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Effects of Pyrethroid Insecticides on Pest Control Operators

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Pyrethroids like cyfluthrin, cypermethrin, permethrin, and deltamethrin are among the most frequently applied insecticides used for indoor extermination. Consequently, pest control operators (PCOs) are often exposed to these insecticides during handling, mixing and spraying.

Pyrethroids are neurotoxic by prolonging the opening of the sodium channel (Aldridge 1990). In humans, a variety of reversible symptoms have been reported (He et al. 1988, 1989), including abnormal facial sensations like burning, itching, or tingling sensation, paresthesia, and irritations of the skin, mucosa, and respiratory tract. Non-specific symptoms for pyrethroid exposure include headache, dizziness, nausea, and epigastric pain.

Pyrethroids are rapidly metabolized by a hydrolytic cleavage of the ester bond, followed by oxidation yielding the non-toxic acid metabolites. These metabolites are partly conjugated and mostly eliminated renally (Eadsforth and Baldwin 1983; Woollen et al. 1992). As markers of absorption the pyrethroid metabolites are useful (Kuhn et al. 1996; Woollen 1993).

The objective of this study was to compare the frequency of complains repoted by PCOs exposed to pyrethroids with a control group of unexposed subjects. A questionaire listing symptoms associated with pyrethroid exposure was developed to analyze any differences specified between these groups. To estimate any ill effects, medical examination as well as complete clinical labor analysis were performed. Furthermore, to assess possible pyrethroid absorption urinary metabolites were measured in both groups.

MATERIAL AND METHODS

A group of 22 male PCOs aged 23 to 59 years (mean ± S.D. : 37.8 ± 10.9 years) and 20 unexposed men aged 26 to 54 years (mean ± S.D. : 38.6 ± 9.3 years) were investigated.

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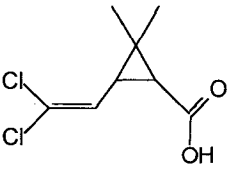
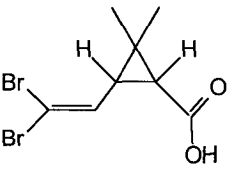
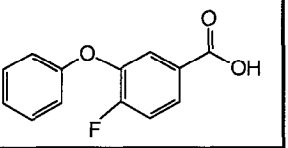
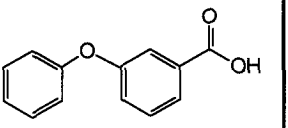
The control group consisted of civil servants, who had no contact to pyrethroids at work or at home. There was no difference in the consumption of alcohol and cigarettes between groups. No chronic diseases were reported. The PCOs had been working in their job between 1 and 21 years (mean: 6.36 years, median: 5.00 years) and had regulary been exposed to pyrethroids during these years. The weekly working time ranged between 40 and 85 hours.

During the week before investigation (monday - friday), all PCOs were handling pyrethroids on a daily basis. In this group, 16 persons were exposed to cyfluthrin (Bayer, Germany), 3 persons to permethrin (Frohwein, Germany), 2 persons to deltamethrin (Frohwein, Germany), and one person to cypermethrin (Deutsche ICI, Germany). The pesticide emulsions were mixed by the PCOs according to the manufacturer's instructions and contained 0.2 - 0.8 % of active pyrethroid. The emulsions were sprayed indoors on average for 4 h each day. The PCOs wore single use protective suits, rubber boots, short-sleeved gloves with plastic palms, and protective masks during spraying.

Table 2. Pyrethroid metabolites tested for biological monitoring in patient's urine specimens

Pyrethroids	Metabolites	Formular
Cyfluthrin Cypermethrin Permethrin	cis-/trans-3-(2,2-**dich**loro-vinyl)-2,2-dimethyl-**c**yclopropane-carboxylic **a**cid (**cis-/trans-DCCA**)	
Deltamethrin	cis-3-(2,2-**dibr**omovinyl)-2,2-dimethyl-**c**yclopropane-carboxylic **a**cid (**cis-DBCA**)	
Cyfluthrin	4-**f**luoro-3-**p**henoxy-**b**enzoic **a**cid (**FPBA**)	
Cypermethrin Deltamethrin Permethrin	3-phenoxy-**b**enzoic **a**cid (**3-PBA**)	

At the end of the week all subjects were interviewed with a questionaire to get information about their socio-demographic status, drinking, eating and smoking habits, former and actual diseases, medication, and possible types of exposure at work and home (including the surrounding area). Furthermore, we asked every person to fillout a symptom questionaire (36 listed), consisting of reversible and nonspecific type symptoms.

