

Inhalation of publicly available indoor insecticide spray caused myocardial infarction type II: a case report

Dirk Habedank^{1*}, Beate Stubbe², Ralf Ewert², Alexandra Kroll¹, Iskandar Atmowihardjo¹ and Birgit Habedank³

¹Clinical Medicine Department of Cardiology, DRK Kliniken Berlin Köpenick, Berlin, Germany; ²Clinical Medicine Department of Pneumology, University Medicine Greifswald, Greifswald, Germany; and ³Section Health Pests and their Control, German Environment Agency, Berlin, Germany

Abstract

We report on a 70-year-old woman who tried to eliminate ants from her kitchen by applying a publicly available insecticide spray. Immediately afterwards, she felt dyspnoea, superseded by heavy chest pain. High-sensitivity troponin concentration increased from 33 to 149 ng/L (cut-off 50 ng/L). Significant coronary stenosis was excluded by coronary angiography, and the myocardial damage was classified as myocardial infarction type II. After exclusion of other potential mechanisms, we consider a cardiotoxic effect of the insecticide mixture of cypermethrin, tetramethrin, and piperonyl butoxide possible. We conclude that consumer information has to be improved. This concerns sustainable control measures adapted to the target insect species (in this case, the black garden ant *Lasius niger*), and differentiation between authorized and non-authorized but notified products. The instructions for use should give clear information on vulnerable groups and recommend personal protective equipment. Physicians and authorities should be alert to cardiac side-effects of insecticides.

Keywords Cypermethrin; Tetramethrin; Piperonyl butoxide; Insecticide spray; Non-professional use; Myocardial infarction type II

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*Correspondence to: Dirk Habedank, Clinical Medicine Department of Cardiology, DRK Kliniken Berlin Köpenick, Medizinische Klinik Kardiologie, S.-Allende-Str. 2-8, D 12555 Berlin, Germany. Phone: +493030353665. Email: d.habedank@drk-kliniken-berlin.de

Introduction

Insecticidal products should be effective against target insects but must not harm human health, other vertebrates, or the environment, assuming application in accordance with the instructions for use.^{1,2} Consumers in the EU might not be aware of differences between authorized biocidal products (identifiable by authorization number²) and notified but not authorized biocidal products (identifiable by N-number). An insecticide spray mixture consisting of propellant gas, solvent, and active ingredients may become toxic if instructions for use are fragmentary or not followed to the letter, or if personal susceptibility is high. Exposure to insecticide products has repeatedly led to toxic effects in humans.^{3–6} Cardiotoxicity of chemicals is not itemized as a separate hazard class,^{7,8} but introduction of this class was recommended recently.⁶ Fixed combinations of active ingredients aim at higher insecticidal efficacy and require a separate toxicity assessment.^{9,10} Against this background, our case report intends to draw attention to severe side-effects of an

insecticide mixture spray (EU notified biocide, product type 18) after application by a non-professional user.

Case report

We report on a 70-year-old woman who noticed several ant trails in the small kitchen of her summer house. The ant species was identified later on as *Lasius niger*. Our patient had a history of coronary heart disease (CHD) with single stent implantation in the left anterior descending (LAD) artery in 2012, arterial hypertension, and follicular lymphoma with curative surgery in 2008. She had neither an allergy nor a pulmonary disease in her anamnesis. When she observed many worker ants in her kitchen, she decided to eliminate them, bought an insecticide spray for non-professional indoor and outdoor use in a DIY superstore, and sprayed in her kitchen along the ant trails. Immediately afterwards, she felt nausea and primarily dyspnoea. The dyspnoea lasted

