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Childhood leukemia and residential proximity to industrial and urban sites

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ABSTRACT

Background: Few risk factors for the childhood leukemia are well established. While a small fraction of cases of childhood leukemia might be partially attributable to some diseases or ionizing radiation exposure, the role of industrial and urban pollution also needs to be assessed.

Objectives: To ascertain the possible effect of residential proximity to both industrial and urban areas on childhood leukemia, taking into account industrial groups and toxic substances released.

Methods: We conducted a population-based case–control study of childhood leukemia in Spain, covering 638 incident cases gathered from the Spanish Registry of Childhood Tumors and for those Autonomous Regions with 100% coverage (period 1990-2011), and 13,188 controls, individually matched by year of birth, sex, and autonomous region of residence. Distances were computed from the respective subject's residences to the 1068 industries and the 157 urban areas with $\geq$ 10,000 inhabitants, located in the study area. Using logistic regression, odds ratios (ORs) and 95% confidence intervals (95%CIs) for categories of distance to industrial and urban pollution sources were calculated, with adjustment for matching variables.

Results: Excess risk of childhood leukemia was observed for children living near ($\leq$2.5 km) industries (OR=1.31; 95%CI=1.03–1.67) – particularly glass and mineral fibers (OR=2.42; 95%CI=1.49–3.92), surface treatment using organic solvents (OR=1.87; 95%CI=1.24–2.83), galvanization (OR=1.86; 95%CI=1.07–3.21), production and processing of metals (OR=1.69; 95%CI=1.22–2.34), and surface treatment of metals (OR=1.62; 95%CI=1.22–2.15) – , and urban areas (OR=1.36; 95%CI=1.02–1.80).

Conclusions: Our study furnishes some evidence that living in the proximity of industrial and urban sites may be a risk factor for childhood leukemia.

1. Introduction

Childhood cancer is the leading cause of disease-related death in childhood affecting both sexes worldwide and, therefore, is an important concern for public health, medical care, and society (Peris-Bonet et al., 2010).

The main group is leukemia, with almost a third of all childhood cancers (Peris-Bonet et al., 2010). Insofar as the etiology of

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Abbreviations: IPPC, Integrated Pollution Prevention and Control; E-PRTR, European Pollutant Release and Transfer Register; RETI-SEHOP, Spanish Registry of Childhood Tumors; UTM, Universal Transverse Mercator; ORs, odds ratios; 95%CIs, 95% confidence intervals; IARC, International Agency for Research on Cancer; VOCs, volatile organic compounds; POPs, persistent organic pollutants; PACs, polycyclic aromatic chemicals; Non-HPCs, non-halogenated phenolic chemicals; PAHs, polycyclic aromatic hydrocarbons

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this disease is concerned, few risk factors for the childhood leukemias are well established. There are evidences that Down syndrome (Mezei et al., 2014) and inherit cancer-predisposing conditions such as ataxia telangiectasia (Bielorai et al., 2013) substantially increase the risk of leukemias (specially for acute lymphoblastic leukemia and acute myeloid leukemia) but account for only a small fraction of cases (5%) (Ross et al., 2011). Investigations of other risk factors, as ionizing radiation (Wakeford et al., 2009), radon (Evrard and Hemon 2005; Tong et al., 2012) or infectious agents (Alexander et al., 1998; Greaves, 2002; Smith et al., 1998), have also indicated increased risk of childhood leukemias. With respect to environmental and parental occupational exposures, several studies have reported risks of leukemias among children whose parents have been occupational exposed to a high level of carcinogenic agents (Perez-Saldivar et al., 2008), pesticides (Ferreira et al., 2013) or involving social contact (Keegan et al., 2012), and some meta-analyses found associations between childhood leukemias and prenatal parental occupational pesticide exposure (Vinson et al., 2011; Wigle et al., 2009). Other exposure to chemicals, as benzene and some volatile organic compounds, has been associated with some type of leukemias (Best et al., 2001; Eden, 2010; Knox, 2005; Steffen et al., 2004), although a review of chemical risk factors and childhood leukemia revealed inconsistent associations (Infante-Rivard, 2008).

