Associations between Pesticide Exposure and Kidney Function Failure

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ABSTRACT

To kill insects and pests that threaten crop yields, agriculturalists use pesticides, many of which on today's market are composed of organophosphates (OPs) that are highly toxic to mammals. To be effective, these pesticides often need to be used in large quantities, which can increase pesticide resistance among targeted pests. Although companies have sought to avoid selective toxicity among pests by developing new pesticides, their efforts have also increased pesticide residues in and around agricultural areas. Furthermore, pesticides can exert significant adverse effects on human health. This paper determined associations between pesticide exposure and kidney function using data available in the National Health and Nutrition Examination Survey (NHANES). Between 2009-2010, 2011-2012 NHANES performed laboratory urinary analysis and reported the level of urinary creatinine, urine osmolality, and pesticide exposure level of 5,422 participants in America along with demographic information. I found that participants categorized as high level of 2,4-dichlorophenols had statistically significant higher level of urinary creatinine and osmolality level. The findings associating with kidney function failure from pesticide exposure will inform people of the necessity of using less toxic pesticides and new regulations regarding pesticides associated with educating farmers to use pesticides properly in safe condition.

KEYWORDS

pesticides, 2,4-dichlorophenol, creatinine, urine, NHANES

INTRODUCTION

The worldwide consumption of pesticides has reached approximately 5.6 billion pounds (Alavanja 2009). The amounts of pesticides used in agricultural areas have grown over time to increase crop yields (Khwaja et al. 2013). To kill insects and pests that threaten crop yields, agriculturalists use pesticides and many available are composed of organophosphates (OPs) that are highly toxic to mammals. This extensive use has resulted in excess pesticide, and many flow into water, into soil, and evaporate into the air (Wilson and Tisdell 2001). The pesticide exposure can affect human health by taking contaminated food, air, and water; numerous negative short- and long-term human health effects have been recorded (Wilson 1998).

Worldwide, approximately 1.8 billion people do farm work and most of them use pesticides for various purposes including protect and increase the amount of commercial products that they produce (Alavanja 2010). Pesticides were very effective to kill pests and to increase agricultural productivity (Wilson and Tisdell 2001). However, the pesticide resistance has been rapidly enhanced since the use of pesticides has been growing rapidly to increase crop yields (Wilson and Tisdell 2001). Thus, many pesticides are introduced to combat development of pesticide resistance. Dichlorodiphenyltrichloroethane (DDT) containing organophosphates compound, a synthetic organic compound, is heavily used as an insecticide for agricultural production in developing countries. The overuse has caused tremendous damage to human health in these regions (Tchounwou et al. 2002).

Widely used in agriculture, pesticides with Organophosphates (OP) can benefit society by protecting crops when used safely, however when mixed and applied, pesticides can endanger people, in open, uncovered spaces, where pesticide residues in the soil or drinking water might increase due to soil erosion and rainfall (Damalas 2011). Such misuses of pesticides can contaminate environment and increase the human exposure to toxins (Praneetvatakul et al. 2013). Pesticides are toxic to humans not only at high doses for acute poisonings, but also in low dosages (Zeliger 2011). Humans are expected to have less effect when they expose to small amounts of pesticides since they are much larger than the expected target species for pesticides (Hernández et al. 2012). However, long-term exposures may cause an array of health effects including cancer and neurodegenerative diseases (Hernández et al. 2012), decreased DNA of brain, inhibition of brain acetylcholinesterase (AchE), and reduced brain weight of offspring (Eskenazi 1999). During the period of development, pesticide effects on human are well established. Exposure to pesticides presents lasting adverse effects in early development of brain and the in endocrine system, which are sensitive targets (London et al. 2012).

