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EXPOSURE EVALUATION IS A CRUCIAL STEP FOR QUANTITATIVE RISK ASSESSMENT OF METHOMYL

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Methomyl, methyl N-[[(methylamino)carbonyl]oxy]ethanimidothioate is a carbamate insecticide with anticholinesterase activity. As a broad spectrum insecticide, it is one of the most frequently used pesticides in tangerine orchards in Thailand. Although methomyl is said to be rapidly eliminated from experimental animals (1) high incidence of acute poisonings was reported among patients occupationally exposed to a powder formulation of methomyl (2, 3). In this passive dosimetry study of tangerine growers, during mixing and overhead spraying of a 90% powder formulation of methomyl, ocular and nasal exposure was measured. Exposure data are discussed in terms of the "potentially absorbed" or "internal dose".

Key terms:
acute poisoning, carbamate insecticide, occupational exposure

Most of the acute episodes of pesticide poisoning occur in developing countries. It has been proposed that the reason for the large number of acute poisonings may be due to the lack of adequate risk management and regulatory response for the highly hazardous pesticide formulations.

From April through June 1993 there were 18 cases of poisoning in Nong Seu province, Patumthani, Thailand which were related to occupational exposure to methomyl. Thirteen of these cases were thought to be related to occupational exposure to a 90% powdered formulation of methomyl with other pesticides. Five cases were thought to involve only the 90% powdered formulation of methomyl. These latter poisoning cases would be classified in the "probable" category under the criteria of the US Environmental Protection Agency (EPA) where there might not be laboratory confirmed data, but there were specific signs and symptoms as well as a history of exposure.

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EXPOSURE TO METHOMYL

Previous illness reports indicated occupational poisonings due to a 90% SP formulation of methomyl in 16 patients out of a total of 25 poisoned by methomyl in 1979 (2).

Recent work of the Joint Meeting on Pesticides also established a no observed effect level (NOEL) for methomyl based on acute toxicity due to cholinesterase inhibition (3). Agricultural practices of Thai tangerine growers such as the open system loading and mixing and high volume overhead spraying with a high pressure pump without proper protective clothing increase the likelihood of exposure to agricultural chemicals.

Interviews of the poisoned patients revealed that irritation of the eyes was experienced regularly (4). According to a survey of 445 growers in Nong Seu district, there was a significant relationship between the pesticide poisoning incidence and the amount of powdered formulations used (5). This study quantifies the degree of exposure of tangerine growers to a 90% powder formulation of methomyl during tangerine growers' working procedures.

METHODS

Workers

Three workers who participated in the exposure trials were growers who routinely applied pesticides. A man aged 57, height 165 cm, right handed, mixed, loaded and sprayed the pesticide. A woman aged 25, right handed, worked as a sprayer only. Another woman, 18 years old, right handed, worked as a boat-puller. The workers were informed of the study and agreed to cooperate. They performed routine spraying with exposure pads on their bodies.

Chemicals

Lannate (methomyl) 90% SP was purchased from a local store in Nong Seu. The volume applied and the dilution rate were 1,000 litres, 18 g formulation per 20 litres of canal water.

Experimental procedure

A high pressure power sprayer was mounted in the middle of a boat. The insecticide was mixed by one sprayer using a reservoir in the boat. The duration of the operation was 20 minutes, two minutes per row were spent mixing and 18 minutes

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were spent spraying. The weather was fair with a little breeze. The wind speed was approximately 2 m/sec, and the temperature was 29.5 °C. The mixer-sprayer stood on the bank of row 2 and sprayed row 1 plants while the other sprayer stood on the bank of row 1 and sprayed the row 2 plants. The mixer-sprayer mixed the pesticide solution once for each row of spraying due to the limited volume of the mixing reservoir. Therefore the mixer-sprayer mixed pesticides 20 times per day of work.

All workers wore long sleeved cotton shirts, long cotton pants, hats (wide-brimmed) and boots. This is the routine clothing used by Thai growers.

Eye exposure pads

For the assessment of the applicator's exposure passive dosimetry techniques were used (6). The pads were constructed from surgical gauze approximately 1 centimetre thick and composed of 40 layers. These pads had been preextracted with water to remove substances that might interfere with residue analysis. An aluminium foil backing square was overlayed with the surgical gauze pads and they were bound together with a masking tape.

The exposure gauze pads were attached to the left hand side of the chemical resistant goggles worn by the mixer and the sprayers.

Respirator exposure pads

The ordinary dust filter was replaced by the gauze filter, which has been described by the Environmental Protection Agency (6). The respirator was manufactured with a cover with an opening middle. The opening was 17 millimetre, using a single unit respirator. The exposure pads were immediately wrapped in an aluminium foil and transported to the analytical laboratory in a refrigerated box on the same day.

