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DDT AND DDE CONCENTRATIONS IN BLOOD OF MEXICAN AMERICANS EXPOSED TO DDT IN MEXICO: THE 1999-2004 NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY.

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Abstract

Concentrations of the pesticide DDT (dichloro diphenyltrichloroethane) and it metabolite DDE (dichloro diphenyldichloroethylene), in the blood of Mexican Americans, born in Mexico, were characterized. The data were derived from the National Health and Nutrition Examination Survey (NHANES) 1999-2004 (unweighted N=648, population estimate=7,490,827). While DDT was banned in Mexico during the year 2000, Mexican Americans who were born in Mexico in 2000 or in prior years and later immigrated to the United States (US) were still likely to have elevated DDT during the NHANES 1999-2004 study period. We sought to identify factors associated with p,p'-DDT and p,p'-DDE concentrations in blood in a population exposed to DDT. The proportion of participants with the isomer p,p'-DDT >0.086 ng/g was highest among women and participants with low acculturation scores, increased with age, and was higher in 1999-2000 than in 2003-2004. In a multiple regression analysis, the concentration of p,p'-DDT was significantly higher among participants who had lived in the US for less than 5 years when compared to those who had been in the US for more than 30 years. Concentrations of p,p'-DDE in blood were also associated with age, survey year, years in the US, and acculturation score in a multiple regression analysis. The decline in DDT and DDE concentrations in blood 3-4 years after the banning of DDT in Mexico in 2000 suggests rapid change is possible once DDT exposure ends. DDT use remains a global public health problem. Economical alternative pesticides are needed before all use of DDT will end.

Key words: DDT (dichlorodiphenyltrichloroethane) DDE (dichlorodiphenyldichloroethylene) Mexican American NHANES (National Health and Nutrition Examination Survey).

INTRODUCTION

DDT was banned in the US in 1972 and banned in Mexico in 2000. The majority of the countries in the world have committed themselves to ending the use of 12 persistent organic pollutants, including DDT, by signing the Stockholm Convention on Persistent Organic Pollutants (United Nations Environment Programme, 2001). However, currently the Stockholm Convention approves DDT for use in 17 countries. For the most part, these exemptions are for malaria control. The countries exempted are: Botswana, Eritrea, Ethiopia, India, Madagascar, Marshall Islands, Mauritius, Morocco, Mozambique, Namibia, Senegal, South Africa, Swaziland, Uganda, Venezuela, Yemen, and Zambia (Stockholm Convention, 2017). Human health consequences of DDT (dichlorodiphenyltrichloroethane) use are thought to include breast cancer, diabetes, decreased semen quality, spontaneous abortion, and impaired neurodevelopment in children (Eskenazi et al., 2009). DDT and its metabolite DDE (dichlorodiphenyldichloroethylene) have half-lives in humans of 6 and 10 years, respectively, and therefore the effects of DDT exposure last for a long time. High concentrations of DDT in serum were found in several studies conducted in Mexico prior

to the banning of DDT there in 2000 (Romieu et al., 2000; Lopez-Carillo et al., 1997; Koepke et al., 2004). Associations of DDT and Type 2 diabetes have been reported in numerous studies and summarized in a meta-analysis (Evangelou et al., 2016). The third tertile of DDT (and its isomer p,p'-DDT) had a summary odds ratio of 2.06 (95% CI 1.05-4.04) for Type 2 diabetes compared to the first tertile, for example. A recent study of Mexican Americans in the 1999-2004 National Health and Nutrition Examination Survey (NHANES), conducted in the United States (US), showed p,p'-DDT >0.086 ng/g to be associated with diabetes (OR = 2.61, 95% CI 1.62-4.22), diabetes without kidney disease (OR = 2.02, 95% CI 1.19-3.44), and with diabetic kidney disease (OR = 4.42, 95% CI 2.23- 8.76) compared to p,p'-DDT <0.086 ng/g (Everett et al., 2017). The purpose of this study was to characterize concentrations of p,p'-DDT and p,p'-DDE in the blood of Mexican Americans, born in Mexico, that were participants in the 1999-2004 National Health and Nutrition Examination Survey. As the time period of the study is 1999-2004 and the youngest participants were born in 1992, all immigrants from Mexico would have likely been exposed to DDT in their lifetime.

