Bull. Environ. Contam. Toxicol. (1995) 55:487–493

Environmental Contamination and Toxicology

Symptoms in Forestry Workers Handling Conifer Plants Treated with Permethrin

B. Kolmodin-Hedman,[1] M. Åkerblom,[2] S. Flato,[1] G. Alex[2]

[1]Karolinska Institute, Dept. of Occupational Medicine, S-141 86 Huddinge, Sweden
[2]National Swedish Laboratory for Agricultural Chemistry, Ultuna, S-750 07 Uppsala, Sweden

Received: 30 July 1994/Accepted: 17 February 1995

In Sweden, an intensive debate is going on about the effects of pesticide handling and pesticide contamination of the environment. So forestry workers are quite worried about the toxicity and symptoms caused by the pesticides in use.

Conifer seedlings were treated with DDT; in 1976, it was outlawed. During the past 10 years, synthetic pyrethroids have been increasingly used to combat the large brown pine weevil (*hylobius abietus*).

Already in 1982, Kolmodin and coworkers reported irritative symptoms in skin and upper respiratory tracts and paresthesia and numbness in the skin of forestry workers, who used fenvalerate and various permethrin isomers (Kolmodin et al, 1982).

Because concern about chemical influence can also create subjective symptoms, the present study was conducted. The purposes of the present study were to:

- Study the frequency of the symptoms in a double-blind design
- Estimate dermal contamination of permethrin
- Estimate possible uptake in the body by checking permethrin metabolite in urine

MATERIALS AND METHODS

Three groups were studied: 18 workers (16 males and 2 females). They were followed for 3 days over a 2-week period during the normal planting season.

Correspondence to: B. Kolmodin-Hedman

By random design, they planted 2 batches of plants:

1. Untreated, where only the vehicle and solvent and water were applied on the plants
2. Plants sprayed with 1.5% permethrin

In a coded way, they planted untreated plants—one week. Then they switched to treated plants—the other week, or vice versa. The plant cartons were coded by number and color for each day. So the order of starting with treated and untreated, respectively, was randomly designed. Field observers did not know this order.

Two batches were treated by the product Ipitox 500EC. One batch had 1.5% emulsion with 15 mg active permethrin per plant. The other batch *did not* contain permethrin; the emulsifier and solvent dose was 20 mg per plant. This treatment occurred centrally, at a plant nursery school. The plants were dried and packed in brown paper cartons and transported to the forest.

The workers wore long cotton or nylon jackets, cotton pants, and short-sleeved gloves with plastic palms. At the end of work day 2, each week, their hands were washed in 40% ethanol and a standardized area of 1 dm^2 on the forearm and 1 dm^2 on the forehead was swabbed with cotton pads soaked in 40% ethanol. Pads were frozen until analysis. At the end of work day 3, each week, urine spot samples were taken. The urine samples were also frozen until analysis.

Before analysis, as an internal standard, esfenvalerate was added to the cotton pads and to the hand rinse.

The cotton pads that were moist from ethanol, were extracted with cyclohexane by ultrasonic treatment. The extract was shaken with sodium chloride solution. The cyclohexane phase was analyzed by gas chromatography.

The hand rinse was evaporated nearly to dryness. The residue was dissolved in cyclohexane acetone. This analysis was done the same way as the pads analysis.

A Hewlett-Packard™ 5890 gas chromatograph with an EC detector was used. It was equipped with a fused silica capillary column that was coated with DB5. Injector and detector temperatures were 280ºC. The oven was temperature programmed from 230ºC to 260ºC by 4ºC/min. Recovery was 70-100%. The detection limit was 0.2 μg for each sample.

Urine was analyzed according to the manufacturer's instructions. With this method, the permethrin and conjugated metabolites are esters that are cleaved by acid hydrolyzed to the metabolites, the acid moiety of which is simultaneously methylated. Determination was made by capillary gas chromatography with EC detection. Recovery was 60-70%. The detection limit was 0.05 μg/ml.

A previously used questionnaire (Kolmodin-Hedman et al, 1990) was completed by the workers at the end of each work day. The questionnaire took up 20 symptoms that consisted of irritative signs and symptoms in the skin, eyes, and respiratory tract. General questions about headache, nausea, and tiredness and 2 specific questions about paresthesia on the face and hands were also included. The last symptoms are characteristic of pyrethroid exposure (He et al, 1989). The questions were ranked from none, slight, modest, to strong. Each day, the field assistant asked about the intensity and character of the reported symptoms and inspected the skin, eyes, and throats for possible signs.

