Drinking Water Contamination and the Incidence of Leukemia: An Ecologic Study

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Abstract: An ecologic study was performed to examine the relation between the incidence of leukemias and the occurrence of volatile organic chemical (VOC) contamination of drinking water supplies within a study area comprised of subpopulations differentially exposed to drinking water VOCs (trichloroethylene and related solvents). Populations served by community water supplies were classified into exposure categories according to VOC contamination status based on 1984–85 sampling data. Leukemia incidence data (1979–84) were collected from a population-based cancer registry. For females, the standardized incidence ratio was elevated only in towns in the highest of three exposure categories. No association was observed in males in any of the exposure categories. A Poisson regression analysis of the data, using finer exposure strata, indicated an increase in risk among females with increasing level of contamination which appeared to be distributed evenly across all age strata. The rate ratio for females at the highest exposure stratum for total non-THM VOCs compared to the least exposed stratum was 1.68. The observed association appears to suggest that drinking water contaminated with VOCs may increase the incidence of leukemia among exposed females, but caution is advised in the interpretation of these results because of the uncertainties inherent in ecologic studies. (*Am J Public Health* 1990; 80:1209–1212.)

Introduction

Since the middle 1970s, there has been considerable epidemiologic interest in the relation between organic contaminants in drinking water and increased cancer incidence in exposed populations. The focus of several studies has been on chlorinated compounds that can form in relatively high concentrations following chlorination of surface water for disinfection. These compounds, some carcinogenic or mutagenic, include the volatile trihalomethanes (THMs) and many nonvolatile substances. There is some evidence that consumption of chlorinated surface water is related to an increased risk of bladder and possibly colorectal cancers.[1–4]

Groundwater was long thought to be relatively protected from such contamination. However, national and state surveys have demonstrated that numerous groundwater supplies throughout the nation have contained volatile organic compounds (VOCs) other than THMs,[5,6] in particular the halogenated solvents trichloroethylene (TCE), tetrachloroethylene (perchloroethylene or PCE), and 1,1,1-trichloroethane (TCA).

In Woburn, Massachusetts, an association was reported between the pattern of VOC water contamination (TCE and others) and the incidence of childhood leukemia.[7] Further epidemiologic analysis of the pattern of non-THM VOC water contamination and the incidence of leukemias is warranted in other geographic areas.

In New Jersey, routine semi-annual testing for 14 VOCs including halogenated solvents has been required of public community water systems since late 1984.[8] Results from 1984 and 1985 showed that about 18 percent of the state's 620 water systems, estimated to serve approximately 20 percent of the state's population, contained detectable levels of non-THM VOCs.[9,10] Data on THM concentrations are also available.

We performed a study of the possible relation between the incidence of leukemia and VOC contamination of drinking water in the state of New Jersey.

Methods

Study Population

In an ecologic study, an ideal geographic area would be completely served by community water systems for which monitoring data are available and would contain subunits that experience a range of contaminant concentrations to ensure exposure differences. The study area that best met these criteria consisted of towns completely within an area bounded by the Lower Passaic River and Saddle River drainage basins. The area is almost completely served by public water supplies, many of which have tapped VOC contaminated groundwater, while others utilize groundwater or surface water free of detectable levels of non-THM VOCs. This portion of the state is primarily urban and residential so that town coding in the Cancer Registry is likely to be accurate, i.e., mailing address and actual residence are likely to be the same.

Towns within the study area were excluded if less than 90 percent of the population was served by public water systems. The age- and sex-specific populations of each municipality were obtained from 1980 US Census summaries.

Exposure Measurement

The New Jersey Department of Environmental Protection compiled all sampling results for each water system serving populations in the study area. The drinking water quality data included the 14 VOCs under the state's monitoring requirements from 1984 and 1985, and THM analyses from 1984 and 1985.

The Department also provided other available sampling data, information on extent of distribution systems, well or reservoir use, and patterns of water purchases among systems so that the water supply of each town could be characterized. Any significant changes in water supply and use patterns in the past decade were noted.

