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Positive correlation between pesticide sales and central nervous system and cardiovascular congenital abnormalities in Brazil

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ABSTRACT

Background: This study investigated the association between pesticide exposure in Brazil (2005–2013) with rates of central nervous system (CNS) and cardiovascular system (CVS) congenital abnormalities in 2014. *Method*: An exposure variable was established from data on production and sales of pesticides (kg) per crop area (ha) for 2012 and 2013 years. The Brazilian states were divided into three categories: high, medium, and low pesticide use and rate ratios were estimated for each group of states (CI: 95 %). *Results*: In 2013 and 2014, the high use group presented a 100 and a 75 % increase, and the medium group a 65 and 23 % increase, respectively, in the risk of CNS and CVS congenital abnormalities at birth, compared to the low use group. *Conclusion*: These findings suggest that pesticide exposure could be associated with increased risk of congenital malformations at birth in Brazil.

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Pesticides; congenital malformations; children; environmental health

Introduction

According to the World Health Organization congenital malformations were the fifth leading cause of death in the neonatal period, worldwide in 2013 (WHO 2015). In the region of Americas, 13 % of deaths in children between 0 and 14 years old in 2002 were due to congenital abnormalities (PAHO 2011).

Congenital malformations are defined as 'structural or functional anomalies (e.g. metabolic disorders) that arise during intrauterine life and can be identified prenatally, at birth or later in life' (WHO 2015). Approximately 30 % of congenital malformations have a known genetic etiology and 10 % are attributable to environmental exposures. However, around 60 % cannot be linked to a specific cause. Risk factors for congenital malformations include adverse socioeconomic and demographic conditions, poor maternal nutrition during pregnancy, infections, and environmental exposures. Maternal exposure to certain pesticides and other toxic chemicals, as mercury, in addition to alcohol, tobacco, radiation during pregnancy, some medications and psychoactive drugs, can increase the risk of occurrence of congenital malformations (WHO 2015).

Pesticides are used for crop production and in urban areas for the control of vector-borne diseases and are potentially toxic to other organisms, including humans (WHO 2016). Pesticides are related to toxic effects on reproductive health associated with their endocrine-disrupting actions on the hormonal regulatory systems that control fetal development in humans (Woodruff et al. 2008; Roberts and

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Karr 2012). The most compelling evidence for associations between pesticide exposure and adverse birth outcomes (premature birth, low birth weight, reduced head circumference, and birth defects) comes from studies of prenatal maternal exposures to organophosphate and organochlorine pesticides (Karr and Rauh 2014).

In Brazil, a sharp reduction of infant mortality from infectious causes has occurred in recent decades, parallel with an improvement in the quality and capacity of reporting of data to the Mortality Information System (SIM) of the Unified National Health System. The proportional mortality from congenital malformations in Brazil increased from a triennial average of 7.1 % in 1983–1985 to 10 % in 1993–1995, and to 14.4 % in 2003–2005 (RIPSA 2009). In 2014, deaths from congenital malformation represented the second leading cause of infant mortality (2.8 per 1000 live births) and the leading cause of postneonatal mortality (28 days–1 year) (DATASUS 2016). In the period from 2007 to 2013, the pesticide sales in Brazil increased steadily, from 643 million to 1.2 billion kg, while the total crop area treated with pesticides rose from 62.33 million to 74.52 million ha, representing a growth of 90.49 % in pesticide sales and of 19.5 % in crop area treated (Brazil 2016). Besides this, there is a current trend of increase of use of pesticides in urban areas due to mosquito control efforts to combat the outbreaks of vector-borne diseases, like Zika virus infection, in Brazil.

This study had the objective of investigating the possible association between pesticide exposure in Brazil, during the years 2005–2013, and the occurrence of Central Nervous System (CNS) and Cardiovascular System (CVS) congenital abnormalities in the year of 2014.

Materials and methods

An exposure variable was established from data on production and sales of pesticides (kg) per crop area (ha) for 2012 and 2013 years. These data were obtained from the National Report of Health Surveillance of Pesticide Exposure Population published by the Health Surveillance Department of the Ministry of Health of Brazil (Brazil 2016). These data comprised all kinds of pesticides produced and traded, into each Brazilian state, which are reported by the industries and dealers to the Ministry of Agriculture.

