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Coffee and tea consumption and risk of leukaemia in an adult population: A reanalysis of the Italian multicentre case-control study

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ABSTRACT

Background: Coffee and tea are the most frequently consumed beverages in the world. Their potential effect on the risk of developing different types of malignancies has been largely investigated, but studies on leukaemia in adults are scarce.
Methods: The present investigation is aimed at evaluating the potential role of regular coffee and tea intake on the risk of adult leukaemia by reanalysing a large population based case-control study carried out in Italy, a country with a high coffee consumption and a low use of green tea. Interviewed subjects, recruited between 1990 and 1993 in 11 Italian areas, included 1771 controls and 651 leukaemia cases. Association between Acute Myeloid Leukaemia (AML), Acute Lymphoid Leukaemia, Chronic Myeloid Leukaemia, Chronic Lymphoid Leukaemia, and use of coffee and tea was evaluated by standard logistic regression. Odds Ratios (OR) were estimated adjusting for the following potential confounders: gender, age, residence area, smoking habit, educational level, previous chemotherapy treatment, alcohol consumption and exposure to electromagnetic fields, radiation, pesticides and aromatic hydrocarbons.
Results: No association was observed between regular use of coffee and any type of leukaemia. A small protective effect of tea intake was found among myeloid malignancies, which was more evident among AML (OR = 0.68, 95%CI: 0.49–0.94). However, no clear dose-response relation was found.
Conclusion: The lower risk of leukaemia among regular coffee consumers, reported by a few of previous small studies, was not confirmed. The protective effect of tea on the AML risk is only partly consistent with results from other investigations.

1. Introduction

The aetiology of leukaemia in adults is poorly understood. Recognized or suspected risk factors include some viral infections (in particular HTLV-1, which may cause a rare form of T-cell lymphoma/leukaemia), chemotherapy, ionizing radiation, smoking habit, alkylating agents, benzene and other hydrocarbons [1–4].

Coffee and tea are by large the most frequently consumed beverages after water over the world [5,6]. Many epidemiological studies have investigated their potential association with the risk of developing different types of malignancies, but those on leukaemia in adults are rare [7,8]. With regard to coffee, a protective effect on the risk of Acute Myeloid Leukaemia (AML) was reported in a USA cohort [9]. A hospital based case-control study in Mumbai (India) reported a reduced risk of all leukaemia among coffee drinkers, whereas a recent population based case-control study in Northern Italy failed to find any association [10].

A regular consumption of tea has been consistently associated with a reduced frequency of both lymphoid and myeloid leukaemia. However, this finding seems to be limited to an intake of high doses of green tea, whereas the possibility of a protective effect of black tea remains controversial [5,11]. The above cited

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Italian case-control investigation reported a protective effect of high tea intake (mainly black tea) on the risk of developing myeloid malignancies (OR = 0.4, 95%CI: 0.2–0.9), but the evidence was based on 10 highly exposed cases only [10].

The present investigation is aimed at evaluating the risk of leukaemia in an adult population among coffee and tea consumers by reanalysing a large multi-centre Italian study.

2. Materials and methods

2.1. Subjects recruitment and interview

The present study is a reanalysis of a large multi-centre population based case-control study including 11 areas in Italy (namely, provinces of Varese, Forlì, Siena, Latina, Ragusa, Imperia, Florence, Novara, Vercelli, and Verona plus the town of Turin) [12,13].

All incident cases of leukaemia, diagnosed between 1990 and 1993, aged 20–74 years at diagnosis, and resident in one of the 11 study areas were considered as eligible. Leukaemia cases were classified according to the International Classification of Diseases, 9th revision (ICD-9): 204–208. The following subtypes were analysed separately: lymphocytic leukaemia (ICD9: 204.0 to 204.9), which included acute (ALL, ICD-9: 204.0) and chronic (CLL, ICD-9: 204.1) subtypes, myeloid leukaemia (ICD9: 205.0–205.9), which also included acute (AML, ICD-9: 205.0) and chronic (CML, ICD-9: 205.1) subtypes, and other leukaemia (OL, ICD-9: 206, 207, and 208). CLL cases were recruited in all areas, while other types of leukaemia were not included in the provinces of Novara, Varese and Vercelli.

