Int J Legal Med (2002) 116 : 238–241
DOI 10.1007/s00414-002-0299-6

CASE REPORT

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Fatal intoxication with omethoate

Received: 11 September 2001 / Accepted: 8 January 2002 / Published online: 17 April 2002

Abstract A case of suicide with the insecticide omethoate is reported. An 18-year-old apprentice gardener had ingested an unknown amount of omethoate. His body was found in his room lying in the storage space under his bed. The autopsy first showed multiple superficial incisions in the skin of his wrists, furthermore hemorrhagic pulmonary oedema, dilation of the right cardiac ventricle and oedema of the brain. The gastric mucosa was swollen and showed a dark brownish colour. An intensive, chemical-like smell rose from the corpse and organs. Toxicological analysis detected omethoate in cardiac blood (208 μg/ml), urine (225 μg/ml) and bile (524 μg/ml), in the liver (341 μg/ml) and kidneys (505 μg/ml). In the gastric content the level was 48223 μg/ml. The amount of the active AChE in peripheral blood serum was reduced to less than 0.2% of the normal level. To our knowledge no case of a fatal suicide by ingestion of omethoate has been reported in literature.

Keywords Organophosphate insecticides · Omethoate · Fatal poisoning · Suicide

Introduction

Omethoate (Dimethoxon; O,O-dimethyl-S-methylcarbamoylmethylthiophosphate, $C_5H_{12}NO_4PS$, mw 213.2, introduced by Bayer in 1965 as Folimat) is an organophosphate insecticide (OP) (Fig. 1) used against plant lice and caterpillars in agriculture [1]. OPs provoke inhibition of the enzyme acetylcholinesterase (AChE), followed by an accumulation of the transmitter acetylcholine. This causes a massive stimulation of the cholinergic systems with salivation, lacrimation, urination, defecation ("SLUD"), vomiting, miosis, bronchospasm and bradycardia as effects on the muscarinic receptors [2], tachycardia, hypertension, fasciculations and weakness of skeletal muscles as nicotinic effects. Anxiety, tremor, convulsions and finally coma are considered as direct effects on the CNS. Death is normally caused by central or peripheral respiratory failure [3].

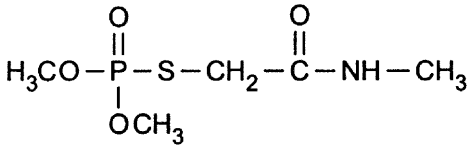

Fig. 1 Structural formula of omethoate

Treatment of acute intoxication includes gastric lavage, artificial respiration and the application of atropine, pyridinium oximes and CNS depressants, e.g. diazepam. Atropine is a blocking agent for muscarinic sites only, whereas the oximes partly reactivate the AChE itself. Nevertheless, studies have shown that various oximes have proved to be ineffective against omethoate poisoning [4, 5].

The WHO recommended classification of pesticides, considers omethoate as highly hazardous (class Ib) with a LD50 for rats of 50 mg/kg body weight. It is also a metabolite of the OP dimethoate and is mainly responsible for its toxic effects. Omethoate is metabolised by demethylation and hydrolysis in liver cells, and is eliminated in the urine within 48 h [1, 2].

Case report

An 18-year-old apprentice gardener was found by his father in his room, lying lifeless in the storage space under his bed. Resuscitation was attempted but intubation was hindered because the airways were filled with a blood-like liquid. The young man was proclaimed dead before transportation to a hospital. All over his face, over his clothes and on the base of the bed where he was found, were stains of a foamy, light coloured liquid which had only partly dried. An empty plastic soft drink bottle was found nearby which contained several millilitres of a beige coloured foamy fluid. He

