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Residential Traffic Density and Childhood Leukemia Risk

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Abstract

Background—Exposures to carcinogenic compounds from vehicle exhaust may increase childhood leukemia risk, and the timing of this exposure may be important.

Methods—We examined the association between traffic density and childhood leukemia risk for three time periods: birth, time of diagnosis, and lifetime average, based on complete residential history in a case-control study. Cases were rapidly ascertained from participating hospitals in northern and central California between 1995 and 2002. Controls were selected from birth records, individually matched on age, sex, race, and Hispanic ethnicity. Traffic density was calculated by estimating total vehicle miles traveled per square mile within a 500-foot (152 meter) radius area around each address. We used conditional logistic regression analyses to account for matching factors and to adjust for household income.

Results—We included 310 cases of acute lymphocytic leukemias (ALL) and 396 controls in our analysis. The odds ratio for ALL and residential traffic density above the 75th percentile, compared with subjects with zero traffic density, was 1.17 [95% confidence interval (95% CI), 0.76–1.81] for residence at diagnosis and 1.11 (95% CI, 0.70–1.78) for the residence at birth. For average lifetime traffic density, the odds ratio was 1.24 (95% CI, 0.74–2.08) for the highest exposure category.

Conclusions—Living in areas of high traffic density during any of the exposure time periods was not associated with increased risk of childhood ALL in this study.

Introduction

Leukemia is the most common cancer in children and the causes of this disease are largely unknown (1). Investigations have focused on the potential role of many environmental exposures, including air pollution from vehicle exhaust. Motor vehicles are a major source of toxic air pollutants in California, accounting for 49% of the outdoor benzene emissions and 45% of 1,3-butadiene emissions (2). Benzene is a known cause of leukemia in adults (3), and 1,3-butadiene has recently been classified as a human carcinogen (4).

The association between heavily traveled roads and childhood leukemia risk was first reported in an early case-control study of electromagnetic fields (5). Four relatively small case-control

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studies (<200 cases each) reported statistically significant positive associations between childhood leukemia and living near high-traffic roads or high estimated exposure to vehicle-related pollutants (5–8), whereas four larger case-control studies found no association (9–13). In addition, ecologic studies from Europe and California found no association between traffic exposure levels and leukemia incidence rates (13).

Exposure timing may be very important in the etiology of childhood leukemia (14). Most studies have considered either exposure at the time of diagnosis or at the time of birth. Only two studies, both conducted in Europe, have examined lifetime traffic exposures based on complete residential history (9,12). In our case-control study of childhood leukemia, we examined traffic density risk estimates for three time periods based on residence at birth, residence at the time of diagnosis, and averaged over the entire lifetime.

Materials and Methods

Study Population

The Northern California Childhood Leukemia Study is an on-going case-control study. The first phase of the study, from 1995 to 1999, included 17 counties in the San Francisco Bay Area. The second phase, from 1999 through 2002, was expanded to include 18 additional counties around Sacramento and Fresno. Cases were rapidly ascertained after diagnosis from participating hospitals in the region. One or two controls were randomly selected for each case from the birth certificate files maintained by the California Office of Vital Records. Controls were matched on age, sex, Hispanic ethnicity, and mother's race. Controls in the first phase of the study were also matched on the county of birth. Subjects were eligible for inclusion if they were a resident of the study area, ages <15 y at the time of diagnosis (or reference date for the controls), had no previous history of cancer, and had an English- or Spanish-speaking parent. If the first choice control could not be located or declined to participate, another birth certificate control was chosen. The overall participation rate was 86% among cases and 84% among control subjects that could be traced and contacted (15).

Extensive demographic and exposure information, such as household income, smoking, and complete residential history, was collected from parents using a self-administered questionnaire and a follow-up in-person interview. Addresses were geocoded using an ArcInfo (ESRI) geographic information system as well as Dynamap/2000 (Geographic Data Technology, Inc.) and NAVTEQ Standard (Navigational Technologies) street geocoding databases. We attempted to manually geocode those residences that did not automatically match.

Use of human subjects in this study was reviewed by applicable Institutional Review Boards and found to be in compliance with their ethical standards as well as with the U.S. Code of Federal Regulations, Title 45, part 46 on the Protection of Human Subjects.

Traffic Exposure Estimates

We obtained yearly traffic counts for 1984 through 2000 from the Highway Performance Monitoring System of the U.S. Department of Transportation, Federal Highway Administration. For years in which no traffic counts were available, we used available traffic data from more recent years as a substitute. Data for years beyond 2000 were not available, so we used traffic-count values for the year 2000 in assigning traffic exposure estimates to addresses in 2001 and 2002. To estimate traffic exposure, we determined the traffic density within a 500-foot (152-meter) radius buffer around each residential address. Traffic density was calculated by multiplying the average daily traffic count by the length of each measured

road segment within the circle, summing these for the entire area, and dividing by the area (11). The resulting units for traffic density are vehicle miles traveled per square mile.