All subjects had a physical and neurological investigastion and routine laboratory tests including blood cell counts, differential white blood cell counts, fat, blood glucose, electrolytes, and parameters of liver and kidney diseases. In our clinical laboratory all data were analyzed according to standard values used in routine clinical testing.

For the biological monitoring, 24 hour urine samples were taken over the week-end (exposure-free time). Volume and level of creatinine of each urine sample were determined. Until analysis, all samples were stored deep frozen (-21° C).

The characteristic pyrethroid metabolites cis-/trans-DCCA, cis-DBCA, 3-PBA, and FPBA served as markers of pyrethroid absorption and were determined in each urine sample of PCOs and control subjects (Table 2). The metabolites in urine were analyzed by a validated GC/MS method (Kuhn et al. 1996; Leng et al 1997).

The urine samples were subject to an acid-induced hydrolytic cleavage of the conjugates, followed by liquid-liquid extraction and methylation of the free acid metabolites.
The prepared derivatives were seperated by diastereoselective gas chromatography using a Hewlett-Packard MS Engine with a 5890 gas chromatograph, an autoinjector 7673 and a 5989 A mass-selective detector. The gas chromatograph was equipped with a nonpolar fused silica Hewelett-Packard Ultra 2 capillary column coated with poly(5%-diphenyl-95%-dimethylsiloxane).
Injection volume was 1 µL with helium as carrier gas. The injector was set at 90° C and programmed from 90° C at 300° C/min to 300° C, holding for 22 min.
The column was maintained at 90° C and programmed from 90° C at 40° C/min to 130° C, holding for 2 min and then at 10° C/min to 270°C, holding for 5 min. Mass spectra were obtained by electron impact ionisation at 70 eV. To enhance the sensitivity of the instrument selected ion monitoring (SIM) was employed.

Quantitation was achieved by internal calibration using 2-phenoxybenzoic acid (2-PBA). Before analysis, the internal standard, 2-PBA was added to every urine sample. Calibration curves of the methylated acid metabolites were linear from 0.5 - 500 µg/L.
The limit of detection (LOD) was 0.5 µg/L with an in-run coefficient of variation of 15 % for all metabolites concerned.

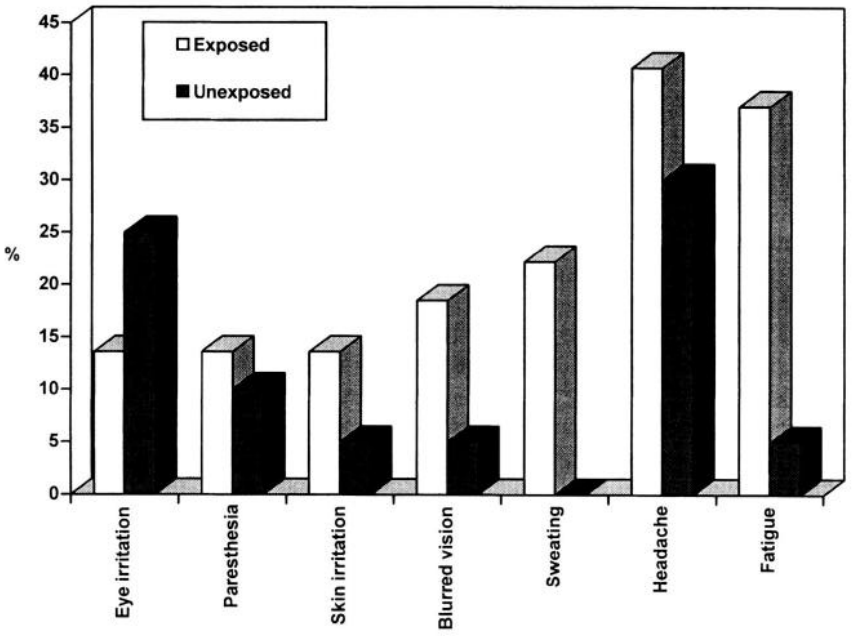


Figure 1. Frequency of reported symptoms (%) in exposed (PCOs) and unexposed group

RESULTS AND DISCUSSION

According to the questionaire, 50 % of the PCOs and 62 % of the control group did not mention any complains. In contrast, among the complains, specific symptoms (eye irritation, blurred vision, paresthesia, skin irritation) were much less reported compared to the unspecific ones (sweating, headache, fatigue). Paresthesia, skin irritation and headache are named by several subjects of both groups.