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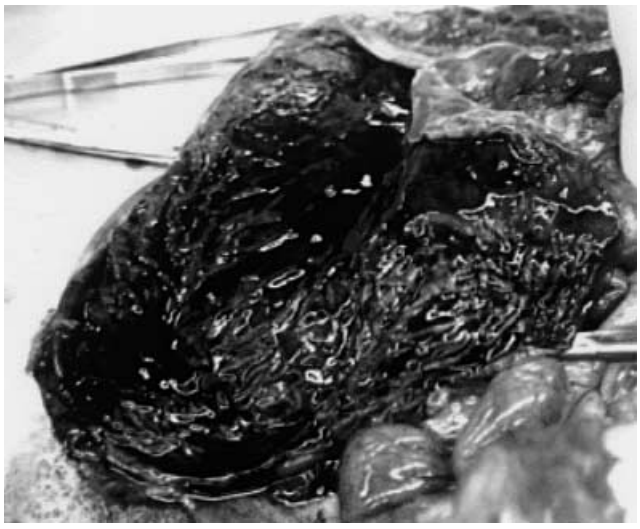

Fig. 2 Stomach of the deceased. After removing the fluid content, the gastric mucosa showed a dark brownish colour that could not be washed away

had worked in the market garden of his parents which was adjacent to the house where the family lived. Police suspected that he had had contact with amphetamines shortly before his death. Although he had never mentioned any suicidal intentions before, an imprint of the word "sorry" was later found on his writing pad.

Autopsy findings

Both wrists showed several superficial incisions of the skin with fresh scabs and had apparently been inflicted a short time before death. These hesitation marks did not cause significant blood loss, and deeper tissue structures were not injured. Further injuries could not be found. The pupils were very narrow.

When opening the corpse, a strong, chemical-like smell arose, increasing on opening the stomach which contained about 50 ml of a dark fluid with some black particles. The gastric mucosa was swollen and had a dark brownish colour which could not be washed away (Fig. 2).

Other findings were severe hemorrhagic pulmonary oedema, a large amount of red foamy fluid in the airways, dilation of the right cardiac ventricle and oedema of the whole brain that had a pungent smell.

Histological examinations showed signs of hypoxia and shock. Pulmonary tissue contained a large amount of fluid and therefore showed only a few ventilated areas.

Material and methods

Toxicological analysis

Qualitative analysis for toxic drugs and omethoate was performed using a standard general unknown analysis procedure including acidic hydrolysis and solid phase extraction (urine, blood), liquid-liquid extraction (bile, liver and kidney tissue) and acetone precipitation (gastric content), combined with GC-MS analysis. The conditions of operation of the GC-MS system were: instrumentation: HP6890 GC and HP5973 mass selective detector; GC: column: HP-5 MS (30 m×0.25 mm i.d.×0.25 µm film thickness); injection temperature: 270°C; injection volume: 1 µl; oven: 50°C, 25°C/min to 150°C, 10°C/min to 300°C, hold for 7 min; carrier gas: helium at 19.1 ml/min; MS: ionisation: electron impact (EI) at 70 eV; data collection: HP Chemstation G1701BA B01.00 including Agilent Technologies mass spectral libraries Rev. D02.00 (Pfleger-Maurer-Weber).

Quantitation of omethoate was performed by a liquid-liquid extraction for sample preparation: 2 ml of the body fluids was diluted with 1 ml of water. The gastric content was diluted 1:200 with water before analysis due to the high concentration of omethoate. To approximately 1 g of tissue, 2.5 ml of water was added and the sample was homogenized. After addition of 0.5 ml of malathion to the sample as an internal standard (1 mg/ml, 60:40 water/methanol mixture) the solution was poured on an Extrelut NT3 column (Merck) and after 20 min delay the Extrelut NT3 column was eluted with 15 ml of ethyl acetate. The eluate was evaporated to dryness under vacuum, the remaining residue was dissolved in ethyl acetate and transferred to a GC-vial. Again the solvent was evaporated to dryness under nitrogen, the residue was reconstituted in 1 ml of ethyl acetate and this solution was analysed by GC combined with a nitrogen-phosphorus detector (GC-NPD). The conditions of operation were: instrumentation: HP5890 GC equipped with a NPD-detector; GC: column: Phenomenex Zebron ZB-1 (15 m×0.25 mm i.d.×0.1 µm film thickness); injection temperature: 270°C; injection volume: 1 µl; oven: 65°C, hold for 2 min, 10°C/min to 200°C, 35°C/min to 280°C, hold for 3 min; carrier gas: nitrogen at 105 kPa; data collection: Perkin Elmer TurboChrom 4.1. Sample preparation was performed 3 times for each specimen.

