Novel Biomarker of Organophosphate Insecticide Exposure in Rats And Humans.

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Abstract: Organophosphorus (OP) pesticides are one of the most widely used insecticides in the world replacing the organochlorines, which are associated with potential carcinogenesis. OP insecticides have a common mechanism of action, even though each of their chemical structure varies in nature. They cause inhibition of the nervous tissue acetylcholinesterase (AChE). Since AChE is also found in the red blood cells (RBCs), measuring the level in RBCs has been the mainstay for detecting functionally significant inhibition of cholinesterase activitiy especially during OP intoxication.

Carboxylesterases (EC3.1.1.1) are the □□hydrolase-fold Proteins. They compose a multigene superfamily, the gene products of which are localized in the endoplasmic reticulum(ER) of many tissues. Among various carboxylesterase isozymes, Egasyn is an accessary protein of □-glucuronidase (BG) in the liver microsomes. Egasyn-□-glucuronidase complex is located at the luminal site of liver microsomal endoplasmic reticulum membrane. When OP insecticides are incorporated into the liver microsomes, they are tightly bound to egasyn, and subsequently, BG is dissociated and released into blood. Consequently, the increase of plasma BG activity becomes a good biomarker of OP exposure. Thus, the single administration of OP increased plasma BG activity in approximately 100-fold the control level in rats. In the repeated administration of OP insecticides to rats, unexpectedly, plasma BG activity was not so increased on days 2 and 3. While, the significant increase of BG was observed again on day 10 after a 7 day interval without OP administration in rats.

On the other hand, a cross-sectional study was conducted to study the effects of acute and chronic OP exposure on the plasma BG enzyme activity among five patients of acute poisoning in Malaysia, 230 farmers and 49 fishermen (control group) in Malaysia. The duration of OP exposure among the patients was unknown, but the plasma samples from patients were collected on day one in the hospital. The duration of OP exposure among the farmers was between 1 and 45 years. The BG activity was compared with plasma cholinesterase activity in the same individual. The plasma cholinesterase activity was significantly reduced among the patients ($P<0.05$), but the inhibition in plasma cholinesterase activity among farmers was not significant ($p>0.05$). On the other hand, the plasma BG activity among the farmers was significantly elevated ($p<0.05$), but not significant among the patients with acute toxicity ($p>0.05$). The plasma cholinesterase activity was positively correlated with the plasma BG activity among the farmers ($r=0.205$, $p<0.01$) but not among the patients ($r=0.79$, $p>0.05$).

In conclusion, the increase in plasma BG activity after OP exposure in rats is a much more sensitive biomarker of acute OP exposure than AChE inhibition. While plasma BG activity can be measured as a biomarker for the chronic OP exposure rather than patients with acute exposure in humans. Further studies need to clarify the discrepancy between rats and humans.