For each water system, we calculated the mean chemical-specific concentrations of VOCs and THMs in distribution system samples for the period 1984–85. Although data were available for later years, the first rounds of monitoring were thought to be more representative of past exposure since corrective actions were taken by many water systems

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TABLE 1—Exposure Classification, Number of Reported Leukemia Cases 1979–84, and Population by Gender

Non-THM VOC rating for SIR	Exposure Stratum for regression (μg/l)*	Leukemia Cases (population) Males	Females	Number of Towns
++	72	1 (5,125)	4 (5,616)	1
	67	5 (11,346)	8 (12,610)	1
	47	0 (1,973)	0 (2,156)	1
	40	8 (12,699)	9 (14,104)	1
	37	11 (8,539)	7 (9,661)	1
		25 (39,682)	28 (44,147)	5
+	12	13 (15,546)	7 (16,683)	1
	9	7 (17,583)	14 (20,738)	1
	7	5 (5,314)	5 (5,488)	1
	5	13 (28,508)	10 (31,078)	4
		38 (66,951)	36 (73,987)	7
−	3	6 (8,358)	3 (8,836)	2
	2	7 (9,385)	4 (10,302)	2
	1	103 (161,195)	74 (182,053)	9
	0	29 (38,478)	19 (44,681)	2
		145 (217,416)	100 (245,872)	15

*Sum of average non-THM VOC concentrations in 1984–85 samples.

following the initial results. The number of distribution system samples for each supply varied from two to 50 in the period. Values for each non-THM VOC, total non-THM VOCs, and total THMs were then assigned to each town based on the water supplies that serve that town.

Disease Measurement

Incident cases of leukemias for the towns within the study area were collected from the New Jersey Cancer Registry for the six-year period 1979–84. Information on each case included date of diagnosis, age at diagnosis, town of residence at time of diagnosis, race and sex, and histologic type according to the International Classification of Diseases for Oncology.[11]

Data Analysis

Based on the 1984–85 contaminant values, towns were categorized as to contaminant status for total non-THM VOCs and for THMs. Categorical exposure levels were defined for each variable, empirically derived from inspection of the distribution of values. For each categorical exposure variable, incidence data for the towns within an exposure category were pooled, and standardized incidence ratios for the combined town groups were calculated. Expected incidence for the grouped areas were derived by applying New Jersey statewide 1982 age-sex-specific rates of total leukemias to the pooled 1980 age-sex-specific populations.[12] (Age-sex-specific rates for specific histologic types are not available.) Standardized incidence ratios (SIRs) were calculated by dividing the observed number of cases by the expected number for each town grouping. The 95% confidence intervals of the SIRs were estimated.[13]

Towns sharing the same values for non-THM VOCs were pooled into exposure strata. For each gender, the number of leukemia cases (total and type-specific) in each exposure stratum and age-group specific population was fitted to a log-linear regression model assuming a Poisson distribution of the counts. Separate regression models were developed for total non-THM VOC and for TCE and PCE, two subsets of that variable.[14,15] Predictor variables included in the models were age group (0–19, 20–49, and 50+) and exposure stratum; interactions were also included. Rate ratios were calculated from the parameters generated by the models. Analysis was performed using the GLIM software package.[16] A hierarchical backward elimination method[17] was used to determine final models.

Results

Three of the 30 towns originally contained in the study area were excluded since approximately 50 percent, 4 percent, and 1 percent of their population, respectively, was served by public community water supplies. Approximately 95 percent to 100 percent of the populations in each of the remaining 27 towns in the study area are served by public community water supplies. These 27 towns contained 688,055 persons (324,049 males and 364,006 females), or 9.3 percent of the population of New Jersey in 1980.

Table 1 includes mean total non-THM VOC values assigned to each town or group of towns for the SIR analysis. TCE, PCE, TCA, and dichloroethylenes (DCE) comprised nearly all of the non-THM VOC. Based on inspection of the average values for each town, three categories of total non-THM VOC status were formed: ++ (72–37 ppb), + (12–5 ppb), or − (3 to less than 1 ppb). Two categories of THM status were also formed: + (76–25 ppb) or − (4–1 ppb).

Figure 1 displays the geographic pattern of this categorization. For THMs, 19 towns were rated plus (+) and eight were rated minus (−).

Over the six-year period 1979–84, 208 leukemia cases occurred among males and 164 among females in the entire study area (Table 1). The most frequently reported histologic type among younger age groups of both sexes was acute lymphocytic leukemia (ALL). Among older age groups, chronic lymphocytic leukemia (CLL), acute granulocytic leukemia (AGL), and chronic granulocytic leukemia (CGL)