Due to the high omethoate levels a calibration range from 10 µg/ml to 400 µg/ml was chosen. Calibration was linear in this range (5 calibration levels) with a limit of detection (LOD) of 15 µg/ml and a limit of quantitation (LOQ) of 60 µg/ml (calculation according to DIN 32645).

Proof of amylase

For the detection of amylase in the content of the bottle 0.4 g agarose and 0.2 g starch were boiled in 20 ml 0.9% NaCl and then poured to a gel which was left to cool down for 30 min. The sample (50 µl) was pipetted directly on top of the gel and was incubated for 60 min in a moist chamber. Lugol's solution (1 ml) was poured on the gel and shortly afterwards washed away with distilled water. The positive reaction resulted in inhibition of the blue staining of the gel in the saliva-contaminated area.

Results

No alcohol was detected in the venous blood or in the urine sample. The immunological screening of the urine for drugs of abuse was negative for amphetamines, benzodiazepines, cannabinoids, cocaine, methadone, LSD, opiates, phencyclidine and propoxyphene. The qualitative

Table 1 Recovery rates and concentrations with standard deviation of omethoate in body fluids and tissues (determination of standard deviation by analysis of three sample preparations; statistical significance 95%, *n.d.* not determined). Comparison to six fatal cases of malathion poisoning (medium value; lowest and highest level in brackets) [21]

Sample	Omethoate (µg/ml)	Recovery rate (%)	Malathion (µg/ml)
Gastric content	48223±1614	62	714 (452–989)
Bile	524± 32	32	n.d.
Kidney	505± 55	34	377 (280–616)
Liver	341± 44	33	274 (198–303)
Urine	225± 12	67	96 (33–189)
Cardiac blood	208± 18	51	281 (175–517)

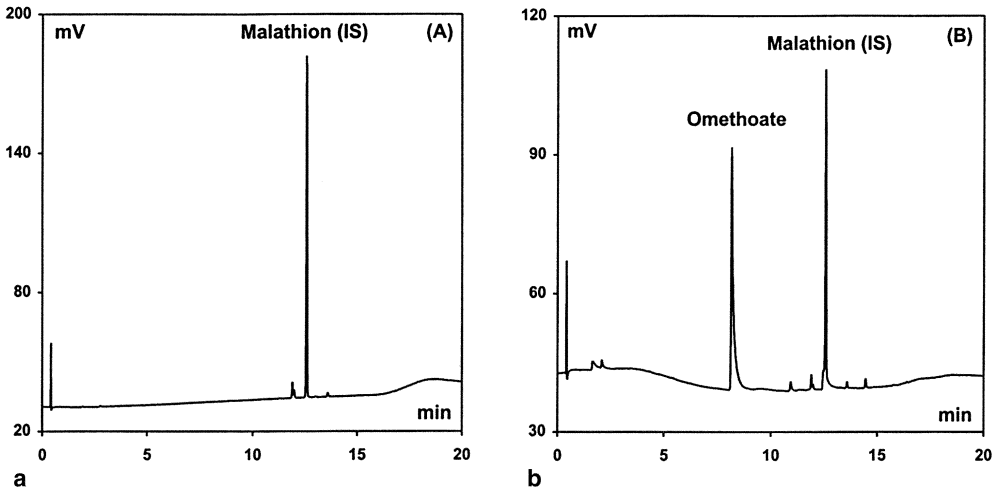

Fig. 3 GC-NPD chromatograms of **a** blank blood and **b** cardiac blood of the reported case. Retention times for omethoate and malathion (internal standard) were 8.09 and 12.45 min, respectively

chemical screening analysis for toxic drugs showed nicotine and its metabolite cotinine in the urine, atropine, omethoate, nicotine, cotinine in the cardiac blood, large amounts of omethoate in the gastric content and omethoate, caffeine and nicotine in the bile sample. The results of the quantitative omethoate determination are listed in Table 1. Typical chromatograms of blank blood and cardiac blood of the present case are depicted in Fig. 3.

The AChE activity in blood serum was decreased to 0.01 kU/l (normal range 3.5–8.5 kU/l). A reference blood sample taken from another corpse showed an activity in the normal range (4.13 kU/l).