The genotoxicity of some environmental contaminants affect human health by damaging genetic system, thereby playing a significant role in the development of cancers (Canales-Aguirre et al. 2011). Accumulating pesticide residues in human body is one of the most common causes of death in the agricultural field (Gunnell et al. 2007). Organophosphates (OP), are a group of insecticides, mainly used in pesticides on today's market acting on the enzyme acetylcholinesterase (AchE), and are especially noted for their toxicity (Damalas 2011). Synthesized OP compounds are predominantly used as pesticides. In the United States most cases of occupational acute pesticide poisoning result in neurotoxicity and are due to exposure to OP or carbamate pesticides (Weisenburge 1993). Many researches have shown that continuous exposure to OP pesticides might impact neurodevelopment and growth of animals and humans (Eskenazi et al. 1999). OP pesticides exert significant side effects in non-target species on human populations (Costa 2005). Although toxicities of OP are known, the extent of exposure and health effects are still debated.

This study will identified the amount of pesticide exposure to people analyzing statistical urinary specimen test data from National Health and Nutrition Examination Study (NHANES) 2009-2010, 2011-2012.

METHODS

Study site

Participants were sampled by the National Health and Nutrition Examination Survey (NHANES) from 2009-2010, 2011-2012. NHANES is a cross-sectional health survey conducted each year by the National Center for Health Statistics (NCHS; CDC) to produce vital health information for epidemiological studies the United States. Demographic data was collected each year from NHANES for five thousand participants in fifteen different locations through interviews. Demographics file from NHANES including all survey volunteers with a interview file.

Urine specimen test

NHANES uses urinary analysis for determining concentrations of pesticide residues in human population. The Measures of the urinary analysis assessed in participants aged 6 years and over within US population is a randomly selected subsample (NHANES 2010). I downloaded 5422 observations aged from 6 years and over of demographic includes gender, age, race, ethnicity, marital status, and pregnancy status within US population. Urine specimens are processed and transferred to the Division of Environmental Health Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention for evaluating. NHANES processed urine specimens to measure human metabolites. They included tests for the pesticides chloropyrifos, chloropyrifos methyl, naphthalene, and creatinine (mg/dL) in urine. The procedure included urine samples by extracting metabolites with an organic solvent and concentration of the solute. NHANES analyzed the concentrate through the National Center for Environmental Health (NCEH) using liquid chromatography combined with tandem mass spectrometric (LC/MS/MS) determination (NHANES 2010).

NHANES Variables

I used National Health and Nutrition Examination Surveys (NHANES) to collect data of prevalence of human exposure and the relevance of human exposure in public health with three variables: Urinary creatinine (mg/dL), dichlorophenol (ug/L), and urine osmolality (mOsm/kg).

2,4-Dichlorophenol

Dichlorophenol (ug/L) is a chemical used in pesticides and is able to be measured in urine. Chlorophenols are used in the wood treatment industry, as intermediates in the production of pesticides, and as antiseptics or fungicides used in industry and home. The purpose of investigating 2,4-dichlorophenol in urine is to determine the human exposure to pesticide compounds. To investigate the amount of pesticide residues in human body, I obtained dichlorophenol result from NHANES.

Creatinine

For this study, I assumed renal failure was present in individuals exhibiting high creatinine levels. The purpose of investigating creatinine level is because kidney function can be assessed by measuring levels of creatinine in urine, because creatinine is not reabsorbed or filtered through renal function. Creatinine is a waste of proteins used in body, such as urea nitrogen and uric acid. Creatinine is used as an energy source in muscle and transformed to creatine or creatine phosphate and excreted through urinary tract after it is released into the blood stream (Lebov et al. 2016). Thus, the concentration of creatinine contained in the urine is used to estimate renal function (Lebov et al. 2015). In the normal state, the creatinine discharge concentration is relatively uniform, and in proportion to the body weight of the individual. The normal range of creatinine level is 0.7-1.3mg/dL for men and 0.6-1.1mg/dL for women because the creatinine level associated with amount of muscle (MedlinePlus 2015) but it increases up to 10mg/dL in patients with chronic renal failure.

Urine Osmolality

The reason why I selected urine osmolality as an indication of kidney function by pesticide exposure is that the urine osmolality is a measurement of the amount of solute fragments contained in urine and it indicates if the urine is overly diluted or concentrated due to hydration status or impaired renal function (NHANES 2011).