MATERIALS AND METHODS

The US National Health and Nutrition Examination Survey (NHANES) 1999-2004 was used to investigate factors related to p,p'-DDT and p,p'-DDE concentrations in the blood of Mexican Americans born in Mexico during the year 2000 or during prior years. Detailed information on the methodology of the NHANES 1999-2004, including laboratory assessment, can be found at the National Center for Health Statistics website (CDC, 2017). The organochlorine pesticide p,p'-DDT, and its metabolite p,p'-DDE, were measured in nonfasting blood samples of a one-third, stratified random, subsample of participants 12 years old or older. We included both teens (12-19 years old) and adults in our sample of Mexican Americans (unweighted N=648, population estimate=7,490,827). High-resolution gas chromatography/isotope-dilution high- resolution mass spectrometry was used to measure p,p'-DDT and p,p'-DDE in serum. The concentrations were expressed per gram of blood, as recommended by Schisterman et al. (2005). Each person had a sample-specific limit of detection. For p,p'-DDT, the maximum limit of detection (MLOD) was 0.086 ng/g. There were 271 participants with p,p'-DDT concentrations above the MLOD, 171 participants with p,p'-DDT concentrations less than or equal the MLOD, but still detectable, and 206 participants with non-detectable p,p'-DDT concentrations. We classified participants' p,p'-DDT levels as >MLOD or <MLOD for analysis of the proportion with elevated p,p'-DDT in blood. For multiple regression analysis, p,p'-DDT measured concentrations for 442 participants were used and non-detectable values, all of which were <0.086 ng/g, set to zero. All of the data for p,p'-DDE were detectable. Factors studied were gender, age, survey year, years in the US and acculturation score. The NHANES visits 15 communities per year, and the data are released every 2 years. The years included in this study were 1999-2000, 2001-2002, and 2003- 2004. Years in the US was classified as: <5 years, 5-30 years, and >30 years. The acculturation score was determined using the Short Acculturation Scale (Marin et al., 1987), a validated five-item Spanish language scale with good internal reliability. The scale consists of the following five questions: • "In general, what language do you read and speak?" • "What was the language(s) you used as a child?" • "What language(s) do you usually speak at home?" • "In which language(s) do you usually think?" • "What language(s) do you usually speak with your friends?" Each question can be answered as "only Spanish," "more Spanish than English," "both equally," "more English than Spanish," or "only English." These responses were scored from 1 to 5 respectively, so that scores ranged from 5-25, with higher scores signifying greater acculturation (Mainous et al., 2006).

Age and acculturation score were analyzed using categories for proportions and as continuous variables for multiple regressions. We used SAS version 9.3 for all analyses (SAS Institute Inc., 2017). The surveyfreq procedure was used for proportions, and the surveyreg procedure used for the multiple regressions. The design of the NHANES is complex and involves stratification, clustering and weighting of the data. Proportions and regressions were calculated using the weights for the organochlorine pesticide subsample. Both minorities and teens were oversampled in the NHANES. A study of Mexican Americans would not have been feasible if this race-ethnicity group had not been oversampled. While 27.8% of all participants in our sample were 12-19 years old, the population estimate, based on the weighted N for this age group was 10.1%. The weighting of the data insures the results apply to the US population (CDC, 2017).

RESULTS AND DISCUSSION

Proportions by gender, age, survey year, years in the US, and acculturation score are given in Table 1. The total sample was 648 Mexican American participants born in Mexico (population estimate = 7,490,827), which differ from the sample used in Everett et al. (2017) due to differences in exclusion criteria in the two studies. The sample in the current study included 180 teens (weighted N = 754,400), 12-19 years old, which represented 10.1% of the total due to the weighting of the data. The NHANES data for years in the US was in 9 categories; we choose to summarize the data in 3 categories following inspection of scatter plots. The proportion that used the Spanish language exclusively, or nearly all Spanish (acculturation score 5-6) was twice that of Mexican, Americans who had been in the US <5 years, indicating it is difficult for these immigrants to learn English.

Table 1. Proportions by gender, age, survey year, years in the US, and acculturation score for Mexican Americans born in Mexico.

