any known chemical exposure. The mean age of the reference group was 30.7 (SD 5.9) years.

With a questionnaire the history of possible liver disease, alcohol consumption, use of oral contraceptives, weight, and height was ascertained from all the subjects, and both groups participated in a periodic health examination.

The groups were followed for one year prospectively. During this period laboratory samples were collected three times, in May, September and again in May. Each sampling took place after overnight fasting. A venous blood sample was drawn in the morning between 0800 and 1000 and stored at —20°C until analyzed. The enzyme tests included the serum activities of aspartate aminotransferase (EC 2.6.1.1.2), alanine aminotransferase (EE 2.6.1.2), and gamma

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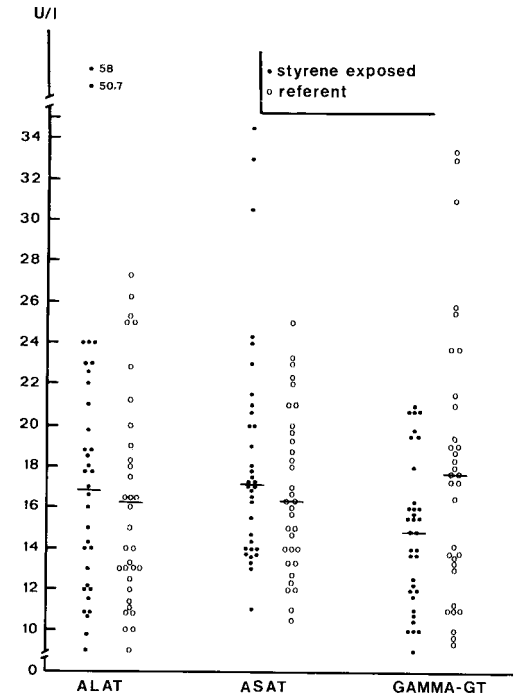

Figure 1. Alanine aminotransferase (ALAT), aspartate aminotransferase (ASAT), and gamma glutamyl transferase (gamma-GT) activity in the serum of 34 styrene-exposed workers and 34 referents (mean of three measurements). (1 U/l = 60 μkat)

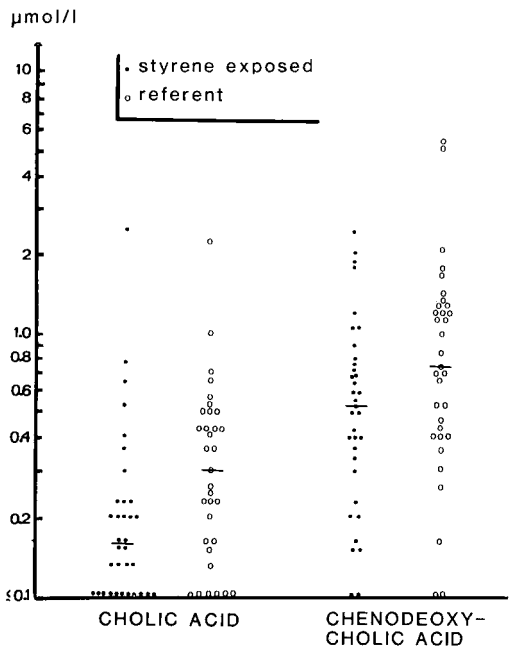

Figure 2. Cholic acid and chenodeoxycholic acid concentrations in the serum of 34 styrene-exposed workers and 34 referents (mean of three measurements).

glutamyl transferase (EC 2.3.2.2). The serum activities of the three enzymes were determined according to the recommended methods of the Scandinavian Society for Clinical Chemistry and Clinical Physiology (3, 4). The cholic acid and chenodeoxycholic acid concentrations were determined by the radioimmunoassay method. The kits for these measurements were purchased from Nordic Lab (Oulu, Finland).

For each subject the means of the transaminase activity and the cholic acid and deoxycholic acid concentrations were calculated.

Exposure

According to earlier hygienic measurements the overall exposure level in the plant in question was about 30—40 ppm. During the hand-laminating and spraying process, the styrene concentration in the breathing zone has been about 50—120 ppm, the highest levels temporarily exceeding 200 ppm. In this context eight urine samples were collected for mandelic acid measurement. The mean of these eight measurements was 819 mg/l (5.38 mmol/l), a level indicating an 8-h time-weighted styrene exposure of about 40 ppm (6).

Results

Altogether 87 samples from the styrene-exposed group and 87 samples from the reference group were analyzed. The styrene-exposed group did not have significantly higher values for any measurement (Student's t-test). Figures 1 and 2 show the distributions of the liver enzyme activities and cholic acid and chenodeoxycholic acid concentrations of the two groups. Two persons in both groups had one sample with enzyme activities exceeding the laboratory reference values (40 U/l or 2,400 μkat). The values of the second sample of these persons were in the normal range however. When the styrene-exposed workers were divided into two groups according to duration of exposure (1—4 years and 5—11 years), there were no statistically significant differences in the enzyme activity levels of the two groups.

Alcohol use was similar in both groups, although 11 of the referents were total abstainers in comparison to only three of the exposed workers. Users of oral contraceptives numbered 17 and 7 among the referents and exposed workers, respectively. The mean height of the styrene-exposed group was 160 (SD 5.6) cm and the mean weight was 60 (SD 8.5) kg. The corresponding values of the reference group were 163 (SD 6.1) cm and 59 (SD 7.3) kg, respectively.

Discussion

In this prospective study the styrene-exposed subjects did not have significantly higher enzyme activities when compared to nonexposed referents. The cholic

and chenodeoxycholic acid concentrations of the two groups were of the same magnitude. This result differs from those of some previous studies, in which styrene-exposed workers had more elevated transaminase values (1, 8) and also high cholic and chenodeoxycholic acid concentrations (5, 12).

Lorimer (8) found styrene-exposed workers to have high gamma glutamyl transferase values even when the use of alcohol was taken into consideration. However, in our series, the tendency was the opposite, even though more referents than exposed subjects were abstainers.

Vihko et al (12) reported the concentrations of chenodeoxycholic acid in the serum of 25 styrene-exposed persons to be more frequently elevated than any other parameter measured when compared to corresponding values of other groups (91 persons in multiple solvent exposure, 41 in polyvinyl chloride exposure, and 76 in vinyl chloride monomer exposure). In addition Edling et al (5) stated that cholic acid may be more sensitive to early liver damage in styrene-exposed groups.

The number of transaminase values exceeding the reference values was of the same magnitude in both groups. When controlled, the abnormal values were within the normal range, and thus there was no indication of a need for further clinical examinations, eg, liver biopsy. In the case of one styrene-exposed subject and one referent, the abnormal values were associated with the use of oral contraceptives. The abnormal transaminase activity of one styrene-exposed worker was associated with changes in the use of psychotropic drugs, and, in the case of one referent, with alcohol. The number of missing samples was 15 in both groups, and therefore this factor did not influence the results. Furthermore the duration of past styrene exposure varied from 1 to 11 years, but no selection due to liver disease or high transaminase values had occurred in this plant.

We could not confirm the superiority of serum cholic acid determinations (12) as an indicator of early liver damage in styrene exposure. Styrene, at concentrations in use at present in hand- and spray-laminating work, does not seem to be a potent hepatotoxin.

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