

LOW DOSE IRRADIATION AND RISK OF LEUKAEMIA: A CASE-CONTROL STUDY

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Abstract. The effect of low dose irradiation (medical X-ray diagnostic) on the developing of leukaemias in adults is investigated. The influence of non-radiation agents (occupational exposure to chemical carcinogens, past viral infections, family aggregations) to leukaemias are considered also. During this retrospective study 228 patients have been examined with the following diagnosis: acute myeloid leukaemia, chronic myelogenous leukaemias, myelodysplastic syndrome and non-Hodgkin lymphoma (diagnosed between 1991 - 1993). Each case has been matched with two controls. Statistically significant increase has been found in the risk of developing leukaemias after X-ray diagnostic irradiation (OR=1.98, 95% CI=1.14 ÷ 3.46). Exposure to chemical agents is also associated with significant increase in the risk (OR=1.98, 95% CI=1.25 ÷ 2.86).

The medical X-ray diagnostics is the dominant “man-made” source of radiation exposure to the Bulgarian population [1]. The aim of this study is to evaluate the relationship between exposure to medical X-ray diagnostic procedures and leukaemias.

1. MATERIALS AND METHODS

The study is of a case control type. The cases, 228, have been recruited from hospital patients, most of them being from the National Centre of Haematology and Transfusion, and the rest - from the Haematology Clinic at the University Hospital and from the Military Medical Academy. All cases are diagnosed during the period 1991 - 1993. The distribution of cases by diagnosis is as follows: acute myeloid leukaemia (AML) - 54; chronic myelogenous leukaemia (CML) - 38; myelodysplastic syndrome (MDS) -34, and non-Hodgkin lymphoma (NHL) - 102. The controls are patients without a malignant disease, matched by sex and age (± 2 years). The interviews are carried out by a special questionnaire and they deal with subjects or with their close relatives if the subjects are too ill to be interviewed.

The data about the medical radiation are for a whole person’s life excluding the last year before the diagnosis or before the interview. The dose of each medical procedure has been taken from the Actualized Methodological Instruction for Determination of Doses Received by Patients from Medical X-rays and Radioisotope Diagnostics [2]. The cumulative equivalent dose to the red marrow and the dose to the whole body are estimated. Using the method of percentile, the patients are distributed into four groups (separately for whole body and red marrow). The patients are distributed into two groups as well, the first one - without any medical procedures, and the second one - with some medical procedures.

The contact with chemical carcinogens is considered according to the occupational route of all patients. As chemical carcinogens are analysed benzene [3] and other petrol products [4], coal tar [5] and magnetic field too [6]. The estimation is not quantitative.

The predisposition factors include hereditary predisposition and viral diseases. The hereditary factors are estimated according to the presence of malignant disease in the family: parents, sisters and brothers [7]. With regard to the viral aetiology, analysed are herpes simplex and herpes zoster [8, 9].

2. STATISTICAL ANALYSIS

The risk of developing leukaemias is estimated as odds ratio (OR) and is presented with a 95% confidence interval (CI). The frequencies of all risk factors under study are calculated for both cases and controls, as well as for each diagnosis. The results are presented in Tables 1 and 2.

3. ANALYSIS

No statistically significant association has been recorded when examining the risk of leukaemias by the method of percentile (the table not seen). The odds ratio for all groups is above 1.0 with the exception of the group with the highest exposure, the significant differences, however, are very wide. There is a significant difference between cases and controls when patients are distributed into two groups (Table 1). The odds ratio suggests high risk for those patients who have received any medical procedures.

The results for non-radiation factors are given in Table 2. The odds ratio suggests an association between chemical agents and leukaemias. The odds ratio for each diagnosis is over 1.0 but the 95% CI for each one is wide.

The risk estimation for leukaemia has shown no association with past viral diseases and hereditary predisposition. OR is over 1.0, excluding AML, but the corresponding 95% CI includes 1.0.

4. DISCUSSION

The results of the study must be interpreted in the context of potential limitations of the study design. The small number of cases for each diagnosis which makes necessary the analysing of four diagnoses simultaneously probably affects the results. Another limitation arises from the choice of the control group. Maybe this is due to the chosen patients with chronic diseases. The cases, by comparison, are often patients without a disease before cancer being diagnosed. There is no Register for Punctual Medical Diagnostic Procedures in Bulgaria. They are registered in the relevant hospital but the filling in of the individual card is not always exact. No dose response analysis can be persuasive in view of the difficulties regarding the control selection.

