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A task-based assessment of parental occupational exposure to pesticides and childhood acute lymphoblastic leukemia

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ABSTRACT

Objectives: Associations between parental occupational pesticide exposure and childhood acute lymphoblastic leukemia (ALL) vary across studies, likely due to different exposure assessment methodologies.

Methods: We assessed parental occupational pesticide exposure from the year before pregnancy to the child's third year of life for 669 children diagnosed with ALL and 1021 controls. We conducted expert rating using task-based job modules (JM) to estimate exposure to pesticides among farmer workers, gardeners, agricultural packers, and pesticide applicators. We compared this method to (1) partial JM using job titles and a brief description, but without completing the task-based questionnaire, and (2) job exposure matrix (JEM) linking job titles to the International Standard Classifications of Occupation Codes. We used unconditional logistic regression to calculate odds ratios (OR) and 95% confidence intervals (95% CI) for ALL cancer risk and pesticide exposure adjusting for child's sex, age, race/ethnicity and household income.

Results: Compared to complete JMs, partial JMs and JEM led to 3.1% and 9.4% of parents with pesticide exposure misclassified, respectively. Misclassification was similar in cases and controls. Using complete JMs, we observed an increased risk of ALL for paternal occupational exposure to any pesticides (OR=1.7; 95% CI=1.2, 2.5), with higher risks reported for pesticides to treat nut crops (OR=4.5; 95% CI=0.9, 23.0), and for children diagnosed before five years of age (OR=2.3; 95% CI: 1.3, 4.1). Exposure misclassification from JEM attenuated these associations by about 57%. Maternal occupational pesticide exposure before and after birth was not associated with ALL.

Conclusions: The risk of ALL was elevated in young children with paternal occupational pesticide exposure during the perinatal period, using more detailed occupational information for exposure classification.

1. Introduction

The evidence for an association between parental occupational pesticide exposure and childhood leukemia has been limited by weaknesses of previous research methods, especially exposure assessment (Jurewicz and Hanke, 2006). Two large studies did not observe an association between parental occupational pesticide exposure and childhood leukemia, however exposure in these studies was based on job title alone and exposure prevalence was very low (McKinney et al., 2003; Rudant et al., 2007). In contrast, two large studies that assessed

Abbreviations: ALL, acute lymphocytic leukemia; CI, confidence interval; JEM, job exposure matrix; JM, job-specific module; CCLS, California Childhood Leukemia Study; OR, odds ratio

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exposure using in-depth parental interviews similar to job modules are consistent with an increased risk of childhood leukemia associated with maternal and paternal occupational pesticide exposure, perhaps due to reduced exposure misclassification (Meinert et al., 2000; Monge et al., 2007). Specifically, a case-control study in Germany that used telephone interviews to obtain detailed information on pesticide exposure observed elevated risk of childhood leukemia associated with both paternal and maternal occupational pesticide exposure during pregnancy with odds ratios (OR) and 95% confidence intervals (CI) of 1.6 (1.1–2.3) and 3.6 (1.5–8.8) respectively (Meinert et al., 2000). A study in Costa Rica conducted using in-depth interviews to collect information on job tasks, a calendar with life events and a pesticide checklist observed an OR=1.5 (1.0–2.3) for fathers occupational exposure to any pesticides during the second trimester and OR=2.4 (1.0–5.9) for mothers exposure during pregnancy (Monge et al., 2007). The findings from meta-analyses of childhood leukemia and parental occupational pesticide exposure support the need to rely more on studies that clearly stipulate exposure to pesticides rather than those that assume pesticide exposure because of farm/agriculture employment (Van Maele-Fabry et al., 2010; Wigle et al., 2009; Bailey et al., 2014).

Job modules have been developed to improve the specificity of occupational exposure assessment by utilizing closed ended branching questions that are task based (Gerin and Siemiatycki, 1991) and a calendar with important life events to assess exposure during critical time periods of development (Monge et al., 2004; Zahm et al., 2001). A comparison of job title as a surrogate for job modules to assess occupational lead exposure found good specificity (~0.9), but only moderate sensitivity (~0.5) (Bhatti et al., 2011). In studies where detailed job module type information is not available, bias analysis can be used to characterize the magnitude of misclassification error from using an exposure surrogate such as job title and quantitative models can be developed to correct point and interval estimates of health effects (Spiegelman, 2010).

