Published in final edited form as:

Int J Hyg Environ Health. 2012 July ; 215(4): 465–473. doi:10.1016/j.ijheh.2011.08.006.

Exposure of flight attendants to pyrethroid insecticides on commercial flights: urinary metabolite levels and implications

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Abstract

Pyrethroid insecticides have been used for disinsection of commercial aircrafts. However, little is known about the pyrethroids exposure of flight attendants. The objective of the study was to assess pyrethroids exposure of flight attendants working on commercial aircrafts through monitoring the urinary pyrethroids metabolite levels. Eighty four urine samples were collected from 28 flight attendants, 18 – 65 years of age, with seventeen working on planes that were non-disinsected, and eleven working on planes that had been disinsected. Five urinary metabolites of pyrethroids were measured using gas chromatographic–mass spectrometric method: 3-phenoxybenzoic acid (3-PBA), *cis*-/*trans*-3-(2,2-Dichlorovinyl)-2,2-dimethylcyclo-propane carboxylic acid (*cis*-/*trans*-Cl2CA), *cis*-3-(2,2-dibromovinyl)-2,2-dimethylcyclo-propane-1-carboxylic acid (*cis*-Br2CA) and 4-fluoro-3-phenoxybenzoic acid (4F-3-PBA). Flight attendants working on disinsected planes had significantly higher urinary levels of 3-PBA, *cis*- and *trans*-Cl2CA in pre, post- and 24hr-post flight samples than those on planes which did not report having been disinsected. Urinary levels of *cis*-Br2CA and 4F-3-PBA did not show significant differences between the two groups. Flight attendants working on international flights connected to Australia had higher urinary levels of 3-PBA, *cis*- and *trans*-Cl2CA than those on either domestic and other international flights flying among Asia, Europe and North America. Post-disinsection duration (number of days from disinsection date to flight date) was the most significant factor affecting the urinary pyrethroid metabolites levels of 3-PBA, *cis*- and *trans*-Cl2CA of the group flying on disinsected aircraft. It was concluded that working on commercial aircrafts disinsected by pyrethroids resulted in elevated body burden of 3-PBA, *cis*- and *trans*-Cl2CA.

Keywords

flight attendant; disinsection; pyrethroid; permethrin; pesticide; metabolite; 3-PBA

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The authors declare they have no competing financial interests.

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Introduction

Many countries have required aircraft disinsection, treating the aircraft landing in their countries using insecticides, since the early 1930s to minimize the spread of non-native potential disease vectors and harmful pests in order to protect their citizens, fauna and flora (Gratz et al., 2000). Currently, the most common products used in aircraft disinsection contain a 2 % synthetic pyrethroid insecticide, typically permethrin or α -phenothrin. Permethrin is widely used for residual, pre-embarkation, and pre-flight treatments, and α -phenothrin is predominantly used for top of descent and on-arrival treatments. Residual treatment is typically done by maintenance staff or professional exterminators prior to or after landing while other disinsection methods are mainly conducted by flight attendants working on the aircraft (AQIS/MAFBNZ, 2010).

The health effects of pyrethroids have been studied prior to their introduction as the most commonly used insecticides in commercial and residential settings. The World Health Organization (WHO) conducted a series of field trials on various materials and methods for the aircraft disinsection (Sullivan et al., 1964; Sullivan et al., 1972), and published the latest recommendations on this basis in 1995 (WHO/HQ, 1995), but additional data have identified new risks that were not considered by WHO in its original risk estimate. Pyrethroids are recognized to be lipophilic components and potential neurotoxins that modify the kinetics of voltage-sensitive sodium and calcium channels (Clark and Symington, 2007; Ray and Fry, 2006; Shafer and Meyer, 2004; Shafer et al., 2005; Soderlund et al., 2002). Studies have suggested that pyrethroids can suppress effects on the immune system and may damage the lymph node and spleen (Repetto and Baliga, 1997). Recent studies found pyrethroids could cause potential developmental neurotoxicity (Bjorling-Poulsen et al., 2008; DeMicco et al., 2010; Shafer et al., 2005). Specifically, permethrin has been reported to be associated with chronic symptoms including headache, loss of memory, fatigue, muscle and joint pain, ataxia, skin rash, respiratory difficulties, and gastrointestinal disturbances (AbouDonia et al., 1996), and suspected to be an endocrine-disrupting chemical (Chen et al., 2002; Kakko et al., 2004; Kim et al., 2004). Phenothrin is suspected of being a kidney toxicant, and was found that exposure to phenothrin used on clothes and bedding could lead to gynecomastia (Murawski, 2005).

Pyrethroids are considered to have low mammalian toxicity (Narahashi, 2001; Soderlund et al., 2002), and the WHO described aircraft disinsection as a procedure that would not cause a risk to human health “if carried out with the recommended precautions” (Rayman, 2006; WHO/HQ, 1995). However, many anecdotal cases of adverse health effects suggested to be due to pyrethroids exposure on aircrafts by flight attendants have been reported to government agencies, labor unions, airlines, and environmental groups, such as irritations of the skin and mucosa, sore throat, vomiting, abdominal pain, headache, dizziness and nausea, etc. (Murawski, 2005; Sutton et al., 2007).