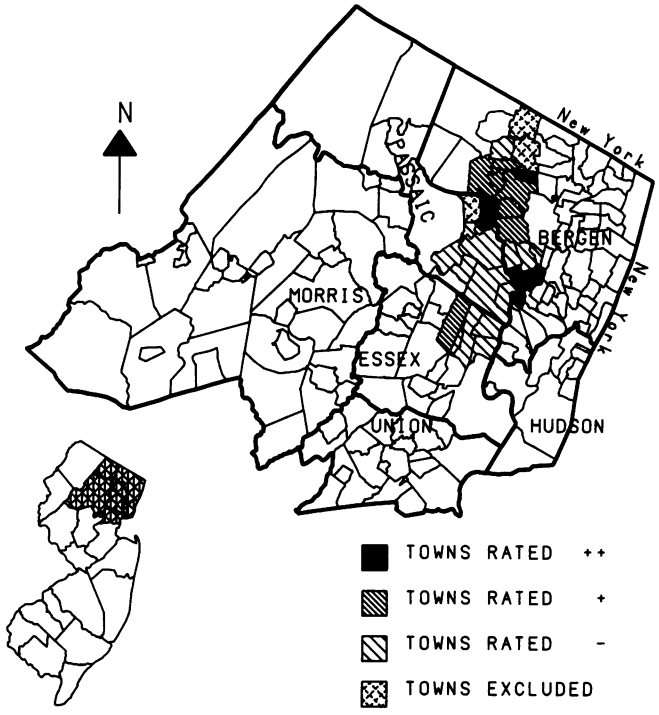

FIGURE 1—Pattern of Total Non-THM VOC Contamination in the Study Area as Categorized for the SIR Analysis

were most frequently reported. Few cases of acute monocytic leukemia were reported, and all were among older males. Twenty-eight percent of the reported cases were coded without specifying histology.

For the entire study area, the observed number of leukemia cases from 1979–84 did not differ from the expected number for either males or females. Among towns classified as ++ for total non-THM VOCs, however, the incidence of leukemia was elevated among females but not in males (Table 2).

No elevation of leukemia incidence was observed for groups of towns classified as either (+) or (−) for THM status among males or females (Table 2).

Regressions were performed for both sexes including categorical age and water quality variables. Results are reported in detail here for females only. The final models of the regression analysis for total leukemias in females (Table 3) do not contain interaction terms between age groups and contaminant status as no p values less than 0.05 were obtained.

The sum concentration of all non-THM VOCs was a statistically significant predictor of total leukemia incidence, adjusted for age. The coefficient for total VOCs was 0.0072 (S.E. =. 0039), and is interpreted as the natural logarithm of the increase in the rate ratio per unit increase in exposure. Thus, for the maximum town average total non-THM VOC concentration observed in the study, 72 μg/l, the rate ratio would be exp[(72 μg/l)(.0072)] = 1.68.

Modeled separately, the age-adjusted coefficients for TCE and PCE concentration were 0.012 (S.E. = .0067) and 0.035 (S.E. = .021), respectively. At the maximum town average TCE and PCE concentrations observed in the study, the rate ratios would be exp[(46 μg/l)(.012)] = 1.74 and exp[(16 μg/l)(.035)] = 1.75, respectively.

When the more common histologic types of leukemia (ALL, CLL, AGL, and CGL) were examined separately, the coefficients for total non-THM VOCs were all of similar direction and magnitude (ALL: 0.016; CLL: 0.0095; AGL: 0.010; CGL: 0.012). There were few cases of each histologic type, hence little power to detect meaningful associations.

TABLE 2—Standardized Incidence Ratios (SIRs) among Males and Females for Groups of Towns Classified According to Various Exposure Categories (Number of cases, 1979–84)

Exposure Category	Number of Cases: Observed	Expected	SIR	(95% Confidence Interval)
Males				
All towns	208	195.7	1.06	(0.92–1.21)
Total non-THM VOCs—1984–85				
++	25	25.0	1.00	(0.65–1.47)
+	38	40.7	0.93	(0.66–1.28)
−	145	130.0	1.12	(0.94–1.31)
Trihalomethanes—1984–85				
+	177	168.5	1.05	(0.90–1.22)
−	31	27.3	1.14	(0.77–1.61)
Females				
All Towns	164	146.8	1.12	(0.95–1.30)
Total non-THM VOCs—1984–85				
++	28	18.3	1.53*	(1.02–2.21)
+	36	30.3	1.19	(0.83–1.65)
−	100	98.2	1.02	(0.83–1.24)
Trihalomethanes—1984–85				
+	140	126.8	1.10	(0.93–1.30)
−	24	20.1	1.20	(0.77–1.78)

*Statistically elevated SIR ($p < 0.05$)

TABLE 3—Poisson Regression Analysis: Final Models for Total Leukemia Cases among Females

