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Ovarian cancer mortality and industrial pollution

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ABSTRACT

We investigated whether there might be excess ovarian cancer mortality among women residing near Spanish industries, according to different categories of industrial groups and toxic substances. An ecologic study was designed to examine ovarian cancer mortality at a municipal level (period 1997–2006). Population exposure to pollution was estimated by means of distance from town to facility. Using Poisson regression models, we assessed the relative risk of dying from ovarian cancer in zones around installations, and analyzed the effect of industrial groups and pollutant substances. Excess ovarian cancer mortality was detected in the vicinity of all sectors combined, and, principally, near refineries, fertilizers plants, glass production, paper production, food/beverage sector, waste treatment plants, pharmaceutical industry and ceramic. Insofar as substances were concerned, statistically significant associations were observed for installations releasing metals and polycyclic aromatic chemicals. These results support that residing near industries could be a risk factor for ovarian cancer mortality.

1. Introduction

In 2012, ovarian cancer was the seventh leading tumor, in terms of new cases and deaths, in women worldwide, and the highest mortality rates were registered in the more developed regions, as Europe and Northern America (IARC, 2015). In Spain, there were 2050 ovarian cancer deaths in 2012 accounting to 5% of all cancer-related deaths in women (Carlos III Institute of Health (2015)). According to EUROCARE-5 (EUROpean CAncer REgistry based study on survival and care of cancer patients) project, relative survival in Spain at five years of diagnosis is 36.8%, figure similar to the European average (De Angelis et al., 2014; Istituto Superiore di Sanità, 2015).

Insofar as the etiology of this cancer is concerned, well-established risk factors are age, family history of ovarian cancer, and infertility, whereas increasing parity, oral contraceptive use, hysterectomy or tubal ligation decrease risk (Hankinson and Danforth, 2006; Lukanova and Kaaks, 2005). Other known environmental exposures include ionizing radiation and asbestos (Hankinson and Danforth, 2006). Lastly, limited evidence exists linking ovarian cancer with pesticides, primarily from women reporting personal use of the herbicide atrazine (Clapp et al., 2005; Dich et al., 1997).

Despite ovarian cancer is primarily a disease of the industrialized world (Mattison and Thorgeirsson, 1978) few factors associated with the industrial processes that contribute to its etiology have been identified (Schwartz and Sahmoun, 2014). Some occupational studies have found associations between women working in graphics and printing industries and increased risks of ovarian cancer (Shen et al., 1998). However, there are no epidemiologic studies that have analyzed the risk of ovarian cancer in populations

Abbreviations: EDCs, Endocrine disrupting chemicals; IPPC, Integrated Pollution Prevention and Control; E-PRTR, European Pollutant Release and Transfer Register; NSI, National Statistics Institute; RRs, Relative risks; IARC, International Agency for Research on Cancer; WHO, World Health Organization; UNEP, United Nations Environment Programme; PACs, Polycyclic aromatic chemicals; Non-HPCs, Non-halogenated phenolic chemicals; POPs, Persistent organic pollutants; 95% CrIs/CIs, 95% credible/confidence intervals; BYM, Besag, York and Mollié; SMRs, Standardized Mortality Ratios; INLAs, Integrated nested Laplace approximations; DIC, Deviance information criterion; PM_{10}, Particulate matter; PAHs, Polycyclic aromatic hydrocarbons.

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near industrial plants. Many types of industries release known or suspected carcinogens (Garcia-Perez et al., 2007; Samet and Cohen, 2006), as well as endocrine disrupting chemicals (EDCs), substances that alter functions of the endocrine system and are related with the increase in incidence of ovarian cancer. Accordingly, it would seem necessary to assess the relationship between facilities that release these types of toxic emissions and the frequency of ovarian cancer in their environs.

In this context, the aims of this study were to: (1) assess possible excess mortality due to ovarian cancer among the Spanish women residing in the environs of industrial installations included in the Integrated Pollution Prevention and Control (IPPC) Register and the European Pollutant Release and Transfer Register (E-PRTR); and, (2) analyze this risk according to the different categories of: a) industrial groups, b) installations releasing carcinogenic substances; and, c) installations releasing EDCs.

