International Journal of Hygiene and Environmental Health 216 (2013) 461–466

Contents lists available at SciVerse ScienceDirect

International Journal of Hygiene and Environmental Health

journal homepage: www.elsevier.com/locate/ijheh

Pesticide use and non-Hodgkin's lymphoma mortality in Brazil

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ARTICLE INFO

Article history:
Received 18 May 2012
Received in revised form 11 March 2013
Accepted 15 March 2013

Keywords:
Pesticides
Non-Hodgkin's lymphoma
Mortality
Epidemiology

ABSTRACT

Introduction: Brazil is one of the major pesticide consumers in the world. The continuous exposure to these substances may be etiologically associated with the development of Non-Hodgkin's Lymphoma (NHL).
Objective: Estimate the correlation between the per capita sales of pesticides in 1985 (exposure) and NHL mortality rates between 1996 and 2005 (outcome), by Brazilian micro-regions.
Method: In this ecological descriptive study, the per capita consumption of pesticides in 1985 was used as a proxy of the population exposure to these chemicals in Brazil. All deaths by NHL occurred in the 446 non-urban micro-regions, between 1996 and 2005, among individuals with ages between 20 and 69, of both sexes, were retrieved from the Brazilian Mortality Information System. Micro-regions were then categorized into low, medium, high and very high pesticide consumption, according to the quartiles of per capita consumption of pesticides. NHL mortality rates and rate ratios for each quartile were obtained using the lowest quartile as reference. In addition, the Spearman's correlation coefficient between pesticide consumption and NHL mortality rates was estimated.
Results: A moderate correlation between per capita pesticides consumption and standardized mortality rate for NHL was observed ($r = 0.597$). In addition, using the lowest quartile of pesticide consumption as a reference, the higher the quartile of pesticide consumption, the higher was NHL mortality risk: men – (second quartile – MRR = 1.69, CI 95% 1.68–1.84; third quartile – MRR = 2.41, CI 95% 2.27–2.57; fourth quartile – MRR = 2.92, CI 95% 2.74–3.11) and females (second quartile – MRR = 1.87, CI 95% 1.69–2.06; third quartile – MRR = 2.28, IC 95% 2.10–2.47; fourth quartile – MRR = 3.20; CI 95% 2.98–3.43).
Conclusion: Our results suggest that pesticide exposure may play a role in the etiology of NHL.

Introduction

Unlike most neoplasms, incidence and mortality of non-Hodgkin's lymphoma (NHL), which is a malignancy that arises from lymphoid tissue, have been increasing since the 1970s as shown by (Alexander et al., 2007; Müller et al., 2005). Although there is no consensus, some studies suggest an increased risk of NHL among agricultural workers as demonstrated (Fleming et al., 2003; Mills et al., 2005; Waddell et al., 2001). The assumption underlying this phenomenon is the exposure to several potentially carcinogenic solvents, dust, animal viruses and various classes of pesticides, experienced by this group of workers as shown by Blair and Zahm (1995). In fact, a recent meta-analysis conducted by Merhi et al. (2003) observed a significant positive association between pesticide exposure and hematopoietic malignancies, including NHL.

The use of pesticides has dramatically increased worldwide, particularly in the second half of the twentieth century as shown by Yudelman et al. (1998). Although diffusion of this agricultural technology has primarily took place in developed countries, its adverse impacts on environmental and human health has been more intensely observed in developing countries as demonstrated by Koh and Jeyaratnam (1996). Due to their possible role as tumor promoters, continuous exposure to pesticides may be etiologically linked to the development of specific types of cancer such as NHL as shown by Collins et al. (2009), Eriksson et al. (2008), and McDuffie et al. (2001).

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http://dx.doi.org/10.1016/j.ijheh.2013.03.007

Currently, Brazil is the world's top consumer of pesticides in the world (Brasil, 2008). Nevertheless, studies that evaluate the impacts of such use on environment and health in Brazil, especially regarding carcinogenic effects, have just recently been initiated by (Koifman et al., 2002; Meyer et al., 2003).