Model	Coefficient	Standard Error
	Exposure: Total non-THM VOCS	
Intercept	−1.85	(0.25)
AGE(20–49)	−0.022	(0.32)
AGE(50+)	1.78	(0.27)
TOTAL VOCS	0.0072	(0.0039)
	Exposure: TCE Concentration	
Intercept	−1.83	(0.25)
AGE(20–49)	−0.021	(0.32)
AGE(50+)	1.78	(0.27)
TCE	0.012	(0.0067)
	Exposure: PCE Concentration	
Intercept	−1.85	(0.25)
AGE(20–49)	−0.019	(0.32)
AGE(50+)	1.78	(0.27)
PCE	0.035	(0.021)

Discussion

Results suggest an association between the contamination of drinking water supplies with non-trihalomethane volatile organic chemicals and an increased incidence of leukemias among females. Because of limitations inherent in the study design, a statement of causal inference cannot be made with confidence at this time.

Ecologic studies are practical because they are quick and inexpensive, but because data reflect the group rather than the individual, the results are best used to develop rather than test etiologic hypotheses. Ecologic studies are susceptible to bias in the estimation of effect if there are factors operating at the individual level that are not accounted for in an aggregate exposure assessment. Additionally, at the group level, the degree of correlation among various predictor variables (multicollinearity) is likely to increase, so that the independent effects of predictors may be difficult to isolate. Potential biases and multicollinearity in ecologic studies can be minimized by using narrow exposure strata and regression to estimate effect.[18]

Misclassification of exposure may exist at both the population and at the individual level. In this study, exposure information (1984–85) was collected at the end of the case collection period (1979–84). Although sampling data prior to 1984 are limited, it was our judgment that these data are reasonable proxies for actual levels years earlier. Since the latency period of chemically-induced leukemias can be relatively short—as little as five years or less for benzene[19]—the problems associated with using exposure information gathered after the development of disease may be lessened.

Within a given population classified according to exposure, there may be significant variability of actual exposure to water-borne contaminants experienced by individuals. Individual-level data on personal tap-water use, residential history and migration patterns, and location of workplace or schools compared to residence were not available for this study.

Additionally, confounding variables such as occupational exposures or local toxic air emissions that may be causally related to the development of leukemias, may be correlated with the pattern of water contamination in the study area. However, each town grouping contained towns with both low and high air emission estimates from the recently available USEPA Toxics Release Inventory database.[20]

At least two of the common contaminants, TCE and PCE, have been shown to be carcinogenic in experimental animal studies, indicating the potential to be carcinogenic in humans.[21–25]

Observations in humans exposed to TCE and PCE or related solvents have not demonstrated a consistent association with leukemias. Studies of the mortality experience of dry cleaning workers have variously reported statistically elevated deaths from a variety of cancer sites. Mortality from leukemia was elevated (but not statistically significant) in one of the studies.[26] In a case-referent study of childhood leukemia, fathers' exposure to chlorinated solvents was associated with excess leukemia in the children.[27]

For TCE and PCE, it has been estimated that daily exposures from these chemicals in the ambient air of New Jersey amount to an average of 90 micrograms per day.[28] Using standard assumptions of drinking water consumption,[29] and assuming an equivalent dose from inhaling volatilized contaminants, drinking water concentrations greater than about 20–25 μg/l would add 80–100 μg of exposure, a doubling of the average daily exposure. This estimate illustrates that drinking water can be an important relative source of exposure at levels encountered in some water supplies.

Although we have analyzed total leukemias in this study, we recognize their clinical and etiologic diversity. Known or suspected risk factors include certain genetic traits (particularly for CGL and CLL), ionizing radiation (apparently most types but CLL), infectious agents, and chemicals such as benzene (primarily AML).[30,31] Combining histologic types together in this ecologic analysis may have obscured an effect if the hypothesized etiologic agent, VOC-contaminated drinking water, is specific to a particular histologic type. A detailed analysis of type-specific incidence in this study was precluded by the small number of cases.

The inconsistency of association with respect to gender in this study cannot be explained given the data and level of analysis used in this study.

Our results suggest that a relation may exist between leukemia incidence and VOC contamination of drinking water, at least among females, although this ecologic study cannot lead to a causal inference. Since the observed association may reflect an underlying causal relation, the potential public health importance warrants further study. In particular, a case-referent epidemiologic study would allow an analysis of several potential risk factors and several histologic types that could not be assessed in this ecologic study.

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