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Blood pressure after a heightened pesticide spray period among children living in agricultural communities in Ecuador

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Abstract

Introduction—Agricultural pesticide spray periods increase the pesticide exposure potential of children living nearby and growing evidence indicates that they may affect children's health. We examined the association of time following a heightened agricultural production period, the Mother's Day flower harvest (May), with children's blood pressure (BP).

Methods—We included cross-sectional information of 313 children ages 4-9 years in Ecuadorian agricultural communities (the ESPINA study). Examinations occurred during a period of low flower production, but within 63-100 days (mean= 81.5, SD= 10.9) following the Mother's Day harvest. BP was measured twice using a pediatric sphygmomanometer and BP percentiles appropriate for age, gender and height were calculated.

Results—Participants were 51% male, 1.6% hypertensive and 7.7% had elevated BP. The mean (SD) BP percentiles were: systolic: 51.7 (23.9); diastolic: 33.3 (20.3). There was an inverse relationship between of time after the spray season with percentiles of systolic (difference [β] per 10.9 days after the harvest: −4.3 [95%CI: −6.9, −1.7]) and diastolic BP (β: −7.5 [−9.6, −5.4]) after adjusting for race, heart rate and BMI-for-age z-score. A curvilinear association with diastolic BP was observed. For every 10.9 days that a child was examined sooner after the harvest, the OR of elevated BP/hypertension doubled (OR: 2.0, 95% CI: 1.3, 3.1). Time after the harvest was positively associated with acetylcholinesterase.

Conclusions—Children examined sooner after a heightened pesticide spray period had higher blood pressure and pesticide exposure markers than children examined later. Further studies with multiple exposure-outcome measures across pesticide spray periods are needed.

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Keywords

pesticides; cholinesterase; agriculture; Ecuador; floriculture

Introduction

Children and other community members living within agricultural communities have an elevated risk of exposure to pesticides during pesticide spray seasons (Crane et al. 2013; Krenz et al. 2015; Peiris-John et al. 2005; Quandt et al. 2015; Singleton et al. 2015; Strelitz et al. 2014). This has been shown even among people who do not work in agriculture but reside near crops (Crane et al. 2013; Galea et al. 2015; Suarez-Lopez et al. 2017a; Thompson et al. 2014). These studies have described greater urinary metabolites of pesticides and lower acetylcholinesterase (AChE) activity during the spray season compared to pre-season levels. AChE is a stable marker of exposure to organophosphate and carbamate insecticides (lower values reflect greater exposure).

Organophosphates and carbamates are commonly used insecticides in agriculture which are designed to inhibit the activity of AChE, leading to cholinergic overstimulation of the nervous system (Crane et al. 2013). Alterations of the cholinergic system can induce physiological alterations in the cardiovascular system (Hall 2010). The relationship between pesticides and blood pressure is unclear, with a limited number of studies reporting positive associations between blood pressure and pesticide exposure constructs based either on self-reports or biomarkers (Grandjean et al. 2006; Ledda et al. 2015; Ranjbar et al. 2015; Samsuddin et al. 2016), while some evidence of negative associations has also been described (Suarez-Lopez et al. 2013). Pesticide exposed workers who were regularly involved in mosquito control, had higher (SBP), diastolic blood pressure (DBP), and heart rate than non-exposed workers. (Samsuddin et al. 2016). In a representative sample of U.S. adults, urinary organophosphate metabolite concentrations were positively associated with higher diastolic, but not systolic, blood pressure (Ranjbar et al. 2015). Additionally, a large cross-sectional study of pregnant women in Italy noted increased odds of gestational hypertension among women who reported agricultural or domestic pesticide exposures compared to unexposed pregnant women (Ledda et al. 2015). Positive associations with SBP and DBP were also observed in an experimental study of rats who were exposed to the organophosphate chlorpyrifos (Gordon and Padnos 2000).

Few studies have assessed the health effects of children in relation to a pesticide spray season. In our previous work among Ecuadorian children as part the Secondary Exposure to Pesticides among Children and Adolescents (ESPINA: Estudio de la Exposición Secundaria a Plaguicidas en Niños y Adolescentes [Spanish]), we previously observed that children examined sooner after the Mother’s Day harvest had lower neurobehavioral performance and lower AChE activity compared to children examined later, (Suarez-Lopez et al. 2017b) particularly among children who lived in close proximity to flower plantations (Suarez-Lopez et al. 2017a).

The purpose of this study was to investigate whether blood pressure differed among individuals examined at different points in time after the end of the Mother's Day flower harvest, which marks the end of a period of heightened pesticide use.

Methods

Study Population

The ESPINA study aimed at evaluating the effects of low-dose environmental pesticide exposure on child development. We examined 313 children of 4-9 years of age living in Pedro Moncayo County, Ecuador, a county with one of the highest concentrations of flower plantations per capita worldwide. The industry employs approximately 21% of adults in the county over an approximate production area of 1,800 hectares (Gobierno Municipal del Canton Pedro Moncayo 2011; Suarez-Lopez et al. 2012). To our knowledge, study participants did not work in agriculture or otherwise.

