

Alcohol consumption and risk of adult-onset acute myeloid leukemia: results from a Los Angeles County case-control study

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Abstract

Few studies have examined the role of alcohol consumption in risk of adult acute myeloid leukemia (AML). Two previous case-control studies resulted in inconsistent findings. We report data from a Los Angeles County population-based case-control study in which 164 matched case-control pairs were asked about lifetime history of alcohol consumption and 136 cases were subtyped according to the French-American-British (FAB) criteria. Estimated categorical odds ratios (OR) adjusted for smoking and education were suggestive of a possible protective effect but trend tests were non-significant. Analyses by FAB subtype did not reveal subtype-specific associations but generally suffered from lack of power. Larger studies are needed to more thoroughly investigate the relationship between alcohol consumption and AML risk.

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1. Introduction

In 1977, the Third National Cancer Survey was the first study to report on the effects of alcohol consumption for leukemia subtypes and suggested a positive but weak association with chronic lymphoid, chronic myeloid, and acute myeloid leukemia [1]. Since then, several studies have analyzed the relationship between alcohol intake and adult leukemia and between maternal alcohol consumption and childhood leukemia. Findings have been generally inconsistent, but interpreting these studies as a group is problematic since leukemia subtypes were not often distinguished. Two case-control studies have specifically reported on acute myeloid leukemia (AML) in adults. One found no evidence of a relationship between alcohol consumption and AML risk [2] and the other found elevated odds ratios (OR) associated with alcohol but no dose-response [3].

Abbreviations: AML, acute myelogenous leukemia; CI, 95% confidence interval; FAB, French-American-British; OR, odds ratio; SES, socioeconomic status

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We report on an analysis of alcohol consumption and AML risk in a subset of a large, population-based case-control study conducted in Los Angeles County. Analyses were done for all cases combined as well as for individual French-American-British (FAB) subtypes of AML.

2. Materials and methods

2.1. Study population

The study has been described in detail elsewhere [4]. Briefly, the study included eligible cases of adult-onset AML (ICDO codes 9861, 9864, 9866, 9867, and 9891) diagnosed in Los Angeles County from January 1987 through June 1994. Proxy respondents (usually the spouse) were used for cases who could not be interviewed. Neighborhood controls were matched by birthyear (± 5 years), ethnicity (African-American or white, including Hispanic), and sex according to a previously established protocol [5]. The study proposal and method of obtaining informed consent from study participants were approved by the USC Institutional Review Board.

2.2. Exposure ascertainment

In interviews conducted from 1992 to 1994, respondents were asked if they had ever drunk alcohol at least once a month for a year or more and, if so, the type of alcoholic beverage they drank. For each type of alcoholic beverage reported, respondents were further asked when they first started drinking, how much they usually drank (per day, week, or month), and when they stopped drinking or changed their drinking pattern for the beverage. Time-weighted average grams (g) of alcohol per day was derived by weighting typical number of drinks per day by g alcohol per drink for each type of beverage (or drinking pattern for a particular beverage) and averaging over all beverage types (or drinking patterns) reported, weighted by number of years of consumption (or drinking pattern). For each type of beverage, g per drink was assigned as follows: 12.8 g for beer, 11 g for wine, and 14 g for liquor [6].

History of smoking was ascertained in a separate section of the interview and is described in detail elsewhere [4]. Respondents also self-reported ethnicity and highest level of education achieved.

2.3. FAB classification

Using the now-standard French-American-British scheme, cases were classified by review of pathology reports or slides by one of us, an experienced hematopathologist (P.W.N.). For cases with FAB subtype not specified on the pathology report or for whom diagnostic information was otherwise incomplete, available peripheral blood and bone marrow slides were reviewed to verify the original AML diagnosis and to establish the FAB subtype.

2.4. Statistical methods

Cutpoints for categorical analyses were chosen by using “abstainers” (those who never drank at least once a month for a year or more) as the reference group and determining tertiles of exposure among the remaining subjects. Education and pack-years of smoking were included as covariates in all analyses and were the only variables considered as possible confounders. Education was categorized as follows: 0, graduate training; 1, college graduate; 2, some college (at least 1 year); 3, high school graduate; 4, some high school; 5, 7–9th grade; and 6, elementary school or less.

