Acute leukemia in professional drivers exposed to gasoline and diesel

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Abstract: The environmental exposure to the petroleum products gasoline, diesel, and their motor exhausts was studied in a case-control interview of 125 patients with acute leukemia and 1 matched control per patient. Odds ratios were calculated by comparing discordant matched patient-control pairs. An excess risk for developing acute leukemia was found for the professional drivers, and odds ratio was determined to be 3.0 (95% CI: 1.1–9.2/$p \leq 0.02$). For those who were exposed for more than 5 years in their life-time, or more than 1 yr during the 5–20 yr period prior to diagnosis, the odds ratio was 5.0 ($p < 0.05$). This finding remains after consideration is given to exposures to organic solvents, smoking and therapeutic x-ray treatment. No excess risk was observed for persons professionally exposed to motor oil and machine oil without exposure to fuels and exhausts. No preferential type of acute leukemia was found to be associated with exposure to fuels and their exhausts. The results indicate an etiological relationship between the development of acute leukemia and exposure to petroleum products as fuels and exhaust.

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Introduction

In a case-control study, we have shown that the regular, professional exposure to organic solvents in painters was associated with a 13-fold increased risk of developing acute leukemia (1). The most probable leukemogenic agents in the organic solvents used by painters are the aromatic volatile compounds benzene, and, to a more limited extent, toluene and xylene (2). Petroleum products, previously implicated as being associated with the development of acute leukemia in exposed patients (3) or in offspring of exposed persons (4, 5), not only contain aromatic solvents but, in addition, saturated and unsaturated hydrocarbons, which can be metabolized to carcinogenic compounds (2).

The same patient material was used for this study as for our previous one evaluating organic solvent exposure (1). The aim of the present study was to analyze the importance of the exposure to petroleum liquids, particularly in professional drivers, as an etiological factor in acute leukemia.

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Material and methods

Patients

One-hundred-and-twenty-five adult patients with acute leukemia who were admitted to one of five hospitals participating in treatment studies organized by the Leukemia Group of Middle Sweden (LGMS) (6, 7) were interviewed during the period September 1980 to May 1983. Before the investigation started the doctors of all the hospitals permitted the interviewer to have access to their patients, who were interviewed in the hospitals after personal introduction by the attending doctors. The LGMS hospitals cover a population of about 1.4 million inhabitants and practically all patients with adult acute leukemia within the area covered are admitted to these hospitals. The patients were of urban and rural origin. Fourteen patients who were in too poor a condition to take part, or who had lost their ability to recapitulate information, were excluded. One patient refused to take part. Seventy-six were men and 49 were women. The mean age was 49 years (range 15–84). The mean age of the women was 51 yr (range 16–84) and of the men 48 yr (range 15–84). The leukemias were classified into FAB types according to Bennett et al. (8) with a slight modification by Öst et al. (9). The numbers of patients in the different leukemia classes were:

trols. The minimum exposure time for being defined as exposed was 1 month. Individuals, who were exposed for longer periods and/or during a defined interval of time were considered to be effectively exposed. The choice of time intervals for effective exposures was based on the observations of the maximum incidence of leukemias in Hiroshima after the atomic bomb explosion in 1945 (12). Effective exposure was defined as either exposure for more than 5 yr during any period of life or exposure for more than 1 yr during the time interval 5–20 yr prior to diagnosis/interview.

Non-professional exposure through the use of different means of transportation was also studied in the same population.

Results

Occupational exposure to petroleum products was noted in different professions such as drivers, car mechanics, gasoline-service station attendants and aircraft-associated occupations. Exposure comparable to occupational exposure was also found in activities such as rally driving.

Eighteen patients and 6 controls had been professional drivers. One further patient/control pair was concordant and disregarded. Thus, the OR of the drivers to develop acute leukemia was 3.0 (Table 1). Three additional patients and 1 control had been rally drivers. Since the rally drivers could be regarded as professional drivers concerning exposure, the OR for both professional drivers and rally drivers was estimated. The OR for the whole group was also 3.0 and the p-value was less than 0.02 (Table 1).

