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A task-based assessment of parental occupational exposure to organic solvents and other compounds and the risk of childhood leukemia in California

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ABSTRACT

Purpose: Data on parental occupational exposures and risk of childhood leukemia lack specificity. Using 19 task-based job modules, we examined the relationship between occupational exposure to organic solvents and other compounds and the risk of leukemia in children.

Methods: Latino (48%) and non-Latino (52%) children with acute lymphoblastic leukemia (ALL; n=670), acute myeloid leukemia (AML; n=104), and controls (n=1021) were enrolled in a study in California (2000–2008). Logistic regression models were used to estimate the odds ratios (ORs) and 95% confidence intervals (CIs), adjusted for socio-demographic factors.

Results: Among children with non-Latino fathers, none of the exposures evaluated were associated with risks of ALL and AML. In contrast, exposure to any organic solvents in Latino fathers was associated with an increased risk of childhood ALL (OR=1.48; 95% CI: 1.01–2.16); in multivariable analyses, the OR for chlorinated hydrocarbons was 2.28 (95% CI: 0.97–5.37) while the ORs were close to one for aromatic hydrocarbons, glycol ethers, and other hydrocarbon mixtures. We also observed an increased risk of ALL with exposure to combustion exhaust/polycyclic aromatic hydrocarbons (PAHs) (ORs=1.70; 95% CI: 1.16–2.57, and 1.46; 95% CI: 0.94–2.26 with and without adjustment for chlorinated hydrocarbons, respectively). Moderately elevated risks of ALL were seen with exposure to metals, paints, and wood dust, although not statistically significant. An increased risk was reported for asbestos based on small numbers of exposed Latino fathers. No associations were reported between maternal exposures to any exposures and childhood ALL and AML.

Conclusions: Our data support associations between paternal occupational exposures to chlorinated hydrocarbons, combustion exhaust, metals, and possibly asbestos and the risk of ALL in the children of Latino fathers only.

1. Introduction

Leukemia is the most common cancer in children leading to approximately 12,000 new cases per year in the United States (US) (Howlader et al., 2013). Acute lymphoblastic leukemia (ALL) accounts for about 80% of leukemias, and occurs mainly in children 2–5 years of age. Acute myeloid leukemia (AML) is rare in children

Abbreviations: ALL, Acute lymphoblastic leukemia; AML, Acute myeloid leukemia; CCLS, California Childhood Leukemia Study; JM, Task-based job-specific module; PAHs, Polycyclic aromatic hydrocarbons; TCE, Trichloroethylene; US, United States

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(Linabery and Ross, 2008). In the US, the incidence of childhood leukemia has increased by 1% annually since the 1970s, with higher rates reported among Hispanic (or Latino) children (Barrington-Trimis et al., 2015), suggesting that environmental factors specific to ethnic groups are contributing to this trend.

Events occurring at critical times during the fetus' and child's development (i.e., before conception, during pregnancy, and the first years of life) are likely to contribute to early-onset leukemia. A two-hit model of leukemogenesis has been postulated, where both prenatal and postnatal cellular insults are necessary to lead to leukemic clones (Greaves and Wiemels, 2003). Carcinogenic compounds encountered at the parents' workplace may induce leukemia in the offspring via damage to the germ and somatic cells (Colt and Blair, 1998) depending on the timing (i.e., preconception, pregnancy, early life) and mode of exposure (e.g., direct for the parents or via take-home for the child). Previous epidemiologic studies have reported associations between parental occupational exposures to solvents, paints, pigments, pesticides, lead, combustion exhaust and the risk of childhood leukemia (Infante-Rivard et al., 2005; McKinney et al., 2008; Reid et al., 2011; Van Maele-Fabry et al., 2011; Vinson et al., 2011; Wigle et al., 2009). Most studies relied on job titles lacking specificity for type and intensity of exposure, and/or had a small sample size (Colt and Blair, 1998; Van Maele-Fabry et al., 2011; Vinson et al., 2011; Wigle et al., 2009; Keegan et al., 2012; Bailey et al., 2014a, 2014b). Few studies used expert occupational exposure assessment (Infante-Rivard et al., 2005; McKinney et al., 2008; Reid et al., 2011; Monge et al., 2007; Perez-Saldivar et al., 2008; Miligi et al., 2013). Among those examining mothers' work history, increased risks of childhood ALL were reported following preconception exposure to aliphatic and aromatic hydrocarbons (Miligi et al., 2013), prenatal exposure to combustion exhaust (Reid et al., 2011), and pre- and postnatal exposure to solvents (McKinney et al., 2008), alkanes and aromatic hydrocarbons (Infante-Rivard et al., 2005). Studies of paternal occupations reported increased risks of childhood ALL with pre- and postnatal exposures to metals (Miligi et al., 2013) and combustion exhaust (Reid et al., 2011; Miligi et al., 2013). Studies of parental occupational exposures and risk of childhood AML are sparse. Previous studies have been mainly conducted in Caucasian populations (Van Maele-Fabry et al., 2011; Vinson et al., 2011; Wigle et al., 2009), and little is known about leukemia risk associated with parental occupational exposures in other ethnic groups (Monge et al., 2007; Perez-Saldivar et al., 2008; Shu et al., 1988; Kishi et al., 1993; Ferreira et al., 2013) that have different work experiences (Bureau of Labor Statistics, 2016).