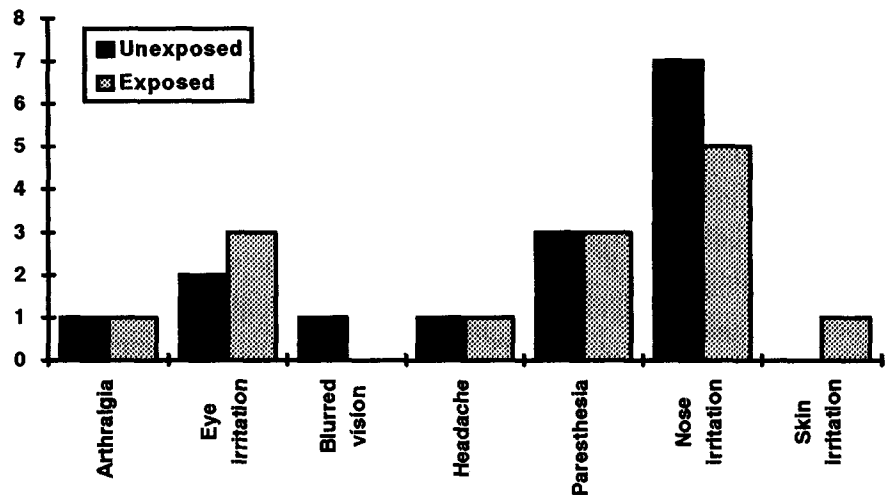

Figure 1. Number of subjects with irritative symptoms and some general symptoms in unexposed (black) and exposed (shaded).

A paired t-test was used. Each person served as his or her own control, where exposed and unexposed weeks were compared. The temperature and relative humidity were measured with an Assman psychrometer (The Lambrecht Co., Germany).

RESULTS AND DISCUSSION

Only a few workers reported symptoms. In Figure 1, seven symptoms are compared. The week with untreated plants (black) is compared with the week with treated plants (shaded). Eye and nose irritation were the 2 most common symptoms. Five never reported symptoms. Three had more symptoms during handling of treated plants—compared to untreated. Three workers reported less symptoms during treatment, while 7 reported minor symptoms both weeks. One worker developed blisters comparable to herpes simplex infection and was sent to a dermatologist. She was given a skin test with pure permethrin and the formula used. She tested negative to both. Another worker had an eczema-like small change on the leg and was also given a skin test, which was also negative.

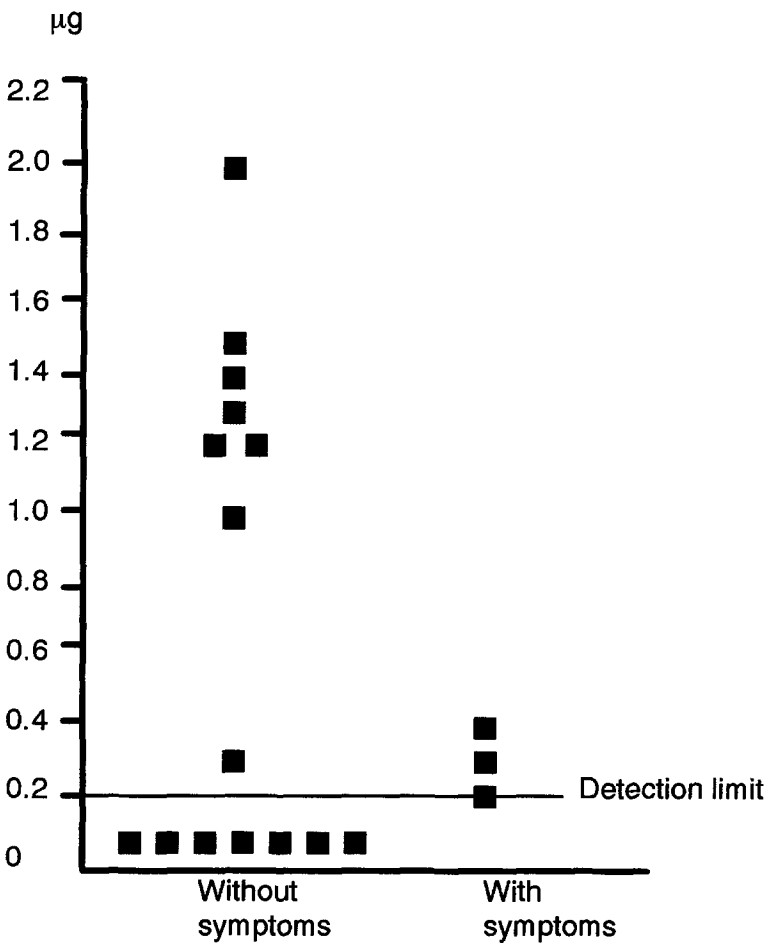

Figure 2. Relationship between dermal exposure of the arm and symptoms on the hand and arm.