Most participants of the ESPINA study (73%) were enrolled through the 2004 Survey of Access and Demand of Health Services in Pedro Moncayo County, collected by Fundacion Cimas del Ecuador in association with the communities of Pedro Moncayo County. That representative survey obtained information on 71% of the population living in Pedro Moncayo County, Ecuador and measured the height and weight of 33% of children younger than 5 years of age. The remaining 27% of participants were new volunteers also living in Pedro Moncayo County, and were recruited through community announcements performed by community leaders, governing councils, and by word of mouth. The ESPINA study aimed to have a balanced distribution of participants living with floricultural and non-agricultural workers (49% lived with one or more flower plantation workers). The study had the following inclusion criteria: participants who lived with a flower plantation worker had to live with the worker for at least one year. For children not living with agricultural workers, participants must have never cohabited with an agricultural worker, never inhabited a house where agricultural pesticides were stored and have had no history of direct contact with pesticides. The ESPINA study included participants residing in all five parishes of Pedro Moncayo County, and had similar socio-economic and racial distributions as the general population of the county. Detailed participant recruitment information has been described previously (Suarez-Lopez et al. 2012).

Informed consent, parental authorization of child participation, and child assent of participants 7 years of age and older was provided for all study participants. This study was approved by the Institutional Review Boards of the University of Minnesota, the University of California San Diego, Universidad San Francisco de Quito, and the Ministry of Public Health of Ecuador.

Measures

Children were examined between July 10 and August 15, 2008, during the period of lowest flower production of the year, and within 100 days after the estimated end of the peak-flower production period (and pesticide use) associated with the Mother's Day flower production and harvest (5/08/2008). During this 37-day period, examinations took place on 20 weekdays days, averaging 15 participants per day. Exams were conducted in 7 schools distributed across the 5 parishes that make-up Pedro Moncayo County during the summer months, when schools were not in session. Assessments were conducted at seven schools across the five parishes that makeup Pedro Moncayo County during the summer break, when schools were not in session.

In-person interviews of parents and other adults cohabiting with the child were used to obtain information on socioeconomic status, demographics, health, and direct and indirect pesticide exposures of household members. Children's height was measured using a height board, following standard methods (World Health Organization 2008), and weight (standing) was measured using a digital scale (Tanita). Body mass index (BMI)-for-age z-scores were calculated using World Health Organization (WHO) growth standards (World Health Organization Multicentre Growth Reference Study Group 2006).

Resting heart rate was measured by a 30-second auscultation, prior to blood pressure measurement. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured with a pediatric Omron aneroid sphygmomanometer (model BF683W), appropriate for the arm size of the children, following protocols recommended by the American Heart Association (Pickering et al. 2005). Namely, measurements were taken after 3-5 minutes of rest. Children were in a seated position with the antecubital fossa supported at heart level, with uncrossed legs and both feet on the floor. Blood pressure was measured twice, and the averages of the two SBP and DBP values were used in the analyses. Blood pressure percentiles appropriate for age, gender and height were calculated using a normative sample of US children and adolescents (Rosner et al. 2008), using a publicly available program (Rosner 2018). This normative sample was based on the sample of the Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents (National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents 2004), but excluded overweight and obese adolescents. Blood pressure status categories were determined based on the American Academy of Pediatrics cut-offs (normal: SBP and DBP $<90^{th}$ percentile, elevated: SBP or DBP $>90^{th}$ percentile to $<95^{th}$ percentile, hypertension stage 1: SBP or DBP $>95^{th}$ percentile to $<95^{th}$ percentile + 12 mm Hg, hypertension stage 2: SBP or DBP $>95^{th}$ percentile +12 mm Hg) (Flynn et al. 2017). It is worth noting that the prevalences of blood pressure status categories presented in this paper are based on a cross-sectional assessment and do not necessarily reflect a clinical diagnosis. It is recommended that multiple blood pressure measurements over time be obtained prior to establishing a diagnosis of hypertension (Flynn et al. 2017).

Erythrocytic AChE activity and hemoglobin concentration were measured from a single finger stick sample using the EQM Test-mate ChE Cholinesterase Test System 400, AChE Erythrocyte Cholinesterase Assay Kit 470 (EQM, Cincinnati, OH).

Distance from the participants' homes to the nearest flower plantation was measured using portable global positioning system receivers. We used geographical coordinates of Pedro Moncayo County homes that were collected in 2004, 2006 and 2010 by Fundación Cimas del Ecuador as part of the System of Local and Community Information (Sistema de

Información Local y Comunitario). Flower plantation edges (areal polygons) were measured and noted by geographical coordinates for each corner of the plantation's perimeter. The distance from each participant's home was calculated to the nearest 1-meter segment of the flower plantation perimeter using ArcGIS 9.3 (Esri, Redlands, CA).