No measurements of urinary metabolite levels of pyrethroid insecticides have been reported for flight attendants though urinary levels at other populations including pregnant women, infants, children and general population exist (Arcury et al., 2007; Barr et al., 2010; Berkowitz et al., 2003; Heudorf and Angerer, 2001; Heudorf et al., 2004; Naeher et al., 2010; Panuwet et al., 2009; Schettgen et al., 2002; Whyatt et al., 2002). In the present study, we investigated the urinary pyrethroid metabolite levels of flight attendants working on U.S. domestic and international commercial aircrafts to assess whether flight attendants working on disinfected flights have elevated pyrethroid body burden compared to those working on planes without being treated with pesticides and the U.S. general population.

Methods

Sample and data collection

The study was reviewed and approved by the Institutional Review Board for human subjects at the University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School. A convenience-based subject recruitment approach was used to recruit eligible participants in collaboration with the Flight Attendant's Union during 2009 – 2010. Briefly, the routes with aircrafts that had high use of pesticides and those with no spraying of pesticides were first identified, and then the flight attendants working on those planes were contacted through notices in newsletters, on-line notices and word of mouth to determine if they were willing to participate in the study. Upon consenting to participating in the study, each participant was provided with one sampling package that included three urine sample containers, a postage paid shipping container certified for biological samples and a log sheet. The study population included actively working flight attendants 18–65 years old. Three samples from each participant were collected, one prior to the boarding, a second one after the flight, and a third one approximately 24 hours later. Urine samples were shipped under the guidelines for biological specimens via a one-day FedEx shipping to the lab, and kept frozen at -20°C until analysis.

To assess the potential effects of exposure conditions on the urinary pyrethroid metabolite levels, the following information was collected from each participant in the study: flight information, including airline, flight number, plane tail number, date of departure, time boarded plane, time disembarked plane, city/country of origin, stopover and destination; disinsection information including whether the flight attendant him/herself was spraying the pesticides, date and time that the aircraft was last disinfected, and name of the disinsection product(s). We also requested information on places the participant stayed overnight, whether they visited or stayed on a farm and the duration stayed for the three days prior to the sample collection and use of residential pesticide and the country or state where they spent most of their non-flying time for the previous month. However, only a limited number of the participants completed this section of the questionnaire.

Twenty eight flight attendants working on commercial aircrafts were recruited with 7 flight attendants flying on domestic routes to or from Minneapolis (MN), Chicago (IL), Detroit (MI), Phoenix (AZ), Los Angeles (CA), San Francisco (CA), Milwaukee (WI), Tri-Cities (TN), Deland (FL), Washington DC, Philadelphia (PA), Sacramento (CA), and Charlotte (NC), and 21 on international flights flying on routes that included landing at Sydney (Australia), Vancouver (Canada), Puerto Vallarta (Mexico), Beijing and Shanghai (China), Bombay (India), Narita (Japan), Seoul (S. Korea), Frankfurt (Germany), Amsterdam (Netherlands) and London (England). Eleven subjects were categorized into a “disinsection group” based on the following criteria: (1) either working on aircrafts that entered countries requiring disinsection, and indications were made that pyrethroids were used to meet the requirement; or (2) information provided by the subjects indicating that the aircrafts had been treated previously using residual treatment method even though they only entered the countries which do not require disinsection. The remaining participants were categorized into the “non-disinsection group”.

Laboratory analysis

Urine samples were prepared using acid hydrolysis, liquid-liquid extraction, and derivatization (Schettgen et al., 2002) using 2-phenoxybenzoic acid (2-PBA) as an internal standard. A slight modification to the method by Schettgen et al. (2002) was used with the residual dissolved into 40 μl rather than 50 toluene. 10 μl of N-tert-Butyldimethylsilyl-N-methyltrifluoroacetamide (MTBSTFA) was then added for derivatisation. 1 μl of the

prepared solution were injected into a gas chromatograph (Hewlett-Packard 6890 II) with a RTX65 column (30 m × 0.25 mm × 0.25 μm) by a Hewlett-Packard 7673 auto-sampler. A mass spectrometer (Hewlett-Packard MSD 5973) operated in electron impact (EI) mode and the selected ion monitoring (SIM) was used for the quantitative analysis. Pyrethroid metabolites measured in the study included 3-phenoxybenzoic acid (3-PBA), *cis*- and *trans*-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylic acid (*cis*- and *trans*-Cl₂CA), *cis*-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane-1-carboxylic acid (*cis*-Br₂CA), and 4-fluoro-3-phenoxybenzoic acid (4F-3-PBA), as listed in Table 1 along with their parental pyrethroids. 3-PBA (certified purity: 98 %), 2-PBA (certified purity: 98 %) and MTBSTFA (certified purity: > 97 %) were purchased from Sigma-Aldrich (St. Louis, MO, USA). *Cis*- and *trans*-Cl₂CA (10 ng/ml in methanol) were purchased from Dr. Ehrenstorfer GmbH (Augsburg, Germany). *Cis*-Br₂CA (100 μg/ml in methanol) was purchased from Chem Service, Inc. (West Chester, PA, USA), and 4F-3-PBA (certified purity: 98 %) was purchased from Cambridge Isotope Laboratories, Inc. (Andover, MA, USA).

