

Association Between Human Paraoxonase Gene Polymorphism and Chronic Symptoms in Pesticide-Exposed Workers

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Abstract

Learning Objectives:

- * Explain the role of paraoxonase (*PON*) in organophosphate metabolism and the implications of polymorphism in the human *PON* gene for farm workers exposed to pesticides.
- * Identify demographic and clinical correlates of chronic toxicity in farm workers exposed to pesticides when applying them to crops.
- * Relate the occurrence of chronic pesticide toxicity to the *PON* genotypes associated with fast and slow enzymatic hydrolysis of toxic pesticide metabolites.

Pesticides, such as parathion, are metabolized by cytochrome p-450 system to paraoxon, which is a potent cholinesterase inhibitor. Paraoxonase (PON) catalyzes the hydrolysis of these toxic metabolites and protects against pesticide toxicity. A glutamine/arginine (Gln/Arg) polymorphism at amino acid position 192 of PON has been described. The Arg/Arg genotype is associated with higher serum paraoxonase activity compared to Gln/Gln. The Arg/Gln genotype is associated with intermediate serum PON activity. The potential association between PON genotype and symptoms of chronic pesticide toxicity was examined among 100 farm workers. As part of a cross-sectional study of pesticide toxicity among mixed-race farm workers in the Western Cape, South Africa, 100 farm workers were genotyped for polymorphism of the paraoxonase gene at amino acid position 192. Subjects with two or more of the following symptoms were considered to have evidence of chronic toxicity: abdominal pain, nausea, rhinorrhea, dizziness, headache, somnolence, fatigue, gait disturbance, limb numbness, paresthesias, limb pain, or limb weakness. In multivariable logistic regression analysis, the independent predictors of chronic toxicity were previous history of head trauma resulting in loss of consciousness (OR 2.8, 95% CI = 1.7-6.7), having worked as a pesticide applicator (OR 5.4, 95% CI = 3.2-8.9), and having one of the two slow metabolism (Gln/Gln or Gln/Arg) genotypes (OR 2.9, 95% CI = 1.7-6.9). Furthermore, the prevalence of chronic toxicity increased in a stepwise fashion from 15% among pesticide nonapplicators with a fast metabolism (Arg/Arg) genotype, to 42.9% among pesticide nonapplicators with slow metabolism (Gln/Gln or Gln/Arg) genotypes, to 58.8% among pesticide applicators with fast metabolism genotype, and 75.0% among pesticide applicators with slow metabolism genotypes ($P = 0.001$). Age, number of years on the job, smoking history, alcohol history, education level, plasma or red blood cell cholinesterase level, or

previous history of acute organophosphate poisoning were not statistically significant predictors of chronic toxicity. The *PON* genotype is an important determinant of a farmworker's susceptibility to chronic pesticide poisoning.