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A Longitudinal Approach of Assessing Urban and Suburban Children's Exposure to Pyrethroid Pesticides

Lu C[1], Barr D[2], Pearson M[1], Bartell S[1], Bravo R[2]

[1] Department of Environmental and Occupational Health, Rollins School of Public Health, Emory University, Atlanta, GA, USA.

[2]National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, GA, USA.

Corresponding author

Chensheng Lu
1518 Clifton Road, NE
Atlanta, GA 30322
(404)727-2131, (404)727-8744 (fax)
clu2@sph.emory.edu

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Abbreviations:

CDC, Center for Disease Control and Prevention
CPES-WA, Children Pesticide Exposure Study-Washington
DBCA, *cis*-2,2-(dibromo)-2-dimethylvinylcyclopropane carboxylic acid
cis-DCCA, *cis*-2,2-(dichloro)-2-dimethylvinylcyclopropane carboxylic acid
trans-DCCA, *trans*-2,2-(dichloro)-2-dimethylvinylcyclopropane carboxylic acid
DVWA concentration, daily volume-weighted average concentration
FPBA, 4-fluoro-3-penoxybenzoic acid
FQPA, Food Quality Protection Act
LOD, limits of detection
OP, Organophosphorus pesticide
PBA, 3-penoxybenzoic acid
USEPA, United State Environmental Protection Agency
USDA, United State Department of Agriculture
NCEH, National Center for Environmental Health

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Outline of section headers

Abstract

We conducted a longitudinal study to assess 23 elementary school-aged children's exposure to pyrethroid pesticides using urinary pyrethroid metabolites as exposure biomarkers. We substituted most of children's conventional diets with organic food items for five consecutive days and collected two daily spot urine samples, first morning and before bedtime voids, throughout the 15-day study period. Urine samples were analyzed for five common pyrethroid metabolites. We found an association between the parents' self-reported pyrethroid use in the residential environment and elevated pyrethroid metabolite levels found in their children's urine. Children were also exposed to pyrethroids through their conventional diets, although the magnitude is smaller than the residential exposure. Children's ages appear to be significantly associated with pyrethroids exposure, which is likely attributed by the use of pyrethroids around the premise or in the facilities where older age children engaged in the outdoor activities. We conclude that residential pesticide use represents the most important risk factor for children's exposure to pyrethroid insecticides. Because of the wide use of pyrethroids in the U.S., the findings of this study are important from both the children's pesticide exposure assessment and the environmental public health perspective.

INTRODUCTION

Pyrethroids, a group of synthetic insecticides, were manufactured in the 1970s after the removal of organochlorine insecticides, such as DDT, from the consumer market. The synthetic pyrethroids not only inherit the biological activity (ability to kill insects) from their natural counterpart, pyrethrin, which is found in chrysanthemums, but also improve their environmental stability. Pyrethroids are widely used in agriculture, forest, textile industry, and public health programs worldwide (Heudorf and Angerer, 2001). With the phase-out of organophosphorus (OP) pesticide use in residential environments in the U.S. (U.S. EPA 1998), the availability of pyrethroids for consumer uses has increased since the late 1990s (U.S. EPA 2005).

Although individual pyrethroid insecticides share some common physical and chemical properties as a group, unlike OP pesticides, their toxicological mechanisms vary in mammals. Pyrethroid insecticides are subject for review as potential developmental neurotoxicants because of their mode of action on voltage-sensitive sodium channels (Shafer et al. 2005). In addition, permethrin, the most widely used pyrethroid insecticide, is suspected as an endocrine disrupting chemical (Chen et al. 2002; Kakko et al. 2004; Kim et al. 2004) and, along with fenvalerate, has been classified as a potential carcinogen at high exposure levels (U.S. EPA 1989). Toxicological studies have also suggested that pyrethroids have a suppressive effect on the immune system and may cause lymph node and spleen damage (Repetto 1996).

Although pyrethroids have been sold in the U.S. consumer market for more than 30 years with the estimated annual use ranging from several thousands to a million

pounds (ATSDR 2003), very few studies have been conducted to quantitatively assess human exposures to pyrethroids. Most of the relevant data were obtained from studies conducted in Germany or in occupational settings (Hardt and Angerer 2003; Leng et al. 2003). Recently, the Center for Disease Control and Prevention reported urinary pyrethroid metabolite levels for the U.S. population aged 6-59 years in the Third National Report on Human Exposure to Environmental Chemicals, which is part of the National Health and Nutrition Examination Survey (NHANES) conducted in 2001-2002 (CDC 2005). All of these studies were conducted cross-sectionally, and therefore, the results only represent exposures over relatively short time periods.

The primary objective of this study was to establish a temporal profile of pyrethroid exposure in a cohort of elementary school-aged children living in an urban/suburban community using urinary pyrethroid metabolites as exposure biomarkers. We also examined the relationship between pyrethroid exposure and children's diets, self-reported residential pyrethroid use, and age.

METHODS

This study is part of the Children's Pesticide Exposure Study (CPES-WA), which took place in Seattle, Washington area from July 2003 to May 2004. Details of the study design and methods have been published previously (Lu et al. 2006). In brief, 23 children ages 3-11 years were recruited from local public elementary and Montessori schools for a 15-consecutive-day sample period in summer 2003, with repeated samplings in fall 2003, and in winter and spring 2004. This report only discusses results of urinary pyrethroid metabolites for the summer 2003 sampling period. Results from

other sampling periods will be reported when they become available. Subject eligibility for enrollment included children exclusively consuming conventional diets and spending most of their time in one residence. Household pesticide use information was obtained via an in-person interview during an in-home appointment prior to the field sampling. Written consent was obtained from parents and older children who can read the consent form, whereas oral assent was obtained from younger children. The University of Washington Human Subject Committee approved the use of human subjects in this study.