Samples were calibrated using ten-point curves with the concentrations ranging from 0.1 to 100 μg/L (0.1, 0.25, 0.5, 1.0, 2.5, 5.0, 10.0, 20.0, 50.0 and 100.0 μg/L) prepared in the pooled urine samples from non-exposed persons. The determined relative standard deviations were from 3.6 to 6.8 % and from 9.3 to 14.7 % for within-series and between-day runs, respectively, and the relative recoveries for the analyzed pyrethroid metabolites were determined to be between 89.1 and 103 % at a spiked concentration of 0.4 μg/L with the analytic limit of detection (LOD) in the study of 0.08 μg/L for all metabolites. The instrumental conditions and calibration curves were checked before running a batch of samples using the spiked calibration standards (1 and 5 μg/L) to make sure all the sample were analyzed under accepted comparable conditions to avoid or reduce the uncertainties in the data analysis. Urinary creatinine concentrations were determined by a modified Jaffe's method using a SpectraMax M5 Microplate Reader (Molecular Devices, Sunnyvale, CA, USA).

Quality control

To ensure the reliability of the data, several quality controls were employed. First, calibrations were made by spiking known amounts of metabolites into the pooled urine, which were prepared and analyzed in the same manner as the samples. Second, one blank sample was prepared in the same manner as the samples using pure water and run after every 10th urine samples. None of the pyrethroid metabolites was detected above LODs in the blank samples, so no blank correction was applied. Third, duplicates were run with each set of samples to check the precision of the method. Finally, statistical analysis was performed using creatinine corrected metabolite concentrations to correct potential interpersonal variability resulted from the urine dilutions in the “spot” urine samples.

Data analysis

Geometric means (GM) and percentiles were calculated for the individual pyrethroid metabolite. For concentrations below the analytic limits of detection (LOD), the value of LOD divided by the square root of 2 was inputted (Hornung and Reed, 1990; Barr et al., 2010). Because the urinary pyrethroid metabolite concentrations were log- normally distributed, urinary levels of pyrethroid metabolites were log-transformed to normalize skewed distributions. Paired *t*-tests were used to compare the differences among pre-, post- and 24hr-post flight samples in the same group. 2-independent sample *t*-test was used to examine the differences in metabolite levels between the two groups defined by whether an individual flew on plane that was disinfected. A nonparametric test (Wilcoxon rank-sum test) was used to assess whether the flight attendants experienced higher exposure to

pyrethroid insecticides than the general U.S. population (Barr et al., 2010). 2-sided p values of < 0.05 were considered statistically significant, and all analyses were performed using SAS software (version 9.0, SAS institute Inc., Cary, NC).

Results

Tables 2 and 3 present the distributions of the volume based and creatinine adjusted concentrations of 3-PBA, *cis*- and *trans*-Cl₂CA, respectively, and those for *cis*-Br₂CA and 4F-3-PBA are presented in Table 4, according to the different sampling groups and exposure conditions. 3-PBA was detected in all urine samples. *Cis*- and *trans*-Cl₂CA levels were above the detection limits in 77 % and 92 % of all urine samples, respectively. *Cis*-Br₂CA and 4F-3-PBA levels were above the detection limits in 24 % and 18 % of all urine samples, respectively. Among all the pyrethroid metabolites, 3-PBA in the disinsection group had the highest total geometric mean (GM) 9.01 $\mu\text{g/g}$ adjusted for creatinine, compared to the total GM of 3-PBA in the non-disinsection group of 1.12 $\mu\text{g/g}$ adjusted for creatinine. The total GM for *trans*-Cl₂CA in the disinsection group was 3.92 $\mu\text{g/g}$ adjusted for creatinine; and that for non-disinsection group was 0.58 $\mu\text{g/g}$ adjusted for creatinine. The total GM of *cis*-Cl₂CA in the disinsection group was 0.98 $\mu\text{g/g}$ adjusted for creatinine, and that for non-disinsection group was 0.23 $\mu\text{g/g}$ adjusted for creatinine. Total GMs for *cis*-Br₂CA and 4F-3-PBA were not calculated because of the small proportion of detects (< 24 %) which could make the GM values unreliable for those two metabolites.

For flight attendants who did not fly on planes that were disinsected, the urinary levels of pyrethroid metabolites in pre-flight samples were not significantly different from those in post-flight samples (3-PBA: $p = 0.34$; *cis*-Cl₂CA: $p = 0.08$; *trans*-Cl₂CA: $p = 0.33$), and also not significantly different from those in 24hr-post flight samples (3-PBA: $p = 0.19$; *cis*-Cl₂CA: $p = 0.63$; *trans*-Cl₂CA: $p = 0.22$). Nor were the post- and 24hr-post samples in the non-disinsection group different (3-PBA: $p = 0.90$; *cis*-Cl₂CA: $p = 0.27$; *trans*-Cl₂CA: $p = 0.67$).

For flight attendants who flew on planes that were disinsected, 3-PBA, *cis*- and *trans*-Cl₂CA in the post-flight samples had significantly higher levels than those in the pre-flight samples (3-PBA: $p < 0.0001$; *cis*-Cl₂CA: $p = 0.0005$; *trans*-Cl₂CA: $p < 0.0001$) with the average increasing percentages of 569 %, 797 % and 857 %, respectively. The post flight samples were also significantly higher than those in the 24hr-post-flight samples (3-PBA: $p = 0.0004$; *cis*-Cl₂CA: $p = 0.01$; *trans*-Cl₂CA: $p = 0.008$). Urinary levels of 3-PBA, *cis*- and *trans*-Cl₂CA in the 24hr-post-flight samples were also significantly higher than those in pre-flight samples (3-PBA: $p = 0.0006$; *cis*-Cl₂CA: $p = 0.001$; *trans*-Cl₂CA: $p < 0.0001$).

