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PON1Q192R genetic polymorphism modifies organophosphorous pesticide effects on semen quality and DNA integrity in agricultural workers from southern Mexico

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ABSTRACT

Pesticide exposure, including organophosphorous (OP) insecticides, has been associated with poor semen quality, and paraoxonase (PON1), an enzyme involved in OP deactivation, may have a role on their susceptibility, due to PON1 polymorphisms. Our objective was to evaluate the role of PON1Q192R polymorphism on the susceptibility to OP toxicity on semen quality and DNA integrity in agricultural workers. A cross-sectional study was conducted in farmers with Mayan ascendancy from southeastern Mexico chronically exposed to pesticides; mostly OP. Fifty four agricultural workers (18–55 years old) were included, who provided semen and blood samples. Semen quality was evaluated according to WHO, sperm DNA damage by *in situ*-nick translation (NT-positive cells), PON1Q192R polymorphism by real-time PCR and serum PON1 activity by using phenylacetate and paraoxon. Two OP exposure indexes were created: at the month of sampling and during 3 months before sampling, representing the exposure to spermatids–spermatozoa and to cells at one spermatogenic cycle, respectively. PON1 192R and 192Q allele frequencies were 0.54 and 0.46, respectively. Significant associations were found between OP exposure at the month of sampling and NT-positive cells and sperm viability in homozygote 192RR subjects, and dose–effect relationships were observed between OP exposure during 3 months before sampling and sperm quality parameters and NT-positive cells in homozygote 192RR farmers. This suggests that cells at all stages of spermatogenesis are target of OP, and that there exists an interaction between OP exposure and PON1Q192R polymorphism on these effects; farmers featuring the 192RR genotype were more susceptible to develop reproductive toxic effects by OP exposure.

Introduction

Genetic polymorphisms as modifiers of human health diseases have received attention in the last decade, and there is an increased interest in conducting studies to explore the gene–environment interactions to detect susceptible populations prone to develop health problems by chemical exposures (Kelada et al., 2003). Recent advances in molecular epidemiology have suggested that polymorphisms on enzymes involved in the metabolism of environmental chemicals would render individual susceptibility to their toxicity. Pesticides are an important class of these environmental chemicals, and included among them are the organophosphorous (OP) insecticides that are used worldwide (IARC, 1991).

OP compounds are among the most widely used pesticides, mainly as insecticides in agriculture, health campaigns and urban pest control. In the last decade, adverse effects of OP exposure on the male reproductive system, along with their mutagenic and carcinogenic activities have attracted attention (IARC, 1991). Workers from a manufacturing plant of OP showed poor semen quality (low concentration and motility) (Padungtod et al., 2000), similar to men environmentally exposed to chlorpyrifos (an OP compound) and carbaryl (Meeker et al., 2004a). In animal models, our previous studies have shown that single doses of methyl parathion and diazinon administered to mice alter sperm quality and DNA integrity, evaluated as the percentage of cells with endogenous nicks (nick translation assay) (Piña-Guzmán et al., 2005, 2006), while Burruel et al. (2000) reported that methamidophos caused a dose–response increase in abnormal sperm morphology, as well as a decreased fertility rate and embryo degeneration in mice.

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Abbreviations: PON1, human paraoxonase 1; OP, organophosphorous pesticides; 8-OHdG, 8-hydroxydeoxyguanosine; NT, nick translation; BMI, body mass index.

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