Null Results in Brief

Solvent Exposure and Non-Hodgkin Lymphoma: No Risk in a Population-Based Study in the San Francisco Bay Area

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Abstract

The literature on environmental exposures and risk of non-Hodgkin lymphoma (NHL) is inconsistent and no occupational exposures have been conclusively identified as causal factors. We used job exposure matrices to assess the association between occupational exposure to solvents in a population-based case-control study of NHL (n = 1,591 cases; n = 2,515 controls) in the San Francisco Bay Area between 1988 and 1995. Occupational histories were collected during in-person interviews and were coded according to the 1980 U.S. Department of Commerce Alphabetic Index of Industries and Occupations. Odds ratios and 95% confidence intervals were adjusted for potential confounders. Our results have provided no support for an association between NHL and occupational exposure to solvents. (Cancer Epidemiol Biomarkers Prev 2009;18(11):3130–2)

Introduction

In 2009, in the United States approximately 66,000 newly diagnosed cases and 19,500 deaths from non-Hodgkin lymphoma (NHL) are expected (1). Few risk factors for NHL have been identified to explain the increase in NHL incidence since the 1970s (2-7). The literature on risk of NHL and environmental exposures, including viral, chemical, lifestyle, and occupational, has identified few etiologic factors (2, 8), with no occupational exposures, including solvents (9-17), conclusively established as causal factors (2, 8-20). To address these inconsistent results in previous studies, we used job exposure matrices to estimate the effect of occupational solvent exposure on NHL risk in our large population-based case-control study of NHL in the San Francisco Bay Area.

Materials and Methods

Detailed methods of patient recruitment previously have been reported (21-25). Briefly, a rapid case-finding system was used to identify NHL patients within approximately 1 mo of diagnosis in hospitals in six San Francisco Bay Area counties. Eligible patients were diagnosed between 1987 and 1993, were between 21 and 74 y of age, and resided in six Bay Area counties at the time of diagnosis. Diagnostic pathology materials were re-reviewed and classified using the Working Formulation by the expert study pathologist. Results are presented for all NHL and common subtypes reflecting recent WHO classifications (26): diffuse large-cell and immunoblastic large-cell (DLCL); follicular lymphomas (FL); chronic lymphocytic leukemia/small-lymphocytic lymphoma (CLL/SLL); and “other” NHL. A total of 1,591 (72%) eligible NHL patients completed interviews. Control participants were identified using random digit dial (27, 28) and were frequency matched to the cases by sex, county of residence, and age in 5-y groups. Eligibility criteria were the same as for cases with the exception of NHL diagnosis. A total of 2,515 (78%) eligible control participants completed interviews.

The University of California-San Francisco Committee on Human Research approved the study protocols and procedures and all participants provided written informed consent before interview. Structured interviews were conducted in-person by trained interviewers. No proxy interviews were conducted. Detailed questions were asked about history of occupational and other exposures and lifestyle factors. Occupational history included jobs held for ≥6 mo when ≥18 y old. Most questions pertained to incidence of exposures or activities up until 1 y before diagnosis (cases) or interview (controls).

The 1980 U.S. Department of Commerce Alphabetic Index of Industries and Occupations was used to code 231 industries and 509 occupations (29). Exposure to any organic solvent and to benzene and formaldehyde was assessed by linking the coded occupation and industry data with job exposure matrices developed by Dosemeci et al. (30, 31) and as described by Wang et al. (14). Each occupation and industry was assigned an estimate of exposure intensity (I) and probability (P) (0, none; 1, low; 2, medium; and 3, high exposure). Exposure I and P were estimated on the expected exposure level for a worker in that industry or occupation. If the exposure...
Formaldehyde
Benzene
Solvents
Total Controls,
Total NHL,
Table 1. ORs and 95% CIs for NHL and NHL subtypes associated with average intensity of solvent exposure, San Francisco Bay Area, California

