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Study on Kidney Function in Female Workers Exposed to Perchlorethylene

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1 Biochemical markers of kidney damage were examined in 16 female workers chrsnically exposed to tetrachlorethylene (TCE) in five dry-cleaning shops. The results were compared with those obtained in 13 females non-occupationally exposed to organic solvents.
2 The intensity of exposure was monitored by personal environmental monitoring. The time-weighed average exposure to TCE amounted to 157 mg m^{-3} (range 9–799 mg m^{-3}). A satisfactory agreement was found between the concentration of TCE in ambient air sampled with the charcoal tube method and with a passive dosimeter.
3 The urinary excretion of lysozyme was increased in the exposed group. No difference was found in the urinary excretion of albumin, β_2-microglobulin, lactate dehydrogenase, total proteins or glucose. The prevalence of abnormal values of biochemical parameters in the exposed group did not differ from that observed in the control group. No correlation was found between the level of TCE exposure and biochemical parameters.
4 The present study suggests that chronic exposure to TCE does not lead to renal damage.

Introduction

Tetrachlorethylene (TCE), an unsaturated chlorinated hydrocarbon is extensively used as an industrial organic solvent for metal degreasing and dry-cleaning. Many studies report the effects of TCE on various organs. The most commonly studied organ is the liver.[1,2] **So** far, very limited information has been available regarding its effects on renal function. In recent studies Goldsworthy *et al.*,[3,4] found nephrotoxicity and renal tumours in male rats gavaged with TCE (1000 mg kg^{-1}). Lauwerys et *al.*[1] did not find any adverse effects of TCE on the kidneys of workers. On the contrary, Franchini et *al.*[5] found increased lysozymuria and activity of urinary p-glucuronidase in workers exposed to TCE.

The aim of the present investigation was to re-examine the nephrotoxic potential of TCE. We measured sensitive markers of tubular and glomerular toxicity in a group of female workers with an average exposure 157 mg m^{-3} TCE.

Methods

The study was conducted on **two** groups of female subjects working in five dry-cleaning shops. The exposed group consisted of 22 workers inhaling TCE. Their working conditions had always remained identical. It was compared with a group of **15** females with only administrative function and with no known exposure to organic solvents.

All participants were asked to answer a self-administered questionnaire in which information was obtained **on** occupational, demographic and health history. Subjects with a present or past history of kidney disease or systemic diseases known for their renal involvement (e.g. diabetes mellitus) were excluded from the statistical analysis of the results.

Exposure of each worker was monitored on the third **or** fourth day of the week over a whole day. Two absorbing systems, namely passive diffusion samplers **(HK85/CKD-Czechoslovakia)** and active charcoal tube samplers (Charcoal tubesconnectedto a personal SKC-222-4 sampling pump – USA, with a flow rate of **55** ml min^{-1}) were positioned in the worker's beathing area, on the left lapel, at 10 cm distance from each other. One-hundred-and-sixty TCE samples (80 coincidental pairs) were carried out on **16** workers

during 1 year. Analyses of TCE were carried out using a gas chromatograph Chrom 61 (Czechoslovakia) equipped with a flame ionization detector after desorption with carbon disulphide.[6]

After the last TCE monitoring, at the end of the working day, a sample of urine from each subject was collected over phosphate buffer (pH 7.4) containing sodium azide as a preservative. All the samples were stored at 4°C until the analyses were performed.

The concentration of β_2-microglobulin (β_{2-m}) and albumin were determined by the RIA-test (UVVVR Prague, Czechoslovakia). Creatinine was measured by the method of Jaffé.[7] The urinary activity of lysozyme was measured by the method of Litwack.[8] Urinary glucose was determined by the Oxochromglucose BIOLA-Test (Lachema, Czechoslovakia). LDH in urine was assayed by the UV-test (Sevac, Czechoslovakia). Total proteins were determined by the BIOLA-Test (Lachema, Czechoslovakia). All urinary parameters were corrected for the creatinine contents. The results of the analysis of the urine samples with creatinine of less than 0.4 g l^{-1} were discarded.

The Kolmogorov–Smirnov test was applied to check if a distribution or its logarithmic transformation was normal. The homogeneity of variances was checked by the F-test. Student's *t*-test was used to compare arithmetic or geometric means. The comparison of prevalence of elevated values was performed with 2 × 2 χ^2 test (with Yates correction) using xs^2 in the control group as a cut-off where x is the geometric mean and s is the geometric standard deviation. The level of significance was taken as $P < 0.05$.