All tests were performed at the 0.05 significance level using SAS statistical software, version 9 (SAS Institute, Inc., Cary, NC). Contingency table analyses were done using Fisher’s exact tests in PROC FREQ of SAS. Maximum likelihood estimates of odds ratios and 95% confidence intervals (CI) were calculated using logistic regression conditioned on matched pairs [7]. Trend tests were performed by modeling categories of exposure as continuous variables. For analyses involving sparse data, exact conditional logistic regression or McNemar’s test was used. PROC LOGISTIC in

SAS was used for conditional logistic regression, including exact methods.

3. Results

Seven hundred twenty-five cases diagnosed from January 1987 through June 1994 who met the age, race and residence criteria were identified. Of these, 188 (26%) were deceased or too ill for interview, 31 (4%) were not contacted as advised by their physicians, and 20 (3%) were lost to followup. Therefore, 67% (486/725) of eligible cases were invited to participate in the study. Since 74 (13%) invited cases refused to participate, the study ultimately included 412 cases (57% (412/726) of those originally identified and 85% (412/487) of those invited). Since a section on alcohol consumption was not added to the interview until 1992, 164/412 case-control pairs (40%) were included in the analysis. Proxy respondents (using a surviving spouse) were used for 77 (47%) of deceased cases.

Distributions for demographic variables and FAB subtype for the 164 case-control pairs included in the analysis are shown in Table 1. As expected, cases and controls were highly comparable on sex and age since these were matching factors. There was a greater proportion of Hispanics among cases than controls because the matching did not distinguish between non-Hispanic whites and Hispanics. Despite neighborhood matching, distribution of education was significantly different by case-control status ($P = 0.01$), with controls being more highly educated than cases. Twenty-eight cases (17%) had unknown FAB subtypes; of these, 25 had inadequate pathology materials available, one had inadequate information in medical records to locate pathology materials, one would not consent to release of pathology materials, and one was unclassifiable after pathology review.

Analysis of time-weighted average g per day alcohol consumption is shown in Table 2. Data on quantity of consumption were available for 146 pairs. While there is some suggestion of either a linear or quadratic downward trend, tests for trend were non-significant. Results were similar when case-control pairs with proxy case respondents were excluded. For index case respondents, distribution of exposure was 35, 19, 23, and 23% for 0, 1–3, 4–10, and more than 10 time-weighted drinks per week, respectively; for proxy case respondents, the distribution was 47, 16, 21, and 16%, respectively.

Analysis of the dichotomous exposure variable “drank at least once a month for a year or more” by FAB subtype was limited by sparse data (Table 3). Among M3 pairs, there were six pairs in which the control but not the case drank alcoholic beverages and no pairs in which the case but not the control did; the case and control were the same race in four of the six pairs (the case was Hispanic and the control was white in the other 2 pairs). Although this distribution of exposure among matched pairs was significant by McNemar’s

Table 1
Gender, age, ethnicity, education, and FAB subtype for subjects comprising 164 case-control pairs with data on alcohol consumption, Los Angeles County, 1992–1994

Characteristic	Cases		Controls		P value
	No.	%	No.	%	
Sex					
Male	88	54	88	54	1.00
Female	76	46	76	46	
Age (years)					
25–39	25	15	23	14	0.96
40–49	22	13	24	15	
50–59	53	32	50	30	
60–75	64	39	67	41	
Ethnicity					
Non-Hispanic white	110	67	127	77	0.18
Hispanic	38	23	25	15	
African-American	14	9	11	7	
Other	2	1	1	1	
Education					
College grad	43	26	63	38	0.04
Some college	47	29	50	30	
High school grad	43	26	28	17	
Did not complete high school	31	19	23	14	
FAB subtype^a					
M0	5	4			
M1	33	24			
M2	38	28			
M3	20	15			
M4 ^b	26	19			
M4E ^b	2	1			
M5 ^c	8	6			
M5A ^c	1	1			
M5B ^c	3	2			
Unknown	28				

^a Percentages are % of cases with non-missing FAB.

^b M4/M4e combined for analysis purposes.

^c M5/M5a/M5b combined for analysis purposes.

test ($P = 0.01$), this result must be interpreted cautiously due to the inability to simultaneously control for potentially important confounders (smoking and socioeconomic status) due to sparse data.

