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Monitoring of organochlorine pesticides in blood of women with uterine cervix cancer☆

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ABSTRACT

In Yucatan, Mexico, chronic exposure of Mayan population to pesticides is expected as about 30 per cent are drinking polluted water. Residues of organochlorine pesticides (OCP) were monitored in 18 municipalities of Yucatan with high mortality rates due to uterine cervix cancer. 70 blood samples collected from Mayan women living in livestock, agricultural and metropolitan area were analyzed for OCP. Solid Phase Extraction was performed on C18 cartridges and analyzed by Gas Chromatography with Electron Capture Detector. The results showed that the highest OCP levels were detected in blood of women living in the livestock area. OCP detected were endosulfan I (7.35 μg/mL), aldrin (3.69 μg/mL), 4,4′ DDD (2.33 μg/mL), 1.39 and 1.46 μg/mL of δ-HCH. Women from the agricultural area had high concentrations of OCP in their blood, particularly dieldrin (1.19 μg/mL), and 1.26 μg/mL of 4,4′ DDE. In the metropolitan area, 0.080 μg/mL of γ-HCH and 0.064 μg/mL of heptachlore were detected. This monitoring study was also based on epidemiological data of uterine cervical cancer. It was found that environmental factors may have facilitated the infiltration of OCP to the aquifer used for potable water supply. These factors in addition to poverty can have impacts on public health. This first exploratory study suggests that monitoring of OCP in human is important for the establishment of health promotion programs. The integrative analysis of both, environmental and social factors would be helpful to characterize the bioaccumulation of pesticides in humans.

1. Introduction

Cancer is a complex disease that relates a sequence of gene and environment interactions, the environmental pollutants can increase the risk of cancer (Tabrez et al., 2014). Organochlorine pesticides (OCP) are environmental contaminants of major concern because their persistence, bioaccumulation, and adverse effects on humans and the environment (Forget, 1991; Carvalho, 2006; Jung-Ho and Yoon-Seok, 2011; Khwaja et al., 2013; Mrema et al., 2013; Sachin et al., 2013; Ruiz-Suárez et al., 2014; Velasco et al., 2014). Humans are exposed to many environmental carcinogens. The increasing prevalence of cancer is partly attributable to exposure to carcinogenic agents in the occupational work (Soffritti et al., 2008).

Gene-Environment-Interaction (GEI) refers to the combined influences of genetic and environmental factors on the health-disease process (Tabrez et al., 2014). The exposure to pollutants under environmental conditions have effects in the genetic polymorphism, promoting the disease initiation. GEI involves the different effects of environmental exposure and the different effects of a genotype in people with different histories of environmental exposure (Berwick, 2000), such interactions may be important determinants in the cancer development (Brennan, 2002). OCP exposure is associated with blood, prostate, pancreas,

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brain, liver and other cancer types related with the gene-environment-interactions (Zahm and Devesa, 1995; Tabrez et al., 2014).

In developing countries, OCP are still use although these countries are part of international conventions and treaties such as the Stockholm Convention, Rotterdam Convention, and the Prague Declaration (Stockholm, 2001; Prague, 2005; Rotterdam, 2013). The changing environmental scenery coupled with various anthropogenic activities, continue to result in the bioaccumulation of many substances, like pesticides (Irigaray et al., 2007; Ali et al., 2014). Exposure to OCP is a risk factor to female cancer because their potential of estrogenic activity (Rachón, 2015) and their immunosuppressive and development of tumor properties (Iscan et al., 2002).

The toxicological effects of environmental pollutants can play an important role on the etiology of several diseases in humans, such as mutagenicity and carcinogenicity (Tabrez and Ahmad, 2009; Waliszewski et al., 2013; Tabrez et al., 2014). The potential association between exposure to pesticides and endocrine activity has been discussed in the last decade (Seidler et al., 2008). OCP are endocrine disruptors chemicals (EDC) interfering with the synthesis, transport, storage, binding, and activity of natural hormones, those may be associated with the cancer risk (Falconer et al., 2006; Mustafa, 2010; Mnif et al., 2011; EEA, 2010), and affect the female reproductive system (Frade et al., 2014). The International Endocrine Society and other international institutions and research groups suggest that EDC have adverse effects on men, such as the prostate cancer, as well as harm the female reproductive system (Lemaire et al., 2006; Crain et al., 2008; Diamanti-Kandarakis et al., 2009). The OCP called xeno-hormones are known to alter the function of the endocrine system by binding with human estrogen receptors. EDC can bind and activate various hormone receptors (AR, ER, AhR, PXR, CAR, ERR) and then mimic the natural hormone's action. Since years 2000's, an increasing number of epidemiological studies tended to link environmental exposure to pesticides and hormone-dependent cancer risks. At the human level, endocrine disruptor such as OCP, have also shown to disrupt reproductive and sexual development, and these effects are depend on several factors, including gender, diet, and occupational factor (Lemaire et al., 2006; Tabrez and Ahmad, 2009; Mnif et al., 2011; Wasi et al., 2013; Tabrez et al., 2014).