for about 1 or 2 min and was superseded by heavy chest pain. Knowing her history of CHD, she called an ambulance. The chest pain had eased off completely at our emergency unit. Electrocardiography (ECG), chest X-ray (*Figure 1*), high-sensitivity troponin T (hsTnT), trans-cutaneous oxygen saturation (96%), and echocardiography were normal. Most laboratory values were within the reference range (in square brackets), except base excess (5.2 mmol/L [−2 to +2 mmol/L]), standard bicarbonate (28.2 mmol/L [21–26 mmol/L]), lactate dehydrogenase (LDH, 239 units/L [135–214 units/L]), and alanine aminotransferase (49 units/L [<31 units/L]). However, hsTnT increased from 33 to 149 ng/L (cut-off 50 ng/L) within 1 h; combined with the preceding chest pain, this led to a suspicion of non-ST elevation myocardial infarction (NSTEMI), and coronary angiography was therefore performed. The left heart catheterization excluded progression of CHD as well as coronary spasm and showed a LAD artery stent without restenosis (*Figure 2*). Thus, the troponin elevation was interpreted as myocardial infarction type II (i.e. caused by an imbalance between myocardial oxygen supply and demand unrelated to coronary athero-thrombosis).¹¹ We consider direct cardiotoxicity as the best explanation for the chest pain and consecutive NSTEMI. The patient remained free of symptoms and was discharged after 48 h.

Discussion

The non-professional over-the-counter insecticide spray used by our patient contains a mixture of propellant gas, solvent, different alkane mixtures, and three active ingredients: the

pyrethroids cypermethrin (with long-term residual efficacy) and tetramethrin (with short-term residual efficacy), and the synergist piperonyl butoxide (PBO; *Table 1*). Warnings on this spray product referred to skin and eye irritation, drowsiness, and dizziness. The safety instructions included precautionary statements⁷ P260 ('Do not breathe the spray:') and P271 ('Use only outdoors or in a well-ventilated area.'). but there was no advice regarding personal protective equipment (PPE). An additional reference to the product's safety data sheet could have improved the consumer's knowledge and hazard awareness. In this regard, a survey by the Organisation for Economic Co-operation and Development (OECD) on regulatory requirements for pesticides reported that consumers 'have no or limited knowledge about pesticides and the associated risks' and may not wear PPE.⁵ A very recent survey on the safe use of chemicals among professionals in Greece suggested that risk awareness campaigns are still necessary even among professional users.¹² In 2020, the Food and Agricultural Organization of the United Nations (FAO) and the World Health Organization (WHO) published international guidelines for the use of PPE when handling or applying pesticides that mainly addressed professional users.¹³ We fully support these recommendations that minimal PPE should also be worn by non-professional users, and we think that advice on PPE should be included in consumers' instructions for use. The FAO and WHO even strongly recommended that 'vulnerable people, such as children, the elderly, and immunosuppressed ... people, [should] not handle ... and apply pesticides'.¹³

Cypermethrin, tetramethrin, and PBO have been widely used in products to control insects for professional and non-professional use. Cypermethrin was approved recently

Figure 1 Chest X-ray at emergency unit excluding pulmonary oedema and infiltration.