Sampling period

As previously reported (Lu et al. 2006), the 15-consecutive-day sampling period was divided into 3 phases. During phase 1 (day 1 to 3) and phase 3 (day 9 to 15), children consumed their normal conventional diets. During phase 2 (day 4 to 8), organic food items, including fresh fruits and vegetables, juices, processed fruit or vegetables (e.g. salsa), and wheat- or corn-based items (e.g. pasta, cereal, popcorn or chips), were substituted for the children's conventional diet. These food items are routinely reported to contain pesticide residues (USDA 2003). Meats and dairy products were not substituted.

Urine sample collection and analysis

For 15 consecutive days, the first morning void and last void of the day was collected from each child. These urine samples were refrigerated or maintained on ice prior to processing in the lab and then stored at -20°C until pesticide metabolite analysis was performed in the National Center for Environmental Health (NCEH) at the Centers for Disease Control and Prevention (CDC) in Atlanta, GA using a liquid

chromatography/ tandem mass spectrometry method (Olsson et al. 2004). The targeted metabolites for pyrethroids included 3-penoxybenzoic acid (PBA), 4-fluoro-3-penoxybenzoic acid (FPBA), *cis*-2,2-(dichloro)-2-dimethylvinylcyclopropane carboxylic acid (*cis*-DCCA), *trans*-2,2-(dichloro)-2-dimethylvinylcyclopropane carboxylic acid (*trans*-DCCA), and *cis*-2,2-(dibromo)-2-dimethylvinylcyclopropane carboxylic acid (DBCA). Kuhn et al. (1999) has demonstrated the relationship of chemical structures between common pyrethroids and their urinary metabolites. The limits of detection (LOD) for the metabolites of pyrethroids insecticides are listed in Table 1.

Data analysis

For data analysis purposes, the reported concentrations were used for samples with detectable (>LOD) or detectable but not quantifiable (<LOD) levels, whereas "0" was assigned for samples where nothing was detected. The daily volume-weighted average (DVWA) of pyrethroids metabolites was calculated by averaging the metabolite concentration in the morning sample with the previous day's bedtime sample normalized by the total volume of these two urine samples (Lu et al. 2006). In cases where only one of the two spot urine samples was collected, the metabolite concentration of the collected sample was used as the DVWA concentration. Urinary concentrations of pyrethroid metabolites were not adjusted by creatinine or specific gravity.

Because the pyrethroid urinary metabolite concentrations were skewed and subject to detection limits, one half of the LOD for each of the pyrethroid metabolites was added to all the respective measured urinary metabolite concentrations before log-transformation. Parametric tests were therefore used for statistical analyses using SPSS 11 (SPSS Inc., Chicago, IL). A linear mixed effects model was used to test the

associations with diet and self-reported residential use of pyrethroid pesticides, which represents the primary risk factors for children's exposure to pyrethroid pesticides. In addition, age was included in the expanded model to determine whether children's age also influenced pyrethroid exposure.

RESULTS

The frequency of detection for the different urinary pyrethroid metabolites varied (Table 1). The most frequently detected pyrethroid metabolite was PBA, a non-specific urinary metabolite for many pyrethroid insecticides (Heudorf and Angerer 2001), such as permethrin, cypermethrin, and deltamethrin, followed by *trans*- and *cis*-DCCA, two urinary metabolites for permethrin, cypermethrin, and cyfluthrin. Very few urine samples had detectable levels of FPBA and DCBA, specific metabolites for cyfluthrin and deltamethrin, respectively.

Table 2 shows the descriptive statistics of the DVWA concentrations for the five urinary pyrethroid metabolites. In parallel to the frequency of detection, PBA has the highest median DVWA level followed by *trans*-DCCA. Since the majority of urine samples had non-detectable levels for *cis*-DCCA, FPBA, and DCBA; their data were not included in statistical analyses. The concentration ratios of *cis*- and *trans*-DCCA, which range from 0.3 to 0.6, correspond to the isomer content of pyrethroid pesticides in most consumer products. For example, the content of permethrin in most commercial products contains either 1:3 or 2:3 of the *cis*- and *trans*-isomer.

Upon visual inspection of the box-plots of the DVWA pyrethroid metabolites in the 23 children during the 15-day study period, no apparent trend due to the dietary

intervention, as was seen for OP pesticides (Lu et al. 2006), can be identified. Many urine samples collected during the organic diet period continue to have detectable levels of all five pyrethroid metabolites. However, when children are grouped by whether or not pyrethroids are used in their household, we found that children of families who used pyrethroids had higher and more variable DVWA PBA and *trans*-DCCA levels than those not using pyrethroids at home (Figure 1A and 1B). Although the detection of FPBA and DBCA in this cohort was rare and the levels were generally low, it is evident that the majority of these exposures were associated with residential use of pyrethroids (Figure 1C and 1D).

Seven of the 23 families reported and were confirmed to use pyrethroid pesticides in their households, both inside and outside the homes (Table 3). Four of the 7 families had an older child (age 8 or above) who participated in this study. Urine samples collected from these seven children routinely contained detectable pyrethroid metabolites levels, and among those urine samples, several of them had the highest concentrations of pyrethroid metabolites. The majority of detectable FPBA and all the detectable DBCA urine samples were collected from these seven children.

Results from the linear mixed effects model (Table 4) demonstrated that both residential pyrethroid use and diet are significant contributors to both PBA and *trans*-DCCA levels in the urine. It is evident from this model that the effect of self-reported residential pyrethroid use is more important than that of diet. Two separate one-way ANOVAs analyzing PBA and *trans*-DCCA data individually for diet or residential use of pyrethroids (Table 5) indicated that the median DVWA PBA and *trans*-DCCA levels are significantly higher in children whose parents reported use of pyrethroids at home than

those who did not (Figure 2A) and during the conventional diet days than during the organic diet days (Figure 2B). The results from the expanded linear mixed effects model suggested that in addition to diet and residential pyrethroid use, children's age is also a significant predictor of PBA and *trans*-DCCA levels in the urine (Table 6). The median DVWA PBA and *trans*-DCCA levels are significantly higher in older children (ages 8-11) than younger children (ages 3-7) (Figure 2C).

