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Pesticide exposures and multiple myeloma in Iowa men

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A population-based case-control study of 173 White men with multiple myeloma (MM) and 650 controls was conducted in Iowa (United States), an area with a large farming population, to evaluate the association between MM, agricultural risk factors, and exposure to individual pesticides. A slight nonsignificantly elevated risk for MM was seen among farmers (odds ratio [OR] = 1.2, 95 percent confidence interval [CI] = 0.8-1.7). Although slight excesses were observed, there were no significant associations between MM and handling either classes of pesticides or specific pesticides. Thus, this study found little evidence to suggest an association between risk of MM and farming or pesticides.

Key words: Case-control study, epidemiology, etiology, farming, multiple myeloma, pesticides, United States.

Introduction

Excess risk for multiple myeloma (MM) has been associated with farming in a number of studies.[1,2] Although pesticides as a generic class of chemicals have been associated with MM, information on risk from use of individual pesticides is limited.[2,3] We analyzed detailed pesticide data from a case-control study among White men in Iowa (United States) to investigate whether risk of MM was related to the use of specific agricultural pesticides. A previous analysis of these data included only classes of pesticides.[4]

Methods

Concurrent, population-based, case-control, interview studies of leukemia, non-Hodgkin's lymphoma (NHL), and MM in Iowa and leukemia and NHL in Minnesota were conducted during 1981-84 using the same questionnaire and controls. Presented in this paper are results for the MM cases and Iowa controls. Details of the pesticide analyses for leukemia and NHL have been published elsewhere.[5,6]

Included in this study were all cases of MM among White men aged 30 or older diagnosed during 1981-84. Cases were identified from the Iowa Health Registry, a member of the Surveillance, Epidemiology, and End Results (SEER) program. To confirm the diagnosis of MM, pathologic material and laboratory reports were reviewed by an expert pathologist. Twenty-five cases of MM for whom adequate information for diagnostic confirmation were unavailable are not included in the analyses.

Three sources of controls were used to select a population-based stratified sample of White men without lymphatic or hematopoietic cancer: random digit dialing [RDD] (living controls under age 65);[7] Medicare records provided by the Health Care Financing

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Administration (living controls aged 65 or over); and state death certificate files (deceased controls). Controls were frequency-matched to the cases by five-year age group and vital status at time of interview. Since the study was designed to evaluate risks for farming and farm-related exposures, we did not match controls to cases on geographic area.

A standardized questionnaire was used to obtain detailed information on general farm activities and the use on the farm of 24 animal insecticides, 34 crop insecticides, 38 herbicides, and 16 fungicides. Questions on pesticide use included whether the subject personally mixed, handled, or applied the pesticide; whether the subject usually used protective equipment when handling the pesticide; and the first and last year the pesticide was used. Information on the frequency of pesticide use was not obtained. In-person interviews lasting approximately 50 min were conducted with subjects or with close relatives, if subjects were deceased. Interviews were completed for 84 percent of the MM cases and 78 percent of the controls. The response rate for the controls includes the 87.5 percent response rate for the RDD controls at the household screening phase. Included in the analysis were 173 (101 alive, 72 deceased) MM cases and 650 (452 alive, 198 deceased) controls.

Logistic models[8] were used to calculate odds ratios (OR) for MM from agricultural exposures and from individual pesticides that were handled personally by at least five cases. This restriction based on the much smaller case-group was made to assure adequate numbers of subjects in each cell for analysis. All ORs were calculated using nonfarmers as the referent group because they were not exposed to any farm-related activities. We felt that subjects who farmed but reported no use of pesticides might be unusual and farmers who did not use a specific pesticide might have been exposed to other potentially carcinogenic pesticides. Vital status (alive, deceased) and age (< 45, 45-64, 65 +), were included in models to adjust for potential confounding. Other factors such as smoking and education were evaluated and found not to be confounders of agricultural risk factors.

Table 1. Risk of multiple myeloma according to number of years farmed and ever use of types of pesticides

	No. of cases	No. of controls	OR[a]	(CI)[b]
Never farmed	62	272		
Ever farmed	111	378	1.2	(0.8-1.7)
Farmed (yrs)				
1-9	40	92	2.0	(1.2-3.2)
10-29	38	101	1.5	(1.0-2.4)
30-44	21	93	1.0	(0.6-1.7)
45 +	8	85	0.3	(0.2-0.7)
Unknown	4	7		
Pesticides	93	318	1.2	(0.8-1.8)
Fungicides	7	35	1.0	(0.4-2.4)
Herbicides	54	194	1.2	(0.8-1.9)
Insecticides	91	308	1.2	(0.9-1.8)

[a] All odds ratio (OR) values relative to subjects who never farmed. All ORs adjusted for vital status and age in a logistic analysis.
[b] CI = 95% confidence interval.

