

Occupational Risk for Hematological Malignancies

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A case-control study was conducted in 620 cases of hematological malignancies and in 1,240 age- and sex-matched controls in order to verify the possible association between occupation, toxic substances exposure, and the risk of hematological neoplasias. The results demonstrate that farmers and industrial workers have a significant risk for hematological malignancies. Exposure to asbestos, aromatic hydrocarbons, fertilizers, mineral oils, pesticides, and radiations is associated with a significant increase in the risk for these malignant diseases. These data are in agreement with previously reported data, and require a confirmation in larger, prospective studies.

Key words: occupation, exposure to toxic substances, case-control study, epidemiology

INTRODUCTION

The incidence of cancer is increasing in western countries [1], and several environmental and occupational risk factors have been suggested to explain this trend. The proportion of cancer deaths attributed to occupational factors is provisionally estimated as 4.0% [2], but this percentage seems to be underestimated [1].

A case-referent study was conducted in order to investigate the possible association between occupation, exposure to occupational toxic substances, and risk of hematological malignancies.

PATIENTS, CONTROLS, AND METHODS

A total of 620 cases of hematological malignancies, 355 males and 275 females, ages ranging from 24 to 85 years, and 1,240 sex- and age-matched hospital controls were considered for the study. Among the patients, there were 59 cases with acute non-lymphoblastic leukemia (ANLL), 29 with acute lymphoblastic leukemia (ALL), 65 with chronic lymphocytic leukemia (CLL), 69 with Hodgkin disease (HD), 108 with non-Hodgkin lymphoma (NHL), 44 with myeloproliferative syndromes (MPS), 48 with myelodysplastic syndromes (MDS), 198 with malignant monoclonal gammopathies (MG), 190 multiple myeloma, and 8 with Waldenstrom's macroglobulinemia. The controls were selected from the same geographic areas as the cases, and were affected with "medical diseases," except cancer or congenital diseases.

All subjects, cases and controls, were interviewed, without knowledge of subject's state, about socioeco-

nomic status [3], area of residence, alcohol intake, tobacco smoking, current or previous occupation, and if they had ever been exposed to one or more of a list of toxic substances. Out of the 620 case interviews, 366 (59%) were obtained directly, whereas 1,054 (85%) of the 1,240 control interviews were provided by the subjects; in the other cases, the information was obtained from their relatives.

Exposures to occupational toxic substances were grouped in 21 risk categories, such as reported by Moms et al. [4]. A matched-pair analysis was used with the relative risk of hematological malignancies estimated by the odds ratio (OR) of discordant pairs (b/c); and the confidence intervals at 95% of probability (95%CI) were computed on the basis of the normal approximation; the statistical significance of each association was calculated using the "Mantel's chi-square test," with a degree of freedom; finally, also the etiological fraction of each association was calculated [5]. All these procedures have been reported previously in detail [6].

RESULTS

Table I summarizes the results. No significant ($P > 0.05$) association was demonstrated for socioeco-

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TABLE I. Association Between Socioeconomic Status, Occupation, Occupational Exposures, and Risk of Hematological Malignancies