DISCUSSION

Despite the wide use of pyrethroid pesticides, the assessment of pyrethroid pesticide exposure in the U.S. population, particularly for children, is limited to a handful of cross-sectional studies. This report consists of data collected as part of the on-going Children's Pesticide Exposure Study (CPES) with a focus on the children's exposure to pyrethroid pesticides. This longitudinal dataset provides a more complete documentation of children's exposure to pyrethroids and examines potential risk factors for higher exposure levels.

The most significant finding of this study - the association between self-reported pyrethroids use in the residential environment by the parents and the elevated pyrethroid metabolite levels found in their children's urine – is important from both the children's pesticide exposure assessment and the environmental public health perspectives. Interventions could be focused on minimizing the use of pyrethroids in the residential environment or eliminating the possible contact with treated areas or objects by children. This finding is consistent with a previous report suggesting that children whose parents reported residential OP pesticide use had higher OP urinary metabolite concentrations (Lu et al. 2001). Although changing children's diets from conventional to organic food

also lowers their exposures to pyrethroid pesticides, the effect of such dietary intervention is not as dramatic for pyrethroid pesticides as it is for OP pesticides (Lu et al. 2006). This pattern is in agreement with the general theory that children are exposed continuously to low levels of pesticides through their diets and that this chronic exposure is modified, usually often increased, by episodes of relatively high exposures from other pathways, such as residential use (Shurdut et al. 1998).

We conclude that residential pesticide use represents a very important risk factor for children's exposure to pyrethroid insecticides. This conclusion is supported by the fact that only seven of the 23 families reported residential pyrethroid use, yet it accounts for more of the variability in the urinary pyrethroid metabolites than the dietary intervention. The results from the mixed effects model indicated that residential use of pyrethroids remains a more significant predictor of both urinary PBA and *trans*-DCCA when different diets were taken into account. The data presented in Table 3 clearly demonstrated that children who lived in households where pyrethroids have been used for pest control purposes have experienced much higher pyrethroid exposures than those whose parents reported no pyrethroid use in their homes. Four of the five highest pyrethroid metabolite levels were found in these seven children. An extreme case was for a 4-year-old child whose parents used permethrin on the furniture, including beds. Several urine samples collected from this participant have the highest DVWA PBA, *cis*- and *trans*-DCCA levels. Other children who lived in homes where pyrethroids were used were continuously exposed to this group of insecticides throughout the 15-day study period. Notably, our pesticide use survey asked whether pesticides are used in and around the home and if so, when the last application occurred. As such, the continuous exposure

to these pesticides throughout the 15-day study period likely reflects residual sources.

Children were also exposed to pyrethroids through diets, although the magnitude was smaller than the residential exposure. Results from studies conducted in Germany have suggested that exposure to pyrethroids in the general population is caused by uptake with the diet (Heufortf and Angerer 2001; Schettgen et al. 2002); however, no direct evidence was provided to support this conclusion. In this study, all five of the measured pyrethroid metabolites were found during the organic diet period, including the two least frequently detected metabolites, FPBA and DCBA, specific metabolites for cyfluthrin and deltamethrin, respectively. Accordingly, the majority of the children's exposures to pyrethroid metabolites are likely to have come from the environment.

In this study, age is a significant predictor for pyrethroid exposure. We found older children, ages 8-11, experienced higher pyrethroid exposures than children ages 3-7. This finding is not consistent with results from other studies, which suggest that younger children tend to have higher pesticide exposure than older children. Younger children are more vulnerable to adverse health risks resulting from pesticide exposures because of the difference in their physiological functions relative to older children and adults. However, it is difficult to draw an absolute conclusion that younger children have higher pesticide exposures, particularly exposures from residential environment, than older children. Although common characteristics of young children, such as mouthing behaviors, close proximity to floor, etc., put them at higher risk of pesticide exposure, it is the pesticide residues found in the environment that serve as the prerequisite for exposure and the subsequent oral ingestion. In this study, we have identified that residential use is the primary source of the children's pyrethroid exposure; however, this

risk factor itself does not explain the age effect as age accounts for more variability in urinary metabolites than residential use in the expanded mixed effect model. One plausible explanation for this finding is that, as reported by their parents, many older children in this study were engaged in outside sports activities, such as swimming or playing tennis, in a neighborhood country club and parks during this sampling period. Pyrethroids may have been used in the premise of those facilities that lead to increased pyrethroid exposure.

With the regulation change that led to the restricted use of OP pesticides in the residential environment (U.S. EPA 1998), we were able to demonstrate that children are exposed to OP pesticides exclusively from their diets in the previous report (Lu et al. 2006). Due to less regulatory restrictions imposed on the pyrethroid use, results from this study suggest that this same group of children are simultaneously exposed to pyrethroids via dietary intake as well as from their residential environments. Such diverse exposure patterns among children may pose a challenge for regulating pyrethroid insecticides as a group under the Food Quality Protection Act (FQPA) (Food Quality Protection Act 1996), which mandates the assessment of exposure in an aggregate manner. The implementation of FQPA for pyrethroids could be even more problematic due to the difficulties of assessing cumulative risks resulting from pyrethroid exposures. Unlike OP or carbamate pesticides, pyrethroids do not appear to exhibit a single common toxicological mechanism in humans.