Results

The characteristics of both groups are summarized in Table 1. They are well matched for the listed criteria (number of subjects, duration of exposure, age, smoking habits, alcohol and analgesic consumption).

There was no appreciable non-occupational exposure to organic solvents in either group.

The mean value and the range of individual values of TCE time-weighed average exposure in five dry-cleaning shops are presented in Table 2. Laboratory tests showed that both the adsorption charcoal tube and the charcoal collector of the passive dozimcter measured TCE with an accuracy ± 20% of the concentration present. This level of accuracy corresponds to the performance of these techniques in industrial pollution control. On average, the exposure level was below the Czechoslovak TWA (*250* mg m^{-3}) but in three dry-cleaning shops 20–80% of individual values exceeded 250 mg m^{-3}.

Data on the urinary excretion of proteins and enzymes in control and exposed subjects are presented in Table 3. Only lysozyme was significantly increased in the exposed group. There were no statistically significant differences in the urinary excretion of albumin, β_{2-m}, LDH or total proteins. No elevated concentrations of glucose were found in control or exposed group (results not shown).

The prevalence of abnormal values in the urinary excretion of proteins or enzymes in the exposed group did not differ from those observed in the control group (Table 4).

Figures 1 and 2 show the distribution of β_{2-m} and lysozyme. The overall distribution of lysozyme is shifted to higher values in exposed workers.

We did not find any significant correlation between the level of TCE exposure and biochemical parameters (results not shown).

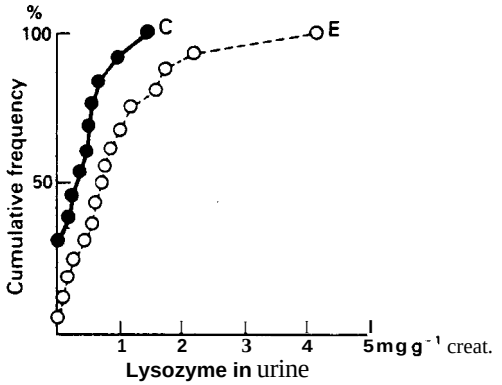

Figure 1 Cumulative frequency distribution of lysozyme in the urine of control (C) and exposed (E) workers.

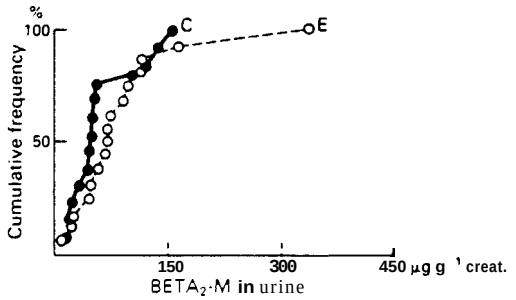

Figure 2 Cumulative frequency distribution of $beta_{2\ m}$ in the urine of control (C) and exposed (E) workers.

Table 1 Charactt

Number volunte
-Number retained
Age/year/mean r
Number of smok
Regular alcohol .
Regular analgesi
Non-occupationa
Duration of empl
Mean (range)

[1] More than five week, [3] More th significant: Studt

Table 2 Time-weighed averag

Shop	*Number of workers*	*Number pairs of measurem*
1	2	20
2	4	14
3	5	22
4	2	12
5	3	12
Total	16	80

[a] A_i,P_i . . . individual values

Table 3 Urin and total prot

Albumin (mg
β_2-microglobul
Lysozyme (mg
LDH (U g^{-1} c
Total proteins

[a] Data are exp Student's *t*-tes

Table 4 Pr and enzym

Urinary pa
Albumin
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shops 20–80% of individual
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E

3 4 5 mg g^{-1} creat.
in urine

frequency distribution of
control (C) and exposed (E)

E

300 450 µg g^{-1} creat.
in urine

quency distribution of $beta_{2-m}$
C) and exposed (E) workers.

Table 1 Characteristics of the control and exposed group.

	Control	*Exposed*	*P*
Number volunteered	15	22	-
Number retained for study	13	16	-
Age/year/mean ± s.d.	36 ± 6	42 ± 10	NS
Number of smokers	6	7	NS
Regular alcohol consumption[1]	3	2	NS
Regular analgesics consumption[2]	1	0	NS
Non-occupational exposure[3]	0	0	NS
Duration of employment/year/ Mean (range)	9 (1–18)	11 (1–25)	NS

[1] More than five glasses of wine. beer or liquor per week, [2] More than one tablet per week, [3] More than 1 h week-' domestic-use of organic solvents, NS: not satistically significant: Student's r-test or χ^2 test with Yates correction.

