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CASE-REFERENT STUDY ON SKIN CANCER AND ITS RELATION TO OCCUPATIONAL EXPOSURE TO POLYCYCLIC AROMATIC HYDROCARBONS. II. STUDY RESULTS

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Abstract. The study was performed on a group of 376 males suffering from skin cancer and on two control groups, 752 males each, matched according to age. Referents were randomly sampled from the general population as well as from hospital wards and dermatological out-patient clinics. The analysis of occupational exposure to different products containing polycyclic aromatic hydrocarbons produced data which indicated an increased risk of skin cancer in persons exposed to mineral oils (odds ratio = 1.46; 95% confidence interval; 1.06–2.05). In the case of exposure to sources of polycyclic aromatic hydrocarbons other than mineral oils, no significant increase in skin cancer risk was noted.

INTRODUCTION

This work presents general results of a case-referent study on skin cancer risk in persons occupationally exposed to polycyclic aromatic hydrocarbons (PAH). Itis a continuation of a study of which the first part "Study design", published in the Polish Journal of Occupational Medicine in 1989 (10), presented the goal, the method and the characteristics of the population under study.

The study covered a group of adult males registered in the Regional Cancer Register, Lodz, during the years 1983–1988, because of the first occurrence of the disease (376 persons)* and two groups of referents (752 males in each). The referents were randomly sampled from the general population (control group I) and from patients of hospital wards and dermatological

*The final verified number of skin cancer patients.

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outpatient clinics (control group II). All these subjects were individually interviewed at their places of residence according to a specially designed questionnaire.

STATISTICAL METHODS

Besides methods of descriptive statistics, a measurement in wide use, namely a relative risk estimator, was employed to assess the effect of given risk factors on the occurrence of skin cancer.

Bearing in mind how cases and referents were matched, the Mantel-Haenszel estimator for data matching 1:2 and dichotomous exposure (exposed and non-exposed) was used in order to estimate the relative risk. The log procedure, in turn, served to estimate the relative risk confidence interval (11). Calculations were done on an IBM microcomputer, fed with our own program.

In certain specific circumstances, like the estimation of the relative risk in groups of a defined period of exposure in relation to non-exposed groups, a relative risk estimator for non-matched data was used. In order to estimate the value of the relative risk estimator, and to test its significance as well as the structure of the confidence interval, the EPIINFO system was employed.

RESULTS

A questionnaire, specially designed by physicians and sociologists, was used to collect data on occupational exposure. The data, obtained during an interview, covered consecutive jobs and posts during the whole period of an individual subject's employment together with job descriptions. The analysis of occupational risk factors of skin cancer included different products which might appear to be the source of polycyclic aromatic hydrocarbons: grease, tar, pitch, soot, mineral oils, creosote oil, anthracene oil, coke, petrol, paraffin, gasoline, paraffin oil, soft asphalt, mazout, bituminous mass, petroleum and asphalt.

Initially, data on exposure to polycyclic aromatic hydrocarbons was analysed. The whole population was stratified into two groups: exposed and non-exposed, regardless of the kind of product. Table 1 displays relevant data. They show that over 50 per cent of males in each of the groups under study have had, during their professional career, an occupational contact with one or more of the products listed above. Nevertheless, differences in the frequency of exposure to polycyclic aromatic hydrocarbons among skin cancer cases and referents were insignificant.

Periods of occupational contact with PAH surpassed, in the majority of subjects, 20 years, and they varied insignificantly in individual groups. Similarly, relative risk estimators calculated according to individual exposure periods were insignificant (Table 2).

TABLE 1. Occupational exposure to polycyclic aromatic hydrocarbons (PAH) in the population under study. Distribution of frequency and magnitude of odds ratio (OR).

	Cases		Control group I		Control group II		OR I	OR II
	n	%	n	%	n	%		
Non-exposed to PAH	160	42.8	349	46.4	348	46.3	1.0000	1.0000
Exposed to PAH	216	57.4	403	53.6	404	57.3	1.1500	1.1400
	376	100.0	752	100.0	752	100.0		

TABLE 2. Occupational exposure to polycyclic aromatic hydrocarbons (PAH) according to the period of exposure. Distribution of frequency and magnitude of odds ratio (OR).