The median exposure time as professional drivers for patients was longer, 9.5 yr, than for the controls, who were exposed during a median time of 1.5 yr (Table 2). However, the exposure time varied considerably and only 10 patients and 2 controls from among the professional drivers were considered to be effectively exposed during their life-time. The OR for this group of patients was 5.0 ($p < 0.05$) (Table 3). For those who were less exposed, the OR was 0.75. Five of the 18 drivers had also worked as painters during other periods. Excluding these 5 patients decreased the significance level to $p \leq 0.10$ in those drivers who were not effectively exposed, but did not decrease the level of significance in drivers who were effectively exposed ($p < 0.05$) (Table 3).

Exposure to petroleum products was noted also in patients with other professions such as car repairer, service station-attendant, air hostess and air field employee, but the number of exposed individuals

Table 1. Odds ratios (OR) for drivers and rally drivers

Profession	Patients/ Controls	OR	95% CI**	p-value
Professional drivers	18/6	3.0	1.1–8.2	≤0.02
Rally drivers*	3/1	3.0		
Total	21/7	3.0	1.2–8.4	≤0.02

* Rally driving was a hobby activity in 3 patients and 1 control.
** Confidence interval.

Table 2. Drivers: Numbers of discordant pairs of patients and controls, median ages, median times as drivers and times from end of exposure to disease or interview, respectively, in professional drivers and in rally drivers as hobby activity

	Patients				Controls			
Exposure to petroleum products	Median age, years (range)	No. of discordant pairs	Median time of exposure, years (range)	Median time from end of exposure to disease, years (range)	Median age, years (range)	No. of discordant pairs	Median time of exposure, years (range)	Median time from end of exposure to interview, years (range)
Professional drivers	49 (18–73)	18	9.5 (0.5–42)	5.5 (0–45)	37 (21–60)	6	1.5 (0.2–27)	3.5 (0–20)
Rally drivers	28 (18–41)	3	7 (4–9)	2 (0–20)	41	1	4	17
Total	45	21	9	5	41	7	2	8

Table 3. OR for drivers and rally drivers alone or in combinations

Professional drivers	Professional drivers, also active as painters	Rally drivers	Rally driver also active as painter	O.R. cases/controls	p-value
+	+	+	-	21/7 = 3.0	≤0.02
-	+	-	-	18/6 = 3.0	≤0.02
+	-	-	-	15/7 = 2.1	≤0.10
-	-	-	-	13/6 = 2.2	0.10 < p < 0.20
Effectively exposed	-	-	-	10/2 = 5.0	< 0.05

The patients with leukemia who had been drivers had a median exposure time of 9.5 yr. Most of the patients had been exposed for more than 5 yr in their lifetime, but 1 had been exposed for less than 1 yr. The OR was estimated to be 5.0 for those drivers who were defined as effectively exposed, but only 0.75 for those who were not. Still, the material is too small to draw any firm conclusion about the minimum exposure time – if any – for developing acute leukemia.

The mechanism by which petroleum products may induce leukemia is unclear. The vapours and exhausts from petroleum products contain aromatic compounds such as benzene, which is well known to be associated with increased risk of leukemia (17). In Sweden, gasoline contains benzene up to a concentration of 5 vol%. Aromatic compounds such as benzene, toluene and xylene are present at up to 30 vol%. The *in vivo* metabolites epoxids and phenols and the polyaromatic hydrocarbons in diesel oil, as well as the gasoline octane-inducing metal lead, are known to be carcinogenic (18–26). Thus it is possible that the key compounds associated with leukemia development in petroleum products may well be the same as those in organic solvents that are present in a variety of paints and which are also known to be associated with the development of leukemia (1).

Petroleum products that were used as machine or motor oil lubricants, containing mainly non-volatile hydrocarbons and without exhaust, were not found in the present study to be associated with an overrisk. The exposure to volatile petroleum products seems to be an independent factor. In a multivariate analysis, no interaction was found between such exposure, organic solvent exposure, smoking habits or therapeutic X-ray treatment (1).

The increased risk of developing leukemia in persons exposed to volatile petroleum products stresses that efforts should be made to minimize such exposure by introduction of new techniques for gasoline loading (27) and by optimal construction of service stations (28). Proper ventilation of working places with the evacuation of volatile compounds can significantly reduce the hazardous effects (29). It seems reasonable to discourage children and adolescents from having regular hobby activities that include the handling of fuel-driven motors.

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