Besides the limitations associated with this study that were discussed previously (Lu et al. 2006), the lack of environmental measures of pyrethroids renders less confirmation of the association between children's exposure to pyrethroids and its

residential use. Systematic quantification of pyrethroids, and other non-persistent pesticides, such as OP, in the environment, via soil, house dust, surface wipe, or personal breathing air collection, remains a daunting task. Substantial numbers of samples are needed in order to minimize the spatial and temporal variations, which is commonly associated with the measurements of non-persistent pesticide exposures (Lu et al. 2004). The cost for analyzing such large numbers of environmental samples would compromise other aspects of a study with a limited research budget, such as reducing the number of participants or collecting less frequent biological samples.

Conclusion

In conclusion, we report the results from the first study of urban/suburban children's longitudinal exposure to pyrethroid pesticides. This study found elevated urinary levels of pyrethroid metabolites associated with both residential pyrethroid use and diets. Pyrethroid use in the residential environment is a particular concern not only because exposures were routinely measured during the days when children consumed an organic diet but also because urine samples collected from this sub-group of children contained the highest levels of four pyrethroid metabolites. The finding of this study provides an opportunity for intervention in which the association between self-reported residential use of pyrethroids and the elevated pyrethroid metabolite levels found in the children can be broken by either minimizing the use of pyrethroids in the residential environment or eliminating the possible contact with treated areas or objects by children.

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Table 1. Limits of detection (LOD) and the number of urine samples (percentages in parentheses) above or below the limit of detections for five common pyrethroid metabolites for 724 urine samples collection from 23 children for a 15-day study period.

	PBA	FPBA	*cis*-DCCA	*trans*-DCCA	DBCA
Detected	596 (82%)	15 (2%)	252 (35%)	517 (71%)	14 (2 %)
< LOD	23 (3%)	41 (6%)	22 (3%)	50 (7%)	15 (2%)
Non-detected	105 (15%)	668 (92%)	450 (62%)	157 (22%)	695 (96%)
LOD (μg/L)	0.1	0.2	0.2	0.4	0.1

Table 2. Descriptive statistics of daily volume-weighted average concentrations (μg/L) of pyrethroid insecticide metabolites for 724 urine samples collected from 23 children for a 15-day study period.

	PBA	FPBA	*cis*-DCCA	*trans*-DCCA	DBCA
Mean[a]	1.22 (2.4)	0.02 (0.2)	0.33 (1)	1.24 (2.6)	0.004 (0.02)
Median	0.45	0	0	0.38	0
G. mean[b]	0.58	0.08	0.4	0.54	0.05
Range	(0 - 25)	(0 - 3.5)	(0 - 15)	(0 - 25)	(0 - 0.1)
Percentiles					
10	0.01	0	0	0	0
25	0.22	0	0	0.14	0
75	0.97	0	0.33	0.99	0
90	2.85	0.05	0.90	3.37	0

a. Standard deviation in parentheses.
b. Geometric mean.

Table 3. Self-reported use of pyrethroid pesticides in the households by the parents, and the numbers of days in which the metabolite concentrations of pyrethroid pesticides in their children's urine samples exceeded the median daily volume-weighted average levels for the respective pyrethroid metabolites.

Child Age	Pyrethroids use (product name)	Location of use	Numbers of days of DVWA exceeded the median level [a,b]				
			PBA	FPBA	*cis*-DCCA	*trans*-DCCA	DBCA[c]
10	Ortho/carpenter ants (permethrin)	Home	3	8	1	2	0
8	Green Light (permethrin/other pyrethroids)	Garden	15	4	7	15	11[d]
7	Terminix (permethrin)	Crawl space	10	1	3	9	3[d]
6	Pyrethroids E.C. (deltamethrin)	Deck	5	0	1	5	0
8	Hot Shot fogger (tetramethrin/permethrin)	Home	16	2	16	16	0
4	RID (furniture/ bedding) (permethrin)	Beds	7[d]	1	6[d]	6[d]	0
11	Hartz (pyrethrin piperonyl butoxide)	Carpet	16	1	16	16	2[d]
	RID (pyrethrin)	Dog					
	Hartz control (allethrin)	Cat					

a Each child has a total of 16 days of DVWA concentration for each of the pyrethroid metabolites.

b Median levels for the DVWA concentration of 5 pyrethroid metabolites are in Table 2.

c All the urine samples with detectable levels were collected from children listed in this table.

d One of the urine samples has the highest level of the respective pyrethroid metabolite among the 724 urine samples collected.

Table 4. Selected SPSS results of a linear mixed effects model for the daily volume-weighted average of 3-phenoxybenzoic acid (PBA) and *trans*-2,2-(dichloro)-2-dimethylvinylcyclopropane carboxylic acid (*trans*-DCCA) concentrations (µg/L) in 23 children's urine samples collected over a 15-day study period.

Source	df[a]	PBA			*trans*-DCCA		
		Sum of squares	Mean Square	*F*-value (Pr>*F*) [b]	Sum of squares	Mean square	*F*-value (Pr>*F*) [b]
Residential Pyrethroids Use	1	9.6	9.6	19.6 *(<.001)*	5.4	5.4	15.4 *(<.001)*
Diets	1	2.0	2.0	4.0 (*0.047*)	1.9	1.9	5.4 (*0.021*)
Error	356	175.4	0.5	124.8	0.4		

a df, degree of freedom
b Pr, probability

Table 5. Daily volume-weighted average concentrations of 3-phenoxybenzoic acid (PBA) and *trans*-2,2-(dichloro)-2-dimethylvinylcyclopropane carboxylic acid (*trans*-DCCA) in urine samples of 23 children over a 15-day study period, compared by diets, residential pyrethroids use, and age.

