Null Results in Brief

No Association Between Residential Exposure to Petrochemicals and Brain Tumor Risk

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Introduction

Evidence to date reveals an inconsistent association between petrochemical exposure and brain tumors (1-5). Community concerns have been raised regarding air pollution caused by the petrochemical industry in southern Taiwan, whereas water pollution has been less addressed because of the central reservoir water supply system. Air monitoring of Kaohsiung conducted by the Taiwanese Environmental Protection Administration (available from January 1993; http://taqm.epa.gov.tw/emc/default.aspx?pid = b0601&cid = b0601) has shown poorer air quality as compared with the average levels in Taiwan (Table 1). However, these pollutants are not spread by the petrochemical industry alone, showing the need for an improved exposure assessment method. Thus, we developed a procedure using geographic information system tools to assign individual residential exposure estimates by accounting for subject mobility, length of stay at each residence, distance to relevant petrochemical plant(s), monthly prevailing wind direction, and multiple petrochemical plant pollution sources (6).

We present the results from a population-based case-control study from 143 cases and 364 controls to assess the association between residential petrochemical exposure and brain tumor risk.

Materials and Methods

Study design. Details regarding the design of our study (cases, n = 143; controls, n = 364) were described previously (6, 7). Briefly, this is a population-based case-control study conducted in the metropolitan area of Kaohsiung, southern Taiwan, excluding the rural areas to avoid the potential confounding effects from pesticide exposure. The study area is ~657.1 km^2. There are four petrochemical industrial complexes in the study area, producing various products from upstream to downstream petrochemicals. Subjects were recruited between November 1997 and June 2003. Eligible cases included all pathologically confirmed incident primary brain tumor cases (benign and malignant: International Classification of Diseases-9 codes, 191-192, 194.3-194.4, and 225) ages 0 to 29 years and currently residing in the study area. Controls were cancer-free current residents of the study area, selected randomly from the population registry data based on the personal identification number system of the Taiwanese government. Each case was matched with three controls on age (±1 year) and sex. In-person interviews were conducted with the parents and/or subjects to collect information regarding descriptive characteristics, residential history, medical history, as well as environmental, occupational, and behavioral factors.

Exposure assessment. Details of the exposure assessment have been described previously (6). Briefly, all long-term residences of each study subject were recorded and then geocoded by a commercial company (MapAsia, Hong Kong). Cases and controls were comparable in address data quality as assessed by geocoding results (non-geocodable addresses: 7% for cases and 9% for controls). Based on previous studies (8-10), we defined potentially exposed areas as areas located within a 3 km radius from the geographic centroid of any of the four petrochemical complexes. Additionally, our group developed a procedure using geographic information system software (ArcInfo, Redlands, CA) to estimate residential petrochemical exposures on an individual level. The exposure estimates from our approach—which we called the exposure opportunity score (EOS)—accounts for subject mobility, length of stay at each residence, distance to petrochemical plant(s), monthly prevailing wind direction, and multiple petrochemical pollution sources. The EOS was log-transformed for normality and was entered in the conditional logistic regression model to calculate the odds ratios (OR) and 95% confidence intervals (CI).

Results

There were no differences in the proportions of exposed individuals according to disease status. Also, the distributions of log-transformed EOS among the exposed individuals did not vary by disease status. No association was seen between the log-transformed EOS and risk of brain tumors (adjusted OR, 0.96; 95% CI, 0.79-1.17; Table 2). Age-stratified analyses did not materially change our results. The inclusion of occupational petrochemical exposure of the subjects

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Note: The members of the Kaohsiung Brain Tumor Research Group are listed in the Appendix.

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Table 1. Comparison of criteria pollutant levels in 2003: Kaohsiung versus Taiwan

Area	PM_{10} ($\mu g/m^3$)	SO_2 (ppb)	NO_2 (ppb)	CO (ppm)	O_3 (ppb)
Kaohsiung	72.90	7.47	23.38	0.71	29.20
Taiwan	55.42	3.83	19.92	0.68	27.80
Taiwanese Air Quality Standards*	65.00	30.00	50.00	9.00 (8 h) or 35.00 (1 h)	80.00 (8 h) or 120.00 (1 h)

NOTE: Criteria pollutant levels for Kaohsiung compared with the whole of Taiwan show similar results during the years 1993 to 2003. Only 2003 data are presented in the table. Data abstracted from the Taiwanese Environmental Protection Administration (http://taqm.epa.gov.tw/emc/default.aspx?pid = b0601 http://210.69.101.141/data/report/air92.pdf) and represent the arithmetic mean of all valid measures taken in the year 2003. Standards for CO and O_3 use 8- or 1-hour averaging times whereas only annual averages were available for the Kaohsiung and Taiwan data.
*Taiwanese Air Quality Standards indicates legal requirements for annual average unless otherwise indicated.

themselves and/or of their parents did not change our conclusion (data not shown). Subgroup analysis of glioma (the most predominant histologic type, accounting for 35% of cases) did not reveal significant associations between residential petrochemical exposures and glioma.