Statistical Analyses

I used R and R Commander (R foundation for Statistical Computing, Vienna, Austria Version 3.31) on levels of creatinine, dichlorophenols, and urine osmolality as described above to see each variable in terms of mean, median, standard deviation, and outliers. I tested for association between 2,4-dichlorophenols and urinary creatinine level by using Chi-square tests. From the Chi-squared test, I considered a p-value less than 0.05 to be statistically significant. I used Fisher's exact test to calculate the odds ratios for significant associations determined by the Pearson's Chi-squared tests. To interpret the odds ratio, I used regression to test for independent associations between pesticide exposure and covariates including gender, ethnicity, body mass index (BMI), and age with the covariates predicting for kidney function failure.

RESULTS

Participants

Standard range of creatinine in urine is 30-170mg/dL for men and 20-162mg/dL for women. I examined a total number of 5422 participants with a 24.44% of participants exhibiting high level of creatinine between 2009, 2010, and 2011 (Table 1).

Table 1. Total number of participants with high creatinine level. Participants were sampled from National Health and Nutrition Examination Survey (NHANES): 2009-2010, 2011-2012.

Urinary creatinine level outside the normal range (# of participants)	**Total # of participants**	**% of participants exhibiting above standard urinary creatinine levels**
1325	5422	24.44%

Participants with higher percentages of urinary creatinine level were largely male. For all other relevant demographics, percentages showed no large difference (Table 2).

Table 2. Aggregate demographics of participants with urinary creatinine level data. N= 5422.

	Total (N)	**Urinary Creatinine level (#)**	**Pesticide - Exposure (#)**	**Urinary-creatinine level (%)**
Gender				
Male	2730	1847	1495	47.66
Female	2692	1425	1327	38.93
Body Mass Index				
Not overweight	2924	583	832	52.09
Overweight	2300	1102	1172	47.91
Ethnicity				
Mexican American	1130	118	972	10.44
Other Hispanic	532	62	490	11.65
Non-Hispanic White	2132	475	1562	22.28
Non-Hispanic Black	1273	421	987	33.07
Other Race	241	32	68	13.28

Association of urinary creatinine level with pesticide exposure

Chi-squared tests showed significant associations between pesticide exposure and creatinine level in urine, and urine osmolality (Table 3).

Table 3. Tests of kidney function by testing urinary creatinine level and urine osmolality with or without 2,4-dichlorophenols. NHANES 2009-2010, 2011-2012.

	% without 2,4-Dichlorophenol	% with 2,4-Dichlorophenol	X^2	P-value	Odds Ratio
Urinary Creatinine Level	30.1	72.2	20.5948	2.2e-16	1.4332
Urine Osmolality	24.6	58.8	58.2253	2.235e-12	1.5424

First I checked the urinary creatinine level to see how many individuals had higher level of creatinine in urine than standard range. Then I looked up their (participants with high level of urinary creatinine level) urinary levels of 2,5-dichlorophenol and urine osmolality results. Results of urinary creatinine level of 500 participants from NHNAES resulted in 117 out of 500 participants had higher level than standard level of urinary creatinine with median levels of about 112 µg/L; or 212 µg/L in people with measurable amount of 2,5-dichlorophenol in urine. The odds ratios of urinary creatinine and urine osmolality had statistically significant associations since both had odds ratios higher than 1 (table 3). The odds of 2,4-dichlorophenol (indicator of pesticides) therefore increased by high level of urinary creatinine and urine osmolality.

DISCUSSION

In this study of a sample of the United States population, I found that kidney function failure is associated with pesticide exposures. This failure occurs even when categorizing participants by urine level based on creatinine and urine osmolality level. Participants categorized as higher level of 2,4-dichlorophenol and 2,5-dichlorophenol had higher level of urinary creatinine and urine osmolality than participants with low level of 2,4-dichlorophenol and 2,5-dichlorophenol. 2,4 and 2,5-dichlorophenol is an indicator of pesticides in participants (NHANES 2009-2010). These results suggest that pesticide exposure is associated with kidney function when measuring value of creatinine in urine and urine osmolality.