2. Materials and methods

We designed an ecologic study to evaluate the association between ovarian cancer mortality and proximity to industrial installations at a municipal level (8098 Spanish towns), over the period 1997–2006.

2.1. Mortality data

Observed municipal mortality data were drawn from the records of the National Statistics Institute (NSI) for the study period, and corresponded to deaths coded as malignant neoplasm of ovary and other uterine adnexa, codes 183 (International Classification of Diseases-9th/ICD-9) and C56, C57(ICD-10). Expected cases were calculated by taking the specific rates for Spain as a whole, broken down by age group (18 groups: 0–4, …, 80–84 years, and 85 years and over) and five-year period (1997–2001, 2002–2006), and multiplying these by the person-years for each town, broken down by the same strata. Person-years for each quinquennium were calculated by multiplying the respective populations by 5 (with data corresponding to 1999 and 2004 being taken as the estimator of the population at the midpoint of the study period).

2.2. Industrial pollution exposure data

Women exposure to industrial pollution was estimated by taking the distance from the centroid of town of residence to the industrial facility. 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. 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. Bearing in mind the minimum induction period for ovarian cancer, generally 10 years (UNSCEAR, 2006), we selected the 1970 installations which released emissions into air, water, land, or generated toxic waste in 2009, and came into operation prior to 1993 (10 years before the mid-year of the study period). Therefore, the facilities were still running to date 2009, i.e., at least, they have worked 17 years. The year of commencement of the respective industrial activities was provided by the industries themselves.

In order to document the location and characteristics of the facilities, Supplementary Data, Figs. S1 and S2 show the geographic distribution of the 1970 installations studied, by industrial group, and the distribution of the years of commencement of operations, by industrial group, respectively. The men year of commencement of operations for industries as a whole was 1964.

Each of the installations was classified into one of the categories of industrial groups listed in Supplementary Data, Table S1. 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.

2.3. Statistical analysis

Four types of analysis were performed to assess possible excess ovarian cancer mortality in towns lying near ("near") versus those lying far ("far") from pollutant industries, known as a "near vs. far" analysis. In all cases, several distances of 2, 3, 4 and 5 km were taken as the area of proximity ("exposure") to industrial installations:

1) in a first phase, we conducted a "near vs. far" analysis to estimate the relative risks (RRs) of towns situated at each one of the above-defined distances from industries as a whole (all sectors). The variable, "exposure", was coded as: a) exposed or proximity area ("near"): towns at $\leq$2, 3, 4 and 5 km from any facility; and, b) unexposed area ("far"): towns having no (IPPC+E-PRTR)-registered industry within each one of the above-defined distances of their municipal centroid (reference group);
2) in a second analysis, we analyzed the risk according to the different categories of industrial groups defined in Supplementary Data, Table S1. To this end, we created a variable of "exposure" for each industrial group in which the exposed area was stratified into the following levels: a) exposed or proximity area ("near"): towns at $\leq$2, 3, 4 and 5 km from any installation belonging to the industrial group in question; b) intermediate area: towns lying at the above-defined distances from any industrial installation other than the group analyzed; and, c) unexposed area ("far"): towns having no (IPPC+E-PRTR)-registered industry within each one of the above-defined distances of their municipal centroid (reference group);
3) in the third analysis, we assessed the relationship between ovarian mortality cancer and municipal proximity to industries releasing substances classified by the International Agency for Research on Cancer (IARC) as carcinogenic (Group 1), probably carcinogenic (Group 2A) and possibly carcinogenic (Group 2B) to humans. To this purpose, we created a variable of "exposure" for each carcinogenic group in which the exposed area was stratified into the following levels: a) exposed or proximity area ("near"): towns at $\leq$2, 3, 4 and 5 km from any installation releasing pollutants including into the carcinogenic group in question; b) intermediate area: towns lying at the above-defined distances from any industrial installation other than the carcinogenic group analyzed; and, c) unexposed area ("far"): towns having no (IPPC+E-PRTR)-registered industry within each one of the above-defined distances of their municipal centroid (reference group); and,
4) lastly, we assessed the relationship between ovarian mortality cancer and municipal proximity to industries releasing EDCs classified into one of the following 8 categories defined by the World Health Organization (WHO) and the United Nations Environment Programme (UNEP) (WHO/UNEP, 2015): a)