With regard to urban and residential traffic exposure, some authors have found associations between childhood leukemia and air pollutants (Boothe et al., 2014; Heck et al., 2014). Nevertheless, there are few studies on exposure to industrial pollution and childhood leukemia (Knox, 1994; Weng et al., 2008), even though industrial plants are known to release carcinogens, such as benzene, dioxins and metals. In relation to industrial sources, the European Commission passed the Integrated Pollution Prevention and Control (IPPC) in 2002 and the European Pollutant Release and Transfer Register (E-PRTR) in 2007. IPPC and E-PRTR records constitute an inventory of geo-located industries with health and environmental impact in Europe, which is a valuable resource for monitoring industrial pollution and, by extension, renders it possible for the association between residential proximity to such pollutants installations and health impacts, such as cancer, to be studied (Lopez-Cima et al., 2011; Lopez-Cima et al., 2013).

In this context, a Spanish population-based case–control study of incident childhood cancer was set in motion to furnish in-depth knowledge of the possible role of residential proximity to both industrial and urban areas as a risk factor for childhood leukemias. In this paper, we analyze the effects of exposure to industrial and urban areas and, including different industrial groups, groups of carcinogenic and other toxic substances, and specific pollutants, on childhood leukemia risk, by incorporating information on industries governed by the IPPC Directive and E-PRTR Regulation.

2. Materials and methods

2.1. Study area and subjects

We designed a population-based case–control study of childhood cancer in Spain. Cases were incident cases of childhood cancer (0–14 years) gathered from the Spanish Registry of Childhood Tumors (RETI-SEHOP) and for those Autonomous Regions with 100% coverage (Catalonia, the Basque Country, Aragon, and Navarre), for the period 1990–2011.

In this study, we select incident cases of childhood leukemia, and corresponded to diseases coded as leukemias, myeloproliferative diseases, and myelodysplastic diseases – code I (International Classification of Diseases for Oncology, 3rd revision) (Steliarova-Foucher et al., 2005). Controls were selected by simple random sampling from among all single live births registered in the Spanish National Statistics Institute between 1996 and 2011, individually matched to cases by year of birth, sex and autonomous region of residence. The final study population comprised 638 cases and 13,188 controls, and both cases and controls were ethnically homogeneous.

2.2. Residential locations

Each individual's last residence was geocoded using Google Map Javascript API v3 (Google Maps, 2015). The obtained latitude and longitude coordinates were projected into the ETRS89/UTM zone 30N (EPSG:25830) using QGIS software (Open Source Geospatial Foundation (OSGeo), 2015), and subsequently converted into the Universal Transverse Mercator (UTM) Zone 30 (ED50) coordinates. Then, we validated the coordinates and kept those where the address and the coordinates matched. For this validation process, we apply the inverse method, getting the addresses of the obtained coordinates and comparing these new addresses (town or city name, street name, and street number) to the original addresses. Lastly, in UTM coordinates of children's residences, the last digit of coordinates (X, Y) was assigned randomly in order to preserve their confidentiality.

With respect to cases, we successfully validated 87% of their addresses. The remaining 13% of cases were fairly uniformly distributed along the different regions and, therefore, we did not think the data were biased in this sense. On the other hand, only 2% of controls did not have valid coordinates. Having had a small number of failures we decided to select more controls to replace this 2%, and we geocoded and validated this last group to end up with more than 20 controls with valid coordinates for every case.

2.3. Industrial facility locations

We used the industrial database (industries governed by IPPC and facilities pertaining to industrial activities not subject to IPPC but included in the E-PRTR) provided by the Spanish Ministry for Agriculture, Food & Environment in 2009, which includes information on the geographic location and industrial pollution emissions of all industrial plants in Spain.

Each of the installations was classified into one of the 25 categories of industrial groups listed in Table 1. These groups were formed on the basis of the similarity of their pollutant emission patterns.

Owing to the presence of errors in the initial location of industries, the geographic coordinates of the industrial locations recorded in the IPPC+E-PRTR 2009 database were previously validated: every single address was thoroughly checked using Google Earth, the Spanish Agricultural Plots Geographic Information System (Spanish Ministry of Agriculture and Food and Environment, 2015), the "Yellow pages" web page, and the web pages of the industries themselves, to ensure that location of the industrial facility was exactly where it should be. We identified a total of 1068 industrial facilities: 1026 installations located in the four areas included in the study and 42 installations located in adjacent regions but very close to the individuals. Table 1 shows the distribution of the number of industrial facilities by industrial group and autonomous region.

2.4. Urban locations

In Spain, municipal centroids are computed by taking only the inhabited area of the designated town into account, and are situated in the center of the most populous zone where the town hall and the main church tend to be located. For the purposes of this study, we considered as urban areas those towns with more