		PBA Mean (Median)	*trans*-DCCA Mean (Median)
Diet	Conventional	1.24 (0.49)[a]	1.25 (0.42)[b]
	Organic	1.16 (0.36)[a]	1.21 (0.28)[b]
Residential pyrethroids use	No	0.94 (0.39)[c]	0.94 (0.35)[c]
	Yes	1.84 (0.6)[c]	1.91 (0.57)[c]
Age	3-7	0.69 (0.37)[c]	0.66 (0.35)[c]
	8-11	1.91 (0.86)[c]	1.99 (0.72)[c]

a Significantly different (one-way ANOVA, p=.023)
b Significantly different (one-way ANOVA, p=.008)
c Significantly different (one-way ANOVA, p<.001)

Table 6. Selected SPSS results of an expanded linear mixed effects model for the daily volume-weighted average of 3-phenoxybenzoic acid (PBA) and *trans*-2,2-(dichloro)-2-dimethylvinylcyclopropane carboxylic acid (*trans*-DCCA) concentrations (μg/L) in 23 children's urine samples collected over a 15-day study period.

Source	df[a]	PBA			*trans*-DCCA		
		Sum of squares	Mean square	*F*-value (Pr>*F*) [b]	Sum of squares	Mean square	*F*-value (Pr>*F*) [b]
Residential Pyrethroids Use	1	4.6	4.6	10.5 (*0.001*)	2.5	2.5	7.9 (*0.005*)
Diets	1	1.8	1.8	4.2 *(0.04)*	1.9	1.9	5.9 (*0.016*)
Age	1	18	18	40.9 *(<.001)*	11.7	11.7	36.7 *(<.001)*
Error	352	155.1	0.4		112.7	0.3	

a df, degree of freedom
b Pr, probability

Figure legends

Figure 1. Box plots, separated by self-reported of residential use of pyrethroid pesticides, of daily volume-weighted average of pyrethroid metabolites concentrations in 23 children ages 3-11 for 15 consecutive days in which conventional and organic diets were consumed: (A) 3-phenoxybenzoic acid (PBA); (B) *trans*-2,2-(dichloro)-2-dimethylvinylcyclopropane carboxylic acid (*trans*-DCCA); (C) 4-fluoro-3-penoxybenzoic acid (FPBA); (D) *cis*-2,2-(dibromo)-2-dimethylvinylcyclopropane carboxylic acid (DBCA). Boxplot : the horizontal lines in each plot represent 10^{th}, 25^{th}, 50^{th}, 75^{th}, and 90^{th} percentiles, bottom to top. Circles represent outlier values. Extreme values are not included in the plots.

Figure 2. Daily volume-weighted average of 3-phenoxybenzoic acid (PBA) and *trans*-2,2-(dichloro)-2-dimethylvinylcyclopropane carboxylic acid in 23 children ages 3-11 for 15 consecutive days grouped by (A) self-reported residential use of pyrethroid pesticides; (B) diet; (C) age. Boxplot: the horizontal lines in each plot represent 10^{th}, 25^{th}, 50^{th}, 75^{th}, and 90^{th} percentiles, bottom to top. Circles represent outlier values. Extreme values are not included in the plots.

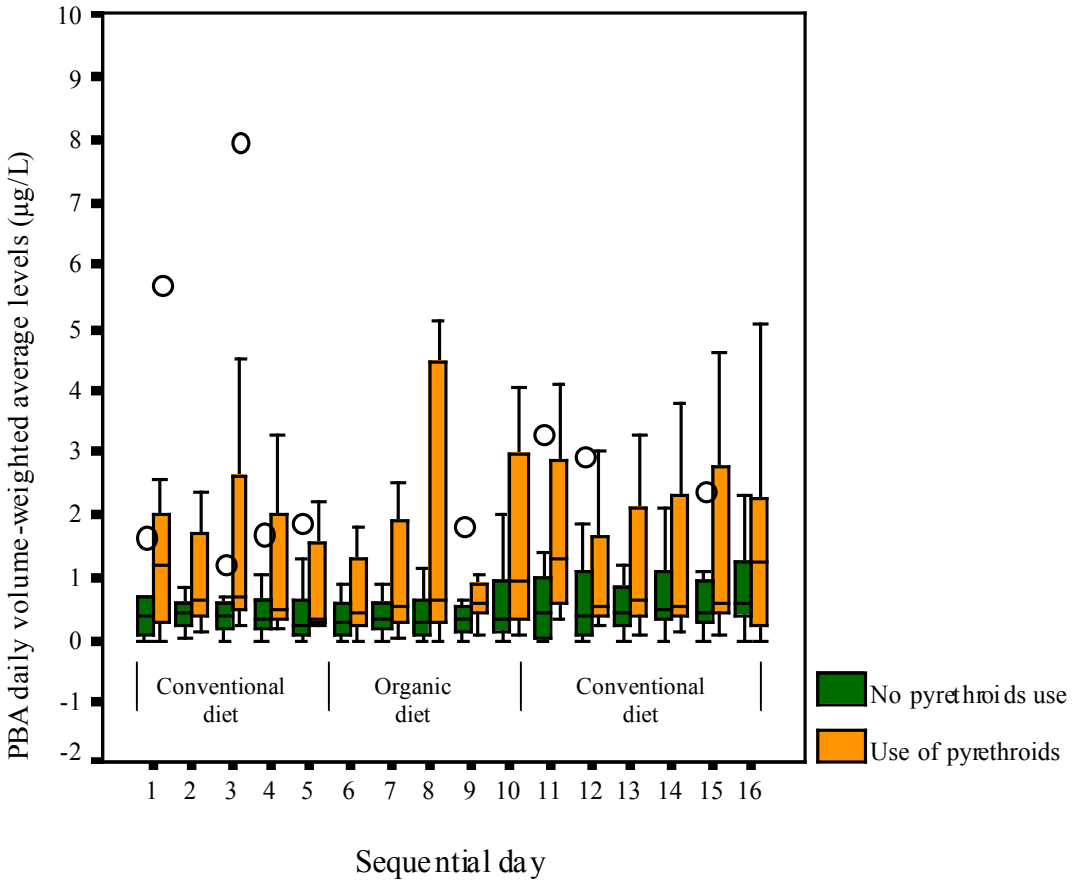

PBA daily volume-weighted average levels (µg/L)
10
9
8
7
6
5
4
3
2
1
0
-1
-2
Conventional diet
Organic diet
Conventional diet
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
Sequential day
No pyrethroids use
Use of pyrethroids

Figure 1A.