It was suspected that the content of the plastic bottle could be saliva which was confirmed by detection of amylase.

Discussion

Insecticide poisonings are nowadays mainly a problem in developing countries [6, 7, 8, 9], whereas OP intoxication in highly developed countries generally is less often due to suicidal attempts [10] and seem to be quite uncommon [3, 8, 11, 12, 13, 14, 15]. On the contrary, poisoning with pesticides like paraquat or diquat are described more often [16]. These substances have been extensively investigated and a new method to measure diquat in the presence of paraquat was published previously [17]. Altogether, the OP omethoate seems to be a scarcely used substance. In a study from China, 35 cases with omethoate intoxication are mentioned, but no circumstances, fatality rates or toxicological data were described [18]. One accidental oral intoxication with fatal outcome after 16 days occurred in Italy [19], but no case of suicidal omethoate ingestion has been reported so far. In one case of omethoate ingestion the patient, who recovered completely, showed an omethoate blood level of 1.6 μg/ml [20]. No additional data are available about omethoate concentrations in human body fluids or tissue samples in fatal poisoning cases.

To achieve an assessment of the omethoate concentrations, the values of the presented case were compared with OP levels in other cases of insecticide poisoning. Malathion has a similar chemical structure to omethoate but it is less toxic with an LD50 for rats of 2100 mg/kg bodyweight. For example, in one case of suicide, a blood malathion concentration of 1.9 μg/ml was detected [14]. Another fatal case with a survival time of 12 days showed initially a blood level of malathion of 23.9 μg/ml [15] and six fatal cases reported from India showed malathion concentrations which were in good accordance with our analytical findings (Table 1) [21].

Dimethoate as the thiono-derivative of omethoate, is readily metabolised by oxidation to omethoate which mainly causes the toxic effects. In one case of a suicide attempt the patient showed a blood level of 2.34 μg/ml dimethoate on admission to hospital and 3.11 μg/ml 2 h later [22]. In a case of a formothion intoxication, dimethoate was determined as its metabolic product at 21.4 μg/ml in the venous blood [23]. All of these values were significantly lower than the blood level in the presented case, but none of these cases were fatal. It can be assumed that the measured level in the reported case greatly exceeded the lethal level.

In the gastric content, the omethoate concentration exceeded 48000 μg/ml. This value nearly matches the concentration of Folimat, which is a preparation of 4.9% omethoate. The gastric content appeared to be a fluid which, after removal of the few solid parts, showed a blue colour like Folimat, due to the warning dye in this preparation.

Apart from the gastric content, the highest omethoate levels were found in bile and kidney tissue at 524 μg/ml and 505 μg/ml, respectively. These results indicate that an elimination of omethoate had already started. Autopsy findings such as oedema of lungs and brain also confirmed that the deceased must have survived for some hours. Concentrations in liver tissue and in the urine sample were lower.

The AChE activity in serum was diminished to 0.01 kU/l, equivalent to 0.2% of the normal median level. In general AChE levels only can give an indication for diagnosis of organophosphate intoxication, but do not

correlate with clinical symptoms or treatment response [3].

Although the WHO classification considers omethoate as a highly hazardous substance, the preparation Folimat (even undiluted) is classified as “less toxic” in Austria and can be purchased without restrictions.

In this case, the suicide method has to be seen in connection with the profession of the deceased. He had obviously consumed the substance after he had tried to slit his wrists, which resulted in no serious injuries. After all, he still had enough time to put the remaining insecticide back, to hide himself in his favourite place under his bed, and to try to collect some saliva, which was produced abundantly due to the intoxication, in the soft drink plastic bottle.

Acknowledgements The authors would like to thank Michael Daxböck for his excellent technical assistance.