Urinary creatinine

Creatinine levels in urine indicate to see how well kidneys are eliminating wastes and excess fluid from the urine, especially environmental chemicals (Mage et al. 2007). Participants with higher 2,4 and 2,5-dichlorophenol had higher urinary creatinine level than individuals with low amount of urinary creatinine level. Kutz et al. (1992) found that an obvious relationship between pesticide concentration and two variables (urine osmolality and urinary creatinine). Creatinine is cleared from blood plasma in the kidney at an approximately constant rate, primarily by filtration (Mage et al. 2004) and not reabsorbed or filtered through renal function. Thus measuring levels of creatinine in urine could estimate the kidney function (Lebov et al. 2015). Ethnicity and BMI were not statistically significant and were not independently associated with kidney function failure. However, gender was statistically significant and associated with kidney function failure from pesticide exposure. Participants with higher percentages of urinary creatinine level were characterized by being male. The 2012 Census of Agriculture collected data on farm that 2,109,303 farmers are in U.S and 86% of them are men (USDA 2012). Since the ratio of men who do farming much higher than the ratio of women, the amount of pesticide exposure had increased for men. This would be one of the factors of men with higher kidney function failure as compared to women. For all other relevant demographics, percentages showed no large difference. Individuals above standard level of urinary creatinine had higher amount of 2,4 and 2,5-dichlorophenol, which are indicators of pesticides, that determined high exposure of pesticides accelerated level of creatinine and urine osmolality by causing kidney function failure.

Urine Osmolality

Participants classified as higher level of urine osmolality had significant positive associations to 2,4-dichlorophenol in this study. Exposure to pesticides led high amount of 2,4-dichlorophenol extracted from human body and it was tested by amount of urine osmolality associated with urinary creatinine level. Urine osmolality should always be considered with urinary creatinine while measuring the level of 2,4-dichlorophenol to see how the kidney function works when they are exposed to pesticide. High level of creatinine in urine has been found to be correlated for higher risk of kidney disease (McQuarrie et al. 2014) because creatinine is removed entirely from kidneys. McQuarrie et al. (2014) stated, "423 patients required renal therapy or who died were identified with mean estimated urinary sodium filtration and urinary sodium to creatinine ratio". Therefore, high exposure of pesticides should be tested by urine osmolality and urinary creatinine level at the same time.

Limitations and Future Directions

This study was conducted with background research and statistical analyses but not using laboratory conditions. Though the laboratory and surveyed data of participants were already conducted and released from NHANES (2009-2010, 2011-2012), additional difficulty against data obtained will not posed. On premises fully obtained data of variables, the p-value and Chi-squared tests will be conducted.

Although the NHANES dataset is experimental study, the population size is not large enough to represent United States. The sample size of this study is 5422 people. NHANES collected laboratory, dietary, and examined data of these population but still the size of populations over four years are still a small sample.

The data set from NHANES also included questionnaire and demographics data with laboratory data, which have possibility of having biases of non-response. Also surveys are not 100% reliable because of their anonymity. Since this study is only based on laboratory data from NHANES, the bias from non-response or anonymity would not be occurred.

Broader Implications

This study will be useful for warning and educating people of the hazardous and indiscriminative use of pesticides without safety education. Furthermore, it will inform scientists and researchers of the necessity of using less toxic pesticides and preventing broad pesticide exposure. Pesticide use poisoned roughly 3 million people and 200,000 casualties each year (FAO 2000), so they should be regulated or limited. However, pesticide use is encouraged in agriculture by market systems aimed at increase the crop yields of farmers (Wilson and Tisdell 2001). If we cannot reduce the amount of pesticides used on farms, then we should find other solutions, such as a prevention act, safety education for farmers, or the development of new pesticides that have no acute or chronic toxicity to mammals.

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