Table 2 Time-weighed average exposure to TCE on the third or fourth working day.

			Exposure level (mg m^{-3})					*% of samples[a]*
			Charcoal tube		*Passive sampler*			
Shop	*Number of workers*	*Number of pairs of measurements*	*Mean ($\bar{A}$)*	*Range*	*Mean ($\bar{P}$)*	*Range*	$\bar{A}/\bar{P}$	$\frac{A_i + P_i}{2}$
1	2	20	319	129–799	262	113–752	1.22	70
2	4	14	84	9–249	72	11–231	1.17	0
3	5	22	283	16–411	276	23–427	1.03	80
4	2	12	41	31–113	34	21–162	1.21	0
5	3	12	60	13–351	51	19–360	1.18	20
Total	16	80	157	9–799	139	11–752		

[a] A_i, P_i . . . individual values

Table 3 Urinary excretion of albumin, β_2-microglobulin, lysozyme, LDH and total proteins in control workers and workers exposed to TCE'.

	Control (n = 13)	*Exposed (n = 16)*	*P*
Albumin (mg g^{-1} creat)	18.9 (5.7–61.4)	19.1 (7.7–97.2)	NS
β_2-microglobulin (µg g^{-1} creat)	45.0 (11.7–153.6)	63.9 (9.9–333.3)	NS
Lysozyme (mg g^{-1} creat)	0.15 (0–1.49)	0.56 (0–4.16)	< 0.05
LDH (U g^{-1} creat)	14.9 (2.7–47.1)	13.5 (2.7–67.1)	NS
Total proteins (mg g^{-1} creat)	103 (32–254)	125 (49–535)	NS

[a] Data are expressed as geometric mean (range), NS: not statistically significant. Student's r-test; creat: creatinine

Table 4 Prevalence of abnormal values' in the urinary excretion of proteins and enzymes in TCE-exposed workers and in their controls.

Urinary parameter	*Control*	*Exposed*	*P*
Albumin	W13	1/16	NS
β_2-microglobulin	0/13	2/16	NS
Lysozyme	0/13	3/16	NS
LDH	W13	1/16	NS
Total proteins	1113	2/16	NS

[a] Higher than the 95th percentile of the values found in the control group. NS: not statistically significant, χ^2 test with Yates correction

Discussion

In the present study the level of TCE was generally below the current TLV (250 mg m^{-3}), but in three dry-cleaning shops 20–80% of individual values exceeded 250 mg m^{-3}. A satisfactory agreement was found between the two sampling methods.

Glomerular permeability did not appear to be affected by TCE exposure as shown by unchanged albumin excretion. No statistically significant differences were found in the urinary excretion of LDH, glucose or β_{2-m} which were used as markers of tubular dysfunction. Only lysozyme, was significantly increased in the exposed group. Its distribution was shifted to higher values in the exposed group.

Decreased tubular reabsorption of lysozyme leads to high concentrations of lysozyme in the urine of leukemic patients, patients who have been treated with aminoglycoside antibiotics and patients who have received kidney transplants. Consequently, lysozyme has become a largely used tool in the diagnosis of tubulopathies and nephrotoxicity.[9–11] Nevertheless, as the urinary excretion of other sensitive markers of tubular dysfunction were normal, it is difficult to interpret the increased lysozymuria as a result of tubular damage due to TCE.

Our results are in agreement with the results of Franchini et *al.*[5] who found a significantly increased lysozymuria and activity of urinary β-glucuronidase and no differences in total proteinuria or albuminuria in female workers exposed to *68.9* mg m^{-3} TCE. Lauwerys *et al.*[1] did not find any significant differences in urinary excretion of albumin and B_{2-m} in female workers exposed to 145 mg m^{-3} TCE.

The renal effects observed in our study seem to be very weak and their occurrence does not correlate with the intensity of exposure. In view of these limitations and results of other authors,[1,5] the existence of a chronic nephrotoxicity of TCE at low exposure levels remains very hypothetical. This conclusion is reinforced by the fact that prolonged exposure to TCE in our study was not associated with an increased prevalence of subclinical renal effects.

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Pre-embarkment I

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1 In order to assess wh
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3 The relationship of the

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Introduction

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amount of paraquat as wc
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Manabe-Shinmachi, Tsuchiura-