Journal of Carcinogenesis

BioMed Central

Short paper

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Prevalence of pesticide exposure in young males (</= 50 years) with adenocarcinoma of the prostate

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Published: 15 July 2003

Journal of Carcinogenesis 2003, **2**:4

Received: 24 March 2003
Accepted: 15 July 2003

This article is available from: http://www.Carcinogenesis.com/content/2/1/4

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Abstract

Evidence implicating pesticides as causative agents of prostate cancer is controversial, and specifically, data in young adults is lacking. Hence, we performed a preliminary study evaluating the relationship between pesticide exposure and prostate cancer in young males. After approval from the University of North Dakota Institutional Review Board and Human Subjects Committee, a retrospective study was performed on all young males (</ = 50 years) with a biopsy-proven diagnosis of carcinoma of the prostate. The records of all patients aged less than/equal to 50 years, with a diagnosis of adenocarcinoma of the prostate, from January 1991 through December 2001 were reviewed. Pesticide risk assessment interviews were performed by a single member of the team, for consistency, via telephone on the basis of a pre-determined questionnaire investigating occupations and hobbies with special emphasis on: Duration of exposure. An exposure index was calculated for each interviewed subject according to the following formula: hours/day × days/year × years. Patients with an exposure index >2400 hours were considered as 'exposed.' The 2400 hour cut-off value was chosen on the basis of previous reports indicating that this figure represents heavy exposure to genotoxic agents. Statistical analysis was obtained using SPSS-10®. Between 1991 and 2001, 61 young males with adenocarcinoma of the prostate were identified, of whom 56 patients with a mean age of 47 years (range: 40–49) had complete records of treatment and could be contacted for completion of the questionnaire. The most common stage at presentation was Stage III and the mean Gleason's score was 7.5 (range 5–9). Interestingly, almost a third (16/56, 28.6%) of patients had stage IV disease at presentation. 37/56 (66.1%) patients had 'significant' exposure in our study. In addition, interestingly, the mean survival in the subgroup of patients with pesticide exposure was 11.3 months (SD: +/- 2.3 months), while the mean survival in the patients without pesticide exposure (n = 19) was 20.1 months (SD: +/- 3.1 months), with p-value <0.01. Although our study is relatively small, it does reveal preliminary evidence linking pesticide exposure to the early development of, possibly aggressive, prostate adenocarcinoma. Future, larger, epidemiological studies are needed to confirm the findings of our study.

Introduction

Adenocarcinoma of the prostate is one of the most frequently diagnosed cancers in men and the second leading cause of cancer-related deaths in men. The incidence of prostate carcinoma in the early 1990s increased, mainly because of an increase in screening for the disease [1]. Many patients with diagnosed prostate cancer have comorbid conditions and die of causes other than prostate cancer [2]. However, this is not true in the case of prostate cancers occurring at a younger age and with an aggressive course. Exposure-response relation may be stronger among young individuals because there is likely to be less misclassification of both exposure and cause of death among the young [3]. Also, despite many associations and attempts to identify specific risk factors for prostate cancer, concrete data regarding the etiology of prostate cancer, except age, are unavailable. Numerous epidemiological reports allude to the positive relation between pesticides and prostate cancer [3–7]. Among whites the mortality rates in the Midwest and north-central regions were significantly higher than the total U.S. rate. Also, positive correlation was observed for people for German and Scandinavian ancestry [8]. However, none of the previously published data addresses the prevalence of 'significant' pesticide exposure among young males with prostate carcinoma. We decided to study young (</ = 50 years) males in North Dakota and Western Minnesota (both predominantly rural/farming communities), with biopsy-proven adenocarcinoma of the prostate, to evaluate the relevance of pesticide exposure and occurrence of prostate cancer.

Materials and Methods

After approval from the University of North Dakota Institutional Review Board and Human Subjects Committee, a retrospective study was performed on all young males (</ = 50 years) with a biopsy-proven diagnosis of carcinoma of the prostate. The records of all patients aged less than/equal to 50 years, with a diagnosis of adenocarcinoma of the prostate, from January 1991 through December 2001 were reviewed. The data collected included the following variables regarding the patient's cancer history: age, socioeconomic status, family history of cancer (if positive, type of cancer), smoking, performance score (ECOG), stage of cancer, treatment modality/modalities for prostate cancer, metastatic sites (other organs) involved, and associated malignancies (if any).

Pesticide risk assessment interviews were conducted by a single member of the team, (for consistency) via telephone, on the basis of a pre-determined questionnaire investigating occupations and hobbies with special emphasis on:

(a) Contacts with mutagenic agents including pesticides (insecticides, herbicides), organic solvents (paints, varnishes, solvents and glues) and petroleum products (diesels, petrol, oils, greases, dyes, inks and colorings).

(b) Type of exposure (preparation and/or spraying of pesticide solutions, direct handling of solvents containing materials or petroleum products).

(c) Use of protective measures in the workplace (dissolving or spraying the pesticide with pressurized containers, using glues or varnishes with adequate ventilation, etc.). In the presence of these effective protection measures the subject was considered as 'non-exposed'.

(d) Duration of exposure. An exposure index was calculated for each interviewed subject according to the following formula: hours/day × days/year × years [9]. Patients with an exposure index >2400 hours were considered as 'exposed.' The 2400 hour cut-off value was chosen on the basis of previous reports indicating that this figure represents heavy exposure to genotoxic agents [10,11]. Statistical analysis was obtained using SPSS-10®.