Discussion

Our study had 80% power at a two-sided $\alpha = 0.05$ level to detect an OR of 1.90 for residential petrochemical exposure. We did not detect any association between residential exposure to petrochemicals and the risk of brain tumors when cumulative exposure levels were assessed by our geographic information system–based approach. In a population-based study in Sweden, occupational exposure to petrochemicals was found to be associated with increased risk of glioma (11). The Swedish study is not directly comparable with ours, however, because of differences in population characteristics, exposure levels, and disease types. To our knowledge, this is the first study which specifically addresses the association between the incidence of brain tumors and residential petrochemical exposure in a population-based case-control setting. Our study has several major strengths including: (*a*) the choice of controls from a population registry, (*b*) the use of complete residential history (rather than only the current residence or the longest held residence) when assigning individual exposure estimates, and (*c*) the incorporation of monthly prevailing wind directions when estimating exposure levels.

Recall bias—differential recall on exposure among cases and controls—is a major concern in case-control studies, as cases may recall exposure more thoroughly than controls (12). In our study, however, the proportions of non-geocodable residences did not vary by disease status (7% for cases and 9% for controls). Because we used geocoded addresses as the basis of exposure assessment, recall bias is not a likely threat to the validity of our study.

Several factors may have contributed to the null association found in this study. First, brain tumor itself is a broad term describing diverse histologic types (benign and malignant) and each of them could have a different etiology. Our sample size was not large enough to assess all subtypes of brain neoplasms. Also, although our approach has significantly reduced some commonly challenged uncertainties in estimating personal exposure, there are still possible sources of exposure misclassification—such as not accounting for indoor pollution sources and not pinpointing specific chemical agents. These sources of exposure misclassification are nondifferential by disease status and would attenuate our OR estimates towards the null. Despite these limitations, our data do not support such an association.

Appendix

Members of the Kaohsiung Brain Tumor Research Group: Kaohsiung Medical University, Chung-Ho Memorial Hospital (Shen-Long Howng, Ann-Shung Lieu, Aij-Lie Kwan); Kaohsiung Chang Gung Memorial Hospital (Jih-Tsun Ho, Teng-Yuan Shih, Tao-Chen Lee, Min-Hsiung Cheng, Wu-Fu Chen, Kuo-Sheng Hung, Shun-Sheng Chen); Kaohsiung Veterans General Hospital (Yuk-Keung Lo, Shu-Shong Hsu); E-Da Hospital, I-Shou University (Han-Jung Chen, Kang Lu, Cheng-Loong Liang, Po-Chou Liliang).

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Table 2. The association between residential petrochemical exposure and brain tumors in Kaohsiung, southern Taiwan

	Exposed individuals	Log-transformed EOS among exposed	OR (95% CI)*	OR (95% CI)*†
	n (%)	Median (min, max)	Crude	Adjusted
All subjects (143 cases and 364 controls)				
Cases (all disease types)	26 (18)	2.43 (1.16, 4.47)	1.00 (0.83-1.12)	0.96 (0.79-1.17)
Controls‡	65 (18)	2.66 (0.42, 4.55)		
Ages 0 to 19 years (72 cases and 186 controls)				
Cases (all disease types)	11 (15)	2.16 (1.29, 4.47)	0.88 (0.65-1.20)	0.82 (0.59-1.16)
Controls‡	34 (18)	2.24 (0.42, 4.41)		
Ages 20 to 29 years (71 cases and 177 controls)				
Cases (all disease types)	15 (21)	2.76 (1.16, 3.86)	1.08 (0.86-1.38)	1.03 (0.79-1.34)
Controls‡	31 (18)	2.72 (0.70, 4.55)		

*ORs and CIs calculated for one unit increase in log-transformed EOS.
†Calculated from conditional logistic regression; adjusted for smoking status, maternal educational status (if subject was aged 0-19 years) or subject educational status (if subject was aged 20-29 years), and diagnostic irradiation.
‡Reference category.

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