We examined traffic density within subjects' buffer areas for three time periods: diagnosis (reference date for controls), birth, and lifetime average. The lifetime average traffic density was calculated by summing the time-weighted traffic density at each address (density multiplied by months at each address) and dividing by age (in months).

Statistical Analysis

We used conditional logistic regression models to account for the matching variables. Because of its association with case status and traffic density, we included household income in the models to control for potential confounding. Income was not reported by 21 subjects, so we assigned them to the median income category (\$45,000–\$59,999 per year) to retain them for our analyses. All analyses were done using SAS, version 9 (SAS Institute, Inc.).

Traffic counts for many lightly traveled residential streets are not measured in the Highway Performance Monitoring System, so subjects with no measured roads within a 500-foot (152-meter) radius of their residence were assigned zero traffic density (reference group). For the remaining subjects, we divided traffic density values into three categories based on percentiles of the lifetime average among the controls. Categories for measured traffic density values were based on cut points of less than the 50th percentile (low exposure), the 50th to 74th percentile (medium), and ± 75 th percentile (high). We also conducted stratified analyses by age group (ages <5 y and 5–14 y).

Subject Inclusion Criteria

For the diagnosis and birth residence analyses, we only included matched sets—one case and at least one control—with the relevant residence geocoded. This inclusion criterion left us with 310 cases and 396 matched controls in our analysis of residence traffic exposure at diagnosis, and 257 cases and 323 controls for our analysis of residence traffic exposure at birth. For lifetime average analyses, we included 248 case and 308 control subjects for whom geocodable address information was available for at least 90% of their lifetime.

Results

Among the 706 subjects included in our analyses, over half were male and under the age of 5 years (Table 1). A large proportion (41%) of the study subjects were Hispanic. The distribution of annual household income varied significantly by case/control status, with controls more likely than cases to be in the higher income group (Mantel-Haenszel χ^2 , $P < 0.0001$).

The odds ratio for acute lymphocytic leukemia and residential traffic density above the 75th percentile compared with subjects with zero traffic density was 1.17 (95% confidence interval, 0.76–1.81) for residence at diagnosis, and 1.11 (95% confidence interval, 0.70–1.78) for the residence at birth (Table 2). For average lifetime traffic density, the odds ratio was 1.24 (95% confidence interval, 0.75–2.09). Assigning a missing indicator to the subjects lacking income data did not appreciably alter the results compared with assigning them to the median income category.

Discussion

We did not observe any significant increase in risk of childhood acute lymphocytic leukemia associated with living near heavily traveled roads in this population. The general lack of association is consistent with our two previous statewide studies, one ecological and one case-control (11,16). Those statewide studies were limited in terms of the timing of the exposure

assessments because each study could only examine traffic levels around one address, either the diagnosis or birth residence. Unlike studies that rely on address information at a single point in time, our use of residential history data prevents exposure misclassification that occurs due to residential mobility. Our present study is the first assessment conducted in the United States of the potential leukemia risk for average traffic exposure estimated over each child's entire lifetime.

Several methodologic differences may account for the inconsistent findings on this topic available in current literature (13). Studies have used various methods for estimating exposure to traffic-related pollutants; moreover, traffic volumes and emission profiles vary between different regions of the world and over time. In addition, the time window of exposure examined may be particularly important, although the critical time, if any, for an environmental exposure leading to the development of leukemia in children is not known.

The optimal spatial scale for estimating relevant traffic-related exposures is not known. We assessed traffic within 500 feet (152 meters) of the home—the same distance used in our previously study (11). The distances used for traffic assessments in other childhood leukemia studies have varied widely—from as little as 164 feet (50 meters; ref. 12), to as much as 1,500 feet (457 meters; ref. 10). In our previous ecological analysis of hazardous air pollutants and childhood cancer incidence, we found a suggested increase in leukemia risk in areas with high levels of potentially carcinogenic air pollutants, based on modeled concentrations at the census tract level—a much larger area than the 500-foot (152-meter) buffer used in our present study (17). In addition, individual air pollutants disperse differently and the concentrations vary with geographic and meteorologic conditions, such as wind direction. These factors were not incorporated in our analyses. In addition, our exposure estimates were limited to residential locations and did not take into account time spent away from home, which could result in exposure misclassification (18).