Categories of risk	Cases	Controls	b/c ^a	OR	95% CI	P	EF, %
Socioeconomic status							
High	172	402	861/97	0.87	(0.68 ÷ 1.08)	ns	—
Medium	245	443	69/164	0.84	(0.63 ÷ 1.11)	ns	—
Low	203	395	811/108	1.50	(1.12 ÷ 1.98)	ns	33.0
Residence							
Urban	326	635	871/163	1.07	(0.83 ÷ 1.39)	ns	6.5
Rural	294	605	931/171	1.09	(0.85 ÷ 1.40)	ns	8.3
Habits							
Alcohol	256	482	68/162	0.84	(0.63 ÷ 1.11)	ns	—
Tobacco	228	425	761/131	1.16	(0.87 ÷ 1.54)	ns	3.8
Occupations							
Private practitioners	55	138	29/83	0.70	(0.46 ÷ 1.07)	ns	—
Office workers	92	228	58/123	0.94	(0.69 ÷ 1.28)	ns	—
Teachers	16	58	11/24	0.92	(0.45 ÷ 1.88)	ns	—
Medical doctors and nurses	23	54	18/27	1.33	(0.73 ÷ 2.41)	ns	24.8
Sales workers	18	43	12/26	0.92	(0.47 ÷ 1.82)	ns	—
Building workers	67	125	39/75	1.04	(0.71 ÷ 1.53)	ns	3.8
Industry workers	105	178	58/39	2.97	(1.98 ÷ 4.46)	<0.0005	66.3
Handcraftmen	38	59	21/26	1.62	(0.91 ÷ 2.88)	ns	38.3
Auto mechanics	8	16	5/9	1.11	(0.37 ÷ 3.31)	ns	9.9
Railroad workers	9	19	7/5	2.80	(0.89 ÷ 8.83)	ns	64.3
Farmers	143	229	71/52	2.73	(1.91 ÷ 3.91)	<0.0001	55.2
Housekeepers	27	58	16/47	0.68	(0.39 ÷ 1.20)	ns	—
Others	19	45	18/32	0.13	(0.63 ÷ 2.01)	ns	11.5
Exposures							
Acids	112	225	31/51	1.21	(0.77 ÷ 1.89)	ns	17.3
Aldehydes and ketones	43	87	21/50	0.84	(0.50 ÷ 1.40)	ns	—
Aliphatic hydrocarbons	102	189	41/67	1.22	(0.83 ÷ 1.80)	ns	18.0
Alkalies	121	258	63/98	1.29	(0.94 ÷ 1.77)	ns	22.5
Aromatic hydrocarbons	64	89	42/39	2.15	(1.39 ÷ 3.32)	<0.001	53.5
Asbestos	68	59	35/23	3.04	(1.79 ÷ 5.14)	<0.001	67.1
Carbon monoxide	85	127	58/95	1.22	(0.88 ÷ 1.69)	ns	18.0
Chemical asphyxiants	30	74	22/59	0.75	(0.46 ÷ 1.22)	ns	—
Chlorinated hydrocarbons	58	95	37/61	1.21	(0.81 ÷ 1.82)	ns	17.4
Dusts	206	376	68/116	1.17	(0.87 ÷ 1.58)	ns	14.4
Dyes and inks	71	85	32/50	1.28	(1.11 ÷ 1.99)	ns	21.9
Esters	35	48	34/47	1.45	(0.93 ÷ 2.25)	ns	31.0
Ethers	64	139	30/75	0.80	(0.53 ÷ 1.22)	ns	—
Fertilizers	136	219	44/54	1.63	(1.09 ÷ 2.43)	<0.05	38.7
Metals	164	319	67/126	1.06	(0.75 ÷ 1.43)	ns	5.7
Mineral oils	98	139	57/44	2.59	(1.75 ÷ 3.84)	<0.0005	61.4
Organically high polymers	49	75	22/37	1.19	(0.70 ÷ 2.02)	ns	16.0
Other caustic substances	30	46	24/41	1.17	(0.71 ÷ 1.94)	ns	14.5
Paints and related products	98	158	48/62	1.55	(1.06 ÷ 2.26)	ns	43.8
Pesticides	151	233	63/46	2.74	(2.14 ÷ 4.01)	<0.0005	63.5
Radiation	46	32	38/15	5.07	(2.00 ÷ 12.87)	<0.0001	86.1

^aDiscordant pair; OR = Mantel-Haenszel odds ratios; 95% CI = 95% confidence intervals EF = etiological fractions.

conomic status, area of residence, and habits. Among the cases, there was a significant ($P < 0.05$) excess of individuals employed in agriculture and in industry. Regarding toxic substances exposure, significant associations ($P < 0.05$) were demonstrated for asbestos, fertilizers, aromatic hydrocarbons, mineral oils, pesticides, and radiations.

When the occupational exposures were analyzed with

respect to each hematological malignancy, significant associations were found between asbestos and MG (OR = 4.61; 95%CI: 1.63 ÷ 12.30; $P < 0.02$) and CLL (OR = 4.71; 95%CI: 1.23 ÷ 18.05; $P < 0.05$); between fertilizers and MG (OR = 3.13; 95%CI: 1.33 ÷ 7.19; $P < 0.05$); between aromatic hydrocarbons and ANLL (OR = 5.28; 95%CI: 2.13 ÷ 13.64; $P < 0.05$); between mineral oils and NHL (OR = 3.4; 95%CI: 1.65 ÷ 7.38;

$P < 0.02$), and MG (OR = 3.00; 95%CI: 1.53 ÷ 6.22; $P < 0.01$); between pesticides and NHL (OR = 4.40; 95%CI: 1.54 ÷ 12.67; $P < 0.05$), CLL (OR = 4.00; 95%CI: 1.52 ÷ 10.73; $P < 0.05$), and MG (OR = 3.55; 95%CI: 1.58 ÷ 7.33; $P < 0.01$); and between radiations and MG (OR = 10.00; 95%CI: 3.00 ÷ 33.84; $P < 0.01$). Work in agriculture was associated significantly ($P < 0.05$) with each malignant hematological disease.

DISCUSSION

This study extends our previous investigation [6], and the results are in agreement with previously reported data [2,4,6-8], suggesting a relationship between some occupational exposures and the risk of hematological neoplasias. Despite the potential limitations to the case-referent studies [4,5], the observation that the farmers have been found to be at high risk in many studies supports the hypothesis that they are exposed to occupational carcinogens, such as fertilizers or pesticides [1,4,6,7], as well as to carcinogen zoonotic viruses [7]. Workers in industry are exposed to many potential carcinogens for blood cells, and the hematotoxicity and carcinogenicity of aromatic hydrocarbons, especially benzene, are well known [9]. Moreover, the negative effect of occupational asbestos exposure on immunological processes, consisting of a defect in cellular immunity and hyperactivity of B-lymphocytes [10], could explain the significant association demonstrated. It is also worth noting that the experimental model for inducing a plasmacytoma in mice is the injection into the peritoneal cavity of mineral oil [6]. Finally, radiation exposure is actually the only

certain environmental factor capable of inducing cancer in humans [1,2].

In conclusion, further special attention might be paid to these substances in occupational epidemiological studies of workers, especially with respect to hematological malignancies; nevertheless, further research appears warranted to assess the strength of any association in prospective, larger population-based studies.

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