The levels of 3-PBA, *cis*- and *trans*-Cl₂CA in pre-flight samples from the disinsection group were higher (approximately twice) than those from non-disinsection group (3-PBA: $p = 0.01$; *cis*-Cl₂CA: $p = 0.01$; *trans*-Cl₂CA: $p = 0.001$). The disinsection group also had higher levels of 3-PBA, *cis*- and *trans*-Cl₂CA in post-flight samples than those in non-disinsection group (3-PBA: $p < 0.0001$; *cis*-Cl₂CA: $p = 0.002$; *trans*-Cl₂CA: $p = 0.0005$), and in 24hr-post-flight samples (3-PBA: $p = 0.0009$; *cis*-Cl₂CA: $p = 0.005$; *trans*-Cl₂CA: $p = 0.002$).

Since the detection frequency of the urinary levels of *cis*-Br₂CA and 4F-3-PBA was low (< 24 %), comparisons among urinary concentration may not provide reliable statistical results. For those concentrations above the LODs, no significant differences were found for *cis*-Br₂CA and 4F-3-PBA among pre-, post- and 24hr-post flight samples both within ($p > 0.18$ for *cis*-Br₂CA and $p > 0.06$ for 4F-3-PBA) and between the two groups ($p > 0.05$ for *cis*-Br₂CA and $p > 0.16$ for 4F-3-PBA). When the LOD divided by the square root of 2 was

included for concentrations below LODs, again, no significant differences were found among different two groups defined.

Figure 1 presents the distribution of the combined urinary pyrethroid metabolite levels by exposure conditions and sampling types. Wide variations in concentrations were measured, ranging from 0.34 $\mu\text{g/g}$ to 11.2 $\mu\text{g/g}$ creatinine in the non-disinsection group, and from 0.60 $\mu\text{g/g}$ to 93.8 $\mu\text{g/g}$ creatinine in the disinsection group. On average, 3-PBA, *cis*- and *trans*-Cl2CA contributed 55%, 9% and 24% to the total metabolite concentration in non-disinsection group, respectively, and contributed 60%, 7% and 27% in disinsection group, respectively. The contributions of *cis*-Br2CA and 4F-3PBA in both groups were below < 10% and < 5%, respectively.

Significant associations were identified between urinary levels of 3-PBA, *cis*- and *trans*-Cl2CA and the post-disinsection duration, the period of the time between when the plane was disinfected and when the post flight urine samples was collected ($R^2 = 0.71, 0.65$ and 0.59 , respectively). This association followed an exponential decay (Figure 2). No obvious variation patterns for *cis*-Br2CA and 4F-3PBA were observed consistent with their precursors being deltamethrin and cyfluthrin, two pyrethroids not reported to be used on planes flown by the study participants.

Volume-based and creatinine corrected GMs and percentiles for 3-PBA, *cis*- and *trans*-Cl2CA, including total and age group 20–59 in the general U.S. population, are also presented in Tables 2 and 3, respectively (NHANES, Barr et al. 2010). For the NHANES data, the percentiles for those metabolite levels were not significant different between the total and age group of 20–59. For comparison with NHANES data, the GM and percentile levels of 3-PBA, *cis*- and *trans*-Cl2CA in the age group 20–59 were used to match with the ages from 18–60 in this study. Both the GMs and the medians of the total levels of 3-PBA in the non-disinsection group were approximately 2–3 times of NHANES levels. However, no significant percentile differences were found between them ($p = 0.69$). Similarly, no significant percentile differences were found between the levels of *cis*-, or *trans*-Cl2CA in the non-disinsection group and NHANES levels (*cis*-Cl2CA: $p = 0.86$; *trans*-Cl2CA: $p = 1.0$).

Urinary levels of 3-PBA in the post-flight samples from flight attendants who flew on planes that were disinfected were more than 10 times higher than the GMs in the NHANES data, as well as for each of the percentiles examined ($p = 0.016$). The GM and median of 3-PBA in the pre-flight samples were 5 times higher than the NHANES levels. For *cis*- and *trans*-Cl2CA in the post- and 24hr-post urine samples from disinsection group were also higher than the NHANES levels at each percentile (75th, 90th and 95th).

Figures 3a and 3b present the urinary concentrations of 3-PBA and *cis/trans*-Cl2CA by domestic and international flight routes, respectively. Those for *cis*-Br2CA and 4F-3-PBA were not listed because their urinary levels did not show significant differences among different flights. Highest urinary pyrethroid metabolite levels were detected in the urine samples from flight attendants on flights connected to Australia compared to the flight attendants on flights flying among U.S., Europe, Asia, and other North American countries.

Discussion

The significantly higher levels of 3-PBA, *cis*- and *trans*- Cl2CA in the post-flight urine samples for the flight attendants who flew on disinfected aircraft and the increase in post to pre-flight samples for that group indicate that residual disinsection of aircraft results in an increase in body burden of pesticides in flight attendants. Permethrin was reported by the flight attendants to be the pesticide used to treat the aircrafts flown. This is consistent with

the pattern of metabolites, 3-PBA, *cis* and *trans*-Cl₂CA, measured to be included in the post-flight samples. The low frequencies of detection of 4F-3-PBA and *cis*-Br₂CA and the lack of any significant differences among the two groups of flight attendants and general US population suggests that the flight attendants in this study were infrequently exposed to cyfluthrin and deltamethrin and that exposure did not occur due to the disinsection of aircraft flown.