Results

Between 1991 and 2001, 61 young males with adenocarcinoma of the prostate were identified, of whom 56 patients with a mean age of 47 years (range: 40–49) had complete records of treatment and could be contacted for completion of the questionnaire. The most common stage at presentation was Stage III and the mean Gleason's score was 7.5 (range 5–9). Interestingly, almost a third (16/56, 28.6%) of patients had stage IV disease at presentation. Although most patients (n = 40, 70.1%) were asymptomatic (from a genitourinary perspective) at presentation, among the patients presenting with symptoms, the most common presentation was hematuria. Treatment ranged from radical prostatectomy/definitive radiation therapy to combination chemotherapy (with estramustine and docetaxel) and local radiotherapy (for bony metastatic disease years).

Of the initial 61 patients identified from our database, only 56 patients/their next of kin could be contacted for completion of the pesticide risk assessment questionnaire. Surprisingly, 37/56 (66.1%) patients had 'significant' exposure in our study. In addition, interestingly, the mean survival in the subgroup of patients with pesticide exposure was 11.3 months (range: 5–19 months), while the mean survival in the patients without pesticide exposure (n = 19) was 20.1 months (range: 9 – 32). The p-value was significant for decreased survival (<0.01) by t-test for independent samples (Table 1).

Table 1: Table showing comparison of survival between exposed and nonexposed males with prostate cancer: (p-value < 0.01).

	Number (n)	Mean Survival (months)	Standard Deviation (+/- months)
Males with significant pesticide exposure	37	11.3	2.3
Males without significant pesticide exposure	19	20.1	3.1

Discussion

Numerous reports over the past few decades have equivocally described the role of pesticides as an etiologic agent for prostate cancer. But, none specifically address the issue in young males. Prostate cancer is a biologically heterogeneous tumor, with some patients suffering rapid debilitation and death and others never developing clinical manifestations of the disease [2]. Our study reveals a possible relation between pesticides and incidence of aggressive prostate cancer resulting in significant morbidity and mortality in young males. This concurs with numerous studies, which have shown a possible relation between occupations involving handling of pesticides and prostate cancer. Morrison et al, in their large study, have shown that there is an exposure-response relation between herbicide exposure and prostate cancer mortality. Their data showed that mortality was related to the number of acres treated with herbicides. They have further shown that phenoxy herbicides may be responsible [3]. Dich et al found an increased risk of prostate cancer in pesticide applicators (who are exposed to pesticides more than farmers) [4]. The results of the study by Mills P showed that exposure to the pesticides 'atrazine' and 'captan' correlated significantly with an increase in incidence of prostate cancer in black males [5]. In two separate studies Fleming et al have reported that pesticide users have a higher risk of cancers than the general population and amongst cancers the incidence and mortality due to prostate cancer is especially increased [6,7].

In predominantly agricultural states like North Dakota and Western Minnesota, exposure to pesticides is a common everyday occurrence. Although animal studies demonstrate that many pesticides are carcinogenic, (e.g. organochlorines, creosote and sulfallate) while others, notably organochlorines (DDT, chlordane and lindane) are tumor promoters, human data is limited to a small number of studies that evaluate individual pesticides [11]. Tessier et al have shown that in human prostate cancer cell lines LNCaP and PC-3, erbB-2 kinase was activated by pesticides of different chemical classes: the organochlorine insectides, beta-hexachloro-cyclohexane (beta-HCH), o,p'-dichloro-diphenyl-trichloroethane (o,p'DDT), heptachlor epoxide, permethrin and chlorothalonil [12].

In occupational epidemiology information is often required about work histories and occupational exposures of study subjects. Objective sources are the best way to gather this data, but, unfortunately, subjects themselves are the only source of the required data. We realize that as with most questionnaire-based studies, a drawback of our study-design is the distinct possibility of a recall bias among the case population. In addition, in cases where the patient was deceased, the data was obtained from the next of kin, who may or may not have had detailed knowledge regarding pesticide exposure of the subject in question. Repeatability of self reported data on occupational exposure has been shown to be high in previous studies [13,14]. Also, accuracy of job history was not influenced by level of education, socioeconomic status or age, especially young males [15–18]. Interviewing technique plays a central role in improving accuracy of the recall and is under the control of the investigator [19]. We tried to minimize the effect of interviewing technique on the results by having one single investigator conduct all the interviews. Also, we used prompted questions, rather than open-ended question during the collection of exposure-data as that has been shown to decrease recall bias [20]. Finally, another potential drawback to our study was the fact that although we gathered enough data regarding the extent of pesticide (insecticide/herbicide) exposure, while implementing our questionnaire, we failed to investigate the extent of exposure to specific pesticides/their components.

Conclusions

Due to the relatively small number of patients included in our study, our results should be considered as only preliminary evidence linking pesticide exposure to the early development of prostatic carcinoma. It is possible that exposure to pesticide(s)/pesticide components leads to alteration of specific biomarker profiles {i.e. her-2/neu, VEGF (vascular endothelial growth factor), UPA-r (urokinase plasminogen activator-receptor)} leading to the development of aggressive adenocarcinoma of the prostate. We are currently in the process of testing specific pesticide components in PC-3 and LNCaP cells to evaluate for overexpression of the above biomarkers. Future, larger, epidemiologic studies would also be helpful to determine which pesticide(s)/pesticide components are indeed associated with the early progression of adenocarcinoma of the prostate, and eventually to diminished survival, so that proper preventative measures may be adopted.

Authors' Contributions

AP conceived and participated in the design of the study and helped draft the manuscript.

AWP helped in the design and coordination of the study and helped in completion of the manuscript.

EL conducted the questionnaire interviews and performed statistical testing.

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