Occupational pesticide use and Parkinson's disease in the Parkinson Environment Gene (PEG) study

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ABSTRACT

Objective: To study the influence of occupational pesticide use on Parkinson's disease (PD) in a population with information on various occupational, residential, and household sources of pesticide exposure.

Methods: In a population-based case control study in Central California, we used structured interviews to collect occupational history details including pesticide use in jobs, duration of use, product names, and personal protective equipment use from 360 PD cases and 827 controls. We linked reported products to California's pesticide product label database and identified pesticide active ingredients and occupational use by chemical class including fungicides, insecticides, and herbicides. Employing unconditional logistic regression, we estimated odds ratios and 95% confidence intervals for PD and occupational pesticide use.

Results: Ever occupational use of carbamates increased risk of PD by 455%, while organophosphorus (OP) and organochlorine (OC) pesticide use doubled risk. PD risk increased 110–211% with ever occupational use of fungicides, herbicides, and insecticides. Using any pesticide occupationally for > 10 years doubled the risk of PD compared with no occupational pesticide use. Surprisingly, we estimated higher risks among those reporting use of personal protective equipment (PPE).

Conclusions: Our findings provide additional evidence that occupational pesticide exposures increase PD risk. This was the case even after controlling for other sources of pesticide exposure. Specifically, risk increased with occupational use of carbamates, OPs, and OCs, as well as of fungicides, herbicides, or insecticides. Interestingly, some types of PPE use may not provide adequate protection during pesticide applications.

1. Introduction

Parkinson's disease (PD) is a chronic and progressive movement disorder. Many previous epidemiologic investigations identified occupational pesticide exposures as risk factors for PD (Brown et al., 2006). Studies reporting associations of PD with occupational exposures to pesticides, herbicides, insecticides, and fungicides, however, are of varying quality, size, and consistency in terms of the agents they examined. Also, some studies assessed exposures rather crudely (ever/never occupational exposure), or employed self-reports only (Brown et al., 2006), with little more than a handful of studies creating job exposure matrixes (JEMs) based on various types of information and levels of detail (Baldi et al., 2003a; Baldi et al., 2003b; Liew et al., 2014; Elbaz et al., 2009; Feldman et al., 2011; van der Mark et al., 2014), and the Agricultural Health Study (AHS) being the only cohort of licensed pesticide applicators and spouses with a prospective design and detailed assessment of pesticide use (Kamel et al., 2007).

In our California population based case control study of PD (Kang et al., 2005; Ritz et al., 2016), we conducted a detailed historical assessment of active occupational use of pesticides and personal protective equipment (PPE) use which we are reporting on for the very first time. Our previous reports relied on extensive information for other sources of pesticide exposure for this population, specifically, household pesticide use and ambient pesticide exposures from agricultural applications at workplaces and residences. Here, we present results for primarily farming-related occupational pesticide use self-reported by participants and complemented by information on chemicals from the California pesticide registration system. Different from

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² Abbreviations: PEG, Parkinson Environment Gene study; PD, Parkinson's disease; OP, organophosphorus; OC, organochlorine; PPE, personal protective equipment; HIPAA, Health Insurance Portability and Accountability Act; MMSE, Mini-Mental State Examination; CAPIT, Core Assessment Program for Intracerebral Transplantation; CDPR, California Department of Pesticide Regulation; PAN, Pesticide Action Network; DDT, Dichlorodiphenyltrichloroethane; TEPP, Tetraethyl pyrophosphate; GIS, geographic information system; DTC, dichlofencarbamate; PQ, paraquat

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previous studies in other populations, we are able to adjust for other pesticide exposures (gardening and household use and ambient bystander exposures) common in agricultural environments; also, we are only the second study to examine whether PPE use modifies risk from occupational pesticide use (Kamel et al., 2007; Furlong et al., 2015).

2. Materials and methods

2.1. Study subjects

The Parkinson Environment Gene (PEG) study is a population-based case-control study of Parkinson’s disease, with participants recruited from the mostly rural California counties Kern, Fresno, and Tulare. Cases were enrolled within three years of PD diagnosis, from 2001 through 2007, and population controls were enrolled between 2001 and 2011. Descriptions of PD case diagnostic criteria (Kang et al., 2005) and subject recruitment (Wang et al., 2011) can be found in our prior publications.

Briefly, through local neurologists, medical groups, and public service announcements, we identified 1167 PD patients. We excluded 397 diagnosed > 3 years before contact, 134 not living in the target counties, 51 without a PD diagnosis, and 22 who were too ill to participate. Of 563 remaining eligible cases, 90 declined, moved, became too ill or died before we could examine them. We further excluded 107 who did not meet criteria for idiopathic PD at exam (Kang et al., 2005), and six withdrew prior to interview leaving us with 360 patients (78.9% acceptance rate for PD cases).