	Unweighted N	Population Estimate	Proportion (%)
Gender			
Male	328	4,299,094	57.4
Female	320	3,191,733	42.6
Age (years)			
12-19	180	754,400	10.1
20-39	205	4,180,460	55.8
40-64	182	2,209,570	29.5
≥65	81	346,397	4.6
Survey Year			
1999-2000	226	1,998,101	26.7
2001-2002	238	2,806,844	37.5
2003-2004	184	2,685,883	35.8
Years in the US			
<5	186	2,072,227	27.7
5-30	358	4,667,044	62.3
>30	104	751,556	10.0
Acculturation Score[1]			
5-6	352	4,153,950	55.4
7-15	250	2,898,876	38.7
16-25	46	438,001	5.8
Total	648	7,490,827	100

[1]5=All Spanish, 25=All English

The proportion with elevated p,p'-DDT levels in blood (>0.086 ng/g) varied significantly in 4 out of 5 variables (Table 2). More women had elevated p,p'-DDT than men. The proportion with elevated p,p'-DDT increased with increasing age, with 12-19 year olds having elevated p,p'-DDT in 25.8% of the participants, and those 65 years old and older having 66.4% with elevated p,p'-DDT. The proportion with elevated p,p'-DDT declined in the later years, with those participating in the 1999-2000 NHANES having 48.4% with elevated p,p'-DDT, and those participating in the 2003-2004 NHANES having 23.3% with elevated p,p'-DDT. The results for the acculturation score were striking with those using primarily the Spanish language (acculturation score 5-6) having 46.5% with elevated p,p'-DDT, and those using a considerable amount of English (acculturation score 16-25) having 9.7% with elevated p,p'-DDT.

Table 2. Number of persons and proportion with p,p'- DDT above the maximum limit of detection (MLOD[1]) by gender, age, survey year, years in the US, and acculturation score for Mexican Americans born in Mexico.

	Unweighted N for *p,p'*- DDT >MLOD / Total	Proportion (%) for *p,p'*- DDT >MLOD	*p*-value
Gender			
Male	115 / 328	32.1	0.0063
Female	156 / 320	43.5	
Age (years)			
12-19	52 / 180	25.8	<0.0001
20-39	71 / 205	31.4	
40-64	93 / 182	46.6	
≥65	55 / 81	66.4	
Survey Year			
1999-2000	120 / 226	48.4	<0.0001
2001-2002	100 / 238	41.9	
2003-2004	51 / 184	23.3	
Years in the US			
<5	78 / 186	39.6	0.2043
5-30	136 / 358	34.4	
>30	57 / 104	45.6	
Acculturation Score[2]			
5-6	188 / 352	46.5	0.0003
7-15	78 / 250	27.3	
16-25	5 / 46	9.7	

[1]MLOD=0.086 ng/g.

[2]5=All Spanish, 25=All English.

When we used multiple regression to estimate p,p'-DDT concentrations in blood there were significant results for survey year, years in the US and acculturation score (Table 3). However, the confidence limits for the estimates were wide, and the primary outcome from this analysis was identification of significant factors influencing DDT levels. Mexican Americans included in the 1999-2000 NHANES had 0.419 ng/g (95% CI 0.068-0.770 ng/g) more p,p'-DDT than those included in the 2003- 2004 NHANES, and those included in the 2001-2002 NHANES had 0.282 ng/g (95% CI 0.088-0.477 ng/g) more p,p'-DDT than those included in 2003-2004 NHANES. Unlike the results reported in Table 1, Mexican Americans residing in the US for <5 years had significantly higher p,p'-DDT concentrations (1.007 ng/g, 95% CI 0.388- 1.627 ng/g) than those who had been in the US >30 years. As shown when looking at the proportion with elevated p,p'-DDT, the acculturation score had a significant negative correlation with p,p'-DDT concentration in blood in the multiple regression, indicating those that used more English had less p,p'-DDT in blood than those who used primarily Spanish.

Table 3. Multiple regression using gender, age, survey year, years in the US, and acculturation score to estimate p,p'-DDT in blood of Mexican Americans born in Mexico.

	Estimate for *p,p'*-DDT (ng/g)	Standard Error for *p,p'*-DDT (ng/g)	*p*-value
Intercept	-0.503	0.434	0.2538
Gender			
Male	0.090	0.104	0.3915
Female	0.00	0.00	
Age (years)	0.010	0.006	0.1166
Survey Year			
1999-2000	0.419	0.174	0.0207
2001-2002	0.282	0.096	0.0056
2003-2004	0.00	0.00	
Years in the US			
<5	1.007	0.306	0.0022
5-30	0.287	0.162	0.0850
>30	0.00	0.00	
Acculturation Score[1]	-0.020	0.008	0.0156

[1]5=All Spanish, 25=All English; estimate per unit of acculturation score.