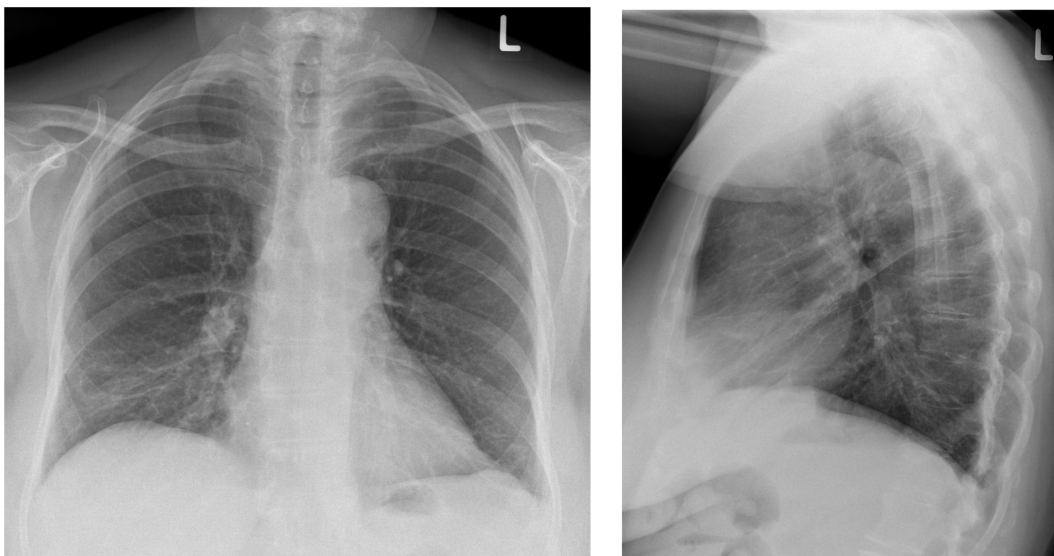
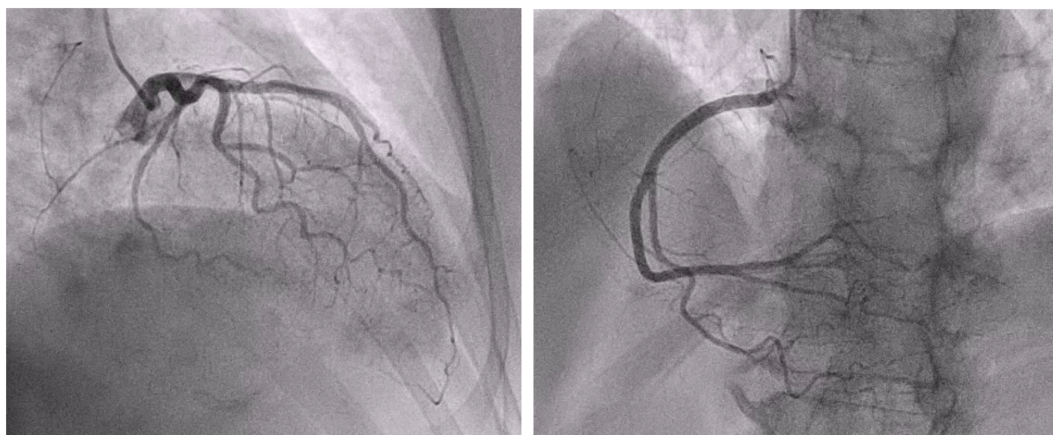


Figure 2 Coronary angiogram excluding progression of the coronary heart disease.**Table 1** Ingredients and their characteristics

Ingredient	Proportion	CAS-/EC-number	DNEL in mg/m ³	AOEL in mg/m ³
Propellant gas (propane and butane)	<80%	68476-40-4	-	1000–2400
Solvent (2-propanol)	<10%	67-63-0	89 c	500
Alkanes	<10%	921-024-6	608 c	2035
Cypermethrin	0.68%	52315-07-8	-	0.06
Piperonyl butoxide	0.51%	51-03-6	1.94 a	3.8
Tetramethrin	0.1%	7696-12-0	-	-

a, consumer acute exposure; AOEL, acceptable operator exposure level; c, consumer chronic exposure; CAS, Chemical Abstracts Service; DNEL, derived no-effect level (according to EU regulation No. 1907/2006); EC, European Community.

by EU regulation 2018/1130¹⁴; tetramethrin is still in the biocidal authorization process. The specific target organ toxicity after single exposure (STOT SE) by inhalation route of cypermethrin and PBO alone is classified as moderate (STOT SE3), and tetramethrin is classified in the potentially more harmful group (STOT SE2).^{15–17} The mode of action of pyrethroids is the alteration of voltage-gated sodium channels, which occur in both neuronal and cardiac cells, with disruption of nervous signalling being responsible for the insecticide effect.⁶ Spencer *et al.*¹⁸ proved in isolated rat hearts that cypermethrin increased the proportion of slowly inactivating current and decreased the fast inactivating current, resulting in a prolonged course of sodium current (I_{Na}), thereby evoking after-depolarizations and arrhythmogenic activity. At the *in vitro* level, both cypermethrin and tetramethrin reduced beating frequency and amplitude in cultured cardiac monocytes.¹⁹ Aside from these acute effects, long-term exposure to cypermethrin induced cardiac dysfunction in male rats, proven by both histopathology and increased plasma concentrations of cardiac markers (LDH, CK-Mb, and troponin T).²⁰ Not only ingestion but also inhalation had cardiotoxic effects in the frog heart.²¹ In man, chronic intoxication led to a permanent third-degree atrio-ventricular block,²² and oral intoxication with suicidal intention led to 48 h of sinus bradycardia.²³ Aside from these case reports, a recent cohort

