

Distribution of PON1Q192R susceptibility genotypes to organophosphate pesticides in agricultural workers from Elqui and Limarí valleys of IV Region, Chile

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In recent years Chile has experienced an enormous increase in agricultural activity, which is reflected in the increased use of pesticides; indeed, the sales of these compounds have increased by more than 400% between 2001 and 2010, exposing local population to new and high levels of contaminants. Although the benefits to agricultural productivity are undeniable, their use is associated to complex human health problems.

Several studies have demonstrated the capability of human plasma to metabolize toxic organophosphate compounds (OP's) and its strong correlation with a serum protein: the Paraoxonase-1 (PON1), but PON1 activity shows a great variability in the population (individuals with low, medium, and high activity level) as a result of a substitution at position 192: glutamine (Q) or arginine (R). Having this polymorphic allele and its relation with metabolic activity, we measured plasma hydrolytic activity in two groups of volunteers (85 exposed to OP's and 103 control) using paraoxon [paraoxonase (PONase) activity], phenylacetate [arylesterase (AREase) activity], and diazoxon [diazoxonase (DZOase) activity] as substrates with standardized spectrophotometric assay. Thus, we determined the *Status* PON1 which is the combination of PON1Q192R genotype by plotting DZOase vs PONase activities and Q192R phenotype using PONase/AREase and PONase/DZOase ratios. Genotypes were verified by qPCR using TaqMan® probes.

Allelic and genotypic frequencies of PON1_{Q192R} polymorphism, as well as their metabolic activities, were established for the first time for a group of agricultural Chilean workers; Q allele was more frequently represented in our exposed and control population (~60%), being this allele less efficient than R allele to metabolize the pesticide *chlorpyrifos*, the most used OP pesticide in this area. Moreover, a great inter-individual variability of PON1 activity was observed suggesting a wide individual susceptibility to these agricultural pesticides, aspect which must be considered in human monitoring studies.