Dietary Folate, Alcohol Consumption, and Risk of Ovarian Cancer in an Italian Case-Control Study

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Materials and Methods

The study was conducted in four Italian areas between 1992 and 1999 (10). Cases were 1,031 women admitted to the major hospitals with incident, histologically confirmed epithelial ovarian cancer. Controls were 2,411 women admitted to the same network of hospitals for acute, nonmalignant, and nongynecologic conditions, unrelated to hormonal diseases or to long-term modifications of diet.

Standard questionnaire was given by centrally trained interviewers during hospital stay, including detailed information on personal characteristics, lifestyle habits, a problem-oriented medical history, history of cancer in relatives, menstrual and reproductive factors, and use of oral contraceptives and hormone therapy. A food frequency questionnaire was developed to assess the usual diet during the 2 years preceding diagnosis (for cases) or hospital admission (for controls). The food frequency questionnaire included 78 foods, food groups, or dishes divided into six sections: first courses, second courses, side dishes, fruits, desserts, and beverages. For a few seasonal vegetables and fruits, duration of consumption was elicited.

Data Analysis. Odds ratios (OR) and 95% confidence intervals (95% CI) were derived using unconditional multiple logistic regression models, including terms for age, study center, year of interview, education, parity, body mass index, alcohol consumption, use of oral contraceptives, physical activity, and energy intake (excluding energy from alcoholic beverages). After adjustment for nonalcohol energy intake, our study had 80% power to detect a 35% reduced risk (i.e., an OR ≤ 0.65) for the highest compared with the lowest quintile of folate intake (x = 0.05).

Results

Table 1 reports the distribution of cases and controls, ORs and 95% CIs of ovarian cancer according to quintiles of folate intake of all women together, by histologic subtype and in separate strata of alcohol consumption, methionine, and vitamin B6 intake. Compared with the lowest quintile of dietary folate, the ORs of ovarian cancer were 1.10, 0.99, 1.02 and 0.98 for subsequent quintiles of intake. When further lifestyle, reproductive, and dietary covariates were controlled for, the ORs were 1.14, 1.12, 1.23, and 1.26. For the highest level of folate, the ORs of serous, mucinous, and other subtypes of ovarian cancer were 1.10, 0.41, and 0.85, respectively. In the stratum of non- and low-alcohol drinkers, the OR for an increase in folate intake equal to an SD was 0.93 (95% CI, 0.76-1.14). In the stratum of moderate/high drinkers, the corresponding OR was 1.02 (95% CI, 0.86-1.23), whereas when we considered folate intake in the stratum of hard drinkers only (5th quintile, i.e., >26 g/d), the OR was 1.14 (95% CI, 0.85-1.54). Ovarian cancer risk for folate intake was somewhat higher in strata of low methionine and vitamin B6 intake (OR, 1.18 and 1.15, respectively) than in strata of high methionine and vitamin B6 intake (OR, 0.79 and 0.88, respectively).

Discussion

Strengths of this investigation are its large size, the use of a validated and reproducible food frequency questionnaire...
(12-14), the low percentage of refusals of the subjects contacted, and the specific interest of the Italian population that has relatively high levels of alcohol (mostly wine) consumption (17). Our results do not indicate a major role of folate in ovarian cancer risk, nor a relevant interaction of folate with alcohol or with methionine or vitamin B6. These findings are in line with previous findings from the Swedish Mammography Cohort (5), but still uncertain because of the small number of mucinous cases in one of the largest data sets of ovarian cancer collected to date, as well as the overall epidemiologic evidence, do not support a role of folate and alcohol in ovarian carcinogenesis (18).

Among possible explanations of the inconsistent findings of the studies, there are potential bias of epidemiologic studies. Case-control studies are generally more liable to bias than prospective ones. However, findings from a companion case-control study of breast cancer, where an inverse association with folate intake (stronger in high alcohol drinkers) was observed (17), are reassuring for the control group that we investigated, because the breast and ovarian studies were conducted on similar populations and shared a number of control subjects too.

In addition, differences in folate intake and alcohol consumption between various populations should be taken into account. In fact, the estimated median intake of folate widely differed between our study (248 μg/d) and the Swedish (178 μg/d) and the Iowa studies (331 μg/d; refs. 5–7). Further, the pattern of alcohol drinking in our investigation was peculiar for this population because we observed a large proportion of nondrinkers (40.6% of controls) as well as of hard drinkers (22.0% of controls had an intake of >25 g/d).

Notwithstanding these considerations, our findings from one of the largest data sets of ovarian cancer collected to date, as well as the overall epidemiologic evidence, do not support a role of folate and alcohol in ovarian carcinogenesis (18).

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References

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