To include most children in multivariable analyses, we imputed missing information for race and residential distance to the nearest flower plantation. Residential distance to the nearest flower plantation was imputed for three participants from a random selection of values generated from a random normal distribution based on the concurrent ESPINA mean ± standard deviation (SD) values. For race, we created a "missing" race category to account for 14 children with missing information. Because only five children in this study were white and two were black, we incorporated these seven children in the mestizo (mix of white and indigenous) category to improve model stability when adjusting for race. The present analyses include the information of 310 children who had information for all variables of interest.

Statistical Analysis

We calculated the means and standard deviation (SD) or proportion of participant characteristics, as appropriate, for all participants and stratified across tertiles of time after the Mother's Day flower harvest in which the examination took place. Time after the Mother's Day harvest was calculated as the number of days between the approximate end of the Mother's Day flower harvest (5/08/2008, 00:00 am) and the date and time of the beginning of the examination. We calculated the p-value for trend (p-trend) for participant characteristics across levels of examination time after the harvest activity using linear regression and modeling time after the harvest as a continuous variable.

The associations of time after the Mother's Day harvest with blood pressure were analyzed using three multiple linear regression models defined a-priori. Model 1 adjusted for a small number of potential confounders including age, gender, race and heart rate. Model 2 further adjusted for height and BMI-for-age z-score, considering the positive associations of these with blood pressure among children (Freedman et al. 2012; He et al. 2000; Hosseini et al. 2010; Regnault et al. 2014). Considering that blood pressure percentiles appropriate for age, gender and height were calculated, the adjustment models for these outcomes do not include age, gender or height. A third adjustment model was conceived as a mediation model, which further adjusted model 2 for two constructs of pesticide exposure including residential distance to the nearest flower plantation (Suarez-Lopez et al. 2017a), and AChE activity (Suarez-Lopez et al. 2012). Mediation by cohabitation with floricultural workers was considered but later removed as we had previously observed that children living with flower plantation workers had lower BP (Suarez-Lopez et al. 2013) and after including it in the model the estimates were unchanged. As a standard practice, all models were adjusted for hemoglobin concentration because variations in hematocrit can alter the values of erythrocytic AChE activity (EQM Research Inc. 2003). We calculated the coefficient of determination (R^2) based on Pearson's correlation coefficient. We then plotted the model 2-adjusted least-squared means and 95% CI of blood pressure percentiles and blood pressure for each sextile of time after the harvest . Additionally, we tested for curvilinear associations by modeling time after the harvest as a quadratic variable (time * time).

Using logistic regression, we calculated odds ratios (OR) and 95% confidence intervals (95% CI) for prehypertension or hypertension combined (vs normotension) for tertiles 1-3 of time after the harvest compared to tertile 4. We combined prehypertension and hypertension given the low prevalence of hypertension in this cohort (see results). The same adjustment models were used in these analyses.

We assessed effect modification by age, sex and BMI-for-age z-score sex and by home distance to the nearest flower plantation. The latter was observed to be an effect modifier in the association between time after the Mother's Day harvest and AChE activity (Suarez-Lopez et al. 2017a). We tested statistical significance of interaction terms ($X\beta_{predictor}$ * $X\beta_{effect\ modifier}$) within models 1 and 2. We then analyzed the associations stratified by categories of the significant effect modifiers. Analyses were conducted using SAS Version 9.4 (SAS Institute Inc., Cary, NC)

Results

Participant Characteristics—Child participants had a mean age of 6.6 years (SD:1.6); 51% were male, 73% mestizo, 21% indigenous, and 49% lived concurrently with at least one floricultural worker. The mean (SD) percentiles for SBP and DBP were 51.7 (23.9) and 33.3 (20.3), respectively. Children were examined between 63 and 100 days after Mother's Day harvest (mean: 85 days, SD: 10.9). Children examined earlier in the examination period (sooner after the end of the Mother's Day harvest) were younger, shorter and more like to live with a floricultural worker compared to children examined later (Table 1). Hemoglobin concentration and AChE activity were both positively associated with examination date. The prevalences of elevated blood pressure and hypertension stage 1 were 1.6% (n=5) and 7.7% (n=24), respectively. No participants were classified as having hypertension stage 2. Participant characteristics are listed in Table 1.

Time after the Mothers' Day harvest and blood pressure

Time after the harvest was negatively and statistically significantly associated with measures of SBP and DBP in all 3 models. In model 2, the differences of SBP and DBP percentiles per 10.9 days (one SD) after the harvest (β) were: −4.3 (95% CI: −6.9, −1.7) and β:−7.5 (95% CI: −9.6, −5.4, Table 2). Corresponding negative associations with SBP and DBP were also observed (Table 2). There was evidence of curvature on the association between time after the harvest and DBP and DBP percentile in all models as observed with the statistically significant quadratic β coefficients. Figure 1 depicts the associations of time after the harvest with SBP and DBP for model 2, and Figure 2 depicts the associations with SBP and DBP percentiles.