We previously published a study that investigated the correlation between per capita consumption of pesticides and cancer mortality rates in 11 Brazilian States and demonstrated a higher risk of death by some types of cancers, including NHL, in states that displayed higher pesticide consumption as shown by Chrisman et al. (2009). In the present study, this correlation was investigated once more, but specifically for NHL, expanded to cover the entire country, and referred to a smaller geographic unit named micro regions. In addition, the correlation between pesticide use and NHL mortality was estimated according to sex, age, and urban/non-urban status.

Methods

Study design

In this ecological descriptive study, the per capita consumption of pesticides in 1985, used here as a surrogate measure of the population exposure to these chemicals, was correlated with NHL mortality rates in Brazil during 1995–2005.

Geographic micro regions

Micro regions are defined by the Brazilian Institute of Geography and Statistics (1990) as sets of adjacent municipalities (clusters) that display similar economic and social characteristics. Accordingly, in 1985, 10–20 years prior to mortality data used in the present study, there were 106 urban and 446 non-urban micro regions in Brazil.

Pesticide sales data

Data on expenditures with pesticides were collected from each farm during Brazilian Agricultural Census, performed in 1985, and were considered as a proxy exposure variable to these chemicals. Expenditure with pesticides was then pooled at the level of a city, and again at the micro region level. The total pesticide expenditures was then divided by the number of inhabitants in each micro region in the same year to obtain the per capita sales of pesticides.

NHL mortality data

Deaths attributed to NHL were obtained from the Brazilian National Mortality System, which is implemented by the Ministry of Health and classifies death causes according to the International Classification of Diseases (ICD) as (WHO, 2007). Thus, information on deaths by NHL (ICD-10: C82–C85) among individuals from both genders, 20–69 years old, was available for each Brazilian micro region from 1996 to 2005. The age standardized mortality rate was calculated through the direct method, having the 1966 world population as reference.

Data analysis

The correlation between per capita sales of pesticides in 1985 and the NHL mortality rates during the 1996 to 2005 period in all 552 Brazilian micro regions, was calculated by means of Spearman's correlation coefficient. Correlation coefficients were calculated according to gender, age strata (20–29, 30–39, 40–49, 50–59, and 60–69 years old), and urban/non-urban micro regions. Non-urban micro regions were further categorized into low, medium, high, and very high pesticide use, according to the quartiles of *per capita* consumption of pesticides. Standardized mortality rates for NHL were then calculated for each quartile. Rate ratios, along with their respective confidence intervals, were obtained using the lowest quartile (first quartile) as reference. Rate ratios were also calculated according to gender and age strata.

In order to improve the analysis and the interpretation of the results, a Poisson negative binomial regression with random effects model was used, employing the pesticide consumption (continuous) and the place of residence (urban/rural) as explanatory variables. Since the micro-regions belong hierarchically to the 26 Brazilian Federative States, these States were employed as a cluster variable on a multilevel model, assuming that the clusters (States) have unmeasured contextual confounders that may explain some of the residual variance of the outcome (Diez-Roux, 2000). One model was estimated for the total population, another for the male population and a third model for the female population.

Results

The population mean by micro region in Brazil was 306,937, ranging from 16,528 to 12,800,000 inhabitants. Considering the rural and urban micro region, the population mean was 168.544 and 889.231 by micro region, respectively.

The *per capita* consumption of pesticides was 3.5 times higher in non-urban micro regions, when compared to urban ones. In

Table 1
Description of mortality from NHL in 1996–2005 and per capita pesticide consumption in 1985 by Brazilian micro regions.

	Urban micro regions (106)	Non-urban micro regions (446)	All micro regions (552)
Population	94,258,522	75,170,744	169,429,266
Pesticide sales ($), 1985	1,198,029,399	3,339,564,941	4,537,594,340
Per capita sales of pesticides (mean)	12.71	44.42	26.78
LNH mortality (1996–2005)			
Men	28.14	15.01	17.53
20–29 years old	7.10	4.82	5.26
30–39 years old	9.71	5.64	6.43
40–49 years old	21.53	11.15	13.15
50–59 years old	43.86	26.19	29.58
60–69 years old	97.45	46.93	56.64
Women	16.33	9.26	10.62
20–29 years old	3.70	2.74	2.93
30–39 years old	6.90	3.94	4.51
40–49 years old	11.68	7.01	7.90
50–59 years old	24.91	16.33	17.98
60–69 years old	58.26	28.08	33.88