Dose-response analysis was performed for FAB subtype M1, and there was no clear evidence of trend (Table 4). Data

Table 2
Risk of AML associated with lifetime time-weighted average grams of alcohol per day, adjusted for smoking (pack-years) and education, case-control study of AML, Los Angeles County, 1987–1994^a

Time-weighted average gram of alcohol per day	Controls					OR	95% CI	Trend P values	
	0	1–3	4–10	>10	Linear			Quadratic	
Cases									
0	24	10	16	12			0.20	0.30	
1–3	5	9	6	5	0.7	0.3, 1.5			
4–10	9	7	10	6	0.7	0.3, 1.4			
>10	4	6	11	6	0.8	0.4, 1.6			

^a Cell entries are numbers of matched case-control pairs.

Table 3
Risk of AML associated with lifetime alcohol consumption by FAB subtype, adjusted for smoking (pack-years) and education, case-control study of AML, Los Angeles County, 1987–1994

Consumed alcohol ^a	Cases	Controls				OR	95% CI
		FAB subtype ^b	No	Yes			
No	M1		5	3			
		Yes	5	20	3.0	0.5, 19	
No	M2		6	5			
		Yes	7	20	1.3	0.3, 5.7	
No	M3 ^c		5	6			
		Yes	0	9	–	–	
No	M4 ^d		3	9			
		Yes	3	13	0.4	0.0, 5.3	
No	M5 ^e		1	4			
		Yes	2	5	–	–	

^a At least once per month for at least 1 year.

^b FAB subtype M0 was not analyzed due to sparse data.

^c Data too sparse for exact conditional logistic regression; $P = 0.01$ by McNemar's test.

^d Exact conditional logistic regression.

^e Data too sparse for exact conditional logistic regression; $P = 0.41$ by McNemar's test.

were too sparse for dose-response analyses for other FAB subtypes.

4. Discussion

Our findings were consistent with those of the case-control study of males in Iowa and Minnesota conducted by Brown et al. [2]. As in that study, we observed decreased but non-significant ORs for alcohol consumption and risk of AML with an upper 95% confidence limit of 1.6 for the highest exposure category. The confidence intervals we observed did not include the elevated ORs reported by Wakabayashi et al. [3], who failed to show dose-response.

Alcohol is associated with reduced risk of coronary heart disease [8] as well as diabetes [9]. In both of those diseases, it appears that the dose-response curve may be quadratic, with a protective effect for moderate levels but increased risk at high levels of alcohol consumption. A biological mechanism

Table 4

Risk of AML associated with lifetime time-weighted average grams of alcohol per day, FAB subtypes M1 and M4, adjusted for smoking (pack-years) and education, case-control study of AML, Los Angeles County, 1987–1994

Time-weighted average g of alcohol per day	FAB subtype	Controls				OR	95% CI	Trend <i>P</i> values	
		0	1–3	4–10	>10			Linear	Quadratic
Cases									
0	M1	5	1	0	2			0.23	0.28
1–3		3	2	1	2	2.7	0.5, 16		
4–10		2	1	2	1	3.3	0.5, 20		
>10		0	2	3	2	2.2	0.4, 12		
0	M4	3	2	5	1			0.90	0.70
1–3		1	1	0	0	1.2	0.1, 11		
4–10		2	1	4	3	0.4	0.0, 5.0		
>10		0	0	0	1	0.0	0.0		

that would exert a similar alcohol effect on AML risk, or on risk of specific FAB subtypes of AML, is not obvious. Nonetheless, our study suggested this type of dose-response curve but did not have sufficient power to detect it.

It is possible that the decreased ORs we observed were due to an unknown, uncontrolled confounder, i.e., a factor that was associated with both alcohol consumption and AML risk. In our study population, alcohol consumption was related to higher socioeconomic status (SES). Therefore, a control sample that had higher SES than cases could produce spuriously reduced ORs. Although controls in our study were neighborhood-matched to cases and education was controlled analytically, residual SES confounding may have resulted in downwardly biased ORs. Another limitation of our study was the extensive use of proxy respondents for cases. Proxies tend to underestimate alcohol intake [10,11], which would also downwardly bias ORs. However, alcohol consumption tends to be underreported in general [12]; thus, it seems likely that control respondents underreported exposure, as well; in fact, we observed similarly decreased ORs when pairs with proxy case respondents were excluded.

Larger case-control studies are needed to more fully explore a possible relationship between alcohol consumption and AML risk. However, based on currently available evidence, it appears that alcohol is not related in any significant way to risk of adult AML.

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