Adverse sub-clinical health effects in pesticide-exposed population: challenges and need for developing non-invasive clinical biomarkers

Over one billion pounds of organophosphorus (OP) chemicals are manufactured worldwide each year due to their increased consumption for agricultural and other purposes. Current methods to monitor environmental and occupational exposures to OP chemicals such as chlorpyrifos (CPS) have limitations, including low specificity and sensitivity, and short time windows for detection[1]. We have undertaken a study on sub-clinical effects like haematological examination (routine), biochemical activity (cholinesterase), pesticides in blood, lung-function test and nerve-conduction studies in 156 pesticide sprayers from Lucknow District, India. The results showed significant decline in peak expiratory flow rate[2], acetyl and butryl cholinesterase activity[3], and sensory and motor nerve conduction velocity[4]. Haematological indices show variations resulting in conditions like leucopenia, leucocytosis, lymphocytopenia, neutropenia, monocytosis, anaemia and thrombocytopenia[5].

Exposure to xenobiotic organophosphates ranges from low-level, chronic exposure during pesticide application (e.g. on farms, in residences or workplace) to high-dose, acute exposures, including release of nerve agents or toxic industrial OP chemicals. The OP chemicals can have both rapid and chronic toxicity, due to their action on specific esterases and lipases, most notably acetylcholinesterase and neuropathic target esterase. In each of the above examples, a rapid and accurate assessment of OP to which the person was exposed, degree of exposure, and period of exposure will help direct therapy to the victim and assess the level of threat to others[1].

Traditionally, assessment of OP chemical exposure is generally based on the analysis of the dialkyl phosphates and other metabolites in blood and urine analysis. The metabolites for specific OP chemicals can be measured in the urine after an exposure, such as 3, 5, 6 trichloro-2-pyridinol for CPS. However, blood and urine analysis provides information about shorter OP chemical exposure, which necessitates interest in using hair analysis of OP metabolites as an exposure indicator due to several advantages over urine and blood. These include: (i) easy collection of hair sample, (ii) non-invasive and high stability on storage and transportation, and (iii) retaining metabolites for longer time (long duration of exposure). Further, the metabolite is excreted in the urine for only a shorter period of several days after significant exposure[1]. In addition, due to the widespread use of CPS and environmental persistence of its breakdown products, the metabolites appear at a high background level in the general population[6]. Their appearance does not indicate whether the individual was exposed to the harmful parent compound, or the harmless breakdown product.

The difficulty of cholinesterase as a biomarker is its inter-individual variability. The intra-individual coefficient of variation (CV)[7] is about 10% and inter-individual CV is 10–40%, which was also observed in our study among pesticide sprayers. Measuring the pre-exposure activity levels of an individual would improve precision, but this is only practical in certain situations, such as monitoring the exposure of agricultural workers during the growing season. Pre-exposure activity levels are rarely available for cases of non-agricultural exposure[1].

In this context, OP metabolites in hair as a biomarker may provide better information on long-term exposure to pesticides than biomarker measures in urine or serum, because of the shorter half-life of the latter biomarkers; these are also considered cost-effective for large epidemiological studies. The absence of drug metabolism in the hair and its fairly uniform growth rate for a given location in the body may present a historical account of OP exposure, provided that the concentrations measured in a given hair segment are related to their distance from the scalp (usually the proximal 1–2 cm). With the advancement of molecular epidemiology and the need for more precise methods of exposure measurement, the hair OP metabolite as a biomarker will likely become a standard measure of pesticide exposure.

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