We also used multiple regression to estimate p,p'-DDE concentrations in blood (Table 4). Age in years, run as a continuous variable, was significant as was survey year, years in the US and acculturation score. As the half-life of DDE is 10 years (Eskenazi et al., 2009) it is not surprising that p,p'-DDE is correlated with age in a multiple regression analysis. In a span of 10 years, p,p'-DDE concentration increased by 4.862 ng/g (95% CI 2.897-6.828 ng/g) in our study participants (0.486 ng/g/year X 10 years). Survey year was a significant variable (p for overall regression = 0.0025) in this analysis, but the confidence interval for those included in the 1999-2000 NHANES was too wide (5.325 ng/g, 95% CI -0.270-10.920 ng/g p,p'-DDE), however those included in the 2001-2002 NHANES had 8.276 ng/g (95% CI 3.635-12.917 ng/g) more p,p'-DDE than those included in the 2003-2004 NHANES. Mexican Americans residing in the US <5 years had 17.656 ng/g (95% CI 8.146-27.167 ng/g) more p,p'-DDE, and those residing in the US 5-30 years had 8.530 ng/g (95% CI 2.295-14.766 ng/g) more p,p'-DDE, than those that had lived in the US for >30 years, respectively. Acculturation score had a significant negative association with p,p'- DDE concentration. Mexican Americans who used more English than Spanish (acculturation score = 20) had 7.995 ng/g lower p,p'-DDE concentrations than those who used only Spanish (acculturation score = 5; difference in score X 0.533 ng/g).

Table 4. Multiple regression using gender, age, survey year, years in the US, and acculturation score to estimate p,p'-DDE in blood of Mexican Americans born in Mexico.

	Estimate for *p,p'*-DDE (ng/g)	Standard Error for *p,p'*-DDE (ng/g)	*p*-value
Intercept	-15.594	7.044	0.0329
Gender			
Male	1.576	2.247	0.4874
Female	0.00	0.00	
Age (years)	0.486	0.097	<0.0001
Survey Year			
1999-2000	5.325	2.764	0.0615
2001-2002	8.276	2.292	0.0009
2003-2004	0.00	0.00	

Continued table 4			
Years in the US			
<5	17.656	4.698	0.0006
5-30	8.530	3.080	0.0086
>30	0.00	0.00	
Acculturation Score[1]	-0.533	0.195	0.0096

[1]5=All Spanish, 25=All English; estimate per unit of acculturation score.

Significant relationships between all 5 variables and the proportion with elevated p,p'-DDT (4 variables) or the concentration of p,p'-DDT (3 variables) were found in this sample of Mexican Americans born in Mexico. As DDT was banned in Mexico in the year 2000, the decrease in p,p'-DDT concentrations in the 2003-2004 NHANES indicates that DDT in blood declines rapidly, once exposure to DDT ends. The length of time spent in the US is also a factor, but the use of Spanish as the principal language spoken may be a surrogate for preference for food imported from Mexico, which prior to 2000 would have been contaminated with DDT, particularly dairy products. However, we knew many of these participants were poor (Everett et al., 2017) and unlikely to afford to travel. To test this hypothesis, we computed the proportion below the poverty threshold (US Census Bureau, 2017) by acculturation score category. The proportion below the poverty threshold was 43.9%, 29.9% and 20.5% for those with acculturation scores of 5-6, 7-15, and 16-25 respectively (p=0.0003). Looking specifically at those who primarily used Spanish (acculturation score of 5-6) we found the proportion with elevated p,p'-DDT (>0.086 ng/g) was not associated with being below the poverty threshold (p=0.34). Hence, we rejected the travel to Mexico hypothesis, in favor of the hypothesis that they were likely consuming food and beverage items imported from Mexico. We have stressed that the multiple regression results are primarily useful for identifying significant variables. The R for the p,p'-DDT model was 0.293, and the R for the p,p'-DDE model was 0.354, indicating much of the variation was not explained by these multiple regressions. It would have been helpful if the place of residence in Mexico immediately prior to the participant immigrating to the US was known, but to our knowledge this information is not collected in the NHANES 1999- 2004.

CONCLUSION

Factors associated with DDT and DDE levels in Mexican Americans exposed to DDT in Mexico were identified. While the magnitude of the exposure is evident and disheartening, the decline in DDT and DDE concentrations in blood 3-4 years after the banning of DDT in Mexico in 2000 is encouraging. Countries currently using DDT, such as India, would see similar benefits if the use of DDT were banned. Of special note, the fact DDE has a half-life of approximately 10 years suggests the legacy of DDT exposure will persist even among the youngest participants in our study who would be 25 in 2017. DDT use remains a global public health problem, economical alternative pesticides are needed before all use of DDT will end.

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