In the first year of our study, controls 65 years or older were randomly selected from Medicare enrollee lists for all three counties, but after the Health Insurance Portability and Accountability Act (HIPAA) was instated, controls were instead randomly selected from residential parcel listings on tax assessor records. We used two strategies to enroll controls. First, we mailed letters to selected residential units and enrolled through mail and phone only. Using a second strategy, we recruited controls from randomly selected clusters of five neighboring households from parcel listings, and trained field staff conducted home visits to determine eligibility and enrolled controls at the doorstep. Only one eligible person per household was allowed to enroll as a control in our study (Liew et al., 2014).

We have depicted control selection in a flowchart in the supplement to this article (Fig. S1, Supplemental material). Using the first sampling strategy, we contacted 1212 potential controls of whom 457 were ineligible (409 were < 35 years of age, 44 too ill to participate, and 4 lived outside target counties). We recruited 346 controls via phone and mail, since an additional 409 eligible controls declined, became too ill, or moved after screening and prior to interview. An additional 5 controls out of the 346 were missing data, leaving 341 controls with complete data. Through an early mailing, for which the number of eligible subjects who did not respond remains unknown, we recruited and interviewed 62 from among controls randomly selected from residential parcel listings. We screened 4753 individuals for eligibility at their door step and found 3512 to be ineligible (88% due to age criteria), leaving 1241 eligible controls, of whom 634 declined participation and 607 enrolled. Of the 607 controls enrolled through the second sampling strategy, 183 subjects agreed to participate in an abbreviated interview only and did not provide occupational information. Altogether, we have 827 controls available.

This study was approved by the University of California, Los Angeles (UCLA) Institutional Review Board, and we obtained written informed consent from all participants.

2.2. Data collection

Trained interviewers collected information by telephone on demographic characteristics, smoking, household pesticide use, lifetime residential addresses, lifetime occupations and addresses, and screened for jobs with exposures of interest, i.e., fertilizers, pesticides, metals, wood, paint strippers, and solvents. We conducted interviews in the preferred language of the participant and employed bilingual staff.

PD cases (290 out of 360) and controls (619 out of 827), who screened positive in this main telephone interview, i.e., reported (1) ever having worked regularly (i.e., once a week or more) with any one of the agents of interest, or who reported having ever (2) lived on a farm, or (3) worked on a farm, were invited for an additional telephone interview to collect more details on specific occupational exposures. We provide a flowchart in the supplement showing the participation in the detailed occupational interview (Fig. S2, Supplemental material).

Of those who screened positive for fertilizers or pesticide use, or ever working or living on a farm (N = 754), 78.7% (192/244) of cases and 80% (408/510) of controls agreed to participate in the detailed occupational interview. Of the 228 cases and 457 controls who participated in the detailed interview, there are 36 cases and 49 controls who screened positive for using chemicals other than pesticides, i.e., metals, wood, paint strippers and solvents and did not report ever working on a farm or living on a farm. Of these, 3/36 (8.3%) cases and 4/49 (8.2%) controls reported pesticide use in the supplemental occupational interview. Therefore, it is unlikely that those who screened positive for using other chemicals only (metals, wood, paint strippers, and solvents), who also reported not living on a farm and not working on a farm, and refused to participate in occupational interviews (10 cases and 60 controls) would have used pesticides occupationally.

All of our PD patients were seen at least once – many multiple times over a period of 10 years – by our UCLA movement specialists to confirm idiopathic PD according to United Kingdom Brain Bank, Core Assessment Program for Intracerebral Transplantation (CAPIT) rating scale, and Gelb criteria (Kang et al., 2005). We also conducted a Mini-mental State Examination (MMSE) over the phone or in person, with phone scores converted into predicted in-person scores as recommended (Newkirk et al., 2004).

2.3. Active occupational pesticide use

In this paper, we utilize extensive information from the additional interview in which participants self-reported active occupational pesticide use of fungicides, herbicides, insecticides, and other pesticides (rodenticides, defoliants) including the name of pesticide products used, purpose or site of usage (e.g., crop, plant, animal, insect), at what ages they used pesticides, duration (in years) of use, location of use (Fresno, Kern, or Tulare counties; California; United States or abroad), whether subjects mixed or loaded pesticides, application methods (tractor with/out an enclosed cab, hand sprayer, backpack or aerial application, etc.), and PPE use (gloves, mask, coveralls, boots, goggles, respirator, etc.). In order to reduce subject burden and recall issues, we started our collection of all self-reported pesticide product and usage data (i.e., purpose, age of use, duration, location, job tasks, and PPE) by asking about pesticide groups (fungicides/herbicides/insecticides/other pesticides). We asked, “Have you ever handled fungicides at work?” If the participant responded, “Yes”, we followed with, “What type of fungicide was it?”、“For what purpose did you use a fungicide?”, etc., collecting self-reported fungicidal product names if the participant remembered them. We asked the same series of questions for herbicides, insecticides, and other pesticides.

We identified the main active ingredient of each self-reported pesticide product, relying on the California Department of Pesticide Regulation (CDPR) product label database (California Department of Pesticide Regulation, 2013), which lists the active ingredients of all pesticide products sold on the California market, with over 70% of products having registrations dated 1970 and later. We obtained the main active ingredient (in terms of product weight), by comparing the reported pesticide product name and purpose of use with CDPR database names, purposes (e.g., crop, plant, animal, insect), use types
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