A χ^2-test (Yates' correction) on a p-level of 0.05 (Sachs 1984) was used. Although, sweating, was more often reported in the exposed group it turned out not to be statistical significant. Only fatigue was statistical significantly more often reported by the PCOs compared to the control. Independent of pyrethroid exposure, this might be explained by PCOs working conditions. All other symptoms named in Figure 1 showed no statistical differences between the groups.

In neither of the two groups, abnormalities of blood, heart, lungs, liver and nervous system were found by physical examination or laboratory tests. Consequently, concerning blood analysis and medical examination, statistical differences could not be established between exposed and unexposed subjects.

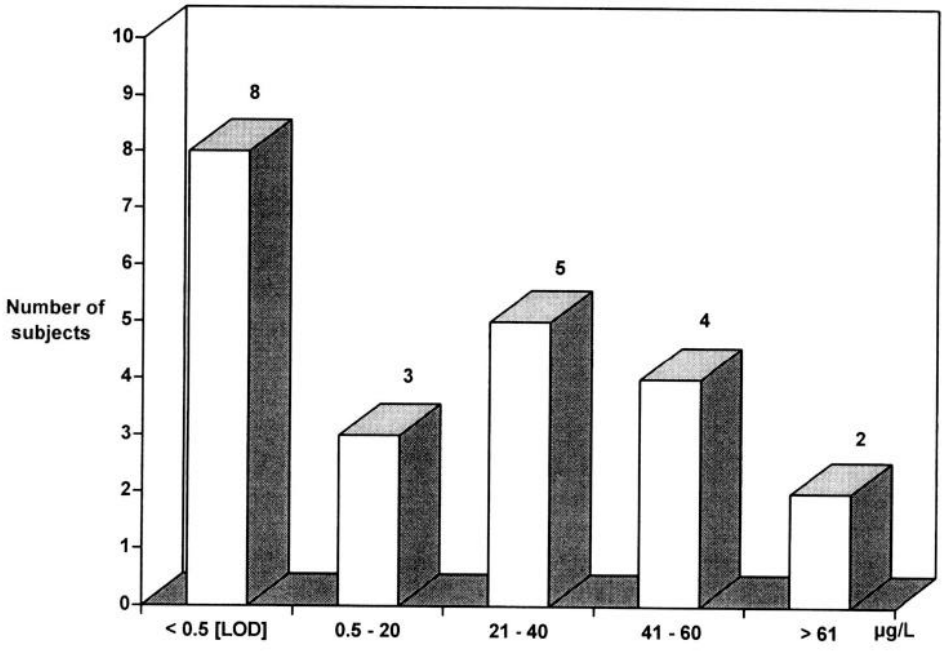


Figure 2. Total metabolite concentration (sum of cis/trans-DCCA and FPBA or 3-PBA) in the urine of 22 PCOs exposed to pyrethroids

In the group of the PCOs, the metabolite concentrations in the urine of 8 subjects were below the limit of detection (< 0.5 µg/L). Furthermore, 14 PCOs (64 %) showed total metabolite concentrations ranging between 0.5 and 277 µg/L urine, the median being 35 µg/L (Figure 2). Even in cases of elevated metabolite concentration in urine, no evidence of ill effects could be found by physical examination and clinical laboratory tests.

In contrast, no pyrethroid metabolites were found in the urine of unexposed subjects (< 0.5 µg/L), showing that no significant uptake of pyrethroids during the time of investigation had occured.

However, for the symptoms eye irritation and headache prominetly named in the control group (Figure 1), no medical cause could not be verified by the applied diagnostic tools (medical examination and clinical laboratory tests). Their complains could may be associated with general and irritative symptoms of *sick-building* syndrom (Kolmodin-Hedman et al. 1995) since all subjects of these group were office employees and did extensive work using personal computers. But it was clearly beyond the scope of this study to verify symptoms not related to pyrethroid exposure.

