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Potential thyroid carcinogens in atmospheric emissions from industrial facilities in Manizales, a midsize Andean city in Colombia

N.E. Arias-Ortiz [a, b, *], P. Ruiz-Rudolph [c]

[a] Programa de Doctorado en Salud Pública, Escuela de Post-Grado, Facultad de Medicina, Universidad de Chile, Independencia 939, Santiago, Chile
[b] Departamento de Salud Pública, Facultad de Ciencias para la Salud, Universidad de Caldas, Carrera 25 N° 48-56, Manizales, Colombia
[c] Programa de Salud Ambiental, Instituto de Salud Poblacional, Facultad de Medicina, Universidad de Chile, Independencia 939, Santiago, Chile

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A B S T R A C T

Background: Manizales is a city in Colombia that presents high rates of thyroid cancer. It has a medium industrial development and there are concerns of the impact of their emissions on health, particularly on thyroid cancer. In this paper we characterize the geographical pattern of industrial atmospheric emissions of suspected thyroid carcinogens.
Methods: We systematized data of industries in two groups. First, those with reports of atmospheric emissions of suspected thyroid carcinogens (reporting facilities – RFs), and then, industries not required to report or facilities with no-available emissions data but belonging to the same SIC-codes than RFs (nonreporting facilities – non-RFs). For non-RFs, annual average atmospheric emissions were estimated using a per-employee algorithm. The spatial pattern of sources emitting carcinogens was represented by plotting facilities by size and amounts of specific pollutants released.
Results: We found 11 RFs and 25 non-RFs in urban Manizales. RFs belong to the metalworking industries, plastics & rubber, manufacture of electrical and electronic devices, waste incineration, cremation, and meat production. Most of them were concentrated in the southeast of the city. Several RFs reported atmospheric emissions of carcinogens exceeding maximum permitted emission limits set in Colombian law. Most of non-RFs were micro and small industries, and were clustered in the southeast of the city and along the main road axis.
Conclusions: We found clusters of pollution sources near densely populated areas. Thyroid cancer incidence might be greater in areas closer to industries than in furthest areas. We will submit a paper that studies this hypothesis soon.

1. Introduction

Thyroid cancer (TC) is the most frequent endocrine cancer but few risk factors have been found, except of exposure to ionizing radiation (Meinhold et al., 2010). TC has presented large increases in incidence recently, specially for differentiated thyroid cancer (DTC) (Benvenga et al., 2015; IARC et al., 2014; Pellegriti et al., 2013).Those raises in DTC has been attributed to improvement in diagnosis technologies and to better health care access, but also occupational and non-occupational studies have pointed out that exogenous factors other than radiation could be contributing to the increased incidence of DTC (Benvenga et al., 2015).

According to United Nations Environment Programme (WHO-UNEP, 2013), close to 800 chemicals used or released by industries are known or suspected to be capable of interfering with

Abbreviations: RFs, reporting facilities or industries required to report atmospheric pollutants releases according to Colombian law; Non-RFs, non-reporting facilities or industries not required to report atmospheric emissions, according to Colombian law; EPA, United States Environmental Protection Agency; TRI, United States Toxic Release Inventory; E-PRTR, European Pollutant Release and Transfer Registry; IARC, International Agency for Research on Cancer; DANE, National Department of Statistics, by its acronym in Spanish; GDP, Gross Domestic Product; PCDDs/DFs, polychlorinated dibenzo-dioxins and dibenzo-furans; PAHs, polycyclic aromatic hydrocarbons; SIC, standard industrial classification; GIS, geographical information system; LCI, Living-Conditions Index, or indicator of socioeconomic position at census tract level; NMVOCs, non-methane volatile organic compounds; MPL, maximum permitted limits for atmospheric emissions.

* Corresponding author. Public Health Department, University of Caldas, Carrera 25 N° 48-56, Manizales, Colombia.
E-mail addresses: nelson.arias@ucaldas.edu.co (N.E. Arias-Ortiz), pabloruiz@med.uchile.cl (P. Ruiz-Rudolph).

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hormone receptors, hormone synthesis or hormone conversión (endocrine disrupters chemicals – EDCs). EDCs have been associated with several human health effects including adrenal, bone, immunological, metabolic, neurodevelopmental, reproductive, and thyroid disorders. Also, exposure to EDCs has been associated with hormonal-related cancers, including breast, ovary, endometrium, prostate, testis and thyroid (WHO-UNEP, 2013). Experts have stated that the increase in incidence of endocrine-related cancers cannot be explained by genetic factors; exposures to pollutants are involved, but very few of these factors have been pinpointed (WHO-UNEP, 2013).

Autoimmune thyroid diseases (AITD) –Hashimoto's thyroiditis and chronic lymphocytic thyroiditis– have been proposed as predisposing factor for TC (Feldt-Rasmussen and Rasmussen, 2010). In turn, EDCs have been associated with thyroid dysfunction and AITD, including smoke and second-hand smoke, dioxins and furans, polyhalogenated biphenyls, chlorinated solvents, plasticizers, phenols, and some heavy metals such as cadmium, lead and mercury. (Benvenga et al., 2015; Leux and Guénel, 2010; Vigneri et al., 2015; WHO-UNEP, 2013). De Coster and van Larebeke (2012) described three mechanisms by which EDCs can alter the functioning of the hypothalamus-hypophysis-thyroid axis: i) directly affecting thyroid gland cells decreasing the synthesis of thyroid hormones; ii) accelerating biliary excretion of thyroxine by induction of glucoronyl-transferase activity; and iii) interfering in the binding of T4 to its specific cellular receptor, leading to inactivation of deiodinase and biliary excretion of the hormone.