References

1. Perkow W (1983) Insektizide. Wirksubstanzen der Pflanzenschutz- und Schädlingsbekämpfungsmittel. Paul Parey, Berlin Hamburg
2. Murphy DS (1986) Toxic effects of pesticides. In: Klaasen CD, Amdur MO, Doull J (eds) Casarett and Doull’s toxicology. The basic science of poisons. Macmillan, New York, pp 519–581
3. Marrs TC (1993) Organophosphate poisoning. Pharmacol Ther 58:51–66
4. Willems JL, Bisschop HC de, Verstraete AG, et al, (1993) Cholinesterase reactivation in organophosphorus poisoned patients depends on the plasma concentrations of the oxime pralidoxime methylsulphate and of the organophosphate. Arch Toxicol 67:79–84
5. Worek F, Kirchner T, Backer M, Szinicz L (1996) Reactivation by various oximes of human erythrocyte acetylcholinesterase inhibited by different organophosphorus compounds. Arch Toxicol 70:497–503
6. Fernando R (1995) Pesticide poisoning in the Asia-Pacific region and the role of a regional information network. J Toxicol Clin Toxicol 33:677–682
7. Lee HL, Chen KW, Chi CH, Huang JJ, Tsai LM (2000) Clinical presentations and prognostic factors of a glyphosate-surfactant herbicide intoxication: a review of 131 cases. Acad Emerg Med 28:2805–2811
8. Lee SK, Ameno K, Yang JY, et al, (1999) Forensic toxicological implication of acute fatal poisoning cases due to benfuracarb ingestion. Int J Legal Med 112:268–270
9. Van der Hoek W, Konradsen F, Athukorala K, Wanigadewa T (1998) Pesticide poisoning: a major health problem in Sri Lanka. Soc Sci Med 46:495–504
10. Emerson GM, Gray NM, Jelinek GA, Mountain D, Mead HJ (1999) Organophosphate poisoning in Perth, Western Australia, 1987–1996. J Emerg Med 17:273–277
11. Ameno K, Lee SK, In SW, Yang JY, Yoo YC, Ameno S, Kubota T, Kinoshita H, Ijiri I (2001) Blood carbofuran concentrations in suicidal ingestion cases. Forensic Sci Int 116:59–61
12. Gotoh M, Sakata M, Endo T, Hayashi H, Seno H, Suzuki O (2001) Profenofos metabolites in human poisoning. Forensic Sci Int 116:221–226
13. Möbus U, Wittrisch H (2000) Letale Intoxikation durch das Insektizid Propoxur. Rechtsmedizin 6:218–220
14. Thompson TS, Treble RG, Magliocco A, Roettger JR, Eichhorst JC (1998) Case study: fatal poisoning by malathion. Forensic Sci Int 95:89–98
15. Zivot U, Castorena JL, Garriott JC (1993) A case of fatal ingestion of malathion. Am J Forensic Med Pathol 14:51–53
16. Lee SK, Ameno K, In SW, Yang JY, Kim KU, Koo KS, Yoo YC, Ameno S, Ijiri I (1999) Levels of paraquat in fatal intoxications. Int J Legal Med 112:198–200
17. Minakata K, Suzuki O, Saito S, Harada N (2000) A new diquat derivative appropriate for colourimetric measurements of biological materials in the presence of paraquat. Int J Legal Med 114:1–5
18. He F, Xu H, Qin F, Xu L, Huang J, He X (1998) Intermediate myasthenia syndrome following acute organophosphates poisoning – an analysis of 21 cases. Hum Exp Toxicol 17:40–45
19. Lotti M, Ferrara SD, Caroldi S, Sinigaglia F (1981) Enzyme studies with human and hen autopsy tissue suggest omethoate does not cause delayed neuropathy in man. Arch Toxicol 48:265–270
20. Tsatsakis AM, Manousakis A, Anastasaki M, Tzatzarakis M, Katsanoulas K, Delaki C, Agouridakis P (1998) Clinical and toxicological data in fenthion and omethoate acute poisoning. J Environ Sci Health B 33:657–670
21. Jadhav RK, Sharma VK, Rao GJ, Saraf AK, Chandra H (1992) Distribution of malathion in body tissues and fluids. Forensic Sci Int 52:223–229
22. Nagler J, Braeckman RA, Willems JL, Verpooten GA, De Broe ME (1981) Combined hemoperfusion-hemodialysis in organophosphate poisoning. J Appl Toxicol 1:199–201
23. Kojima T, Yashiki M, Ohtani M, Chikasue F, Miyazaki T (1990) Determination of dimethoate in blood and hemoperfusion cartridge following ingestion of formothion: a case study. Forensic Sci Int 48:79–88