Period of occupational exposure	Cases		Control group I		Control group II		OR I	OR II
	n	%	n	%	n	%		
Non-exposed								
0	160		349		348		1.0000	1.0000
– 9	49	22.7	75	18.6	78	19.3	1.4251	1.3663
10–19	42	19.4	76	18.9	79	19.6	1.2054	1.1563
20–29	36	16.7	101	25.1	101	25.0	0.7775	0.7752
30–	89	41.2	151	37.5	146	36.1	1.2856	1.3259
	100% = 216		100% = 403		100% = 404			

Mean latency periods, estimated by the number of years between the beginning of exposure to PAH and the onset of skin cancer were very long and they ranged, depending on the kind of product, from 23.9 to 45.6 years for mineral oils; the figure was equal to 34.5, on average.

In the course of analysis, the subjects exposed to PAH were stratified into sub-groups according to the products with which they had had an occupational contact. It should be stressed that a number of difficulties was faced during the classification procedure. Just a few subjects had had contact with only one out of 17 afore-said products, whereas the majority of them had had concurrent contact with a number of them. When products were selected one by one, it was, by necessity, decided to consider them hypothetically as the only hazards of a particular working environment. For example, when persons exposed to mineral oils were looked for, all males who had had any occupational contact with these oils, regardless of possible concurrent contact with other products, were placed in the same group. Data stratified in such a way were then analysed and products which emerged sporadically in the population under study were excluded (creosote and anthracene oils, gasoline, soft asphalt, mazout and asphalt). The results are presented in Table 3. Out of 11 products, only in the case of mineral oils, were differences in the frequency distribution of exposure significant in the group of cases and in the group of referents sampled from the general population.

TABLE 3. Analysis of occupational exposure to polycyclic aromatic hydrocarbons (PAH) in the population under study. Distribution of frequency and magnitude of odds ratio (OR) according to individual products.

Product	Cases		Control group I		Control group II		OR I	95% confidence interval	OR II
	n	%	n	%	n	%			
Non-exposed to PAH	160		349		348				
Exposed to PAH – total	216		403		404		1.15		1.14
Grease	172	45.7	325	43.2	313	41.6	1.15		1.20
Tar	28	7.4	56	7.4	61	8.1	1.09		1.00
Pitch	15	3.9	35	4.7	38	5.1	0.93		0.86
Soot	29	7.7	52	6.9	65	8.6	1.22		0.97
Mineral oils	99	26.3	148	20.0	163	21.7	1.46	(1.06–2.05)	1.32
Coke	32	8.5	54	7.2	70	9.3	1.29		0.99
Petrol	71	18.9	119	15.8	139	18.5	1.30		1.11
Paraffin	24	6.4	29	3.9	37	4.9	1.81		1.41
Petroleum	57	15.2	106	14.1	112	14.9	1.17		1.11
Paraffin oils	8	2.1	17	2.3	10	1.3	1.45		1.74
Bituminous mass	13	3.5	14	1.9	14	1.9	2.03		2.02
	100% = 376		100% = 752		100% = 752				

OR calculated in relation to persons non-exposed to PAH

TABLE 4. Magnitude of odds ratio (OR) in the population under study in relation to the period of exposure to mineral oils.

Period of exposure in years	Cases		Control group I		Control group II		OR I	95% confidence interval	OR II
	n	%	n	%	n	%			
0 (non-exposed to PAH)	160		349		348				
– 9	23	23.2	30	20.3	32	19.6	1.67		1.56
10–19	19	19.2	25	16.9	30	18.4	1.66		1.38
20–29	21	21.2	44	29.7	43	26.4	1.04		1.06
30–	36	36.4	49	33.1	58	35.6	1.60	(0.98–2.63)	1.35
	100% = 99		100% = 148		100% = 163				

The relative risk estimator in subjects exposed to mineral oils, plus other products, was significantly higher when compared with those not exposed to polycyclic aromatic hydrocarbons. The comparison between persons exposed only to mineral oils and those not exposed to PAH, as well as persons exposed

to products comprising these compounds (except mineral oils) produced similar results (odds ratio = 1.48; 95% confidence interval: 1.09 – 2.00). In order to confirm a significant role of mineral oils in evoking skin cancer, another comparison was made between persons exposed to PAH, except mineral oils, and persons not exposed to these compounds, but the differences were insignificant.

An increased risk of skin cancer found in subjects exposed to mineral oils, in principle, was not determined by the period of exposure. Only in cases of contact lasting for 30 or more years did the risk reach the limits of statistical significance (Table 4).