Typical usage of pyrethroid insecticides on different aircrafts flying domestically and internationally was reflected by the specific profile of pyrethroid metabolites in the urine samples from the flight attendants. The urinary levels of 3-PBA, *cis*- and *trans*-Cl₂CA being comparable across the pre, post and 24 hour post flight samples for the flight attendants on domestic flights is consistent with that the United States not requiring disinsection of arriving aircraft since 1979 nor pyrethroid being approved for current use on aircraft (Smith, 1996). Internationally, aircraft disinsection is still required by many countries, e.g., Australia, New Zealand, Barbados, Cook Islands, Fiji, Jamaica and Panama, and most countries reserve their right for this practice on flights from particular regions of endemic diseases (OSTPXWEB, 2010). Among the countries flown to in this study, the higher concentrations of 3-PBA, *cis*- and *trans*-Cl₂CA were measured among the flight attendants on the airlines flying to or from Australia. This result is consistent with Australia requiring that the international flights landing on Australia be routinely disinfected (AQIS/MAFBNZ, 2010).

Previous studies revealed rapid metabolism and excretion of pyrethroids. In a metabolism study with cypermethrin (1:1 *cis/trans* mixture) by Eadsforth et al. (1988), 72 % of the *trans* isomer dose and 45 % of the *cis* isomer dose were excreted through human subject urine within 24 h, respectively. Recent human volunteer studies with oral administration of deltamethrin found that its metabolite was essentially completely excreted within 24 h of exposure with peak levels being detected around 4 h post-dose (Sams and Jones, 2011). Following an inhalation exposure to 160 µg/m³ of cyfluthrin for 10–60 min, 93% of the metabolites were excreted within the first 24 h with the peak excretion rates between 0.5 and 3 h, and the mean half-lives of 6.9 h for *cis*-Cl₂CA, of 6.2 h for *trans*-Cl₂CA and of 5.3 h for 4F-3-PBA (Leng et al., 1997). In dermal studies with cypermethrin and permethrin, the elimination half-life was reported to be longer, from 29 to 38 hours (Woollen et al., 1992; Tomalik-Scharte et al., 2005). Similar phenomena were observed in this study. Levels of 3-PBA, *cis*- and *trans*-Cl₂CA in 24hr-post flight urine samples were greatly decreased compared to those in post-flight samples at all percentiles.

In spite of the rapid metabolism and excretion of pyrethroids, the creatinine adjusted levels of urinary permethrin metabolites in pre-flight samples from participants who flew on routes to countries requiring disinsection were above the corresponding background levels observed in the U.S. general population and flight attendants who flew domestic routes. Their levels at the 50th percentile were nearly twice of that in non-disinsection group, indicating elevated body burden of pyrethroid metabolites existed in the flight attendants in the disinsection group, which could be affected by the flying frequencies or the duration between two working flights. Longer duration between two flights made a longer period for the flight attendants away from the occupationally related pyrethroid exposure, resulting in lower urinary pyrethroids metabolite levels. Similarly, shorter duration between two flights could lead to higher body burden. Considering each flight as a single exposure event, the urinary levels of pyrethroid metabolites could be gradually built up in “wave-like” short-term exposure pattern and finally reached the steady-state in a long-term period, assuming flight attendants had regular flying schedules.

Permethrin on the internal surfaces of airlines, the residual levels of permethrin on the airline seats and carpets were identified to decay with time (Mohan and Weisel, 2010), from which, it can be assumed that flight attendants would be exposed to varying pesticides levels existing within the aircraft environment post-disinsection. The relationships between post-disinsection duration and the concentrations of 3-PBA, *cis*- and *trans*-Cl₂CA in the study did follow exponential decay trends, indicating the closer the date/time of the flight to when the disinsection was done, the higher the levels expected within the aircraft cabin, and therefore, the higher the body burden of pyrethroids.

Few data are available in the open literature with which the results in this study can be compared with although pyrethroid metabolites in urine have been studied for almost 30 years in different occupational settings. In a study by Kolmodin-Hedman et al. (1982), the highest urinary level of permethrin metabolites detected were 260 µg/L in the morning void in one forestry worker following a 6-hour permethrin exposure to 11–85 µg/m³, but no detectable amount of metabolites were observed in the afternoon samples. Concentrations of 3-PBA in urine samples from ten workers working in greenhouses for more than 12 h after application of deltamethrin ranged from < LOD – 52 µg/L (Tuomainen et al., 1996). Pest control workers had reported concentrations of 3-PBA from < 0.5–277 µg/L (Leng et al., 1997). These results suggested that urinary metabolite levels of pyrethroids varied greatly among different occupations. In this study, the creatinine adjusted concentrations of 3-PBA ranged from 2.18–71.0 µg/g for flight attendants flying on disinfected aircrafts through residual treatment, suggesting their exposure to permethrin is similar to pesticides applicators.

None of the flight attendants in this study reported spraying pesticides themselves, rather the aircrafts they flew on had been treated previously on the ground using the residual disinsection method to meet the requirement. Exposure to residual treatment would likely be associated with dermal uptake of pyrethroids as flight attendants spend up to 15 hours working, sitting and sleeping on surfaces in the international flights that were treated. In addition, potential non-intentional ingestion of pyrethroids contaminated food could also occur if hands or food contacted pesticide treated surfaces, e.g. tray tables. Potential inhalation exposure can not be ruled out since permethrin is a semi-volatile organic compound that could slowly partition into the gaseous phase from the internal surfaces of the aircraft, and be consequently inhaled into their bodies. In addition, the resuspended particles containing permethrin could also be inhaled particularly when laying down in the crew rest areas.

