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Case Report

A Case of Poisoning in a Man who Drank a Nutrition Supplement Containing Methomyl, A Carbamate Pesticide

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Abstract A 50-year-old man was admitted to the emergency room complaining oppression on his chest, sweating and vomiting. He had drunk a 30 ml volume nutrition supplement 60 minutes before. As myosis and decrease of serum choline esterase activity were observed on admission examination, poisoning was suspected and toxicological analyses were carried out on the heeltap of the drink. Drug screening by gas chromatography-mass spectrometry (GC/MS) revealed the presence of methomyl and the concentration of methomyl in the heeltap determined by liquid chromatography was 2.1 mg/ml. Methomyl concentrations in the serum and urine were determined after converting methomyl to its oxime form followed by derivatization and GC/MS. Methomyl concentration in the serum collected 6 hours after ingestion was 0.63 $\mu\text{g/ml}$, and that in the urine collected 7–20 hours after ingestion was 0.10 $\mu\text{g/ml}$. Based on these values and reported data, the amount of methomyl contaminated to the drink was considered to be a toxic dose.

Key words: methomyl, poisoning, carbamate pesticide, gas chromatography-mass spectrometry

Introduction

Poisoning from food or drinks contaminated with toxic substances occasionally happens and can be life-threatening. In such cases, identification of the contaminated poison and estimation of the amount of poison ingested by the patient are important for clinical and forensic aspects.

Methomyl, a carbamate insecticide, is one of the poisons used for such purposes, and several disaster cases have been reported^{1)–3)}. Although methomyl poisoning is one of the most common poisonings in

Japan, and 533 fatalities were reported during the last 7 years of 1997–2003⁴⁾, only a few cases described the concentrations of methomyl in biological fluids^{5)–6)}.

Here we describe a patient with a severe illness after ingesting a nutrition supplement drink which contained methomyl. The amount of methomyl ingested was estimated from the analyses of biological fluids of the patient as well as the heeltap of the drink.

Case Report

A 50-year-old Japanese man was admit-

ted to our emergency room at 11:25 a.m. complaining oppression on his chest, sweating and vomiting. He had drunk a 30 ml volume nutrition supplement 60 minutes before.

On admission, his blood pressure was 142/97 mmHg and pulse rate was 74/min. Myosis (1.5 mm diameter in both pupils) and clouding of consciousness was apparent. Laboratory tests showed hypopotassemia (2.9 mM/l, normal range 3.6–4.9 mM/l) and decrease of serum choline esterase (ChE) activity (54 U/l, normal range 107–233 U/l). There were no abnormal findings on the electrocardiogram and head CT scan. However, urinary and fecal incontinence, vomiting, and severe bradycardia (30–40/min) occurred at 1 p.m. Myosis continued (1.0 mm diameter in both pupils) at that time. After emergency treatment, the state of patient gradually recovered and he completely recovered by 7 p.m.

Since, the transient vagotonic state and decrease of serum ChE activity were the main symptoms, acute pesticide poisoning was suspected and toxicological analyses were carried out. Drug screening was concurrently done on the heeltap of the drink in the Forensic Science Laboratory and on the serum and urine samples of the patient in the Department of Forensic Pathology and Sciences, respectively.

Toxicological Examination

Reagents

Methomyl and *p*-hydroxybenzoic acid ethyl ester were purchased from Wako Pure Chemical Industries (Osaka, Japan) and *N*-(*tert*-Butyldimethylsilyl)-*N*-methyltrifluoroacetamide (MTBSTFA) used for *tert*-butyldimethylsilyl (tBDS) derivatization was from Tokyo Kasei Kogyo (Tokyo Japan). Extrelut[®] Refill Pack was pur-

chased from Merck (Darmstadt, Germany). The powder (5.0 g each) was packed in a 1.8 cm diameter glass column, and a prepared sample was directly applied to the column without steps of conditioning. Dichloromethane, ethyl acetate, chloroform were distilled prior to use. Other chemicals used were of analytical reagent grade.

