ENVIRONMENTAL TOXICOLOGY AND PHARMACOLOGY 38 (2014) 220–229

Available online at www.sciencedirect.com

ScienceDirect

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

Placental oxidative status in rural residents environmentally exposed to organophosphates

Graciela Chiapella[a,b,*], *Susana Genti-Raimondi*[c], *Gladis Magnarelli*[a,b]

[a] *Facultad de Ciencias Médicas, Universidad Nacional del Comahue, Cipolletti, Río Negro, Argentina*
[b] *LIBIQUIMA, Instituto Multidisciplinario de Investigación y Desarrollo de la Patagonia Norte (IDEPA), CONICET – Universidad Nacional del Comahue, Neuquén, Argentina*
[c] *Centro de Investigaciones en Bioquímica Clínica e Inmunología (CIBICI-CONICET), Departamento de Bioquímica Clínica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba, Argentina*

ARTICLE INFO

Article history:
Received 17 March 2014
Accepted 3 June 2014
Available online 10 June 2014

Keywords:
Pesticides
Placenta
Catalase
Placental index

ABSTRACT

The impact of environmental organophosphate pesticide exposure on the placenta oxidative status was assessed. Placental samples were collected from women residing in an agricultural area during pesticide pulverization period, non-pulverization period and from control group. Carboxylesterase activity was significantly decreased in pulverization period group. Enzymatic and non-enzymatic defense system, the oxidative stress biomarkers and the nuclear factor erythroid 2-related factor levels showed no differences among groups. However, in the pulverization period group, an inverse association between catalase activity and placental index, a useful metric for estimating placental inefficiency, was found. This result suggests that catalase may serve as a potential placental biomarker of susceptibility to pesticides. Further studies designed from a gene-environment perspective are needed.

1. Introduction

Organophosphorus (OP) compounds are a class of widely used pesticides which represent the most commonly chemical applied in agricultural pest control programs. The primary acute toxicological effect of OPs is associated with inhibition of acetylcholinesterase (AChE) and pseudocholinesterase enzymes. Cytochrome P450 family enzymes have been shown to carry out activation of phosphorothionate and phosphoroditionate compounds to the oxon products (Chambers et al., 2010; Ojha et al., 2011). The oxon derivatives are the actual powerful inhibitors of type "B" esterases such as AChE and carboxylesterase (CaE) (Barata et al., 2004), whereas the products of the dearylation reaction and the oxon hydrolysis represent the main detoxification metabolites (Buratti et al., 2007). The balance between OP activation and detoxification establishes their risk to humans.

In addition to esterase enzyme inhibition, several studies provide evidence that OP exposure induces oxidative stress affecting different systems and organs such as the immune system (Richter et al., 2009), brain (Mekail and Sharafaddin, 2009), liver (Mink et al., 2012; Mostafalou et al., 2012), hematological system (Van der Oost et al., 2003), and reproductive system (Agarwal et al., 2012).

* *Corresponding author at*: IDEPA-CONICET, Buenos Aires 1400, Neuquén 8300, Argentina. Tel.: +54 2994490300/461; fax: +54 2994490461.
E-mail addresses: grachiapella@live.com.ar, chiaper@fibertel.com.ar (G. Chiapella), sgenti@fcq.unc.edu.ar (S. Genti-Raimondi), ggmag23@gmail.com (G. Magnarelli).
http://dx.doi.org/10.1016/j.etap.2014.06.001
1382-6689/

Oxidative stress is defined as an imbalance between the generation of reactive oxygen species (ROS: superoxide, H_2O_2 and $^{\bullet}OH$) and the ability of antioxidant enzymes to scavenge ROS (Myatt and Cui, 2004). The participation of ROS in pesticide toxicity may occur at different levels: by enzymatic conversion to secondary reactive products and/or ROS, depletion of antioxidant defenses, impairment of antioxidant enzyme function (Franco et al., 2009), or by alterations of metabolic links, which indirectly increase ROS generation (Mekail and Sharafaddin, 2009; Southorn and Powis, 1988). In fact, agriculture workers exposed to OP presented a depletion in erythrocyte antioxidant enzymes (Myatt and Cui, 2004) and an increase in the products o lipid peroxidation (López et al., 2007; Rastogi et al., 2009).