Previous studies have shown that the ratios of *trans*- to *cis*-Cl₂CA concentrations were different among oral, inhalation and dermal administration. The ratio was approximately 1:1 after dermal exposure to cypermethrin, and was 2:1 after oral ingestion (Wilkes et al., 1993; Woollen et al., 1992). Inhalation of cyfluthrin resulted in the ratio from 1.8 to 2.2 (Leng et al., 1997). The ratio of *trans*- to *cis*-Cl₂CA in this study varied from 2.1 to 6.9 (GM: 4.1), and from 1.0 to 6.4 (GM: 2.6) in the urine samples from disinsection and non-disinsection groups, respectively. In the NHANES data (Barr et al., 2010), this ratio ranged from 0.001 to 5800 with the vast majority between 3 and 4. Several studies attempted to determine the exposure routes of pyrethroid uptake based on the ratio of *trans*- to *cis*-Cl₂CA (Hardt and Angerer, 2003; Heudorf and Angerer, 2001). However, indications for the predominant exposure routes based on the ratios of *trans*- to *cis*-Cl₂CA may not be reliable since the ratio could vary with product formulation, differential metabolism, half-lives in environmental media, and environment conditions, et al. (Barr et al., 2010). Thus, a more detailed analysis is need to investigate the contributions of oral, inhalation and dermal exposures to the internal doses for the current study.

Conclusions

In this study, we found that the flight attendants working on the pyrethroids disinfected commercial aircraft had significant higher concentrations of 3-PBA, *cis*- and *trans*- Cl₂CA in the post- and 24hr-post flight urine samples than those working on non-disinfected aircrafts and the general U.S. population, indicating they had elevated body burden due to the practice of disinsection of aircrafts with pyrethroids, predominantly permethrin. The creatinine adjusted levels of 3-PBA, *cis*- and *trans*- Cl₂CA in the post-flight urine samples reflected the short-term exposure to pyrethroids, while those in the pre-flight urine samples suggested an elevated body burden from a long-term exposure for those flight attendants routinely working on pyrethroid treated aircrafts. Post-disinsection duration was positively associated with the levels of 3-PBA, *cis*- and *trans*- Cl₂CA. This study suggests that an evaluation of the potential health risks from this occupational exposure to pyrethroids should be done.

Acknowledgments

The authors thank Dr. Dana Boyd Barr for graciously providing the pyrethroid metabolite standard of trans-chrysanthemumdicarboxylic acid, and thank Drs. Jeffrey Laskin, Yi-Hua Jan for their laboratory support. Drs. Michael Gochfeld, Mark Gregory Robson, Sastry Isukapalli, Lori A. White and Pamela A. Ohman Strickland are acknowledged for their helpful comments. Kristin Borbely and Teresa Boutillette are also acknowledged for helping sample shipping.

The research reported in this paper was funded in part by the U.S. Federal Aviation Administration (FAA) Office of Aerospace Medicine through the National Air Transportation Center of Excellence for Research in the Intermodal Transport Environment under Cooperative Agreement 07-C-RITE-UMDNJ. Although the FAA has sponsored this project, it neither endorses nor rejects the findings of this research. This research was supported in part by the NIEHS sponsored UMDNJ Center for Environmental Exposures and Disease, Grant #: NIEHS P30ES005022.

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Figure 1.
The distribution of the combined urinary pyrethroid metabolite levels by exposure conditions and sampling types

Figure 2.
Post-disinsection durations and the urinary concentrations of pyrethroid metabolites in the disinsection group

Figure 3a

Figure 3b

Figure 3.

Figure 3a. Urinary concentrations of 3-PBA by domestic and international flights in the disinsection group.

Figure 3b. Urinary concentrations of *cis*- and *trans*-Cl₂CA by domestic and international flights in the disinsection group

Table 1

Pyrethroids and their corresponding urinary metabolites.

Pyrethroid	Urinary metabolites
Permethrin	3-PBA, <i>cis</i> - and <i>trans</i> -Cl ₂ CA
Cypermethrin	3-PBA, <i>cis</i> - and <i>trans</i> -Cl ₂ CA
Deltamethrin	<i>cis</i> -Br ₂ CA, 3-PBA
Cyfluthrin	4F-3-PBA, <i>cis</i> - and <i>trans</i> -Cl ₂ CA

Table 2

Distribution of volume-based urinary concentrations of pyrethroid metabolites among the flight attendants ($\mu\text{g/L}$)