The exposed gauze pads were analysed (82% recovery) by means of a high pressure liquid chromatography method developed by *Hunt and Langdon* (7).

RESULTS

Results show that a mixer-sprayer was exposed to a much higher amount of methomyl per square centimetre on exposure pads than a boat puller or a sprayer (Table 1).

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Table 1 *Methomyl exposure of tangerine growers*

	Amount of methomyl on pad per row (μg/cm²)	Amount of methomyl received per day (μg)
Eye exposure		
boat puller	0.47	9.4
sprayer	0.45	9.06
mixer and sprayer (n=3)	10.76±2.75	215.26
Respirator exposure		
boat puller	2.2	44
sprayer	2.7	54
mixer and sprayer (n=3)	6.04±2.93	120.80

For sprayer and boat puller, the value is an average of three row-spraying, without changing of pads.
For mixer and sprayer, pads were changed after each row of spraying, the value is an average of three measurements ± S.D.
Normally, workers spray 20 rows of tangerine per day.

DISCUSSION

This study showed that the eyes and the nasal region of the growers were highly exposed to methomyl. The grower who was a pesticide loader, mixer and sprayer received a much higher combined exposure than the sprayer alone or the boat puller. This higher exposure may be explained by the agricultural activities as well as by the high concentration of the powder formulation used.

In assessing risk from nasal exposure, it is essential to consider the differences in regional deposition patterns. Different species exposed to the same dust particles of the same chemical in comparable regions of the respiratory tract may not receive an identical "internal dose". The deposition and adsorption of dust particles in the nasopharyngeal area will depend on the physico-chemical properties of the particles, regional airway geometry, airflow characteristics and airway physiology (8).

The amount of absorption of methomyl will be a result of competition between mucociliary clearance and permeation through the mucosal surface. The methomyl which is not absorbed from the nasal cavity can also be removed into the pharynx.

In addition, the rate of clearance of a chemical will influence the rate of cholinesterase inhibition.

Methomyl is a small molecule (relative molecular mass 162) and is highly soluble in water (3). The nasal epithelium is a single layer, one cell deep. The different epithelial paths may differ widely in the permeability of their junctions: namely transcytosis, transcellular or paracellular (through the cell-cell junctions).

Non-specific diffusion between the cells of the nasal mucosa imposes a size restriction on permeability.

McMartin and co-workers (9) reported a high degree of absorption for low molecular weight polar compounds. From the physico-chemical characteristics of methomyl it is expected that methomyl will be readily absorbed by any route of exposure. This is consistent with the information that methomyl may be absorbed through the conjunctiva of animals resulting in systemic intoxication and cholinesterase inhibition (1).

Technical grade methomyl is highly toxic by the oral and respiratory routes of exposure while dermal toxicity is low. Methomyl inhibits acetylcholinesterase rapidly but spontaneous reactivation of carbamylated cholinesterases is also rapid, the half-life being between 2 and 240 minutes (10). The metabolism by various esterases to non-inhibitory products is also rapid (3). The major metabolic components in the expired air were carbon dioxide and acetonitrile in the ratio of about 2:1. The major metabolite in urine was the mercapturic acid derivative of methomyl, equal to 17% of the dose (3).

If one considers total exposure to methomyl through nasal absorption to be the "absorbed dose", the margin of safety to achieve the "effective dose" is a little over one hundred, not considering dermal exposure which is generally considered to be the major route of exposure to pesticides during occupational exposure (3). However, for methomyl, exposure evaluation is a crucial step for risk assessment. Further evaluation such as through biologically based pharmacokinetics may provide a more accurate quantitative risk assessment.

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Sažetak

PROCJENA IZLOŽENOSTI METOMILU ODLUČUJUĆI JE KORAK U KVANTITATIVNOJ OCJENI RIZIKA

Metomil, metil N-[[(metilamino)karbonil]oksi]etanmidotioat je karbamatni insekticid s antikolinesteraznim djelovanjem. Kao insekticid širokog spektra nalazio se među pesticidima koji su najviše upotrebljavani u voćnjacima mandarinki u Tajlandu. Premda je na osnovi eksperimenata na životinjama poznato da se metomil brzo izlučuje, ustanovljena je visoka učestalost akutnih trovanja među ljudima profesionalno izloženima praškastoj formulaciji metomila. U ovoj pasivnoj dozimetrijskoj studiji mjerena je izloženost putem očiju i nosa uzgajivača mandarinki tijekom miješanja i prskanja 90% praškaste formulacije metomila. O podacima se raspravlja u smislu eventualno apsorbirane ili interne doze.

Ključne riječi:
akutno trovanje, karbamatni insekticid, profesionalna izloženost

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