study of 2116 US adults found an association (hazard ratio [HR] 3.0, 95% confidence interval [CI] 1.0–8.8) between urinary pyrethroid metabolites and cardiovascular mortality.²⁴ This is supported by a smaller Chinese study which found an association between pyrethroid metabolites and CHD (odds ratio 4.6, 95% CI 1.8–11.5).²⁵ In these studies, general population and non-occupational users of insecticides had been considered, respectively. The authors stated that further investigations are necessary to verify these findings, for example, the exclusion of further confounders might be necessary. However, the Agricultural Health Study considered the occupational use by licensed pesticide applicators and did not find an increased risk of myocardial infarction mortality associated with pyrethroids (HR 0.81; 95% CI 0.54–1.22).²⁶ Both pyrethroids (cypermethrin and tetramethrin) may irritate the mucosa of the respiratory tract, and inhalative resorption²⁷ and association with chronic obstructive pulmonary disease are possible.²⁸ Notably, cypermethrin persisted in high concentrations on surfaces and in dust samples for more than 112 days after indoor application.²⁹

PBO, an approved active substance in biocidal products of EU product type 18 until 2028,³⁰ delays the detoxification of insecticides by inhibiting a cytochrome p450 enzyme (e.g. the insecticide effect of pyrethroids is increased up to 30-fold). Long-term exposure to cypermethrin elevates micronuclei

and telomerase activity as measures of genotoxicity, and co-exposure with PBO increases these effects up to four-fold.^{9,31} In man, combined exposure to pyrethrins and PBO has been reported to increase respiratory symptoms such as bronchospasm and dyspnoea,¹⁷ but robust studies on pulmonary irritation are lacking. In summary, at least three ingredients may irritate the respiratory mucosa, and two ingredients have shown *in vitro* evidence suggesting cardiac toxicity, with clinical data also suggesting an association with cardiovascular mortality in man.

Against this background, the symptoms and troponin elevation in our patient could have four pathophysiological explanations: (1) coronary spasm—this is unlikely with a normal ECG and a normal coronary angiogram; (2) bradycardia—based on the symptoms of nausea and dyspnoea and the *in vitro* studies mentioned above, transient bradycardia seems possible; (3) transient hypoxia due to toxic lung injury or allergic reaction—we consider this less probable because oxygen saturation, chest X-ray, and pulmonary function test results the next day were normal, and white blood cell differentiation counted only 0.08 eosinophilic granulocytes per nL; and (4) cardiotoxic effect of pyrethroids in a susceptible patient—in weighting probabilities of the given mechanisms, we think this is the most likely explanation.

One last aspect regards the biology of ants. Workers of ant colonies can rapidly invade areas in human flats where they find food and become visible on their ant trails. This can lead to panic of the human inhabitant and finally to overdosing of insecticides. However, insecticide spraying to kill foraging ant workers will not eradicate the ant colony, as the queen in the ant nest will continue reproduction. Thus, the ant species must be identified and the nest located. The case presented here involved *Lasius niger*, which typically nests outside a facility with only foraging workers following the ant trails. Treatment should include removal of food sources, mechanical removal of ants, cleaning of trails with detergents, and putting up mechanical or adhesive tape barriers. If ants still appear inside the house, insecticide baits are the products of choice. These enable foraging ant workers to transport low-dosage insecticides into their nest, where nursing

workers will feed them to the queen and larvae, causing their death.

The evident finding in this case report is that an insecticide spray containing pyrethroids and PBO may induce severe dyspnoea, chest pain, and consecutively even myocardial infarction type II in a patient with cardiac comorbidity. Our report underlines the necessity of studies on insecticide mixtures. Physicians are asked to report side-effects to authorities (e.g. in Germany³²), and insecticide producers are requested to label their products with clear information on risk, vulnerable groups, and PPE.

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Conflict of interest

The authors declare no conflict of interest.

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Author contribution

DH and BH wrote the manuscript. BH wrote the regulatory and ant control aspects and identified the ants. BS and RE contributed to the pulmonary and toxicological part. AK performed the left heart catheterization, and AK, DH, and IA treated the patient and reviewed the manuscript.

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