The none - versus - some medical exposure is likely to be more reliable than the amount of medical exposure, since it is easier to remember if you have ever been exposed to X-rays than to remember how many X-rays you have had, where and when. The results of other studies are controversial [9, 10]. In the present study a statistically significant

leukaemia risk is observed only when patients are distributed into two groups. This means that the effect of recall bias is not likely to be as great as in the none - versus - some medical exposure.

The results of this study confirm the relationship between risk of leukaemias and occupational chemical carcinogens [3, 8]. Retroviruses have long been suspected as a cause of human leukaemias [8, 11]. The case-control studies show the role of family aggregation in the aetiology of leukaemias [7, 8]. The present study, on the contrary, does not show such relationships.

TABLE 1. OR with 95% CI for selected leukaemias regarding medical X-ray diagnostic procedures

	AML		CML		MDS		NHL		ALL	
	Co	Ca	Co	Ca	Co	Ca	Co	Ca	Co	Ca
no	28	9	11	0	7	2	27	9	73	20
yes	80	45	65	38	61	32	177	93	383	208
total	108	54	76	38	68	34	204	102	456	228
OR	1.75		-		1.13		1.58		1.98	
95% CI	0.7 ÷ 4.4		-		0.3 ÷ 4.0		0.7 ÷ 3.8		1.1 ÷ 3.5	

TABLE 2. OR with 95% CI for selected leukaemias regarding non-radiation agents

	AML	CML	MDS	NHL	ALL
Chemical agents					
OR	1.60	3.92	3.58	1.32	1.89
95% CI	0.6 ÷ 4.5	1.3 ÷ 12.2	1.2 ÷ 11.0	0.8 ÷ 2.4	1.2 ÷ 2.9
Viral disease					
OR	0.61	0.54	0.39	1.03	0.71
95% CI	0.2 ÷ 1.6	0.2 ÷ 1.5	0.11 ÷ 1.3	0.6 ÷ 1.9	0.5 ÷ 1.1
Hereditary predisposition					
OR	0.58	2.19	1.87	1.26	1.30
95% CI	0.1 ÷ 2.4	0.6 ÷ 8.5	0.5 ÷ 7.0	0.6 ÷ 2.5	0.7 ÷ 2.1

REFERENCES

- [1] VASSILEV, B., Exposure of the Bulgarian population to ionising radiation. Analysis, retrospection, predictions. 1950 - 2000. "Although" Publishing House, Sofia, (1994).
- [2] Actualized methodological instruction for determination of doses received by patients from medical X-rays and radioisotope diagnostics. Sofia (1988) 6-7, 18-32.
- [3] CHEKOWAY, H. et al., An evaluation of the association of leukaemia rubber industry solvent exposures. Am. J. Ind. 5 (1984) 239-249.
- [4] AUSTIN, H., COLE, P., McCRAW, O.C., A case-control study of leukaemia at an oil refinery, J. Occup. Med. 28 (1986) 1169-1173.
- [5] ADAMSON, R.H., SEIBER, S.M., Chemically induced leukaemia in humans, Env. Health Persp. 39 (1982) 93-102.

- [6] SAVITZ, D., Overview of epidemiologic research on electric and magnetic fields and cancer, *Am. Ind. Hyg. Assoc. J.* 54 (1993) 197-204.
- [7] SHPILBERG, O. et al., Familial aggregation of haematological neoplasms: a controlled study, *Br. J. Haem.* 84 (1994) 75-80.
- [8] LINET, M., CARTWRIGHT, R.A., "The leukaemias", *Cancer epidemiology and prevention*, (SCHOTTENFEILD, D., FRAUMENI, J., Jr., Ed.), Oxford University Press, Oxford (1996) 841-890.
- [9] BOICE, J.D., et al., Diagnostic X-rays and risk of leukaemia, lymphoma and multiple myeloma, *JAMA* 265 (1991) 1290-1294.
- [10] FLODIN, U., et al., Acute myeloid leukaemia and background radiation in an expanded case-referent study, *Arch. Environ. Health*, 45 (1990) 364-366.
- [11] CLARK, D.A., et al., The seroepidemiology of human herpesvirus-6 (HHV-6) from a case-control study of leukaemia and lymphoma, *Int. J. Cancer*, 47 (1991) 803-810.