<table>
<thead>
<tr>
<th>Solvents</th>
<th>Total Controls, n = 2,094</th>
<th>Total NHL, n = 1,262</th>
<th>DLCL, n = 497</th>
<th>FL, n = 340</th>
<th>CLL/SLL, n = 148</th>
<th>Other NHL, n = 277</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>526 (25) 344 (27)</td>
<td>1.0</td>
<td>140 (28)</td>
<td>1.0</td>
<td>92 (27)</td>
<td>1.0</td>
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<tr>
<td>Ever</td>
<td>1,568 (75) 918 (73)</td>
<td>0.95 (0.80-1.1)</td>
<td>357 (72) 0.93 (0.74-1.2)</td>
<td>248 (73) 1.1 (0.79-1.4)</td>
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<td>Low</td>
<td>1,147 (55) 662 (52)</td>
<td>0.95 (0.79-1.2)</td>
<td>250 (50) 0.89 (0.69-1.1)</td>
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<td>80 (54) 0.97 (0.63-1.5)</td>
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<td>Med-high</td>
<td>421 (20) 256 (20)</td>
<td>0.95 (0.78-1.2)</td>
<td>107 (22) 1.1 (0.78-1.4)</td>
<td>67 (20) 1.1 (0.75-1.5)</td>
<td>27 (18) 0.90 (0.53-1.5)</td>
<td>35 (20) 0.88 (0.59-1.3)</td>
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†The number of participants may vary because of missing data.

Results

The mean age for NHL and control participants was 57 and 54 years, respectively, after removal of HIV-positive cases. Cases were somewhat less educated and a greater proportion were men. The median lifetime number of jobs for NHL and control participants was four and five, respectively. There was no association between average intensity (Table 1) and probability (Table 2) of solvent, benzene, or formaldehyde exposure and NHL risk for all NHL, DLCL, FL, CLL/SLL, or other NHL. Results did not differ when men and women were analyzed separately, and there were few women in the various exposure subgroups (data not shown).

Table 2. ORs and 95% CIs for NHL and NHL subtypes associated with average probability of solvent exposure, San Francisco Bay Area, California

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*Age-, sex-, education-, race-, and ethnicity-adjusted values.

American African, Asian, other), and education level (≤12, >12 y). Analyses were restricted to HIV-negative participants (n = 1,262 cases; n = 2,094 controls).

Depended on occupation or industry only, then the exposure score was the square of the exposure estimation for that occupation or industry (I = P and P = P). If the exposure depended on occupation and industry, then the exposure score was the product of the occupational and industrial exposure estimate (I = I × P). For each study participant, this information was combined with job duration in years (D) to estimate average exposure intensity, and probability, and median lifetime number of jobs categorized as never exposed (0), low (<3), medium (3-5), and high intensity / probability (≥6).

Unconditional logistic regression was used to obtain odds ratios (OR) as estimates of relative risk (hereafter called risk) and 95% confidence intervals (95% CI) in SAS (v. 9.1, SAS Institute). All statistical tests were two-sided. All models were adjusted for age in 5-y groups, race/ethnicity (Hispanic White, non-Hispanic White,


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Discussion
This large population-based case-control study provides no support for an association between occupational exposure to solvents and NHL. Several factors may contribute to the inconsistent results across previous studies that have evaluated the relationship between occupational solvent exposure and NHL (8, 16, 18, 32, 33). Studies that assume exposures based on job titles lack specific individual-level exposure information. Many occupational settings entail exposure to multiple chemicals that, when coupled with exposure levels presumed by specific job titles, can lead to substantial measurement error and exposure misclassification. Exposure studies often lack complete job and lifestyle histories that may confound or modify the main occupational effects.

This study has several strengths, including its large sample size, study design diminishing potential selection bias (e.g., random digit dial to identify age-, sex- and county-matched controls from the same population from which the cases arose), and rapid case ascertainment to identify all incident NHL cases diagnosed in six Bay Area counties between 1988 and 1993. To diminish interviewer bias, the study hypotheses were not known to the experienced interviewers who conducted in-person interviews with participants. Because specific occupations are not known to be risk factors for NHL, there was less likelihood of response bias. The design of this case-control study allowed us to adjust for potential confounders and examine potential risk factors by NHL subtype. With this study, we were able to adjust for potential confounders and examine potential risk factors by NHL subtype. With our large sample size, we had 80% power to detect an OR of ≥1.5 for the lowest frequency exposure (5%).

In conclusion, we found no evidence that occupational exposure to solvents was associated with NHL. Examination of other potential risk factors including viral, chemical, lifestyle, and occupational exposures is needed to increase our understanding of the etiology of NHL.

Disclosure of Potential Conflicts of Interest
No potential conflicts of interest were disclosed.

Acknowledgments
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References
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