The associations in the mediation model, which accounted for 2 pesticide exposure constructs (residential distance to the nearest flower plantation and AChE activity), were minimally stronger for SBP measures but unchanged for DBP measures. There was no evidence of effect modification by age, gender, BMI-for-age z-score, residential distance to the nearest flower crop.

In multivariate models of the combined outcome of elevated blood pressure, or hypertension stage 1 or stage 2 , we observed that for every SD (10.9 days) decrease in time after the harvest there were significantly increased ORs in all 3 models (model 2 OR: 2.0, 95% CI: 1.3, 3.1). The associations were strongest for model 2, and weakest in mediation Model 3 as hypothesized (Table 3). When time after the harvest was analyzed as tertiles, substantial ORs were observed (3.2, 95% CI: 1.2, 9.3 in model 2, Table 3) when comparing children examined between 63-81 days after the harvest (tertile 1) with children examined between 91 and 100 days (tertile 3). As expected, weaker associations were observed in participants examined in tertile 2 (82 – 91 days) vs tertile 3 (OR: 1.2, 95% CI: 0.4, 3.9). The associations using the mediation model weakened and became non-significant, as hypothesized (OR for tertile 1 vs 3: 2.6). Of the constructs of pesticide exposure, AChE activity accounted for most of the weakening of the association in the mediation model. Model 2 further adjusted for AChE and hemoglobin yielded an OR per SD decrease in time after the harvest of 1.83 (95% CI: 1.17, 2.84), whereas model 2 further adjusted for residential distance to flower crops yielded an OR of 1.88 (95% CI: 1.20, 2.94) which is closer to that of model 2 alone.

Time after the Mothers' Day harvest and heart rate

Time after the Mother's Day harvest was not associated with heart rate in any of the models. In model 2 the difference of heart rate per 10.9 days after the harvest was 0.34 beats per minute (95% CI: −0.97, 1.64). There was no evidence of curvilinear associations or effect modification by age, gender, BMI-for-age z-score, residential distance to the nearest flower crop.

Discussion

Our findings suggest that pesticide exposures, as a result of a peak pesticide use period in floriculture, may result in short-term alterations in both systolic and diastolic blood pressure among children living in agricultural communities. We observed that children examined sooner after the harvest had lower AChE activity (reflecting greater exposure to cholinesterase inhibitor pesticides in this context) and higher SBP and DBP than children examined later during a period of decreased flower production. These inverse associations between time and blood pressure continued through 100 days after the Mother's Day harvest. In this setting, these findings expand the body of evidence documenting physiological and neurobehavioral alterations in children associated a peak pesticide-use period (Suarez-Lopez et al. 2017b, 2017a).

Peak pesticide spray seasons have been found to be associated with statistically significantly lower cholinesterase activity and higher urinary metabolites of pesticides among agricultural worker and non-agricultural worker children (Crane et al. 2013; Thompson et al. 2014). Potential pathways of exposure of non-worker children associated with pesticide spray seasons include increased off-target drift of pesticides onto nearby homes, schools and playgrounds, in addition to increased introduction of pesticides into homes by agricultural workers.

In our study population, we previously observed that the children's pesticide exposure related to the Mother's Day harvest did not appear to be influenced by cohabitation with a flower plantation worker (e.g. introducing pesticide contaminated clothing, tools, etc.) but rather by off-target pesticide drift onto nearby homes, particularly if they live near a flower crop (Suarez-Lopez et al. 2017a). While we did not observe effect modification by residential distance to flower crops or cohabitation with a flower plantation worker on the associations between time after the harvest and blood pressure, we did observe that the reported associations were partially mediated by residential distance to crops. For instance, most of the attenuation of the associations between time after the harvest and OR for hypertension or prehypertension, resulted from adjusting for residential distance to plantations and AChE activity (Table 3), whereas cohabitation with a flower worker had a negligible effect on the estimate (data not shown).

The present findings concur with our previous observations that residential proximity to flower plantations and higher areas of flower plantations near homes were associated with higher SBP in children (Suarez-Lopez et al. 2018). Interestingly, we have also reported positive associations between AChE activity and blood pressure in children of the ESPINA study (Suarez-Lopez et al. 2013). This, in addition to the positive association between time after the harvest and AChE activity, possibly explain why adjustment for AChE activity in the mediation analysis using the linear variables of time and blood pressure resulted in a stronger association. This divergence of associations with blood pressure across exposure constructs within the same study population may be due to the influence of different classes of pesticides. AChE activity is a marker of exposure to cholinesterase inhibitors, whereas time after a peak-spray season and residential distance to flower plantations are indicators of pesticide drift for many classes of pesticides. Floriculture in Pedro Moncayo county actively uses many classes of fungicides, insecticides and herbicides (Harari 2004; Suarez-Lopez et al. 2017a). In fact, 23 different cholinesterase inhibitor insecticides and over 50 fungicides, in addition to pyrethroid and neonicotinoid insecticides, were reported to be used (Suarez-Lopez et al. 2017a). Although information of other pesticides are non-existent, the cholinesterase inhibitor exposure levels that children in Pedro Moncayo County are subjected to may not be very different from those of similar communities in the USA and other developed countries (Barr et al. 2003; Grandjean et al. 2006; Higgins et al. 2001; Suarez-Lopez et al. 2013, 2012).

