The Examination of the Relation of Organophosphate Exposure to Neurologic and Neurobehavioral Outcomes in Farmworker Children

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Abstract

Organophosphate pesticides are extensively used in California. Very few studies have been conducted on the adverse effects of prolonged organophosphate exposure to human health, specifically children's health. This paper evaluates the relationship between moderate to high levels of organophosphate exposure and adverse neurologic and neurobehavioral effects in migrant farmworker children. From preliminary data, there seems to be a higher prevalence of a certain type of organophosphate metabolite called Dimethylthiphosphate (DMTP) in children who have parents working with or near organophosphate pesticides than that of children whose parents have minimal exposure.

Introduction

Pesticide use in the agricultural industry has increased since the beginning of modern agricultural practices throughout the world. Modern pesticide use began in 1934 with the discovery of DDT and it is estimated that 1.16 billion pounds of pesticides were used in the United States in 1990 (Cunningham 1997). Such an increase in agricultural pesticide use results in increased health risks for farmworkers who are regularly exposed to certain pesticides. In addition, these farmworkers may not only be increasing health risks for themselves, but also for their immediate family, specifically, children who were conceived during the time the farmworker had significant exposure to hazardous pesticides. It is now believed that farmworkers who are exposed to pesticides show increased risk of birth defects in their offspring (Garcia 1998). Regular exposure to pesticides may also result in childhood leukemia. A study conducted by the Children's Cancer Study Group found that paternal exposure to pesticides for more than 1,000 days nearly tripled the risk of childhood acute nonlymphocytic leukemia (Buckley *et al.* 1989).

Pesticides are classified by their chemical structure. The seven pesticide classifications include inorganic, organic, fumigants, chlorinated hydrocarbons, carbamates, microbial agents and biological control, and organophosphates (Cunningham 1997). Organophosphates are used extensively in California as insecticides and defoliants. For instance, in 1988 over 9 million pounds of organophoshate pesticides were used on over 10 million acres during a twelve month period (Gold *et al.* 1997). Organophosphates are used on a variety of crops such as cotton, melon, nut trees, and fruit trees. Human exposure to agricultural applications of organophosphates can result in systemic illnesses because they inhibit the enzyme acetylcholinesterase at nerve endings, causing accumulation of the neurotransmitter acetylcholine in the nerve and effector organs. According to annual reports by the Worker Health and Safety Branch at the California Environmental Protection Agency, at least 15% of pesticide-related illnesses are associated with organophosphate exposure (Gold *et al.* 1997). Organophosphates have been known to cause these symptoms in adults: headaches, nervousness, nausea, blurred vision, cramps, diarrhea, muscle twitching, and in severe cases, neuropathies, convulsions, coma, and loss of reflexes and muscle control (Davies and Peterson 1995).

The levels of occupational risks and hazards associated with agricultural work in California are among the highest in the United States (Gold *et al.* 1997). The population that is at greatest risk is migrant farmworkers who perform most of the pre-harvest and harvest work. Women and children compose at least 28% of the total migrant farmworker population in California, thus it is important to study the effects of organophosphate exposure to the neourologic outcomes in children. Children have a higher risk of health problems because of their vulnerability to adverse effects of exposure from organophosphates. A study conducted by Abou-Donia showed that the blood brain barrier in children is more permeable to harmful substances and offers less protection than that of adults. It is also believed that the greater permeability of infant skin may facilitate the absorption of organophosphates (Fenske *et al.* 1990).

Currently a team of researchers headed by Dr. Ellen Gold at UC Davis is conducting a study on organophosphate exposure in farmworker children. The researchers have assayed urine samples from mothers and their children in the study in order to look for alkyl phosphate and phenolic metabolites. Being rapidly excreted from the body, alkyl phosphate and phenolic metabolites have proven to be usable indices of recent exposure. Davies and Peterson (1995) stated that cholinesterase surveillance, the mainstay of present pesticide occupational surveillance, has many limitations and at times is inadequate, nonspecific and unpredictable. Cholinesterase surveillance is used in order to detect nonspecific exposure, thus it is a good indicator of general organophosphate pesticide exposure. Over the last two decades, however, increased interest has been shown in surveillance by urinary metabolites, which is capable of identifying subtle differences in groups of workers. For example, exposure to the organophosphate pesticide Mevinphos (Phosdrin) will result in the presence of the Dimethylphosphate (DMP) metabolite. The idea is that if a specific metabolite is detected from a person's urine sample, it is likely that he or she was exposed to the specific pesticide which results in that metabolite. Surveillance by urinary metabolites can also measure "…small incidental exposure of the general population to these pesticides in the environment." Comparing the two methods of detection, surveillance by urinary metabolites does a better job of detecting specific exposure whereas the cholinesterase surveillance detects nonspecific exposure.

