Medical Xpress

Pesticide susceptibility in children lasts longer than expected

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Although it is known that infants are more susceptible than adults to the toxic effects of pesticides, this increased vulnerability may extend much longer into childhood than expected, according to a new study by researchers at the University of California, Berkeley.

Among newborns, levels of paraoxonase 1 (PON1), an enzyme critical to the detoxification of organophosphate pesticides, average one-third or less than those of the babies' mothers. It was thought that PON1 enzyme activity in children approached adult levels by age 2, but instead, the UC Berkeley researchers found that the enzyme level remained low in some individuals through age 7.

Based upon the findings, reported this month in the journal *Environmental Health Perspectives*, the study authors recommend that the U.S. Environmental Protection Agency (EPA) re-evaluate the current standards for acceptable levels of pesticide exposure.

"Current EPA standards of exposure for some pesticides assume children are 3 to 5 times more susceptible than adults, and for other pesticides the standards assume no difference," said Nina Holland, UC Berkeley adjunct professor of environmental health sciences and senior author of the paper. "Our study is the first to show quantitatively that young children may be more susceptible to certain organophosphate pesticides up to age 7. Our results suggest that the EPA standards need to be re-examined to determine if they are adequately protecting the most vulnerable members of the population."

In 2001, the EPA began restricting organophosphate pesticides in products sold for use in homes, mainly because of risks to children. However, organophosphate pesticides, such as chlorpyrifos and diazinon, are still used in agriculture in the United States and elsewhere.

The study, conducted by UC Berkeley's Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS), involves 458 children from an agricultural region who were followed from birth through age 7. Cord blood samples were collected from all children to determine their PON1 genotype and to obtain baseline measures of the enzyme's activity level.

For more than 100 of the children in the study, researchers were able to obtain at least four additional measurements - at ages 1, 2, 5 and 7 - of PON1 activity. Almost all the children in the study had 2 to 3 time points assessed, for a total of 1,143 measurements of three types of PON1 enzyme activity.

One's PON1 genotypic profile determines how effectively the enzyme can metabolize toxins. For example, people with two copies of the Q form of the gene - known as a QQ genotype - produce a PON1 enzyme that is less efficient at detoxifying chlorpyrifos oxon, a metabolite of chlorpyrifos, than the enzyme produced by people with two R forms of the gene. Similarly, individuals with two T forms of the PON1 gene on a different part of the chromosome generally have a lower quantity of the enzyme than do those with two C forms of the gene.

Previous research led by Holland found that some of the QQ newborns may be 50 times more susceptible to chlorpyrifos and chlorpyrifos oxon than RR newborns with high PON1 levels, and 130 to 164 times more susceptible than some of the RR adults.

Of the children in this latest study, 24 percent had the QQ genotype, and

18 percent had the TT genotype, both of which are associated with lower activity of the PON1 enzyme. Moreover, 7.5 percent of the children had both QQ and TT genotypes, which is considered an even more vulnerable profile.

On average, the quantity of enzyme quadrupled between birth and age 7. The greatest rise in enzyme activity was among children with the RR and CC variants of the PON1 gene, which quickly outpaced the increase in children with the QQ and TT genotypes.

The fact that enzyme activity remained low for certain kids with vulnerable genotypes well past age 2 was surprising for the study authors. The researchers are continuing to collect data for these children as they grow older to see if the pesticide susceptibility continues.

"In addition to its involvement in the metabolism of pesticides, many studies are now finding that PON1 may play an important role in protecting against oxidative stress, which is linked to diseases from asthma to obesity and cardiovascular disease," said study lead author Karen Huen, a UC Berkeley Ph.D. student in environmental health sciences. "The children in our study whose genotypes are related to lower PON1 activity may not only be more susceptible to pesticides throughout much of their childhood, they may also be more vulnerable to other common diseases related to oxidative stress."

Notably, other studies have found that PON1 genotypes vary by race and ethnicity, with the Q variants more common among Caucasians, less common among Latinos, and least common among African Americans. The majority of the subjects in this study were Mexican-American.

"What's important about this study is that it shows that young children are potentially susceptible to certain organophosphates for a longer period of time than previously thought," said Brenda Eskenazi, UC

Berkeley professor of epidemiology and director of CHAMACOS and the Center for Children's Environmental Health Research. "Policymakers need to consider these vulnerable populations when establishing acceptable levels of exposure to different pesticides."

Source: University of California - Berkeley (news : web)