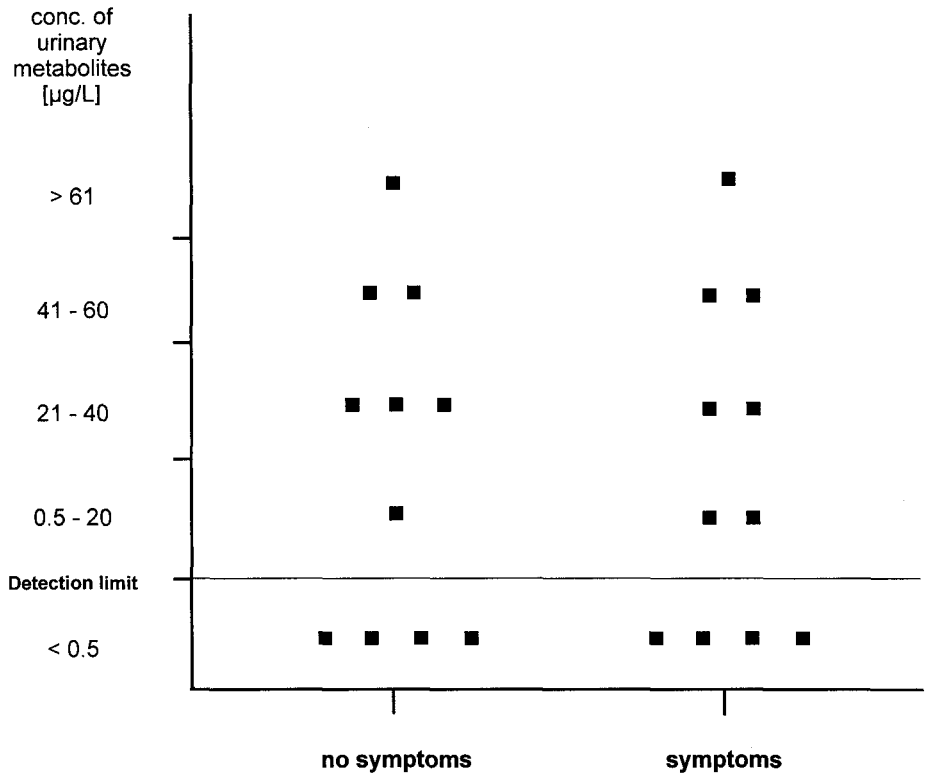


Figure 3: Relationship between pyrethoid metabolite concentration in urine and reported symptoms of 22 PCOs

In Figure 3 the relationship between the concentration of metabolites in urine and the reported symptoms for the PCOs is compaired, showing a nearly equal distribution of values in both groups. The Mann-Whitney U test on a *p*-level of 0.05 (Sachs, 1984) showed no relationship between type and number of complains reported by the PCOs and concentration of pyrethroid metabolites in urine.

These findings are in agreement with a study of forestry workers in Sweden (Kolmodin-Hedman et al. 1995). In the Sweden study, no correlation was found between the degree of dermal exposure to permethrin and the concentration of urinary pyrethroid metabolites (their limit of detection: 50 µg/L) and the frequency of symptoms. In further investigations about subjects engaged in packaging or spraying pyrethroids, no relationship were reported between symptoms, clinical findings, and biological monitoring (He et al. 1988;. Zhang et al. 1991). Generally, it is difficult to draw correlations between symptoms obtained from questionaire and a pesticide exposure, because of the variety of factors influencing peoples behaviour when outfilling questionaires (Barrot, 1996).

On the whole, no correlation between symptoms reported by subjects exposed to pyrethroids, the urinary concentration, or total amount of the eliminated metabolites could be found.
However, a sensitive biological monitoring assessing the absorption of pyrethroids by measuring their metabolites in urine is still usefull in toxicology, occupational medicine, and risk assessment. Nevertheless, due to many known and unknown variables e.g. interindividual differences of excretion rates, personal hygiene, major route, and extend of absorption, biological monitoring was of limited use for the interpretation of symptoms in our field study.

In general, from these findings it should not be extrapolated that pyrethroid exposure and absorption can not cause ill effects on human health. It must be taken into account that there are risk groups like very sensitive subjects and humans with metabolic deficits or polymorphism. In such cases, relationships between biomakers of absorption and reported symptoms are more likely to find.

Since only pyrethroids and not their detoxified metabolites are known to cause neurotoxic effects (Aldridge 1990), probably there would be a correlation between the concentration of intact pyrethroids in blood and health effects reported by susceptible persons. The measuring of pyrethroids in blood as markers of adverse effects is difficult to implement in field studies, because of their rapid enzymatic degradation (Leng et al. 1997). Nowadays, a quantitation of these pesticides in blood is limited to a monitoring of severe intoxications under emergency conditions.

Futher research is recommended to extend knowledge about the relationship between human pesticide exposure, extend of absorption, and possible ill effects.

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