The California Childhood Leukemia Study (CCLS) is a large, population-based case control study. We developed task-based, job-specific modules in the CCLS to assess occupational exposures including pesticides (Reinier et al., 2004). Utilizing the relatively large number of cases and controls in the CCLS, our goals in this analysis are to evaluate misclassification of exposure from using job titles alone compared to job modules and to estimate risks of childhood ALL by age, ethnicity and leukemia subtype.

2. Methods

2.1. Study population

We used data from the CCLS, a case-control study conducted in 35 California counties from 1995 to 2008. As described previously (Bartley et al., 2010; Metayer et al., 2013), participants from the study area were eligible if they were less than 15 years of age at the time of diagnosis (or referent date for the controls) and had a parent that spoke English or Spanish. Among eligible cases, 86% consented and participated in the study. One or two controls were randomly selected from California birth certificate files and individually matched to cases by child's age, sex, race, and Latino ethnicity, and maternal race. About 87% of eligible controls were enrolled in the study and a review of the control selection methods indicates that socio-demographic and birth characteristics of participating and non-participating controls are similar in the CCLS (Ma et al., 2004). The study was approved by the University of California Committee for the Protection of Human Subjects, the California Health and Human Services Agency Committee for the Protection of Human Subjects, and the institutional review boards of all participating hospitals. Written informed consent was obtained from the parents of all participants.

The main CCLS in-person interview includes extensive time-specific exposure information collected from the parents (97% mothers), such as home use of pesticides, parental smoking, job titles for parental occupational histories, and mother and child's residential histories. For each question, parents were asked about use/exposure at critical windows of exposure related to childhood leukemia: the year before birth and from birth to age three years (Daniels et al., 1997; Colt et al., 1998; Anderson et al., 2000; Wigle et al., 2009; Van Maele-Fabry et al., 2010). During this initial interview, a complete occupational history (i.e., job title and duties, company name and type, dates of employment) was collected separately for each parent for any full and part time jobs reported for more than one month (paid or volunteered) from one year before the child's birth until the child's third birthday or diagnosis date (or reference date in control children), whichever came first. We also collected information on the parent's current job or occupation and industry and their usual job and industry since 18 years of age. In the main interview, specific questions were asked regarding whether or not the parent worked regularly with pesticides, insecticides, fungicides, or herbicides along with whether the parent worked in common agricultural occupations (e.g. farm or ranch worker, gardener, groundskeeper, landscaper, garden nursery worker, etc).

2.2. Pesticide exposure assessment using completed task-based job modules (complete JM)

Nineteen job modules were developed for the CCLS to obtain the detailed occupational information necessary to provide semi-quantitative estimates of parental occupational exposure including the timing (i.e., the year before pregnancy to the child's third year of life or to diagnosis/reference date, whichever came first), frequency, duration and intensity of exposure (Reinier et al., 2004; Metayer et al., 2016). Four of the nineteen job modules were developed for occupations with potential pesticide exposure in our study population: farm or ranch worker; gardener, landscaper, nursery worker or groundskeeper; agricultural packer; and pesticide applicator. All interviews and study material were available in English and Spanish.

Based on the complete occupational history gathered in the main interview as described above, parents were assigned one of the pesticide-related job-modules, and pesticide exposure was determined from the detailed task-based questions (Table 1). If no pesticide related job modules were deemed necessary based on job history, the parents were considered unexposed. Assignment of all job-modules was independently reviewed for quality control. Job-module interviews were administered in person with the mothers and possibly the fathers. To increase fathers' participation, phone interviews were proposed when in-person interviews were not feasible. No surrogate interviews were conducted (see detailed methods in Metayer et al., 2016). Of the 1690 participants included in this study from 2000 to 2008, 277 were assigned and completed pesticide related job modules based on their detailed job history. Job modules were coded blinded to the participants' case-control status. For each time period, we asked participants about the crops that they worked with and specific tasks they performed. If the participant applied pesticides, we asked about the target pests and pesticide products or active ingredients that they applied and whether they mixed or loaded pesticides.

Table 1.
Information used to assess parental occupational pesticide exposure using job exposure matrix (JEM), and partial or complete job modules (JM).

Data Collected	JEM	Partial JM	Complete JM
Job-title	X	X	X
What did the company make or do?		X	X
What were your work duties?		X	X
Description of tasks			X
Expert rating			X

Abbreviations: JEM = job exposure matrix, high and moderate probability of exposures; JM = job modules.