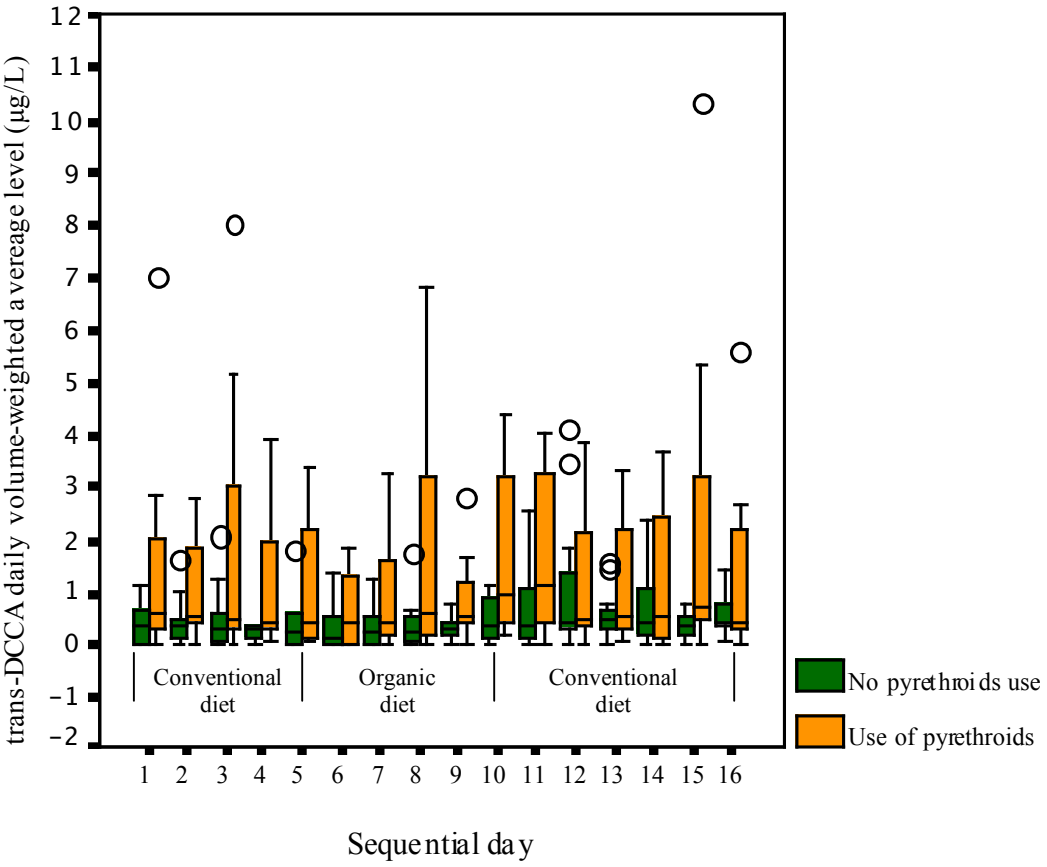

trans-DCCA daily volume-weighted average level (µg/L)
12
11
10
9
8
7
6
5
4
3
2
1
0
−1
−2
Conventional diet
Organic diet
Conventional diet
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
Sequential day
No pyrethroids use
Use of pyrethroids

Figure 1B.