The outcome variables examined were rate of congenital abnormalities at birth (%) and the infant mortality (less 1-year-old) rate from congenital abnormalities (per 1000 live births) of the CVS and of the CNS. The information on all live births and all live births with congenital abnormality were collected from the National Information System on Live Births (SINASC) and on all deaths and all deaths from congenital abnormalities among infants less 1 year of age were acquired from the SIM from the Health Information Department of the Unified National Health System (DATASUS 2016), Ministry of Health of Brazil, by state, for 2013 and 2014 years. Information was collected on all births and on all deaths from congenital abnormalities of the CVS or of the CNS, items Q20-Q28 and Q00-Q07 in Chapter XVII of International Classification of Diseases (ICD-10), respectively, in the years of 2013 and 2014.To examine the possible effect of maternal age on the occurrence of outcomes, the rates, by year and state, were adjusted for maternal age between 20 and 40 years old, considering the standard of age group distribution of mothers registered by SINASC.

To investigate possible associations between congenital malformations and pesticide use by state, the Brazilian states were organized into three groups, according to the kg pesticide per crop area (ha) in the 2012 and 2013 years: High Use: above 20.00 kg/ha; Medium Use: 10.00–19.99 kg/ha; and Low Use: 0.01–9.99 kg/ha. Rate ratios (RR) to infant death rate and congenital abnormalities at birth were estimated for each group, taking the low use group as reference. The 95 % confidence intervals (CI) were calculated using χ^2 test.

Results

The Table 1 presents the total number of births with CNS and CVS malformations and deaths caused by CNS and CVS malformations, for the years of 2013 and 2014. The rates of CNS and CVS congenital malformation at birth were 0.18 and 0.73 %, respectively, in these years. The infant mortality rates

Table 1. Congenital malformations indicators to the 2013 and 2014 years. Brazil, pesticide use groups.

Period	Brazil	Low use group	Medium use group	High use group
Number of states and FD[a]				
2012	27	13	8	6
2013	27	12	13	2
Total Amount of Pesticide commerce (kg/ha)				
2012	453.99	72.78	90.87	275.98
2013	426.46	68.54	186.75	171.17
% CVS and CNS Birth Defects				
2013	0.18	0.10	0.17	0.22
2014	0.73	0.55	0.68	0.96
CVS and CNS Mortality Rate (per 1000)				
2013	2.27	2.33	2.53	2.10
2014	2.36	2.52	2.26	2.37

[a]FD: Federal District.

Table 2. Risk ratios to CVS and CNS congenital abnormalities in the years of 2013 and 2014 according to the pesticide use groups (kg/ha).

	CVS and CNS Birth Defects			Infant death rate from CVS and CNS Birth Defects		
Period	Cases	Birth Lives	RR(95 %IC)	Deaths from CVS/CNS Birth Defects	Birth Lives	RR (95 %IC)
2013: pesticide use 2012						
Low group (0.95–9.14)	609	595,758	1	1387	595,758	1
Medium group (10.09–18.37)	1001	594,542	1.65* (1.489, 1.821)	1505	594,542	1.09* (1.011, 1.169)
High group (20.57–136.35)	2421	1,084,040	2.19* (1.999, 2.388)	2279	1,084,040	0.90 (0.844, 0.965)
2014: pesticide use 2013						
Low group (1.77–9.26)	3327	605,346	1	1526	605,346	1
Medium group (11.91–19.75)	7011	1,034,273	1.23* (1.184, 1.285)	591	1,034,273	0.898 (0.841, 0.957)
High group (35.72–135.45)	6737	701,309	1.75* (1.677, 1.822)	1152	701,309	0.941 (0.878, 1.009)

*$p < 0.01$.

due to CNS and CVS malformations were 2.27 and 2.36 per 1000 live births respectively, in 2013 and 2014 years.

The analysis of rate ratios of the CNS and CVS congenital abnormalities outcomes according to the three pesticide use groups (kg/ha) is shown in Table 2. In 2013, the high use group presented a rate ratio of 2.19 times and the medium use group of 1.65 times the risk to CNS and CVS congenital abnormalities at birth, compared to the low use group. Concerning the infant mortality rate due to CNS and CVS congenital abnormalities, the medium group presented 1.09 times taking as reference the low group. The RR to the high group was lower than unit though statistically significant. In 2014, the high group presented a rate ratio of 1.75 times and the medium group of 1.23 times the risk to CNS and CVS congenital abnormalities at birth, compared to the low use group. The mortality rate ratio (RR) from CNS and CVS defects were, in general, lower than unity though statistically significant, taking as reference the low group.