Cases were identified by systematic searches in departments of haematology, general medicine, surgery, and pathology in all hospitals of the above-mentioned areas. Furthermore, specialized hospitals outside these areas, where such patients could have been admitted, were also considered. Diagnoses were based on histological analyses for CLL, and on morphologic, cytochemical, and immunological analyses for the other types of leukaemia. All diagnoses of CLL were classified by an experienced pathologist.

The control group was selected by random sampling of the resident population and frequency matched to cases by age (±5 years) and gender. Control selection was carried out through record linkage with population computerized files in all areas.

Information about the known or alleged risk factors was collected through person-to-person interview. A standardized questionnaire was administered to cases and controls by trained interviewers to obtain detailed information about socio-demographic characteristics, residential history, occupational exposures, medical history, and lifestyle habits. When subjects were deceased or too ill close relatives were interviewed, instead. Interview lasted on average one hour in both cases and controls. With regard to coffee and tea consumption, information about exposure duration and the average number of cups per day was available. Subjects who stopped drinking within six months prior to their inclusion in the study were considered as exposed. With regard to coffee, the daily mean number of cups was estimated considering the major types of beverages containing coffee, namely: espresso, cappuccino and “caffelatte” (Italian white coffee obtained mixing an espresso with a cup of milk). Because 8.8% of cases and 7.6% of controls were no coffee consumers, they were aggregated to the lowest exposure category in any analysis.

All subjects gave their informed consent to participate in the study.

More details about the study design and the questionnaire structure have been published elsewhere [12,13].

2.2. Statistical analysis

The association between leukaemia risk and coffee and tea consumption was assessed by multivariable unconditional logistic regression [14]. The five major subtypes of leukaemia (ALL, CLL, AML, CML and OL) were considered both separately and after aggregating lymphoid and myeloid cases, in order to make results comparable to that of other previous investigations.

Exposure was expressed by an intensity score (*IS*), obtained by multiplying the average daily consumption (*ADC*) by the estimated number of exposure days divided by 1000:

$$IS = (ADC * 365.25 * NY)/1000$$

where *NY* represents the number of years of exposure.

For example, *IS* = 11 corresponds to a regular consumption of one cup of coffee per day for 30 years or, equivalently, of three cups per day for 10 years. Analyses were also performed by using the mean number of cups per day.

Odds ratios (OR) were adjusted for gender, age (continuous linear and quadratic terms), residence area, educational level (illiteracy or primary school, middle school, high school/university), alcohol consumption (cumulative exposure), previous chemotherapy treatment, exposure to electromagnetic fields, radiation, pesticides and aromatic hydrocarbons (exposed vs. unexposed), and smoking habit (current, former and never smokers). Smoke intensity was estimated by multiplying the number of cigarette packs daily smoked by the duration of smoking and inserted into the model as nested variables [15]. The mutual potential confounding effect of coffee and tea was also assessed.

In order to reduce the possible effect of recall bias, all analyses were repeated after excluding next-of-kin and allegedly poor quality interviews (*i.e.*, those that lasted less than 45 min) [16].

Selection of predictors in logistic regression analysis was performed by a standard backward procedure [17], using R language (version 3.2.2.17). All the other analyses were carried out by Stata for Windows statistical package (release 12.1, Stata Corporation, College Station, TX).

3. Results

During the study period 1774 controls (81%) and 651 leukaemia cases (88%) were interviewed. The latter included: 264 lymphoid leukaemia (49 ALL, 214 CLL and 1 unspecified lymphoid leukaemia), 329 myeloid leukaemia (223 AML and 106 CML), and 58 OL.

Information about coffee consumption was missing for three controls. Moreover, eight controls and 53 cases (12 lymphoid, 30 myeloid and 11 OL, respectively) were unable to provide information on exposure duration. One control did not provide any information about tea consumption, while 3 controls and 32 cases (13 lymphoid, 14 myeloid and 5 OL) had missing data for the duration of tea intake.

Table 1 summarizes the main characteristics of interviewed subjects. Compared to controls, ALL cases were on average younger and CLL slightly older. Males and females were nearly equally distributed among controls, females were more prevalent among ALL cases and less frequent among the other groups of cases. Educational level was higher in OL and slightly lower in CLL than in controls. The proportion of next-of-kin interview was higher in any group of cases, with the highest proportion observed among CLL. Prevalence of tobacco smoking was higher among ALL and OL. Previous exposure to radiations, EMF and chemotherapy treatment was rare in all considered groups. Pesticide exposure was slightly higher among CLL and CML, and CLL also declared to be more exposed to aromatic hydrocarbons.