Our findings agree with the few existing studies on the relationship between pesticide exposures and blood pressure. In rats, increased doses of organophosphate insecticides led to prolonged systolic and diastolic pressure elevation (Gordon and Padnos 2000; Smith and Gordon 2005). In humans, persistently exposed male workers involved in mosquito control were found to have an increased prevalence of higher brachial and aortic blood pressure, increased heart rate and increased oxidative stress markers compared to unexposed workers (Samsuddin et al. 2016). Similarly, adults with detectable levels of the organophosphate metabolites (dimethylphosphate, diethylphosphate, and diethyldithiophosphate) had higher diastolic blood pressure, lower high-density lipoprotein cholesterol and higher triglyceride levels compared to people with non-detectable levels in a representative survey of the United States of America (USA) (Ranjbar et al. 2015). Among pregnant women in Italy, the incidence of gestational hypertension was twice as high among women occupationally exposed to pesticides (12%) compared to those who had indirect or domestic exposures (6% and 7% respectively), and four times greater than the incidence among unexposed women (4%) (Ledda et al. 2015). Furthermore, statistically significant increased odds ratios for gestational hypertension were observed with self-reports of exposure to diazinon (OR= 1.09) and malathion (OR= 1.14) compared to unexposed women. In the same source population as our study, a pilot study found that maternal occupational pesticide exposure while pregnant was associated with significantly increased systolic blood pressure in children ages 6-8 (Harari et al. 2010). However, concurrent exposures to pesticides were not associated with blood pressure in that study. Research is needed to understand how various classes of pesticides such as fungicides, herbicides, neonicotinoids, pyrethroids and others may affect the cardiovascular system.

From the toxicological perspective of cholinesterase inhibitors, the inhibition of AChE activity by organophosphates results in heightened cholinergic stimulation of muscarinic and nicotinic receptors in the central and peripheral nervous systems (Taylor 2011). The overstimulation of nicotinic receptors can result in increases in blood pressure and heart rate (Hung et al. 2015; Roberts and Karr 2012). Neonicotinoid insecticide exposures also lead to overstimulation of nicotine receptors; however, human studies are lacking on their associations with hemodynamic constructs such as blood pressure. The potential mechanisms of increased blood pressure of these and other classes of pesticides is a topic for further research.

A limitation of our study is its cross-sectional design in which we measured blood pressure at a single point in time for each child. The ESPINA study in 2008 was not designed to assess health effects of pesticide spray periods; however, the short examination period in 2008, which occurred relatively soon after the Mother's Day harvest, made these analyses possible. Conducting blood pressure assessments before, during and after a peak pesticide spray season is difficult in this population because the heightened pesticide-use periods start at approximately October/November and remain relatively high until early May. Nonetheless, studies assessing blood pressure measures before, during and after a pesticide spray season are needed.

Limitations of this study also include our inability to account for factors plausibly related to blood pressure such perinatal health history, concurrent and previous dietary patterns (e.g., salt and fat consumption), etc. We do, however, account for heart rate, age, height and BMI. Another limitation is our inability to discern which pesticides may be driving the observed associations. Although a growing number of pesticides can be quantified in urine, accurate methods to quantify many other pesticides, including most fungicides and herbicides, have not been developed. AChE activity is a biomarker of exposure that reflects a physiological change associated with cholinesterase inhibitor exposures. It has lower sensitivity to exposure than measurements of pesticides or pesticide metabolites in bio-specimens; however, it is also a more reliable (lower within individual variability) indicator of cholinesterase inhibitor exposure (Lefkowitz et al. 2007; Griffith et al. 2011; Bradman et al. 2013) and provides a much wider exposure window than bio-specimen quantification (mean of 82 days, 95% CI: 72-98 days) (Mason 2000).

The concomitant use of a variety of chemicals in agriculture, including substances for stimulating plant growth or pesticides is a challenge for understanding of the role of specific environmental pollutants on health. In this regard, pesticide exposure constructs such as time after the end of a known exposure period or residential proximity to plantations provide valuable exposure information that crudely accounts for a mixture of exposures. As a result, this study prompts the need to further study the role of agrochemicals on hemodynamic markers in children.

This is one of the largest studies to date to estimate the associations between a known pesticide exposure period and physiological changes in children. Our logistical approach to participant examination allowed us to measure blood pressure on 20 different days (once per participant) within 100 days from Mother’s Day harvest, averaging 15 participants per time point. The well-established partnerships and ongoing community involvement that we have developed in Pedro Moncayo County resulted high participation rates, fast recruitment and examination of participants. This allowed us to have approximations of seasonal changes in blood pressure, although with cross-sectional data. Further research is needed to assess the associations of pesticide spray seasons on the health of children living in agricultural communities.