The forehead and forearm showed levels of permethrin from nondetectable to 2.0 μg per sample. The mean value for arm exposure was 0.3 μg. Hand rinses varied from nondetectable levels to 1.8 μg per hand rinse with a mean of 0.7. Seventeen of 18 workers had measurable permethrin on their hands.

Figure 2 shows the relationship between exposure of hands and arms in workers with symptoms and without—on hands and arms. On the whole, the Mann-Whitney analysis showed that eye, nose, and skin symptoms could not be related to the degree of skin exposure. Urine from 4 workers who had the highest exposure on their hands (2 with 1.8 μg and 2 with 1.6 μg) was analyzed for permethrin and its acid metabolite. In all 4 cases, no permethrin or acid metabolites were detected. The detection limit was 0.05 μg per ml urine.

In a working population, reports occur about eye, skin, and general symptoms such as headaches and tiredness. Previous studies in control populations in *sick-building* investigations show irritative symptoms in the control populations to be less than 5% and general symptoms and irritative symptoms to be less than 10%. Concern about expected ill effects from the environment can increase these figures appreciably (Kolmodin-Hedman, 1990).

From the literature about the use of pyrethroids, Flannigan and coworkers (1985) reported skin irritation in doses of more than 130 μg per cm^2, that is, 13 mg on 1 dm^2. The present study calculated an extrapolated dermal dose of 0.001 mg/dm^2. This is well below the figures reported by Flannigan. So no over representation of skin symptoms related to permethrin would be expected.

The characteristic paresthesia that was reported earlier by workers using permethrin and other synthetic pyrethroids is caused by a transient irritation of the peripheral nerves (Kolmodin-Hedman, 1982; Ray, 1991). In high doses, (as reported by Chinese agricultural workers) both CNS and PNS might be affected (He et al, 1989). Permethrin's allergy-causing potential in humans is low. Two workers who had had mucosal blisters and 1 who had eczema on the leg were given skin tests with permethrin and the formula. The tests were negative. This agrees with our previous investigation in 1982, where 8 tested persons with skin symptoms did not react to skin tests.

In a previous investigation by Kolmodin-Hedman et al (1982), a maximal inhalation concentration of permethrin during a 6-8 hour work day was 0.04 mg/day.

In the present study, maximal dermal exposure, if the whole body area of 170 dm^2 would have been exposed, gives a value of 0.2 mg. A median exposure of 0.04 mg was found. Some parts of the body are covered, so they would not be exposed. The hands and face are most commonly exposed.

A 100% uptake of 0.2 mg would give a permethrin dose of 0.003 mg/70 kg person body weight. Calculated with the mean exposure of 0.04 mg and a theoretical dermal uptake of 10%, gives a dose of 0.0006 mg/kg.

Pyrethroids are not easily absorbed by the skin (Ray, 1991). Dermal LD50 in rats is given to be more than 2500 mg/kg. NOEL for permethrin is calculated to 5 mg/kg bw and day. WHO has set ADI to 0.05 mg/kg bw. The values found in the present study are well below this limit.

Oral uptake of permethrin is metabolized rapidly by esterases and then excreted in urine. The present study analyzed urine samples from 4 workers with the highest dermal exposure. But no metabolites were found with a detection limit of 0.05 mg/l.

Dermal exposure was measured on hands in 17 out of 18 workers—despite the use of gloves. Appropriate use and change to new gloves are important. So is good hygiene before meals, breaks, and at the end of the work day—to avoid exposure.

REFERENCES

Flannigan SA, Tucker SB, Key MM, Ross CE, Fairchild EJ, Grimes BA, Harrist RB (1985) Synthetic pyrethroid insecticides: A dermatological evaluation. Br J Ind Med 42:363-372

He F, Wang S, Liu L, Chen S, Zhang Z, Sun J (1989) Clinical manifestations and diagnosis of acute pyrethroid poisoning. Arch Toxicol 63:54-58

Kolmodin-Hedman B, Swensson Å, Åkerblom M (1982) Occupational exposure to some synthetic pyrethroids (permethrin and fenvalerate). Arch Toxicol 50:27-33

Kolmodin-Hedman B, Jönsson E, Andersson C, Stjernberg N (1990) Symptoms in a population from northern Sweden—a cross-sectional study. 1st Int Congress of Behavioral Medicine Proceedings p 39.

Mann Whitney (1988) Nonparametric statistics for the behavioral sciences. Siegel S, Castellan JN Jr. (eds). McGraw-Hill

Ray DE (1991) Pesticides derived from plants and other organisms. In: Hayes WJ, Laws ER, Handbook of pesticide toxicology, Academic Press, New York, pp 585-636