Using detailed task-based job modules (JMs) and expert exposure rating, we evaluated whether paternal and maternal exposures to organic solvents and other compounds increase the risk of childhood ALL and AML, overall and separately in Latinos and non-Latinos, the two major ethnic groups participating in a case-control study in California.

2. Methods

2.1. Study population

The present analysis includes cases and controls enrolled in the California Childhood Leukemia Study (CCLS) and for which detailed occupational exposures were collected from 2000 to 2008. The CCLS is a population-based case-control study conducted in 35 counties in Northern and Central California, as previously described (Metayer et al., 2013; Bartley et al., 2010). Cases were identified within 72 hours after diagnosis at 9 hospitals and were eligible for participation if they were younger than 15 years of age at diagnosis, had an English or Spanish speaking parent, lived in one of the 35 counties that comprised the population base at the time of diagnosis, and had never been previously diagnosed with cancer. Children of all racial and ethnic backgrounds were eligible. Comparison of case ascertainment in the 35-county study area to the California Cancer Registry showed that the CCLS ascertained 93% of cases diagnosed from the participating hospitals. When considering both participating and non-participating hospitals within the 35 study counties, 76% of all diagnosed cases in California were ascertained in the CCLS. Of these, 86% of cases were eligible and consented to participate.

Eligibility criteria for leukemia-free controls were similar to those for cases. Controls were randomly selected using birth certificates obtained through the California Office of Vital Records, and one or two controls were matched to each case on child's date of birth, sex, Hispanic ethnicity defined as either one or both parents being Hispanic as indicated on the birth certificate record (also referred to as Latino in the text), and maternal race as indicated on the birth certificate record. Among those contacted and eligible during this study period, approximately 90% agreed to participate in the study.

2.2. Data collection

General information on socio-demographic characteristics, home use of chemicals, residential characteristics, mother's and child's medical histories and diets, lifestyle, smoking, social contacts, and family history of cancer, was collected through home-based, in-person interviews, mainly with the biological mother (97%). During this initial interview, a complete occupational history (i.e., job title and duties, company name and type, dates of employment) was gathered 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. The mother provided information on her job history, as well as the father's job history if the father was not available. When available, the father (55%) provided information on his job history either by phone or in a home-based, in-person interview.

In order to capture detailed parental occupational exposures, a team of scientists in the fields of industrial hygiene, environmental epidemiology, occupational medicine, and toxicology developed 19 additional JMs (Table 1) that were adapted from those designed by the National Cancer Institute (US) (Stewart et al., 1996, 1998). Detailed methods are provided elsewhere (Reinier et al., 2004). In brief, the JMs were designed to test *a priori* hypotheses for the development of leukemia in children, and to capture critical periods of parental occupational exposures, i.e., prenatally (the three months before conception, during pregnancy including 1st, 2nd, and 3rd trimesters) and postnatally (1st, 2nd, and 3rd year after birth or diagnosis/reference date, whichever came first). The JMs included questions about tasks likely to involve exposures of interest such as chemicals and agents identified as possible leukemogens or carcinogens (as described in the introduction), and other products commonly used like disinfectants. Information on the use of protective equipment was also collected. For certain occupations with high certainty of exposure to chemicals (e.g., dry cleaners and exposure to perchlorethylene) or mixtures of chemicals (e.g., parking attendants and exposure to vehicle exhaust), JMs were not developed and relevant exposures were assigned directly (Supplementary Fig. 1). Following the initial interview, trained interviewers assigned JMs based on the parent's job title, industry and a brief job description. No more than two JMs were assigned per family. In the event a family was eligible for more than two JMs (5%), the following selection criteria were applied. The first criterion was the timing of the occupation (i.e., any job