Conclusions

We observed that children examined sooner after a peak pesticide-use period had higher systolic and diastolic blood pressures and lower AChE activity compared to children examined later during a period of moderate or low pesticide use. This suggests that pesticide spray seasons increase the pesticide-exposure potential of young children who do not work in agriculture, but also that such exposures may lead to short-term increases on blood pressure. These findings, although cross-sectional, build on a growing number of studies that have characterized subacute effects of pesticide exposures. Studies with repeated exposure and outcome measures before, during and after pesticide spray seasons are needed.

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Highlights

- We assessed blood pressure (BP) in children examined after a pesticide spray period
- BP was higher in children examined sooner (vs later) after the pesticide spray period
- Elevated odds of hypertension/prehypertension were present in those examined sooner
- Time after the spray season was positively associated with acetylcholinesterase

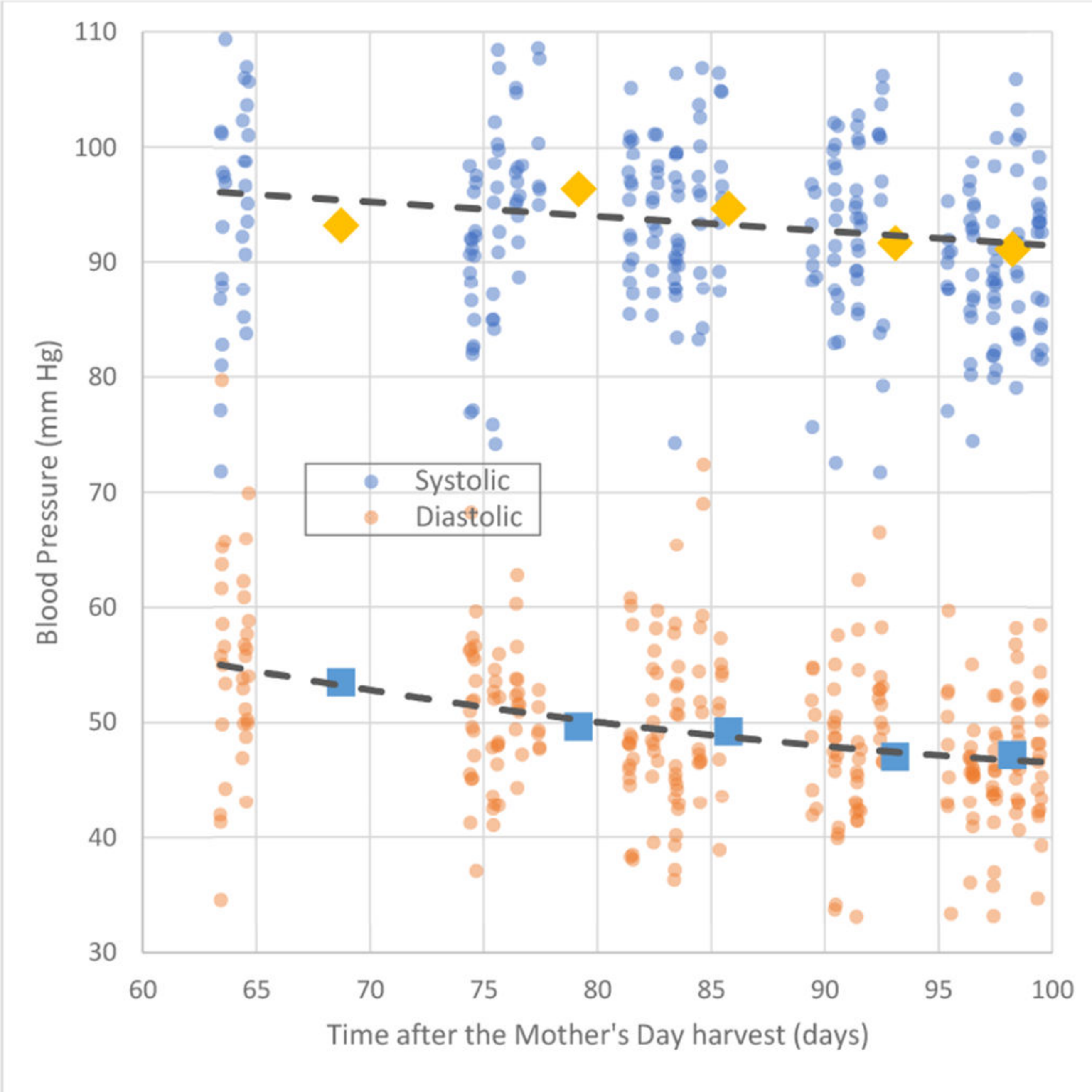

Figure 1.

Adjusted associations between time after a peak pesticide use period (the Mother's Day Flower Harvest) and blood pressure in children (n=310).

Adjusted for: age, gender, race, height, heart rate and BMI-for-age z-score (Model 2).