Non-occupational exposure to nitrates by drinking water has also been proposed as a risk factor capable of triggering AITD and hypothyroidism, but the evidence regard nitrate exposure and thyroid cancer is inconclusive (Benvenga et al., 2015). On the other hand, exposure to EDCs in the general population surrounding waste sites have been studied (Leux and Guénel, 2010), but thyroid disruption has been poorly addressed by chemical tests currently listed in the OECD conceptual framework (WHO-UNEP, 2013).

Many chemicals are released into the environment from industrial facilities, with many of them being unknown or whose effects on human health have not yet been tested (United States Government Accountability Office, 2005). Populations might be exposed to these substances both occupationally, *i.e.* inside industrial facilities, and in the general environment, *i.e.* outside the facilities. These aspects, coupled with the large variety of substances handled in a single facility, make the exposure assessment –both occupational and environmental– very difficult and highly uncertain. Although it is widely accepted that exposures to high concentrations of carcinogens occur more frequently in the work environment, they are also found in the general environment (Boyle and Levin, 2008). Usually, occupational studies at high exposure levels are considered as first evidence of potential risks at lower level population exposures (Cogliano et al., 2011).

In addition, several pollutants released or used by industries have been declared by IARC as carcinogenic agents for some neoplasms. However, carcinogens may be non-specific for one cancer, but the same agent or the same exposure circumstance may be associated with one or more neoplasms (IARC, 2016). For example, exposure to arsenic is associated with an increased risk of lung, bladder and skin cancer (Steinmaus et al., 2013), or exposure to dioxins is associated with all cancer sites combined (IARC, 2016). This lack of specificity is a major challenge for epidemiological studies, and many of them cannot easily pinpoint specific chemicals (WHO-UNEP, 2013).

On the other hand, environmental regulations of industrial sources might not be protective enough for population (Ruiz-Rudolph et al., 2016) as i) facilities might emit several pollutants simultaneously, with potential synergistic effects, ii) pollutants usually present linear dose-response risks and, hence, no safe limits can stated, iii) many pollutants might be unknown or untested, iv) 'pollution standards' are built under cost-benefit frameworks, and v) many industries, especially small and micro facilities in developing countries, may fail in monitoring and/or meeting environmental standards because they do not have the financial resources to invest in cleaner production, which can lead to higher cumulative effects than larger industries (Dolinoy and Miranda, 2004).

In Colombia, since the 80s, authorities regulate stationary emission of air pollutants through emission permits (Ministerio de Ambiente Vivienda y Desarrollo Territorial (Colombia), 2010, 2008, 2006). These control activities are managed by decentralized public corporations within well-defined territorial jurisdictions (*Corporaciones Autónomas Regionales*), which collect local information on industrial pollution. In 2008 a new regulation set down the maximum permissible limits for criteria air pollutants (particulate matter, SOx, NOx, CO) emissions from stationary sources, and incorporated compulsory measurement of specific pollutants like dioxins and furans, heavy metals, hydrocarbons, and volatile organic compounds for specific industrial processes (Ministerio de Ambiente Vivienda y Desarrollo Territorial (Colombia), 2008). Some of the pollutants listed above have been pointed out like potential thyroid carcinogens, although evidence is still weak and need to be further studied (Aschebrook-Kilfoy et al., 2014; Leux and Guénel, 2010; WHO-UNEP, 2013).

Manizales is a middle-size city in the Andean region of Colombia and it has a population-based cancer registry certified by IARC that have reported thyroid cancer incidence rates higher than incidence in other cities in Colombia and South America. For the 2003–2007 period the age-standardized incidence rates (ASIR) were 12.4 per 100,000 person-year in women and 3.7 in men (López-Guarnizo et al., 2012), being the third most frequent cancer site in women, while in other Colombian cities -such as Bucaramanga, Cali and Pasto-the ASIRs were 9.6, 11.3, y 8.4 for women and 2.6, 2.3 y 2.4 for men, respectively (Bravo et al., 2012; Uribe et al., 2012; Yépez et al., 2012). In South America, only São Paulo, Aracajú and Goiânia (Brazil) and Quito (Ecuador) show higher rates for thyroid cancer, while worldwide Manizales is in the top 50 of cities with population-based cancer registries (IARC et al., 2014).

Given this context, we attempt to study the impact of industrial sources on thyroid cancer in Colombia using a small-areas approach. We present Manizales as a case study as i) the city has hosted pollution-generating industries for decades, ii) it has topographical and climatic characteristics that facilitate the accumulation of air pollutants, with many densely populated residential areas nearby, iii) data on atmospheric emissions of pollutants are available and iv) city presents a population-based cancer registry certified by the International Agency for Research on Cancer (IARC), showing some of the highest incidence in Latin America.

In this paper, we describe the characteristics and spatial distribution of industrial sources for potential thyroid carcinogens in Manizales, and explore associations with socioeconomic conditions. In short, we will submit a second paper in which we analyze the incidence of thyroid cancer in small areas and the spatial association with sources that emit atmospheric pollutants suspected of inducing thyroid carcinogenesis.

2. Methods

2.1. Study site and design

Colombia is an upper-middle income country with a Gross National Income of USD 7910 per capita (World Bank, 2015), and industry participation of about 18%(Santa María et al., 2013). It has a population of 48 million inhabitants, divided into 32 provinces