The field study was first conducted in 1996 in six state-funded Migrant Housing Centers (MHC's) in Colusa, Woodland, Winters, Madison, Esparto, and Dixon. The study included approximately 300 women and 300 children. Each woman and child was assigned to a job category based on the expected levels of organophosphate exposure to the mother and father. The mothers and children were asked to give at least one urine sample in order to screen for organophosphate metabolites (Marcia Woodby 1999, pers. comm.).

In addition, U.C. Davis graduate student Marcia Woodby surveyed the women and children as part of this study. Her survey was designed to evaluate the link between neurologic and neurobehavioral outcomes from pesticide exposure. The survey conducted in 1996 and 1997 collected the following information from the participating families: demographic, medical and work history, nutritional information to assess adequacy of diet, lifestyle habits, child care practices and access to health care.

Methods

This research project is designed to address whether or not mothers exposed to organophosphate pesticides increase the chance of adverse neurologic outcomes in their offspring compared to mothers who have little or no exposure to organophosphates.

In order to find the answer to this question, I separated this research into two steps. In the first step I analyzed the organophosphate metabolite data obtained early in the study to determine whether the mothers and children in three job categories were exposed to different amounts of pesticides. The second step of this research project is the neurologic survey analysis in which we see the relationship between levels of organophosphate exposure in mothers and potential adverse neurologic performance of their children based on their Job Category

Job Category The participants were chosen based on the likely familial exposure to organophosphates. The mothers and children participating in the study were each assigned a Human Subject Number (H.S.N.), one number corresponding to a mother and child. An M (mother) or C (child) behind the H.S.N can differentiate the mother and child. Participants were placed in Job Category 1 if the mother works in agriculture, meaning working with crops in the fields, driving a tractor, sorting vegetables, hoeing, as well as other activities that may expose the person to pesticides. Families placed in Job Category 2 include mothers that do not do agricultural work, but fathers that do agricultural work. Finally, families that are placed in Job Category 3 include mothers and fathers that do not work in agriculture.

The metabolite data was separated by the field study years of 1996 and 1997. I cleaned up the data by checking for any duplications or incorrect H.S.N.'s. I then separated the 1996 and 1997 data into mothers and children based on their Job Category classification and urine sample number. The urine sample number represents which urine sample was analyzed for metabolites, since many participants gave two or more urine samples. After this stage I made a table showing the H.S.N., Job Category, and the amount of metabolite found in each urine sample. From this table I was able to analyze the prevalence of the six metabolites in each of the job categories.

Organophosphate Metabolites Analysis Under the supervision of Dr. Buckpitt, a metabolic toxicologist in the department of Epidemiology and Preventive Medicine at U.C. Davis, I coded organophosphate metabolite results from urine samples from farmworker children. I also analyzed the prevalence of the six organophosphates in all of the samples collected. The six metabolites are Diethylphosphate (DEP), Dimethylphosphate (DMP), Dimethyltriphosphate (DMTP), Dimethylditriphosphate (DMDTP), Diethyltriphosphate (DETP), and Diethylditriphosphate (DEDTP). The metabolites were measured in ng/ml of urine. These alkyl phosphate and phenolic metabolites are a result of exposure to certain pesticides such as ethyl parathion and mevinphos. For example, ethyl parathion exposure results in the metabolites DEP and DETP being identified. DETP will also result from exposure to the diazinon organophosphate. Dimethythiphosphate (DMTP) may result from exposure to azinphos-methyl. In addition, exposure to the organophosphate pesticide called Mevinphos (Phosdrin) will result in the presence of the Dimethylphosphate (DMP) metabolite. According to Woodby, the metabolites Dimethylditriphosphate (DMDTP) and Diethylditriphosphate (DEDTP) are derivatives of DMTP and DETP.