Metabolite	GM (SD)	Range	Percentile ^d				
			25th	50th	75th	90th	95th
3-PBA							
Non-disinsection ^a							
Total	0.96 (0.88)	0.11–3.86	0.30	0.70	1.45	1.97	2.84
Pre-flight	0.86 (0.86)	0.11–3.40	0.24	0.54	0.90	1.78	2.26
Post-flight	1.01 (0.60)	0.22–2.33	0.61	0.84	1.38	1.77	1.96
24-hr-post	1.06 (1.13)	0.13–3.86	0.25	0.48	1.57	2.53	3.45
Disinsection ^b							
Total	7.06 (15.00)	0.30–81.53	1.34	2.18	4.93	19.48	25.80
Pre-flight	1.36 (1.20)	0.30–3.62	0.37	1.07	1.85	3.26	3.44
Post-flight	14.40 (22.97)	0.78–81.53	2.08	5.16	17.13	25.95	50.98
24-hr-post	4.53 (5.86)	1.34–20.78	1.95	2.39	4.03	7.06	13.92
NHANES 2001–2002 ^c							
Total	0.318			0.27	0.70	1.73	3.54
Age 20–59	0.314			0.27	0.67	1.65	3.25
<i>cis</i> -CI2CA							
Non-disinsection							
Total	0.21 (0.26)	<LOD–1.21	<LOD	0.11	0.23	0.60	0.73
Pre-flight	0.14 (0.19)	<LOD–0.66	<LOD	0.09	0.19	0.51	0.58
Post-flight	0.28 (0.28)	<LOD–0.89	0.09	0.16	0.36	0.71	0.83
24-hr-post	0.20 (0.29)	<LOD–1.21	<LOD	0.10	0.24	0.39	0.57
Disinsection							
Total	0.68 (1.03)	<LOD–3.70	0.15	0.22	0.53	2.19	3.37
Pre-flight	0.14 (0.09)	<LOD–0.29	<LOD	0.12	0.21	0.25	0.27
Post-flight	1.31 (1.42)	0.10–3.70	0.20	0.63	2.27	3.46	3.58
24-hr-post	0.53 (0.62)	0.15–2.25	0.19	0.37	0.52	0.70	1.48
NHANES 2001–2002							

Metabolite	GM (SD)	Range	Percentile ^d				
			25th	50th	75th	90th	95th
Total				<LOD	0.17	0.51	0.91
Age 20–59				<LOD	0.17	0.51	0.96
<i>trans</i> -C12CA							
Non-disinsection							
Total	0.49 (0.53)	<LOD–2.14	0.11	0.26	0.62	1.15	1.58
Pre-flight	0.39 (0.51)	<LOD–2.02	0.11	0.21	0.51	0.85	1.30
Post-flight	0.55 (0.46)	<LOD–1.60	0.23	0.42	0.73	1.25	1.43
24-hr-post	0.53 (0.63)	<LOD–2.14	0.08	0.21	1.00	1.31	1.67
Disinsection							
Total	2.94 (4.86)	<LOD–22.62	0.52	0.95	3.11	8.72	11.28
Pre-flight	0.45 (0.31)	<LOD–1.04	0.17	0.49	0.65	0.75	0.90
Post-flight	5.74 (6.96)	0.38–22.62	0.65	3.15	8.68	14.36	18.42
24-hr-post	2.31 (2.48)	0.55–8.81	0.98	1.31	2.74	4.01	6.41
NHANES 2001–2002							
Total					0.43	1.18	2.60
Age 20–59					<LOD	1.17	2.56

Abbreviations: GM, geometric mean; SD, standard deviation.

^aIncluding flight attendants working on disinsected aircrafts.

^bIncluding flight attendants working on non-disinsected aircrafts.

^cData for general US population from Barr et al. (2010).

^dLimit of detection of 0.08 µg/L

Table 3

Distribution of creatinine corrected concentrations of pyrethroid metabolites among the flight attendants ($\mu\text{g/g}$ creatinine)

Metabolite	GM (SD)	Range	Percentile				
			25th	50th	75th	90th	95th
3-PBA							
Non-disinsection							
Total	1.12 (1.02)	0.15–5.89	0.53	0.83	1.33	2.12	2.92
Pre-flight	1.09 (1.26)	0.15–5.22	0.39	0.73	1.17	1.99	3.52
Post-flight	1.17 (0.86)	0.27–3.83	0.71	0.92	1.44	1.83	2.29
24-hr-post	1.36 (1.38)	0.23–5.89	0.60	0.87	1.37	2.57	3.38
Disinsection							
Total	9.01 (15.21)	0.26–71.00	2.16	4.13	6.91	21.55	36.27
Pre-flight	2.26 (1.89)	0.26–6.79	1.12	1.74	3.05	3.53	5.16
Post-flight	17.59 (20.87)	2.18–71.00	4.84	6.88	21.60	43.25	57.01
24-hr-post	5.45 (5.55)	1.20–19.15	2.53	3.29	4.75	11.94	15.55
NHANES 2001–2002							
Total	0.324		0.29	0.60	1.54	3.35	
Age 20–59	0.311		0.30	0.60	1.59	3.43	
cis-C12CA							
Non-disinsection							
Total	0.23 (0.31)	<LOD–1.85	<LOD	0.11	0.28	0.51	0.73
Pre-flight	0.13 (0.13)	<LOD–0.51	<LOD	0.10	0.12	0.39	0.35
Post-flight	0.29 (0.28)	<LOD–1.05	0.09	0.15	0.42	0.63	0.80
24-hr-post	0.27 (0.44)	<LOD–1.85	<LOD	0.12	0.25	0.49	0.94
Disinsection							
Total	0.98 (1.60)	<LOD–7.06	0.26	0.46	0.91	2.40	4.30
Pre-flight	0.26 (0.18)	<LOD–0.65	<LOD	0.20	0.31	0.48	0.57
Post-flight	1.94 (2.18)	0.27–7.06	0.47	0.76	2.44	4.93	6.01
24-hr-post	0.62 (0.48)	0.11–1.60	0.28	0.47	0.83	1.25	1.43
NHANES 2001–2002							
Total			<LOD	0.23	0.46	0.90	