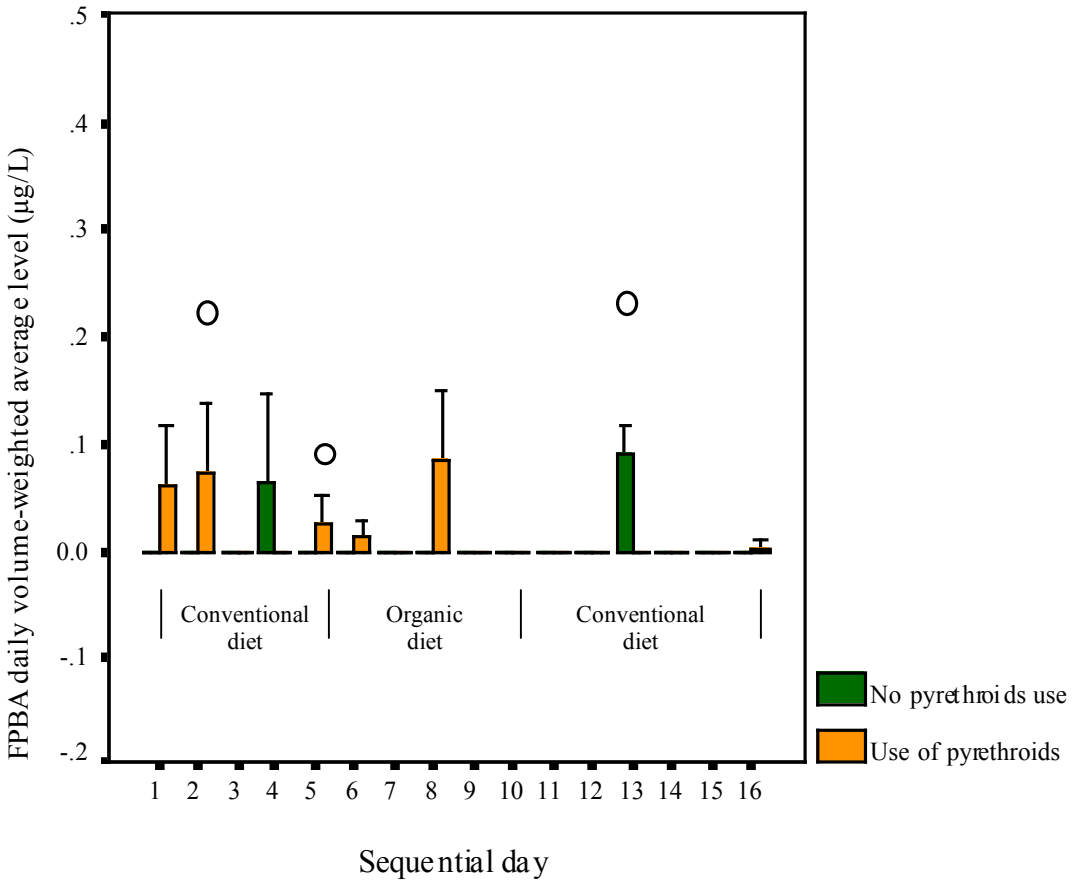

.5
.4
.3
.2
.1
0.0
-.1
-.2
FPBA daily volume-weighted average level (µg/L)
Conventional diet
Organic diet
Conventional diet
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
Sequential day
No pyrethroids use
Use of pyrethroids

Figure 1C.

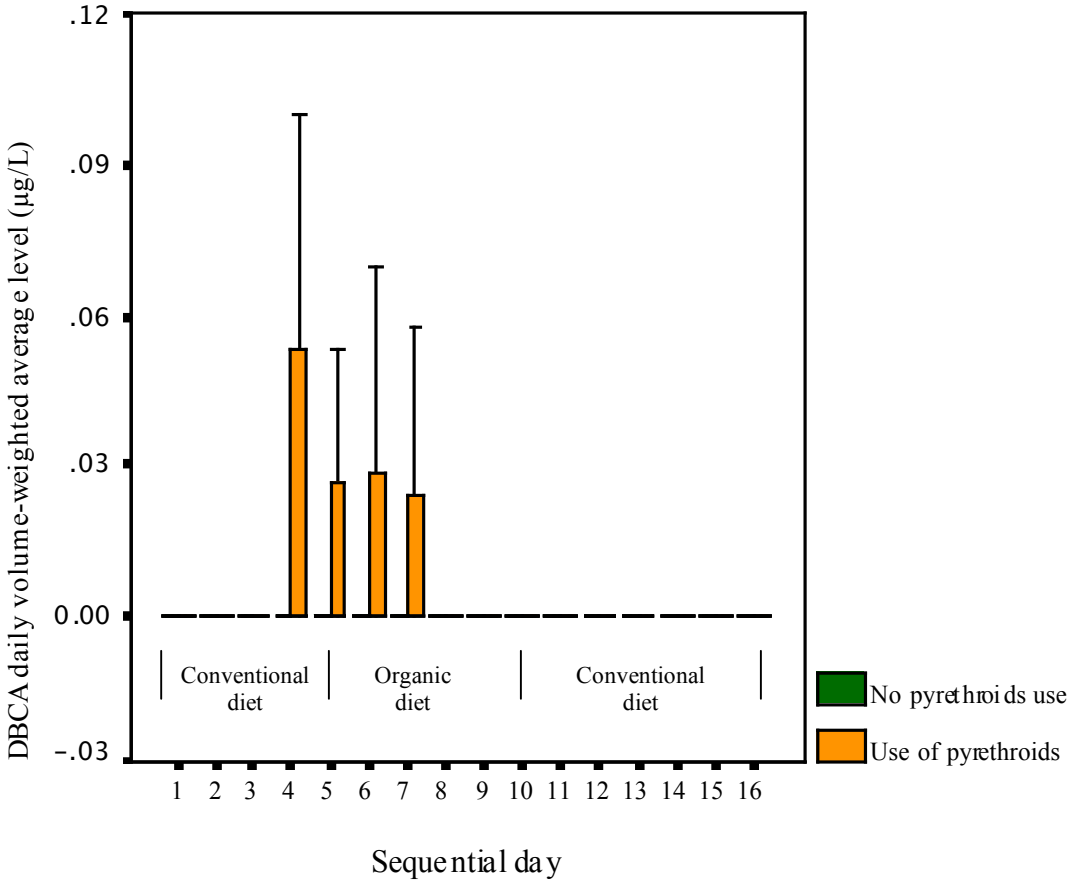
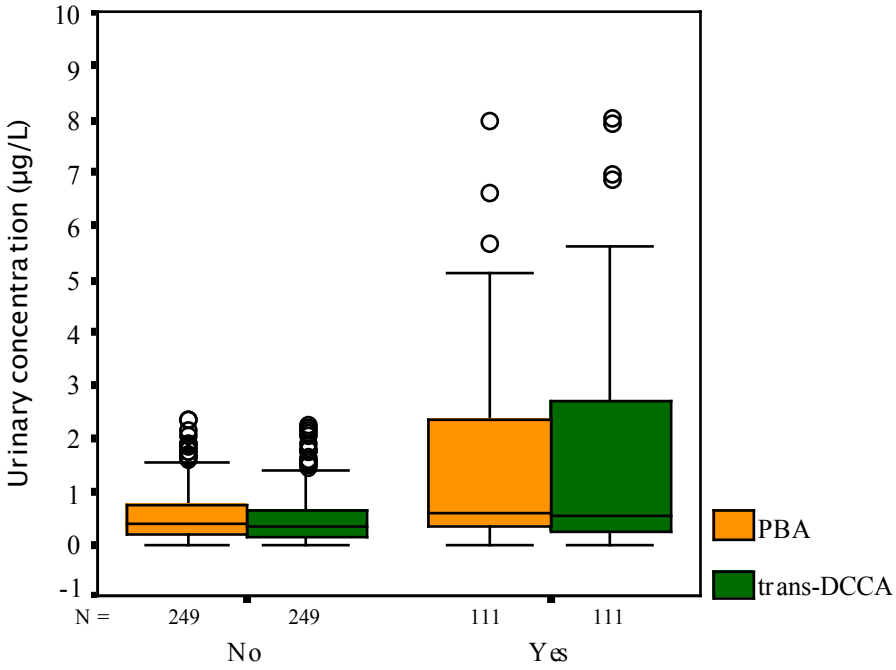

