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Childhood cancer in small geographical areas and proximity to air-polluting industries

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ABSTRACT

Aim: Pediatric cancer has been associated with exposure to certain environmental carcinogens. The purpose of this work is to analyse the relationship between environmental pollution and pediatric cancer risk.
Method: We analysed all incidences of pediatric cancer (< 15) diagnosed in a Spanish region during the period 1998–2015. The place of residence of each patient and the exact geographical coordinates of main industrial facilities was codified in order to analyse the spatial distribution of cases of cancer in relation to industrial areas. Focal tests and focused Scan methodology were used for the identification of high-incidence-rate spatial clusters around the main industrial pollution foci.
Results: The crude rate for the period was 148.0 cases per 1,000,0000 children. The incidence of pediatric cancer increased significantly along the period of study. With respect to spatial distribution, results showed significant high incidence around some industrial pollution foci group and the Scan methodology identify spatial clustering. We observe a global major incidence of non Hodgkin lymphomas (NHL) considering all foci, and high incidence of Sympathetic Nervous System Tumour (SNST) around Energy and Electric and organic and inorganic chemical industries foci group. In the analysis foci to foci, the focused Scan test identifies several significant spatial clusters. Particularly, three significant clusters were identified: the first of SNST was around energy-generating chemical industries (2 cases versus the expected 0.26), another of NHL was around residue-valorisation plants (5 cases versus the expected 0.91) and finally one cluster of Hodgkin lymphoma around building materials (3 cases versus the expected 2.2)
Conclusion: Results suggest a possible association between proximity to certain industries and pediatric cancer risk. More evidences are necessary before establishing the relationship between industrial pollution and pediatric cancer incidence.

1. Introduction

Pediatric Cancer (PC) was the leading cause of disease-related death in children under 15 in 2014 in Spain (INE, 2016). The most common tumours (age-adjusted rates per million for children aged 0–14) are leukaemia (Spain 47.0, Europe 44.0), central nervous system tumours (CNST) (Spain 33.2, Europe 29.9) and lymphoma (Spain 19.4, Europe 15.2) (Peris-Bonet et al., 2010; Stiller et al., 2006). The causes of PC are largely unknown, although in recent years an increase in incidence rates has been detected (Kaatsch, 2010; Ward et al., 2014). The reason for this increase is unknown, although it is believed that environmental changes are a contributing factor (Buka et al., 2007; Kaatsch, 2010).

Ambient air, especially in big cities and in the vicinity of industrial pollution foci, contains a wide variety of known human carcinogens, including polycyclic aromatic hydrocarbons, dioxins, arsenic, benzene, fine and ultrafine particles, asbestos and volatile organic compounds. In adults, it is estimated that 1–2% of cases of lung cancer can be associated with the presence of a high concentration of these compounds (Alberg and Samet, 2003). In Europe, national registers of polluting industries have increased awareness of the activities and

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emissions of the main foci of industrial pollution, which has facilitated the analysis of emissions and their effects. Several works have identified residential areas that are in the vicinity of industrial pollution foci as higher-risk cancer areas for adults (Bulka et al., 2013; Garcia-Perez et al., 2015a, 2015b; Morton-Jones et al., 1999; Ramis et al., 2009; Reynolds et al., 2003). Based on this empirical evidence, the World Health Organisation (WHO) has confirmed that air pollution is a human carcinogen, owing to the direct link between it and lung cancer (Loomis et al., 2013).

The presence of spatial clusters in pediatric cancer (PC) cases has been analysed in the search for etiological factors (Alexander et al., 1998; Demoury et al., 2012; McNally et al., 2009; Ramis et al., 2015). Observational studies that relate PC and air pollution are scarce (Garcia-Perez et al., 2016a; Reynolds et al., 2003), and in most cases focus on traffic density and the proximity of high-capacity roads; no consistent results on a global scale have been reached to date. Regarding industrial pollution, several works recently published in Spain argue for the relationship between exposure to industrial pollution and leukaemia, neuroblastoma, kidney and bone tumours in children aged 0–14 (Garcia-Perez et al., 2015b, 2016a, 2016b; García-Pérez et al., 2017). The low incidence of PC, the high degree of uncertainty associated with the variables under consideration, and the formation of micro-clusters emphasise the need to carry out spatial epidemiological studies, which can then be used to analyse the incidence of cancer in small urban units (Ortega-García et al., 2016).

The target of this work is to undertake a preliminary analysis, based on empirical evidence, of the spatial distribution of PC around industrial facilities in a European region (Region of Murcia, Spain).

