

No acute behavioural effects of exposure to styrene: a safe level of exposure?

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ABSTRACT To determine whether exposure to low levels of styrene (below 110 mg/m³) causes acute behavioural effects and symptoms that may be related to concentrations of styrene in air or urinary mandelic acid or both, 12 men occupationally exposed to styrene were studied and compared with a reference group of 10 unexposed men. Simple reaction time was measured before and after work and information about symptoms was obtained by questionnaire. Active and passive sampling of airborne styrene was carried out and urinary mandelic acid concentrations were measured. Although the size of the study groups is small, the results indicate that exposure to styrene below 110 mg/m³ does not cause any acute adverse effects on the central nervous system.

Styrene is one of the most commonly used raw materials for making plastics. Occupational exposure to styrene occurs during the production of the monomer, in polymerisation plants, during the fabrication of plastic products from monomeric or partly pre-polymerised styrene, and during the transportation and handling of liquid styrene.¹ Styrene is taken up mainly through the lungs and is readily soluble in the blood.² It is biotransformed in man and the main metabolites, mandelic acid and phenylglyoxylic acid, are excreted in the urine.³

Styrene causes irritation of the mucous membranes and is toxic to the central nervous system.⁴ Symptoms of fatigue, difficulties with concentration, and irritation have occurred among exposed workers; "prenarcotic symptoms"—for example, nausea, dizziness, and a drunken feeling—have also been reported.⁵ Exposure chamber studies have shown a significant slowing in reaction time after exposure to styrene,⁶ and studies of workers exposed to styrene in the field have reported prolonged reaction times at the end of the work shift⁷⁻⁹ as well as deterioration in performance in other psychological tests.¹⁰ Early morning urinary mandelic acid concentrations after two days without exposure correlate with the simple reaction time measured on arrival at work, and there is a considerable difference in the rate of clearance of mandelic acid between different sub-

jects.^{9,11} This indicates that both exposure and the rate of metabolism may be important when evaluating the health and safety of workers exposed to styrene. Nevertheless, most studies in the exposure chamber, as well as those in the field have been performed with exposure at relatively high concentrations of styrene (more than 200 mg/m³), not taking into account the improved occupational hygiene standard during recent years.

In Sweden the threshold limit value has gradually been lowered from 210 mg/m³ to 110 mg/m³, but no studies have been conducted to determine whether or not this concentration is low enough to exclude adverse effects on the central nervous system. The present study was carried out to determine if exposure to low concentrations of styrene (below 110 mg/m³) causes acute behavioural effects and symptoms which may be related to the levels of styrene in air or the urinary mandelic acid concentration, or both.

Material and methods

SUBJECTS

Twelve men with a mean age of 30 (SD = 10 years) and with a mean exposure to styrene of 2.5 years (range 0.5-4 years) took part in the study. They manufactured styrene based sewage pipes and worked in two shifts (0600-1400, 1400-2200), changing their shift every week. Measurements were made on two successive Mondays, and all men had been free of exposure for at least 24 hours.

A reference group of ten men working between 0700–1500 at the same factory was used to evaluate the reaction time measurements for the morning shift. Their mean age was 34 (SD = 8 years). A non-exposed reference group was not available for the afternoon shift.

QUESTIONNAIRE

Before work each man completed a questionnaire containing 16 items relating to neuropsychiatric symptoms which have been reported to be sensitive to long term effects of exposure to solvent.¹² Since recent data indicate that alcohol ingestion might interfere with the kinetics of mandelic acid excretion¹³ the questionnaire also included questions concerning alcohol intake in general and in particular on the days before exposure as well as medication and sleeping hours during the weekend preceding the measurements.

ASSESSMENT OF EXPOSURE

Active sampling of airborne styrene was made with a Sipin-pump and SKC-charcoal tubes. Simultaneous passive sampling was made with a Porton Down charcoal cloth diffuse sampler.¹⁴ The dosimeters and the charcoal tubes were placed in the breathing zone of the men and the tubes and filters were changed simultaneously after two to four hours. Determination of styrene in the charcoal tubes and in the charcoal filter was made with a conventional technique: desorption with carbon disulphide and GC analysis (Varian 3700).

Urine was collected on the Monday morning before work and the following Tuesday morning. The mandelic acid concentrations were measured by isotachopheresis, essentially as described by Sollenberg and Baldesten,¹⁵ and corrected for creatinine.