Systolic slope= β: −1.4 mmHg (95% CI: −2.2, −0.6); R^2= 0.26

Diastolic slope= β: −16.6 mmHg + $\beta_{quadratic}$: 0.93 mmHg, 95% CI for $\beta_{quadratic}$: (0.18, 1.67); R^2= 0.27

Blue and orange circles are adjusted individual systolic and diastolic blood pressure values, respectively. Diamonds and squares are systolic and diastolic blood pressure means for each sextile of time, respectively. The dashed line is the slope of the adjusted linear regression model.

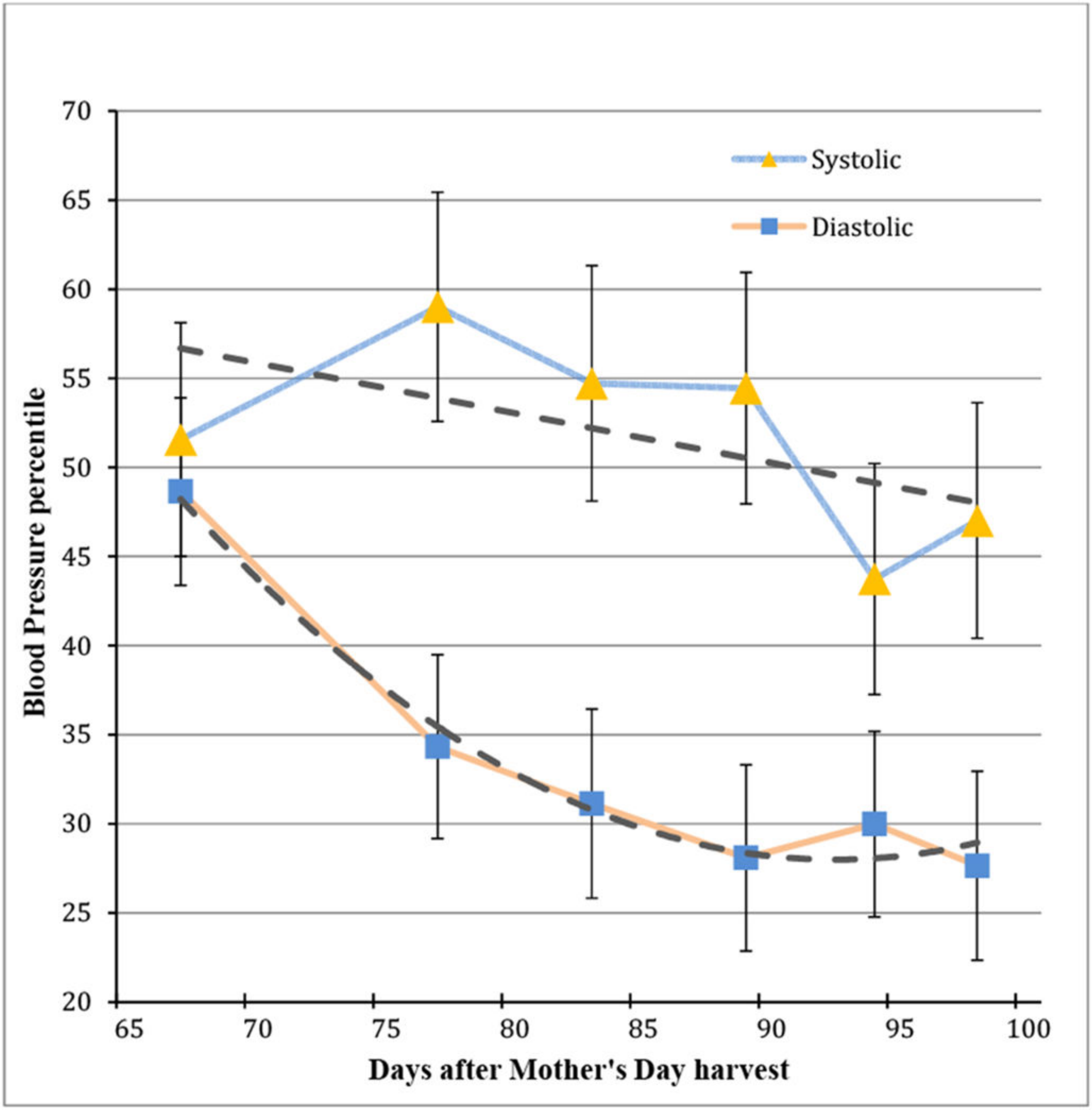

Figure 2:

Adjusted association between time after a peak pesticide use period (the Mother's Day Flower Harvest) and blood pressure percentiles in children (n=310)

Adjusted for: race, heart rate and BMI-for-age z-score (Model 2).

Systolic slope= β: −4.3 (95% CI: −6.9, −1.7); R^2= 0.05

Diastolic slope= β: −54.8 + $\beta_{quadratic}$: 3.11, 95% CI for $\beta_{quadratic}$: (−0.92, 5.30); R^2= 0.19

Triangles and squares are the adjusted blood pressure percentiles for systolic and diastolic blood pressure across each sextile of time after the Mother's Day harvest, respectively. Error bars represent 95% CI for each sextile. The dashed line is the slope of the adjusted linear regression model. Lines between sextiles were added for visual purposes. Individual data points are not plotted due to substantial overlap between diastolic and systolic blood pressure percentiles.