Neurological Survey Analysis I assisted Marcia Woodby with the analysis of the survey data that was obtained from Woodby's two-year field research in migrant farm camps throughout California. Since many types of tests were given to the children, I chose to look at the Purdue Picture and Vocabulary Test (PPVT), the Purdue Peg Board test, and a neurologic test that exams gait, balance, and shoulder elevation. The PPVT is a picture vocabulary test that tests cognitive functions. The Purdue Peg Board tests for motor functions. Finally, tests for gait, balance, and shoulder elevation are standard in a neurological test. For the PPVT and Purdue Peg board, a higher score reflects a greater likelihood of a problem with either cognitive or motor functions. I conducted an internal comparison of the test scores based on Job Category. For instance, I took the mean score of the PPVT from Job Category 1, Job Category 2, and Job Category 3 in order to compare the means of each of these Job Categories.

Results

When comparing the prevalence of the six metabolites in Job Categories 1, 2, and 3, the prevalence of DMTP is higher in Job Category 1 than in 2 and 3. Table 1 shows these results. Table 1 shows that the prevalence of the metabolites DMP and DEDTP are relatively similar in all job categories. The prevalence of DEP and DETP decreases slightly from Job Categories 1,2, and 3. The prevalence of DMDTP decreases from 20% in Job Category 1 to 16% and 15% in Job Categories 2 and 3, respectively. A chi-square test was used to evaluate the differences across job categories for each metabolite, and the resulting p-values are included in Table 1.

	Job Category 1 (n=318)	**Job Category 2** (n=277)	**Job Category 3** (n=303)	**P-value**
DMP	10%	11%	10%	0.89
DEP	13%	8%	8%	0.09
DMTP	52%	39%	30%	1.05
DMDTP	20%	16%	15%	0.30
DETP	15%	13%	11%	0.40
DEDTP	2%	3%	3%	0.64

Table1. Prevalence of the six organophosphate metabolites in children

The means of the two neurologic tests are given below in Table 2, along with the p-values from an ANOVA analysis for differences in the means across job categories for each test. The PPVT Raw score represents the unconverted test score. This number allows us to compare the scores internally. The PURDUE scores used to calculate the mean were standard test scores that do not need to be converted for this study.

JOB CATEGORY	PPVT RAW	PURDUE
1	93.7	28.6
2	92.3	25.9
3	85.9	24.6
P-value (across groups)	0.020	0.002

Table 2. Mean test scores.

The neurological test used for gait, balance and shoulder elevation was conducted on the children. Almost every child had a normal score for these tests so I did not include a table of results because they are the same for about 99% of the children.

Discussion

It is interesting to note that the prevalence of DMTP in Job Categories 2 and 3 are relatively high. This may suggest that a greater population, including those that do not work in agriculture, are commonly exposed to the pesticide that results in this metabolite which is azinphos-methyl. To add, Dimethyltriphosphate (DMTP) seems to be most prevalent in Job Category 1, so I believe that the pesticide that caused the excretion of this metabolite is used extensively in California agriculture. This pesticide may be azinphos-methyl, this information is based on a previous study conducted in Washington State during the summer of 1995 (Loewenherz *et al.* 1997).

The analysis of Table 1 suggests that the prevalence of DMP and DEDTP are similar in all three Job Categories. Thus the exposure to the pesticides that result in the identification of these metabolites is similar in all three populations.

The prevalence of DEP and DETP is shown to decrease slightly when comparing Job Categories 1,2, and 3. This may suggest that the exposure to the specific pesticides is a result of relatively similar exposure in all populations.

The means of the neurologic test scores show an interesting trend. The test scores decrease when comparing Job Category 1, 2, and 3. This shows that for children who have a greater chance of exposure to organophosphate pesticides are likely to have neurologic complications. The P-value for both the PPVT and Purdue test shows that these results are statistically significant and that children who have exposure to organphosphate pesticides in general have a greater chance of decreasing their neurologic health.

Conclusion

This study was designed to see whether or not farmworker children who were potentially exposed to organophosphate pesticides had a greater chance of decreasing their neurologic health. As the study has shown, there is a correlation between mothers and fathers who are exposed to organophosphates and the increase in the chance that their children will be neurologically affected. The team at UC Davis is hoping to share this knowledge with the agricultural and medical community once they complete their research in the near future.

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