

Is plasma cholinesterase a reliable biomarker for prolonged exposure to cholinesterase inhibitors?

**Introduction:** The use of pesticides, including insecticides, has increased in Brazil. Beyond their role in agricultural production, insecticides are also used to control urban pests and endemic diseases. Plasma or Butyrylcholinesterase (BCHE) is required for the biological monitoring of occupational exposure to organophosphates (OP) and carbamates. However, there are controversies regarding its validity. This study aimed to assess this biomarker in OP and Carbamates long term exposure.

**Methods:** A two-steps cross-sectional study was conducted among 492 pesticide applicators in tobacco farming. Sociodemographic and occupational data; use of protective equipment; BCHE levels during low and high exposure, using kinetic method; pesticide exposure, characterized by type of chemical and date of last exposure, were investigated. Acute pesticide poisoning was evaluated by symptoms related to pesticides (according to World Health Organization criteria), standardized medical examinations and by toxicologists incorporating previous evaluations and lab tests. Data analysis was performed using the chi-square test, t-test for mean comparisons and Poisson regression.

**Results:** Among the 492 tobacco growers studied, 210(42.7%) had been exposed to OP within the previous 15 days or to carbamates within the last day. The mean BCHE level during the reference period was 5012.5 increasing to 5159.1 U/L ( $p < 0.001$ ) during high exposure. A reduction of  $\geq 20\%$  in BCHE levels was observed in 2.4% of participants, while 12.9% demonstrated an increase of  $\geq 20\%$ . No association was found between BCHE levels and any criteria for acute pesticide poisoning (including toxicologist's assessment).

**Conclusions:** The increase in BCHE during the period of high exposure and the lack of association between BCHE reduction and acute pesticide poisoning, contradict both existing literature and legal assumptions. These results might be related to tolerance to prolonged exposure to relatively low doses, variabilities in laboratory methodology (compared to Ellmann's method), small sample size, genetic polymorphism differences, among others. These findings suggest that the use of BCHE as biomarker for occupational exposure to OPs and Carbamates may require reevaluation of its validity and appropriated cutoff points. Additionally, the development of new biomarkers is essential for monitoring exposure to cholinesterase inhibitors and other pesticides.