2. Methods

2.1. Study area and population

Census track (CT) represents the smallest territorial unit for which population data are available in Spain. The region of Murcia (RM) is a European Region (NUTS II in Eurostat terminology) located in south-eastern of Spain and is divided in 2011 into 1220 CT. We consider this spatial unit as reference to evaluate risk and spatial clusters. A latitude and longitude coordinates (centroid) was assigned to each CT and the distance between two CT was defined as the distance between centroids.

Reference population (risk population) came from Spanish Census 2001 and 2011. The total population (< 15 years) was 207,822 in 2001 and 259,083 in 2011. We performed linear interpolation to estimate the population between the censuses. For each CT we used the population at the census times immediately preceding and immediately following. For times before the first census time, the population size is set equal to the population size at that first census time, and for times after the last census time, the population is set equal to the population size at that last census time.

2.2. Cases

The subjects of analysis were PC (< 15) cases diagnosed in the RM between January 1998 and December 2015 by the MACAPEMUR (Environment and Pediatric Cancer in the RM) project. MACAPEMUR is a project for the compilation of Pediatric Environmental History in newly diagnosed cancer patients since 1998 in the RM (Cárceles-Álvarez et al., 2015; Ferris Tortajada et al., 2004; Ortega-García et al., 2011). The single-province character of the RM and the centralized care reference units of Pediatric Oncohematology and the Pediatric Environmental Health Speciality Unit site at the Clinical University Hospital Virgen of Arrixaca facilitated the access to medical records. The hospital registry from the Clinical University Hospital Virgen of Arrixaca register 100% of the children diagnosed with cancer in the RM. The classification of the cases is done by checking the clinical-pathological diagnosis with the international classification of diseases for oncology (ICD-O-3) (IARC, 2011) and the International Classification of Childhood Cancer (ICCC-3) (Steliarova-Foucher et al., 2005) within 0–2 months after of diagnosis. Over 99% of the cases are morphologically verified. Annually, a medical doctor performs an additional check of all cases to verify the correct classification and elimination of double registrations.

In all cases, the families were contacted by phone or in person. Once the diagnosis is made, a face-to-face interview is carried out by one doctor trained in pediatric cancer, environmental health and risk communication, which collect information on addresses at diagnosis; as well as another series of environmental data (Cárceles-Álvarez et al., 2015; Ferris Tortajada et al., 2004; Ortega-García et al., 2012). In this study, inclusion criteria comprised: children (< 15) diagnosed with cancer between 1998 and 2015 with an address in the RM corresponding to at-diagnosis residence. A total of 669 children were diagnosis with cancer during this period. Of these, we excluded 45 cases because they simply went to the RM in order to obtain a second opinion or complete the diagnostic and therapeutic process. Another 6 cases rejected to participate in the study. Finally, 624 cases were included in the study. Information on the residence at the time of diagnosis was then collected. These addresses were georeferenced and assigned a CT.

In order to reduce the border effects an exhaustive revision of hospital-based records of adjacent regions (Castilla-La Mancha and Comunidad Valenciana) was performed. This review did not provide new case studies.

The project was approved by the ethics research committee of Clinical University Hospital Virgen de la Arrixaca. Informed consent forms signed by all parents and children over 12 were collected.

2.3. Polluting industries

The identification of industrial pollution foci in the RM was carried out by studying the national emission and pollution register, which is maintained by the Spanish environment ministry (PRTR-Spain, http://www.prtr-es.es/). This register takes into consideration air pollution emitted by industrial facilities in the RM, and excludes the agricultural and animal-husbandry sectors. The geographical coordinates of industrial complexes were compiled using Google Maps and on-the-ground survey. Facilities located within 2 km of one another were grouped together in a single foci, which was, for analytical purposes, located in the geographic centroid. In total, the list includes 88 facilities, of which only 28 produce emissions; these were grouped in 12 foci. Fig. 1 illustrates the locations of these foci. Five types of industrial activity were defined (NACE Rev.2, http://ec.europa.eu/eurostat/web/nace-rev2) and foci were assigned accordingly: energy industries (2 foci); organic and inorganic chemical industries (5 foci); pharmaceutical industries (3 foci); building material industries (2 foci); industries concerned with the incineration or valorisation of dangerous waste (4 foci). Some foci were assigned more than one category because of the presence of industrial facilities of different kinds. Table 1 provides further details about the facilities that make up each industrial foci and the exposure of the population under 15 in 2011.

2.4. Statistical analysis

In first place, a descriptive analysis of the main diagnostic groups according to age group and sub-period was carried out, which involved the calculation of standardised incidence ratio (SIR) and its confidence intervals (CI) by cancer type and sub-periods. In second place,[1] we calculated several risk indicators (observed cases; expected cases and crude incidence rate; lowest number of observed cases which would be statistical significant at the one sided 5% type one level or less; exact

[1] Thanks to anonymous referee for this suggestion.