Three million cases of intoxication by pesticides and 220,000 of deaths are annually registered worldwide (WHO, 1992). In Mexico, although statistics may not be reliable due to the lack of specific records linked to intoxications by OCP, intoxications and poisonings are causing 1400 death (87% adults and 13% children). Exposure to pesticides is the third cause of intoxication with a rate of 13.9%. The agricultural and industry workers are the most affected (Rodríguez et al., 2005). In Mexico, OCP are sold in stores of agricultural products and in the municipalities without restriction (Polanco et al., 2015b).

Cervical cancer is the second most common mortality cancer in developing countries (Ferlay et al., 2015). In Mexico it is distributed mainly in the poor states in the South of the country including the Maya area, and is directly related to poverty, marginalization, low education levels, as well as insufficient access to services adequate of health (Palacio-Mejía et al., 2003). In Yucatan, the national average mortality of cervical cancer was 29.02 $\times$ 100,000 during 1990–2005 (Fig. 1) (SSY, 2006). During 2006–2010, Yucatan was the second State with cervical cancer related mortality with 94 deaths in 2010 (SSY, 2011). Overall, over the period 1990–2010, Yucatan had the highest mortality rate.

Yucatan has high agricultural activity, (579,000 ha of land for livestock; 145,715 ha of corn; 13,325 ha of citrus, and more than 10,000 ha for other crops) (SAGARPA, 2012). High level of poverty exists in Yucatan (CONAPO, 2010), therefore farmers use agrochemicals to improve agricultural yields while ignoring the health impacts of OCP. The areas with highest pesticides use are Tzucacab, Ticul, Tekax, Peto, and Oxkutzkab at south in the agricultural area, as well as the livestock region of Tizimin and the surrounding areas of Dzilam Gonzalez and Buctzotz, in the northeast (INEGI, 2007). About 86% of the population is applying agrochemicals, 94% of the population believes that the agrochemicals do not pollute the groundwater, around 30% of the population is drinking polluted water from wells and sinkholes, and these risk factors cause chronic exposure to OCP and their bioaccumulation. The sociocultural background and low educational levels of the Mayan communities (45% of illiteracy) explains their low perception of risk in relation to the process of contamination by OCP (Polanco et al., 2015b).

Recent study has detected OCP in water of 11 municipalities of the Ring of Cenotes (sinkholes), which is the main aquifer in the area. Very high concentrations were found during the dry season for heptachlor (13.617 mg/mL), α-HCH (6.538 mg/mL), endrin (3.265 mg/mL), 4,4′ DDE (1.255 mg/mL), δ-HCH (10.864 mg/mL) (Polanco et al., 2015a,b). Yucatan has a context of high vulnerability in their natural landscape, such as well their karst soils, which easily filters all contaminants to the groundwater. There is also a high density of sinkholes in the state interconnected to the groundwater, with more of 4000 (Seduma, 2012), which allows the distribution of pollutants (Marin and Perry, 1994; Escolero et al., 2000; Marin et al., 2000; Escolero et al., 2002). Furthermore, there are faults and fractures in the ground surface (INEGI, 2010), that facilitate the filtering of pollutants to the groundwater (Bauer et al., 2011), as well as 30% of deforestation in Yucatan (Andrade, 2010), which increases the vulnerability process for the contamination of water. In the few monitoring studies on bioaccumulation of OCP in breast milk, high levels of OCP were found for women from Chelem, Yucatan, in the coastal town (Rodas-Ortíz et al., 2008); and for women in the metropolitan, agricultural and the coastal areas of Yucatan (Polanco et al., 2016).

This study is the first and unique survey conducted in Yucatan up-to-date to address environmental and health related issues linked to the use of OCP (Polanco et al., 2015a). The objective of this exploratory study is the monitoring of pesticides in the blood of Maya women with cervix uterine cancer in relation to the environmental and social vulnerabilities.

2. Material and methods

2.1. Study area

The study was conducted in 18 municipalities in Yucatan, Mexico known for the high mortality of cervical cancer (Fig. 2). This area includes the main livestock zone in the northeast, the main agriculture zone in the south, and the metropolitan zone of the State.

2.2. Sampling

Sampling was carried out between 2009 and 2011. Prior to sampling strategy design, the available official information on mortality caused by uterine cervix cancer in Yucatan in the last 20 years was analyzed. Clinical records were obtained from the Health Secretary State of the Government of Yucatan. The population sample was chosen in agreement with the Ministry of Health. It covers 18 municipalities with highest cervical cancer mortality. Prior to the study, meetings with members of the Health Secretary State and directors of the field clinics of health in the municipalities were organized. The inclusion criteria were based on occupational factors: women with agricultural activity in their backyards and use

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