REACTION TIME TEST

Simple reaction time was measured for 10 minutes using the type of modified cassette recorder that has been used in previous studies.^{11,16} A practise session was given the week before the study began. The subject's task was to press a white button in response to a red light which appeared in the stimulus window. The stimuli were presented randomly at intervals from three to 12 seconds. The

Table 2 Mean reaction time in the study groups

Group	Reaction time (msec)			
	Before work		After work	
	Mean	SD	Mean	SD
Morning shift	267	42	247	36
Afternoon shift	247	38	253	50
Reference group	262	23	234	24

mean reaction time was computed from the individual responses recorded.

STATISTICAL EVALUATION

Differences between means were tested with Student's *t* test and correlations were calculated with Pearson's product moment correlation.

Results

The mean eight hour time weighted concentration of styrene in air, measured by passive dosimetry, was 43 ± 28 mg/m³ for the morning shift group and 54 ± 37 mg/m³ (table 1) for the afternoon group. The correlation between active and passive sampling was 0.92 ($p < 0.001$).

The answers on the questionnaire showed no differences in number of positive answers on subjective symptoms between the groups. On average the men gave two positive answers out of the 16. There was no indication of alcohol or drug abuse or of sleep disturbances, nor was any high alcohol intake reported for the weekend before the measurements were performed.

Simple reaction time before and after work showed a non-significant speeding up of mean reaction time in the morning shift group and a non-significant slowing down in the afternoon group (table 2). The mean reaction times before and after work of the exposed morning shift group did not differ significantly from that of the reference group.

The correlation between mandelic acid concentration before work and the reaction time before work was -0.17 for the men in the morning shift group and -0.37 for the afternoon group, both are non-significant. The end of shift reaction time did not correlate significantly with air borne styrene exposure during the working shift ($r = -0.22$) or with

Table 1 Number of subjects, age, and environmental measures for exposed and reference groups

Group	No of subjects	Age		Personal exposure (dosimetry, mg/m ³)	
		Mean	SD	Mean	SD
Morning shift	12	30	10	43	28
Afternoon shift	12	30	10	54	37
Reference group	10	34	8	—	—

urinary mandelic acid concentration of the next morning ($r = -0.28$).

Discussion

A cross sectional study design may have certain drawbacks due to selection processes, work organisation, and the number of available employees, thereby limiting the validity of the study. A reference group for the afternoon shift group would have been desirable in order to draw conclusions on the association between styrene exposure and acute behavioural effects. The present design, however, with measurements before and after work, makes it possible to correlate levels of exposure and performance by relating each individual to his own performance before work. Another advantage of the design is that the same individuals are studied on both the morning and the afternoon shift, which will balance possible selectional bias.

There were no indications from the questionnaire that the workers had an excess of symptoms which might be due to the chronic effects of exposure to styrene. On the other hand, the mean exposure time was only 2.5 years, and the general experience is that an exposure time of about nine years or more is needed for solvent induced neuropsychiatric disorders.¹⁷

In some other studies different neuropsychological tests have been used to evaluate the possible behavioural effects of styrene.^{9,10} In this study only reaction time was used since it has been reported to be sensitive in showing any impairment due to solvents,⁸ an experience confirmed by the results of earlier studies.^{9,10} Cherry *et al* reported considerable individual differences in rate of clearance of styrene and its metabolites and suggested that the rate of clearance may determine the behavioural effects of styrene exposure.¹¹ Individuals with a slow clearance of mandelic acid had a prolonged mean reaction time in that study. The results of the present study indicate that such individual differences in metabolic rate and in behavioural effects may not be apparent with low levels of exposure.

An improvement in reaction time after exposure has also been suggested to be related to an inhibitory effect on styrene metabolism or an inhibition of the excretion of metabolites caused either by styrene itself or an early metabolite.⁷ In this study there was no correlation between start of shift reaction time and early morning urinary mandelic acid concentrations. Such interference with metabolism is therefore not likely at this exposure level. Mutti *et al* also suggest that at levels below 110 mg/m³ (mean daily exposure) behavioural effects are less likely.¹⁰ The differences between this study and others may there-

fore be primarily due to differences in the levels to which the subjects were exposed.

The speeding up of reaction time in the morning shift group and the slowing down in the afternoon group may be explained by a normal biological circadian rhythm with a shorter reaction time in the afternoon than in the morning.¹⁸ The lack of difference in mean reaction time before work between the morning shift group and the reference group and the small association between end of shift reaction time and the eight hour time weighted concentrations of styrene in the air further support this interpretation.

Although the size of the studied groups is small, this study indicates that exposure to styrene below the current Swedish TLV (110 mg/m³) does not cause any acute adverse effects on the central nervous system. Neither are there any apparent individual differences in the rate of the biotransformation or in the behavioural effects at such levels.

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