Normal pregnancy is a state close to the limit at which oxidative stress may become pathological (Roberts and Hubel, 2009). Decreased antioxidant capacity and increased ROS have emerged as likely promoters of several pregnancy-related disorders such as low birth weight, preeclampsia, and preterm birth (Al-Gubory et al., 2010; Roberts and Hubel, 2009) as well as with lower fetal growth in normal pregnancies (Kim et al., 2005). Evidence for a weak correlation between urinary stress oxidative biomarkers of midterm pregnancy and oxidative stress levels of placental delivery with birth size were also reported (Min et al., 2009). Moreover, Luo et al. (2006) hypothesized that "oxidative stress may be the key link between adverse insults and fetal or developmental programming of the metabolic syndrome".

Despite the recognition that the health of the placenta is a prerequisite for the health of fetus (Gupta, 2007) and that this organ may function as an OP temporary depot (Abdel-Rahman et al., 2002; Abu-Qare et al., 2000), few studies have focused on placental OP toxicity. Microscopic examination of placenta samples derived from OP exposed women showed atypical characteristics of tertiary villi (Levario-Carrillo et al., 2001) and alterations in the maturity homogeneity within placental tissue (Acosta-Maldonado et al., 2009). We have previously demonstrated increased AChE and catalase (CAT) activities (Rovedatti et al., 2012; Souza et al., 2005) and changes in mitochondrial and nuclear lipid profiles (Vera et al., 2012) in placenta of women living in agricultural area exposed to OP applications. Recently, we have reported up-regulation of enzymes which are implicated in tissue repair associated to the inhibition of placental CaE (Bulgaroni et al., 2013). Nevertheless, studies exploring the extent to which OP environmental exposure during pregnancy affect the placental oxidative condition are very few.

The present study was conducted to assess the potential impact of environmental pesticide exposure on the placenta oxidative status of women residing in an agricultural area. The enzymatic and nonenzymatic antioxidant defense parameters as well as the oxidative stress indicators were studied. Additionally, the nuclear factor erythroid 2-related factor 2 (Nrf2) levels which plays a crucial role in the cellular redox homeostasis (Niture et al., 2010) and was associated with the pathogenesis of preeclampsia (Chigusa et al., 2012) was explored.

2. Materials and methods

2.1. Chemicals

Reduced glutathione (GSH), 5′-dithiobis (2-nitrobenzoic acid), glutahione reductase, nicotinamide adenine dinucleotide phosphate-reduced tetrasodium salt (NADPH), and bovine serum albumin (BSA) were purchased from Sigma Co. (St. Louis, MO, USA). All the other reagents used were of analytical grade.

2.2. Antibodies

Polyclonal rabbit Nrf2 (C-20) antibody was purchased from Santa Cruz. Mouse monoclonal anti β-actin and horseradish peroxidase-conjugated donkey anti-rabbit antibodies were from Sigma.

2.3. Participant recruitment and sample collection

The study included seventy healthy pregnant women (15–35 years old), enrolled through 2009–2011, who delivered single healthy babies at term by vaginal mode. Forty-six women recruited in the public Hospital in General Roca City, Rio Negro, situated in the northern part of Argentine Patagonia were included in the rural group. They are residents of farms or small rural communities surrounding fruit cultivation areas of the Río Negro River Valley where OPs such as azinphos methyl, phosmet, chlorpyrifos, and dimethoate, are applied 3 months per year. Pesticides are usually finely dispersed as droplets or particles at the time of pulverization and aerial drift from the target area is frequent, increasing the potential environmental exposure of this population. Samples collected from October to December were considered as pulverization period samples (PP), and those collected from April to August were considered as non-pulverization period samples (NP). Both groups were matched for self-reported passive smoking. Another group of pregnant women with no history of pesticide exposure, attended to the Castro Rendón Hospital in Neuquén City ($n = 24$), was considered as control group (CG).

A brief questionnaire to each woman was requested to document about occupation, education, smoking habits, housing, diet, and household use of pesticides. Obese women and those with anemia, overweight, X-ray exposition, on medication, or suffering from any complications including pregnancy complications or with documented infection were excluded from the study. Maternal clinical background data were taken from medical histories. We also restricted the study to mothers who had not smoked, used drugs or drunken alcohol during the pregnancy and the labor lasted less than 10 h. Informed consent was obtained prior to the enrollment in the study. The study protocol was approved by the ethical committee of the local Advisory Committee of Biomedical Research in Humans.

For analytical determinations, sample tissues were obtained from the central area of the placenta maternal side to avoid variation in the antioxidant enzyme activities (Hempstock et al., 2003). Placental samples were snap frozen in liquid nitrogen and transported to the laboratory where they were stored at −80 °C until analysis.