

EFFECT OF PARAOXONASE-1 (PON1) POLYMORPHISM AND PESTICIDE EXPOSURE ON BIOMARKERS OF HEPATOTOXICITY

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Background and aims. Exposure to pesticides which are metabolically activated in the liver may elicit subtle and early biochemical changes of hepatotoxicity. This study assessed whether long-term exposure to pesticides in occupational settings (intensive agriculture within plastic greenhouses) induces changes in liver function parameters. The interaction effect between exposure to pesticide compounds and polymorphisms in pesticide-metabolizing genes is also evaluated.

Methods. A longitudinal study was conducted on a population of intensive agriculture workers from Andalusia (South Spain), during two periods of high and low-intensity levels of pesticide application. A structured questionnaire containing questions on sociodemographic and occupational characteristics was completed by workers. Blood samples were taken for the measurement of biomarkers of exposure (serum and erythrocyte cholinesterases), susceptibility (Paraoxonase-1 – PON1-) and effect (liver biochemistry, including aspartate and alanine transaminases –AST and ALT, respectively-, cholestasis enzymes (gamma-glutamyl transpeptidase and alkaline phosphatase) and serum lipids –triglycerides, total cholesterol, HDL-cholesterol and LDL-cholesterol). Interaction effects between cholinesterases and PON-1 polymorphisms on biological indicators of hepatotoxicity were performed by generalized estimating equations (GEE) models.

Results. Short-term exposure to pesticides as measured by a reduction in serum cholinesterase was associated with decreased levels of liver parameters and serum lipids with the exception of HDL-cholesterol. By the contrast, cumulated exposure to pesticides (as reflected by reduced erythrocyte cholinesterase) was associated with increased levels of AST and alkaline phosphatase and increased levels of serum lipids (triglycerides, total cholesterol and LDL-cholesterol) and reduced levels of HDL-cholesterol. PON1 polymorphisms significantly contributed to changes in ALT. A significant interaction effect was found between the PON1-192Q allele and erythrocyte cholinesterase on triglyceride and HDL-cholesterol levels.

Conclusions. Pesticide exposure may induce a different profile of hepatotoxicity depending on the exposure (either short- or long-term). In the latter, pesticides exposure was associated with a proatherogenic lipid profile and this involved particularly the PON1-192Q allele.