Various consumer products, cigarette smoke, and wood smoke from fireplaces and stoves are all potential indoor sources of some of the same carcinogenic chemicals found in vehicle exhaust, such as benzene, polycyclic aromatic hydrocarbons, and 1,3-butadiene (19). These indoor sources may be more important than outdoor sources for estimating personal exposure, due to the amount of time children spend indoors (20,21). Fathers' preconception smoking was suggestive of increased risk for acute lymphocytic leukemia in this study population (odds ratio, 1.32; 95% confidence interval, 0.86–2.04), although maternal smoking was not (15). When we included fathers' preconception smoking in our multivariable models, the results did not appreciably change.

A potential limitation of this study was that the control subject families had a higher average annual household income than did case families. Potential controls from lower income families may have been harder to locate and less likely to participate in the study than were those from higher income families. Socioeconomic status is strongly related to residential traffic exposure. In a previous analysis, we found that low income children were more likely to live in areas with high traffic density than were high income children (22). Although we controlled for household income in our multivariable models, possible effects of selection or participation bias cannot be ruled out.

This study offers a number of strengths. The cases were representative of the population-based cases occurring during the study time period. By comparing cases identified in the study with those recorded in the California Cancer Registry, we determined that we ascertained 88% of the population-based cases in the study area. The use of birth certificate records for control selection gave us controls that seemed to be generally representative of the source population (23), and such controls may be less subject to selection bias than are those selected through

random digit dialing (24). We used a geographic information system, detailed yearly vehicle-count data, and lifetime residential history to assign traffic exposure estimates for specific time periods during the child's lifetime. Because they were not self-reported, the traffic measures were not subject to recall bias. Previously, we found good correlation between traffic density measures and ambient air monitoring levels of benzene, 1-3 butadiene, and carbon monoxide (22).

In summary, despite careful assignment of traffic exposure values that incorporated variations in both time and place, we did not see compelling evidence that living in areas of high traffic density is related to an increased acute lymphocytic leukemia risk in children. However, we cannot exclude a small association with traffic-related air pollution given the limited study size. Future studies should examine how well traffic-related measures correlate with levels of carcinogenic air pollutants, incorporate measures of regional air quality, factor in predominant wind direction and speed, and use comprehensive measures of indoor exposures.

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Table 1
Demographic characteristics of the acute lymphocytic leukemia cases and controls

Demographic factors	No. of cases	%	No. of controls	%
Age *				
0–4	180	58	234	59
5–9	92	30	113	29
10–14	38	12	49	12
Sex *				
Male	165	53	189	52
Female	145	47	207	48
Hispanic ethnicity *				
Yes	128	41	163	41
No	182	59	233	59
Maternal race *				
White	267	87	344	86
Black	9	3	11	3
Asian or other	34	10	41	11
Annual Household income †				
<\$15,000	40	13	32	8
\$15,000–29,999	58	19	57	14
\$30,000–44,999	49	16	46	12
\$45,000–59,999	51	16	50	13
\$60,000–74,999	32	10	52	13
≥ \$75,000	72	23	148	37
Refused or unknown	8	3	11	3
Total	310	100	396	100

NOTE: Among the 706 subjects included in the diagnosis residence analysis.

* Matching criteria.

† Mantel-Haenszel χ^2 test $P < 0.0001$.

Table 2
Residential exposure to traffic and childhood acute lymphocytic leukemia risk, by residential location

Traffic density	No. of cases	No. of controls	OR [*]	95% CI
At birth residence (<i>n</i> = 580)				
No measured road (38% of subjects)	93	127	1.0	
0–49th percentile (1–38,499)	72	73	1.42	0.90–2.26
50–74th percentile (38,500–91,461)	36	55	0.91	0.54–1.53
75th percentile and above (≥91,462)	56	68	1.11	0.70–1.78
At diagnosis residence (<i>n</i> = 706)				
No measured road (42% of subjects)	129	168	1.0	
0–49th percentile (1–38,499)	74	104	0.90	0.60–1.34
50–74th percentile (38,500–91,461)	37	57	0.79	0.48–1.29
75th percentile and above (≥91,462)	70	67	1.17	0.76–1.81
Average lifetime (<i>n</i> = 556)				
No measured road (27% of subjects)	63	88	1.0	
0–49th percentile (1–38,499)	84	110	1.04	0.66–1.65
50–74th percentile (38,500–91,461)	49	55	1.18	0.70–2.00
75th percentile and above (≥91,462)	52	55	1.24	0.74–2.08

Abbreviations: OR, odds ratio; 95% CI, 95% confidence interval.

* Odds Ratios from conditional logistic regression to account for matching factors and household income category. Categories are based on percentiles of the lifetime average among the controls, excluding zero.