Archives of Medical Research 47 (2016) 694–705

Archives of Medical Research

ORIGINAL ARTICLE

Road Traffic Pollution and Childhood Leukemia: A Nationwide Case-control Study in Italy

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Received for publication January 2, 2017; accepted February 23, 2017 (ARCMED-D-17-00020).

Background. The association of childhood leukemia with traffic pollution was considered in a number of studies from 1989 onwards, with results not entirely consistent and little information regarding subtypes.

Aim of the study. We used the data of the Italian SETIL case-control on childhood leukemia to explore the risk by leukemia subtypes associated to exposure to vehicular traffic.

Methods. We included in the analyses 648 cases of childhood leukemia (565 Acute lymphoblastic−ALL and 80 Acute non lymphoblastic-AnLL) and 980 controls. Information on traffic exposure was collected from questionnaire interviews and from the geocoding of house addresses, for all periods of life of the children.

Results. We observed an increase in risk for AnLL, and at a lower extent for ALL, with indicators of exposure to traffic pollutants. In particular, the risk was associated to the report of closeness of the house to traffic lights and to the passage of trucks (OR: 1.76; 95% CI 1.03−3.01 for ALL and 6.35; 95% CI 2.59−15.6 for AnLL). The

Ethical Aspects: The SETIL study was authorized by the Ethical Review Board for the Piedmont Region (authorization n. 2886, on 15/2/1999; letter n. 1852/28.3 on 17/2/1999) and later by the corresponding board of each participating research unit. Parental informed consent was obtained before the interview.

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http://dx.doi.org/10.1016/j.arcmed.2017.02.001

association was shown also in the analyses limited to AML and in the stratified analyses and in respect to the house in different period of life.

Conclusions. Results from the SETIL study provide some support to the association of traffic related exposure and risk for AnLL, but at a lesser extent for ALL. Our conclusion highlights the need for leukemia type specific analyses in future studies. Results support the need of controlling exposure from traffic pollution, even if knowledge is not complete. © 2017 IMSS. Published by Elsevier Inc.

Key Words: Childhood, Leukemia, Acute non Lymphoblastic Leukemia, Road Traffic, Environment.

Introduction

Leukemia is the most frequent neoplasm in childhood, with incidence rates of 35.9 per million children-year for Acute Lymphoblastic Leukemia (ALL) and of 6.5 for Acute non Lymphoblastic Leukemia (AnLL) in European countries (1). Analyses of incidence trends showed an increase, in particular in the EU and USA (1,2). Despite its relative frequency and the large number of studies, exposure to ionizing radiation is the only exposure unequivocally associated to childhood leukemia (3−5). A large number of putative risk factors has been studied, including among others: infectious agents and immune stimulation, parental and child exposure to: chemical agents, solvents, pesticides, tobacco smoking, Extremely Low Frequency Magnetic fields (ELF-MF) and Radiofrequency fields, and exhaust gases from traffic pollution (3,4,6−11). Traffic pollution causes exposure to a large number of chemicals, including some with known carcinogenic effect, such as benzene and polycyclic aromatic hydrocarbons (PAH). Diesel exhaust was classified in the IARC Monographs as Human Carcinogen (group 1), but only limited information was available on childhood leukemia (12). Benzene is a known carcinogen causing leukemia and lymphoma, but evidence for childhood leukemia is limited (13). Three recent metaanalyses observed an association of childhood leukemia and traffic related exposures (14−16).

Etiological factors for childhood leukemia were investigated in Italy in a large national population-based case-control study, including 683 cases of leukemia and 1044 matched controls (17). Exposure to traffic pollution was one of the main factors considered, with information based on the geocoding of all reported addresses and on questionnaire information on the area of residence and on the house characteristics. A pilot study was conducted including area and personal measurement of benzene exposure, showing that exposure was higher in wintertime, and it was not affected by gender, age or area of residence. The pilot study size was too limited to investigate association with leukemia and to conduct analyses by subtype (18). An analysis of SETIL main study focused on distance from main roads and estimates of exposure to pollutants from Land Use Regression (LUR) and dispersion models observed no association of traffic exposure indicators and leukemia status (19). The present study further investigates with further analyses on leukemia risk and traffic exposure, using both questionnaire information and geocoded home addresses to identify traffic related exposure variables. Present analyses were conducted separately for ALL and AnLL, in order to contribute information on etiological factors specific for leukemia type.

Material and Methods

Study Population

The SETIL study is a population based case-control study including the cases of acute childhood leukemia diagnosed in children aged 0−10 in 14 Italian regions in 1998−2001. Cases were identified from the national registry of the Italian Association of Pediatric Hematology and Oncology (AIEOP) (20), that provided descriptive and clinical information, including cytological diagnosis. For each case, two controls were randomly sampled from the rosters of the National Health Service, matched by birth date (+/−15 d), gender and region. Age range (0−10) corresponds to the primary (elementary) school in Italy. Parents of cases and controls were interviewed at home with a structured questionnaire administered by a trained interviewer. Interviews took place during 1999−2002. Subjects were invited after approval from the attending oncologist for cases, and after information of the GP for the controls. Details of the study design were presented elsewhere (17) and are only summarized here.

The study included 683 leukemia cases out of 745 eligible (participation rate 91.7%) and 1044 controls out of 1475 eligible (70.8%). Among controls, family refusal was the most common reason of non participation (70.3%); medical refusal was 6.2%, while the untraced proportion was 21.8%, and the remaining 1.6% included non-participants for other reasons (17). Subjects not participating for any reasons were not substituted.

Cases were classified using the ICCC-3 classification (21), according to the confirmed cytological diagnosis recorded at AIEOP registry (20). Cytological types of participant cases included: 601 (88%) Acute Lymphocytic Leukemia (ALL, ICCC I a), 82 cases (12%) of Acute non Lymphoblastic Leukemia (AnLL—ICCC I b-e). The ALL group included for the analyses 7 cases of Acute Hybrid Leukemia (1%). The frequency distribution of AnLL by cytological subtype was:

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