In general, there was a trend of decrease of 6 % in the amount of pesticide traded in Brazil (kg/ha) from 2012 to 2013 year. In fact, there was a decrease in the number of states with amount of pesticide traded above 20 kg/ha (high group use) and an increase in the number of states encompassed in the medium use group (10–19.99 kg/ha). This result is consistent with the Brazil Health Ministry report (Brazil 2016) referring a general tendency of decrease of pesticide commerce related to the crop area (kg/ha) in most states of Brazil.

Discussion

We used data on pesticide production and sales per crop area (kg/ha) as a proxy of pesticide exposure of Brazilian population. This can be a potential limitation of this study because does not constitute a specific measure of individual exposure. Nevertheless, the amounts of pesticide traded have been applied as an exposure indicator by many researchers in Brazil, and worldwide, that have published studies on this field (de Siqueira et al. 2010; Cremonese et al. 2014; McKinnish et al. 2014; Oliveira et al. 2014; Markel et al. 2015).

Cremonese et al. (2014) studied the association between per capita pesticide consumption in the years 1985 and 1996 and infant mortality rates from CNS and CVS congenital malformations in the 1986–1990 and 1997–2001 periods, respectively, in the South and Southeast regions of Brazil. They divided the study area in microregions and classified them as rural and urban. The authors referred a significant trend of increase in infant mortality rate ratio for the two types of malformations, in rural micro regions, but not, in the urban regions. The authors suggested that 'pesticide exposure may play an important role in the geographical distribution of mortality from congenital malformations only in rural areas' there being other intervenient factors in urban areas. A similar analysis was done by Oliveira et al. (2014). The authors selected eight municipalities with the higher amount of pesticide traded per crop area in the study region (Mato Grosso state) and observed that maternal exposure to the pesticide was significantly associated with higher incidence of congenital malformations.

This study did not classify and analyze the data according to urban or rural areas of pesticide exposure, neither selected small study areas with the intensive use of pesticides. It can represent a potential weakness since that most of Brazilian population live in urban areas and this condition can be masking the results. de Siqueira et al. (2010) also developed an ecological analysis of pesticide exposure including the 26 Brazilian states. The authors observed that pesticide exposure was weak but, significantly correlated with infant death rate by the congenital abnormality ($r = 0.49$; $p = 0.039$) and medium but, not significantly correlated with congenital abnormality at birth ($r = 0.65$; $p = 0.664$).

In 2013, this study found a 100 % increase in the risk of CVS and CNS congenital malformations in the high use group, comprising eight states, with an amount of pesticide traded above of 20 kg/ha. In 2013, only two states were encompassed in the high use group. There was an increase in the number of states in the medium group (from 10 to 19.99 kg/ha). In despite this, this study still observed an increase in the risk of CNS and CVS congenital abnormalities at birth to the high group (75 %) and medium group (23 %) in 2014 year. These results could suggest that the amount of pesticide traded is an important factor in determining the exposure and occurrence of adverse effect. Both in the studies above cited as, in this study, the correlation and the rate ratios seem to reflect the increase in exposure due to the higher amount of pesticide traded.

In Brazil, many projects have examined the contamination of the environment and resultant exposure of the population to these chemicals. The Program of Assessment of Pesticides Residues in Food (*Programa de analise de Residuos de Agrotoxicos em Alimentos* – PARA) has been developed by Agency of Sanitary Surveillance (ANVISA) of Brazil, since 2001. This program measured the concentrations and sort of active ingredient residues in crops. The analysis of 1397 crop samples, in the year of 2012, detected active ingredient residues above the maximum limits (MLR – maximum limit of residue) or non-legalized active ingredients in 25 % these (PARA 2014).