Table 2. Risk of multiple myeloma for mixing, handling, or applying specific pesticides

Pesticides	No. of cases	No. of controls	OR[a]	(CI)[b]
Animal insecticides				
Chlordane	9	29	1.6	(0.7-3.6)
Coumaphos	5	16	2.0	(0.7-5.8)
DDT	20	84	1.1	(0.6-1.9)
Dichlorvos	7	21	2.0	(0.8-5.0)
Lindane	16	75	1.1	(0.6-2.0)
Malathion	6	44	0.8	(0.3-1.9)
Nicotine	6	22	1.4	(0.5-3.6)
Crop insecticides				
Aldrin	22	89	1.1	(0.7-2.0)
Carbofuran	12	49	1.2	(0.6-2.5)
Carbaryl	6	20	1.5	(0.6-3.9)
DDT	20	52	1.7	(0.9-3.1)
Fonofos	5	22	1.4	(0.5-3.8)
Lindane	5	19	1.2	(0.4-3.4)
Malathion	8	24	1.9	(0.8-4.6)
Phorate	11	41	1.4	(0.7-3.1)
Terbufos	10	33	1.8	(0.8-4.0)
Herbicides				
Alachlor	13	73	0.9	(0.5-1.7)
Atrazine	12	74	0.8	(0.4-1.6)
Bentazon	9	38	1.3	(0.6-2.8)
Butylate	8	36	1.3	(0.6-3.1)
Chloramben	6	47	0.6	(0.3-1.6)
Cyanazine	11	51	1.2	(0.6-2.4)
2,4-D	35	150	1.0	(0.6-1.6)
Dicamba	10	43	1.3	(0.6-2.8)
Glyphosate	11	40	1.7	(0.8-3.6)
Metribuzen	7	36	1.2	(0.5-3.0)
2,4,5-T	7	39	0.9	(0.4-2.1)
Trifluralin	17	69	1.2	(0.7-2.3)

[a] All odds ratios (OR) values relative to nonfarmers (62 cases, 272 controls). All ORs adjusted for vital status and age in a logistic analysis.
[b] CI = 95% confidence interval.

Results

Some farming activity was reported by 64 percent of the cases and 58 percent of the controls (OR = 1.2; Table 1). The farming-associated risk was greater for subjects less than 65 years (OR = 1.4, 95 percent confidence interval [CI] = 0.7-2.8) than for subjects 65 years of age or older (OR = 1.1, CI = 0.7-1.7). Years engaged in farming appeared to be inversely associated with risk of MM (P for trend < 0.05), even though the median year first (1932) and last farmed (1968) were the same for cases and controls. Similar patterns in risk were seen for both younger (< 65 years) and older (65 + years) subjects (not shown). The ORs were not elevated significantly among farmers reporting the use of any pesticide (OR = 1.2), any fungicide (OR = 1.0), any herbicide (OR = 1.2), or any insecticide (OR = 1.2; Table 1).

Risks for MM were not increased significantly for farmers who personally mixed, handled, or applied any specific insecticide or herbicide (Table 2). Nonsignificantly elevated ORs of 1.5 or greater were seen for the animal insecticides chlordane, coumaphos, and dichlorvos; the crop insecticides carbaryl, dichlorodiphenyl-trichloroethane (DDT), malathion, and terbufos; and the herbicide glyphosate. Failure to use protective equipment was associated with a higher risk of MM for chlordane (OR = 1.9), coumaphos (OR = 2.4), DDT (OR = 1.8), terbufos (OR = 2.1), and glyphosate (OR = 1.9), but not for dichlorvos (OR = 2.0), carbaryl (OR = 1.4), and malathion (OR = 1.4). Risks were generally higher for deceased than alive subjects and for older than for younger subjects. Risks were not elevated for subjects who handled the phenoxy herbicides 2,4-dichlorophenoxyacetic acid (2,4-D) and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T). As previously reported for these data,[4] ORs for farmers exposed to any chemical class of pesticides (*e.g.*, chlorinated hydrocarbon or organophosphate insecticides) were not significantly elevated.

Discussion

This study of White men in Iowa was designed to evaluate the association betweeen MM and agricultural risk factors, as well as exposure to individual pesticides. There was a slight, nonsignificantly elevated risk for MM among farmers (OR = 1.2), with the greatest risk seen for farmers of shortest duration (< 10 years, OR = 2.0). In other studies where positive associations with farming have been reported, risks generally have been in the range of 1.2 to 2.2.[1,3,9] However, two recent studies conducted among White men in Missouri[10] and Nebraska[11] found no association between MM and farming. Various farm-related exposures have been suggested as potential risk factors for lymphatic and hematopoietic cancers including pesticides, viruses, or chronic antigenic stimulation.[12]

Positive associations between MM and use of pesticides in general have been reported previously in some studies,[3,13-16] but not in others.[17] In our study, we found no significant associations between MM and the handling of pesticides in general, classes of pesticides, or specific pesticides. Risks were not elevated for exposure to phenoxy herbicides as has been reported for MM in a recent Swedish study[3] and for NHL in a number of studies.[18-21] The slightly elevated risks seen for a number of animal and crop insecticides were often greater among deceased than living subjects, suggesting that other factors such as recall bias or chance, due to relatively small numbers of cases and controls or multiple statistical comparisons, may play a role.

This study, where over half of the subjects were farmers, found little evidence of an association between risk of MM and farming. These data also do not provide strong support for an association with specific agricultural chemicals.

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