Table 1:

Participant characteristics across tertiles of days; N=310

	Days after Mother's Day harvest (tertiles)[a]			
	1st	**2nd**	**3rd**	**P-Trend**
N	**103**	**104**	**103**	
Range (days)	**63.4-81.4**	**81.5-91.4**	**91.5-99.6**	
Age (years)	6.2 (1.5)	6.7 (1.6)	6.8 (1.7)	0.01
Sex, male	47	56	51	0.84
Race, mestizo	86	60	83	0.84
Race, indigenous	12	36	17	0.76
Heart Rate (bpm)	85.5 (11.7)	84.1 (14.0)	85.0 (11.9)	0.59
BMI-for-age Z-score (SD)	0.27 (0.88)	0.53 (0.70)	0.24 (0.75)	0.62
Height (cm)	111.1 (9.5)	111.0 (9.9)	114.3 (11.1)	0.02
Home distance to nearest flower plantation (m)	516.3 (438)	325.1 (250)	505.9 (299)	0.11
Hemoglobin (g/L)	12.3 (1.1)	12.7 (1.2)	12.9 (1.0)	<0.01
Acetylcholinesterase (U/mL)	3.02 (0.47)	3.12 (0.52)	3.27 (0.44)	<0.01

Table entries are percentage or mean (SD)

[a]Days after Mother's Day harvest mean (SD): 85 days (10.9)

Table 2.

Linear associations between time after a peak-pesticide spray period (the Mother's Day flower harvest) and blood pressure in children.

	Blood pressure difference per SD[*] of time after the harvest (β, 95% CI)		
	Model 1	**Model 2**	**Model 3**
SBP, mmHg	−1.3 (−2.2, −0.5)	−1.4 (−2.2, −0.6)	−1.6 (−2.4, −0.7)
DBP, mmHg	−2.4 (−3.2, −1.7)[a]	−2.5 (−3.2, −1.8)[b]	−2.4 (−3.2, −1.7)
SBP percentile[**]	−4.3 (−6.9, −1.6)	−4.3 (−6.9, −1.7)	−5.5 (−8.2, −2.8)
DBP percentile[**]	−7.5 (−9.5, −5.4)[c]	−7.5 (−9.6, −5.4)[d]	−7.5 (−9.7, −5.3)[e]

[*] SD: 10.9 days

[**] blood pressure percentiles appropriate for age, gender and height

[a] β: −17.1 mmHg + $\beta_{quadratic}$: 0.96 mmHg, 95% CI for $\beta_{quadratic}$: (0.21, 1.72)

[b] β: −16.6 mmHg + $\beta_{quadratic}$: 0.93 mmHg, 95% CI for $\beta_{quadratic}$: (0.18, 1.67)

[c] β: −51.0 + $\beta_{quadratic}$: 2.86, 95% CI for $\beta_{quadratic}$: (0.68, 5.04)

[d] β: −54.8 + $\beta_{quadratic}$: 3.11, 95% CI for $\beta_{quadratic}$: (−0.92, 5.30)

[e] β: −53.4 + $\beta_{quadratic}$: 2.99, 95% CI for $\beta_{quadratic}$: (0.25, 5.73)

Associations were estimated using linear regression.

Model 1 for SBP: age, gender, race, heart rate

Model 1 for SBP percentile: race, heart rate

Model 2 for SBP: model 1 + height and BMI-for-age z-score

Model 2 for SBP percentile: model 1 + BMI-for-age z-score

Model 3 (mediation): model 2 + residential distance to nearest flower plantation, AChE activity and hemoglobin

Table 3.

Odds ratios for elevated blood pressure, hypertension stage 1 or hypertension stage 2* associated with time after the Mother's Day harvest.

	Time after the Mother's Day Harvest and OR (95% CI)		
	Per SD decrease**	**Tertile 1 vs 3**	**Tertile 2 vs 3**
Model 1	1.95 (1.28, 2.97)	3.26 (1.14, 9.34)	1.28 (0.41, 3.97)
Model 2	2.01 (1.31, 3.08)	3.22 (1.12, 9.28)	1.23 (0.39, 3.90)
Model 3	1.76 (1.11, 2.80)	2.63 (0.87, 7.92)	1.32 (0.41, 4.31)

*Blood pressure cut-offs appropriate for age, gender and height.

**SD: 10.9 days

Days after Mother's Day harvest tertile ranges - Tertile 1: 63.4-81.4, Tertile 2: 81.5-91.4, Tertile 3: 91.4-99.6.

Associations were estimated using logistic regression.

Model 1: age, gender, race, heart rate

Model 2: model 1 + height and BMI-for-age z-score

Model 3 (mediation): model 2 + residential distance to nearest flower plantation, AChE activity and hemoglobin