.12
.09
.06
.03
0.00
-.03
DBCA daily volume-weighted average level (µg/L)
Conventional diet
Organic diet
Conventional diet
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
Sequential day
No pyrethroids use
Use of pyrethroids

Figure 1D.



Self-reported residential use of pyrethroid pesticides

Figure 2A.

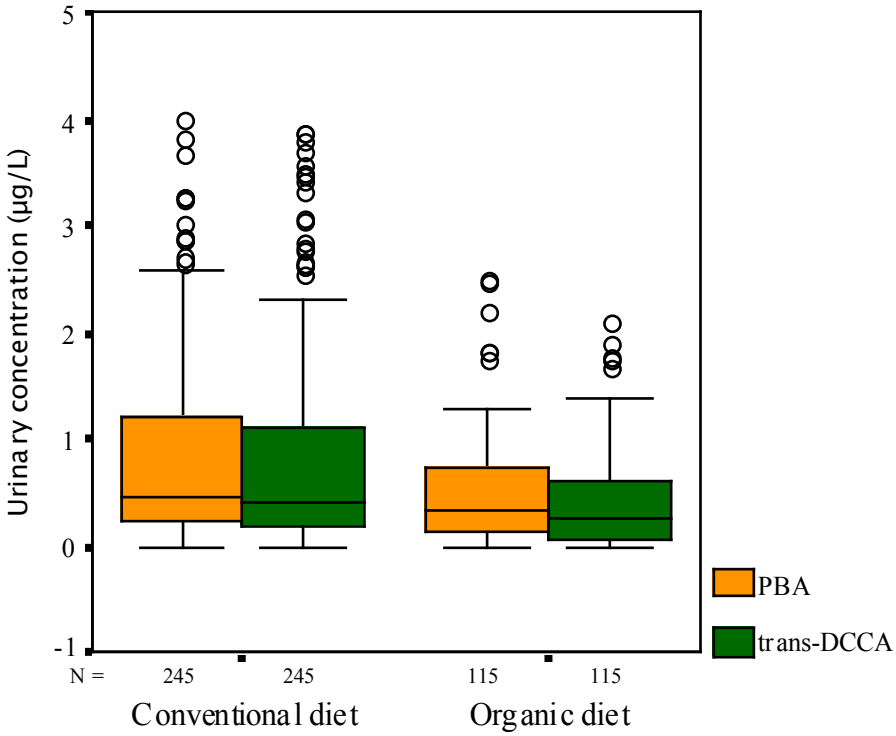

Urinary concentration (µg/L)
5
4
3
2
1
0
-1
N =
245
245
115
115
Conventional diet
Organic diet
PBA
trans-DCCA

Figure 2B.

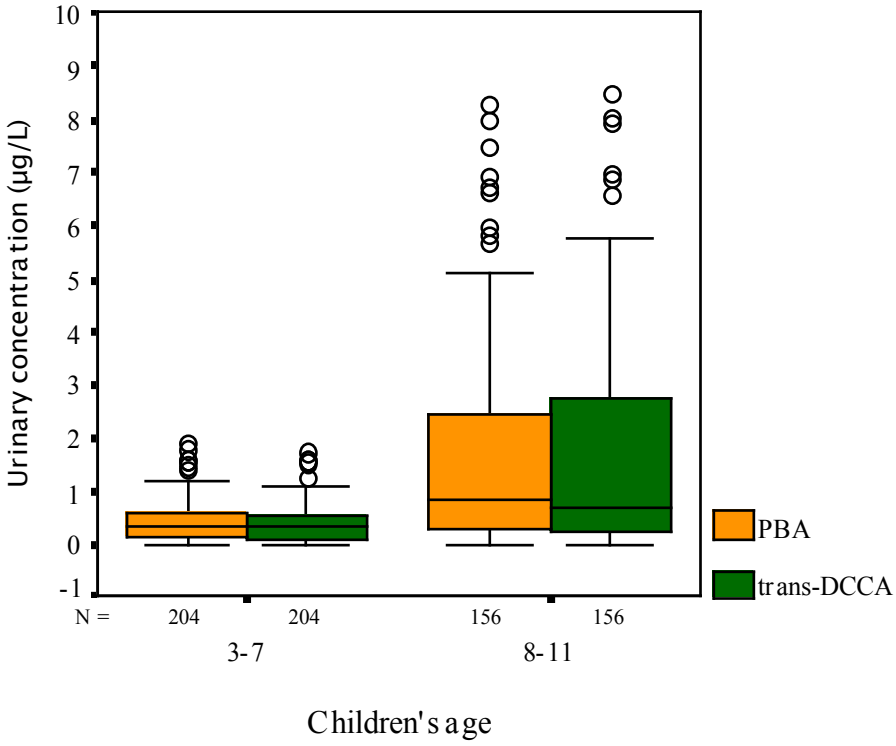

Urinary concentration (µg/L)
10
9
8
7
6
5
4
3
2
1
0
-1
N =
204
204
156
156
3-7
8-11
Children's age
PBA
trans-DCCA

Figure 2C.