Metabolite	GM (SD)	Range	Percentile				
			25th	50th	75th	90th	95th
Age 20–59				<LOD	0.26	0.58	1.05
<i>trans</i> -C12CA							
Non-disinsection							
Total	0.58 (0.67)	<LOD–3.26	0.17	0.32	0.64	1.53	2.00
Pre-flight	0.38 (0.41)	<LOD–1.84	0.17	0.32	0.39	0.61	0.86
Post-flight	0.64 (0.56)	<LOD–1.88	0.20	0.33	1.12	1.36	1.60
24-hr-post	0.71 (0.92)	<LOD–3.26	0.15	0.34	0.78	2.14	2.39
Disinsection							
Total	3.92 (5.42)	<LOD–19.69	0.90	1.71	3.37	13.94	15.78
Pre-flight	0.79 (0.56)	<LOD–1.96	0.43	0.68	0.88	1.50	1.73
Post-flight	7.51 (6.86)	0.94–19.69	2.09	3.75	14.04	15.92	17.64
24-hr-post	2.74 (2.30)	0.40–8.40	1.56	2.02	2.88	5.09	6.75
NHANES 2001–2002							
Total					0.74	1.47	2.62
Age 20–59					<LOD	1.87	2.89

Table 4Distribution of urinary concentrations of *cis*-Br2CA and 4F-3-PBA in the flight attendants

Metabolite	GM	Range	Percentile				
			25th	50th	75th	90th	95th
cis-Br2CA							
Non-disinsection							
Total ^a	NC ^c	<LOD-1.14	<LOD	<LOD	0.12	0.30	0.74
Pre-flight ^a	NC	<LOD-0.90	<LOD	<LOD	0.20	0.33	0.56
Post-flight ^a	NC	<LOD-1.14	<LOD	<LOD	0.16	0.60	0.89
24-hr-post ^a	NC	<LOD-0.16	<LOD	<LOD	<LOD	0.10	0.13
Total ^b	NC	<LOD-1.25	<LOD	<LOD	0.20	0.30	0.33
Pre-flight ^b	NC	<LOD-0.33	<LOD	<LOD	0.21	0.29	0.31
Post-flight ^b	NC	<LOD-1.25	<LOD	<LOD	0.19	0.44	0.76
24-hr-post ^b	NC	<LOD-0.30	<LOD	<LOD	<LOD	0.25	0.29
Disinsection							
Total ^a	NC	<LOD-0.54	<LOD	<LOD	0.11	0.20	0.43
Pre-flight ^a	NC	<LOD-0.54	<LOD	<LOD	0.26	0.53	0.53
Post-flight ^a	NC	<LOD-0.17	<LOD	<LOD	0.11	0.12	0.15
24-hr-post ^a	NC	<LOD-0.08	<LOD	<LOD	<LOD	0.08	0.08
Total ^b	NC	<LOD-0.70	<LOD	<LOD	0.18	0.39	0.56
Pre-flight ^b	NC	<LOD-0.70	<LOD	<LOD	0.38	0.61	0.66
Post-flight ^b	NC	<LOD-0.30	<LOD	<LOD	0.18	0.28	0.29
24-hr-post ^b	NC	<LOD-0.33	<LOD	<LOD	<LOD	0.16	0.24
4F-3-PBA							
Non-disinsection							
Total ^a	NC	<LOD-0.29	<LOD	<LOD	<LOD	0.13	0.20
Pre-flight ^a	NC	<LOD-0.19	<LOD	<LOD	<LOD	0.11	0.14
Post-flight ^a	NC	<LOD-0.29	<LOD	<LOD	<LOD	0.14	0.23

Metabolite	GM	Range	Percentile				
			25th	50th	75th	90th	95th
24-hr-post ^a	NC	<LOD-0.20	<LOD	<LOD	<LOD	0.12	0.16
Total ^b	NC	<LOD-0.42	<LOD	<LOD	<LOD	0.13	0.22
Pre-flight ^b	NC	<LOD-0.42	<LOD	<LOD	<LOD	0.09	0.18
Post-flight ^b	NC	<LOD-0.40	<LOD	<LOD	<LOD	0.13	0.20
24-hr-post ^b	NC	<LOD-0.26	<LOD	<LOD	<LOD	0.13	0.17
Disinsection							
Total ^a	NC	<LOD-0.36	<LOD	<LOD	<LOD	0.18	0.24
Pre-flight ^a	NC	<LOD-0.36	<LOD	<LOD	<LOD	0.30	0.33
Post-flight ^a	NC	<LOD-0.09	<LOD	<LOD	<LOD	<LOD	<LOD
24-hr-post ^a	NC	<LOD-0.18	<LOD	<LOD	<LOD	0.12	0.15
Total ^b	NC	<LOD-1.07	<LOD	<LOD	<LOD	0.27	0.63
Pre-flight ^b	NC	<LOD-1.07	<LOD	<LOD	<LOD	0.55	0.81
Post-flight ^b	NC	<LOD-0.21	<LOD	<LOD	<LOD	<LOD	<LOD
24-hr-post ^b	NC	<LOD-0.73	<LOD	<LOD	<LOD	0.24	0.49

^aVolume-based concentration (μg/L);

^bCreatinine adjusted concentration (μg/g creatinine)

^cNot calculated due to small detection percentage (< 24 %)