The Health Surveillance Department of the Ministry of Health of Brazil has been undertaking the National Program of monitoring of pesticides residue in drinking water, in all municipalities of the country, since the last decade. In the year of 2013, samples of drinking water were collected in 1598 municipalities. The analysis identified at least one sample above the maximum limits of pesticides residues in the drinking water in 337 (21 %) municipalities (Brazil 2016). In a systematic review of Brazilian children's exposure to environmental contaminants, Froes Asmus et al. (2016) reported seven studies that detected organochlorine pesticides in breast milk, children's blood, maternal blood, and umbilical cord blood.

Although a better recognition and reporting of cases of congenital malformation in Brazil has been occurring, the underreporting of data can constitute a limitation of this study. Studies done in Brazil analyzing the quality of data obtained from birth certificates, based on SINASC (Live Births National Information System) showed an under notification of congenital malformation at birth in many regions of country (Costa et al. 2006; Drumond et al. 2008; Guerra et al. 2008). Luquetti and Koifman (2009) examined the quality of notification of congenital malformations in the city of Campinas (São Paulo state, Southeast Brazil), based on the SINASC (Live Births National Information System) and observed underreporting of 46.8 % for all congenital defects and 36.4 % for major birth defects.

Additionally, in the present study, data were obtained from the national information system, which does not register individual data related with the factors such as education, cigarette smoking, alcohol and drug consumption, health history, and pregnancy illness. The lack of information on these potential risk factors is a limitation of this study since it could have produced biased risk estimates.

The mortality data are another potential source of bias in this study. The implementation of Unified National Health System (SUS) in the 90s, in Brazil, catalyzed enhancement of the SIM and led to creation of the National Information System on Live Births (SINASC) through DATASUS. Although there has been constant improvement of the reach and recording capacity of these systems, the register of births and deaths in Brazil still has failed, mainly in the regions far from the great metropolitan centers. This situation can be interfering with the records observed, since many live births with congenital abnormalities and infant deaths from congenital abnormalities may not be registered.

The CVS malformations are the most prevalent of all congenital malformations and the first trimester of pregnancy is the most susceptible period of exposure to occurrence of these sort of birth defects. Some specific CVS malformations as transposition of great arteries were related with exposure to herbicides and rodenticides (Gorini et al. 2014). The main pesticide used in Brazil is glyphosate (Brazil 2016), an herbicide whose teratogenic action still is controversial (Kimmel et al. 2013). However, glyphosate has been considered, at least, as a contributing factor to occurrence of congenital abnormalities in population living in and near farming regions in which this pesticide is applied (Myers et al. 2016).

These considerations indicate the necessity of the enhancement of control of pesticide use, associated with a strict assessment of these contaminants in the environment, including food, drinking water, air, and soil. This conduct is still more necessary and critical due to the growth of pesticides application into urban areas, to control the current outbreak of Zika virus infection, in Brazil. This action can potentially raise the pesticide exposure for the entire population, including pregnant women, far beyond the mosquito control efforts.

The potential impact of pesticides on human health has been a relevant topic of debate in the international scientific society. Considering that, in Brazil, the pesticide commerce has presented an exponential growth in the last 10 years, the establishment of health surveillance actions and the accomplishment of searches on population potentially exposed constitute a priority. Under these circumstances, this study believes to be contributing to the development of knowledge about the effects of pesticide exposure on the maternal-infant health, in Brazil.

Conclusion

Infant mortality has declined sharply in Brazil in recent decades reflecting improvement in living conditions, with declining of infant deaths from infectious diseases. As a consequence of this overall decline, deaths from congenital malformations have emerged as one of the main causes of infant mortality. Risk of death from congenital malformations is exacerbated by difficulties of access to prenatal and neonatal health care, in many regions of the country.

In the same time period, pesticide sales and population exposure to pesticides has increased hugely in Brazil, and many studies suggest an association between the expansion of pesticide trade and the growth of occurrence of congenital abnormalities, independently of the decline of infant deaths by infectious diseases.

In an ecological study like this, it is not possible to establish a cause–effect relationship between pesticide exposure and congenital malformations. Nevertheless, findings from the present study suggest that pesticide exposure could be related to increased incidence of major congenital malformations at birth. This correlation is especially clear in the states of Brazil with high pesticide commerce. This finding calls for urgent follow-up investigation.

Institution and ethics approval and informed consent

This is a study with ecological design in which the personal identification of study subjects is not possible.

Disclosure statement

The authors declare no conflicts of interest.

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