DISCUSSION

Among exogenous causes of neoplasm, factors present in the working environment do not prove to be the most important ones (3, 6, 14). In the case of skin cancer, besides solar radiation (a very rare occupational factor in Poland), and ionizing radiation, arsenic and polycyclic aromatic hydrocarbons are the main causes of this disease (4, 5, 12, 13). Polycyclic aromatic hydrocarbons represent a very large group of chemical compounds occurring in the working environment. Occupational exposure to PAH is associated with production, processing and use of oil- and coal-derived materials. Although those materials are in common use, we still lack epidemiological data on the carcinogenity of individual hydrocarbons. This can be explained by the fact that, except anthracene, they always, take on the form of multi-component mixtures. Hence data on products which are made up of them but not on individual hydrocarbons. The carcinogenity of products which contain PAH differs; some of them are even not carcinogenic at all. In addition, investigations carried out in different research institutions do not always produce the same resulst. The reason lies in the quantitative and qualitative composition of oil- and coal-derived materials. The composition varies and depends on the kind of raw material and production process. Moreover, the concentration of PAH changes in the same product under different handling conditions. It has been recently proved that the content of polycyclic aromatic hydrocarbons increases in mineral oils under the operational process (1).

The observations show that this is a problem of great complexity, which justifies diverse opinions on the carcinogenic effect of polycyclic aromatic hydrocarbons on skin. These opinions are reflected in evaluations made by the Working Group of the International Agency for Research on Cancer (IARC) (7 – 9). How to obtain sufficiently large and homogeneous exposure groups is the greatest difficulty faced by epidemiologists working on this subject. The same problem emerged in the study presented. However, the obstacles anticipated and associated with the availability of persons sampled from the general population did not, finally, threaten the implementation of the study, and they appeared to be even less distressing than in the group of patients from hospital wards and dermatological out-patient clinics.

CONCLUSIONS

1. Following the analysis of occupational risk, it was found that the skin cancer risk in persons with past exposure to mineral oils was significantly greater in comparison with those non-exposed to polycyclic aromatic hydrocarbons, however, the relationship between the increased risk and the exposure period was rather limited. Only in the case of exposure lasting 30 years or longer did it become statistically significant.

2. No significant relationship between skin cancer risk and exposure to polycyclic aromatic hydrocarbons from other sources than mineral oils was found.

3. The matching of referents from the general population did not cause difficulties as great as had been theoretically anticipated. The availability of persons was higher than expected.

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REFERENCES

1. Adamiak-Zięba J, Ciosek A, Grochulska J, Krysiak B. Carcinogenic substances in the working environment. Vol. 2. Polycyclic aromatic hydrocarbons. Institute of Occupational Medicine, Lodz 1987 (in Polish).
2. Breslow NE, Day NE. Statistical Methods in Cancer Research. Vol. 1. The analysis of case-control studies. IARC, Lyon 1980.
3. Doll R, Peto R. The causes of cancer. J Nat Cancer Inst 66, 1193–1308, 1981.
4. Emmett EA. Occupational skin cancer-review. J Occup Med 17, 44–49, 1975.
5. Everall JD, Dowd PM. Influence of environmental factors excluding ultra-violet radiation of the incidence of skin cancer. Bull Cancer 65, 241–247, 1978.
6. Higginson J, Muir CS, Environmental Carcinogenesis: Misconceptions and limitations to cancer control. J Nat Cancer Inst 63, 1291–1218, 1979.
7. IARC Monographs on the evaluation of carcinogenic risk of chemicals to humans. Vol. 28. The rubber industry. Lyon 1982.
8. IARC Monographs on the evaluation on the carcinogenic risk of chemicals to humans. Vol. 33. Polynuclear aromatic compounds. Part 2. Carbon blacks, mineral oils and some nitroarenes. Lyon 1984.
9. IARC Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Vol. 35. Polynuclear aromatic compounds. Part 4. Bitumens, coal-tars and derived products, shale-oils and soots. Lyon 1985.
10. Kubasiewicz M, Starzyński Z. Case-referent study on skin cancer and its relation to occupational exposure to polycyclic aromatic hydrocarbons. I. Study design. Pol J Occup Med 2, 221–228, 1989.
11. Miettinen OS. Estimation of relative risk from individually matched series. Biometrics 26, 75–86, 1970.
12. Urbach F. UV radiation and skin cancer in man. Prev Med 9, 227–230, 1980.

13. Urbach F. Epidemiology and etiology of skin cancer in man. Cancer Campain New York, 213–227, 1982.
14. Wynder EL, Gori GB. Contribution of the environment to cancer incidence: an epidemiological exercise. J Nat Cancer Inst 58, 825–832, 1977.

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