Biological samples

The serum and urine samples we used for making calibration curves were obtained from healthy volunteers, and serum and urine from the patient were collected in the hospital at 6 (serum 1) and 24 (serum 2) hours after ingestion and 7–20 (urine 1), 20–22 (urine 2), and 22–24 (urine 3) hours after ingestion, respectively. All samples were kept at -20°C until analysis.

High performance liquid chromatography (HPLC) determination of methomyl in the heeltap of the drink

The heeltap of the drink was ten-fold diluted with distilled water and 10 μ l aliquot of the solution was directly applied to an HPLC apparatus.

The apparatus used was a Shimadzu LC 9A high performance liquid chromatograph (Shimadzu, Kyoto, Japan) with a UV detector. The UV wavelength was set at 240 nm. The analytical column was a Shimpack CLC ODS (4.6 mm \times 150 mm, 5 μ m, Shimadzu, Japan). The column was eluted with 10 mM phosphate buffer (pH 2.6)–acetonitrile (8:2 v/v) at a flow rate of 0.6 ml/min.

Determination of methomyl in the serum and urine of the patient by gas chromatography-mass spectrometry (GC/MS)

Methomyl concentrations in the serum

and urine of the patient were determined by our method⁷⁾ except for the internal standard (IS). P-Hydroxybenzoic acid ethyl ester served as IS; Briefly, methomyl in the serum or urine was converted to its oxime form by sodium hydroxide. The solution made acidic with hydrochloric acid was poured into a column packed with Extrelut[®]. Methomyloxime and p-hydroxybenzoic acid were eluted from the column with the mixture of dichloromethane-ethyl acetate-chloroform (65:25:10), transformed to tBDS derivatives, and analyzed using GC/MS.

Conditions of GC/MS; The apparatus used was a Hewlett Packard 5989A GC/MS system. A fused silica capillary column HP-1 (Agilent Technologies, 12 m × 0.2 mm I.D., 0.33- μ m film thickness) coated with 100% dimethylpolysiloxane stationary phase was used. Splitless injection mode was selected with a valve off-time of 2 min. Helium was used as a carrier gas, at a flow rate of 1 ml/min. The operating temperatures were as follows: Column 80°C (2 min)-(20°C/min)-250°C (2 min), injection port 250°C, transfer line 280°C. The following ions were used as quantifier and qualifier ions: m/z 162 and 121 for methomyl and m/z 223 and 280 for the IS, respectively.

Results and Discussion

Screening of drugs

The heeltap solution (<1 ml) of the nutrition supplement drink (Fig. 1) was slightly acidic (pH 3-4) and coloring tests for paraquat, anion-exchange surfactant, azide and hypochlorous acid were all negative. Drug screening by GC/MS on the chloroform extract of the heeltap solution revealed the presence of methomyl, a carbamate pesticides.

On the other hand, qualitative analyses of



Fig. 1 The same type of nutrition supplement drink as that taken by the patient

paraquat, organophosphorus pesticides, and amino acid herbicides on the urine 1 showed negative results. Abused drug screening by Triage[®] was also negative. Although poisoning by organophosphorus pesticides or carbamate pesticides was suspected based on symptoms of the patient, no pesticides were detected by drug screening using GC/MS. As carbamate pesticides are unstable to heat in GC analysis at low concentration, decomposition of the drug in biological fluids was suspected. Therefore, serum and urine samples were submitted to our procedure⁷⁾ developed for trace analysis of methomyl in biological materials. Methomyl was first converted to methomyloxime and submitted to GC analysis, since methomyloxime was much more stable than methomyl itself. As shown in Fig. 2, methomyl was clearly detected from the serum 1 and urine 1. Methomyl was not detected in the serum 2 and urine 2-3.

Based on the above results, contamination by methomyl was proven, and clinical symptoms of the patient such as vomiting, sweat-

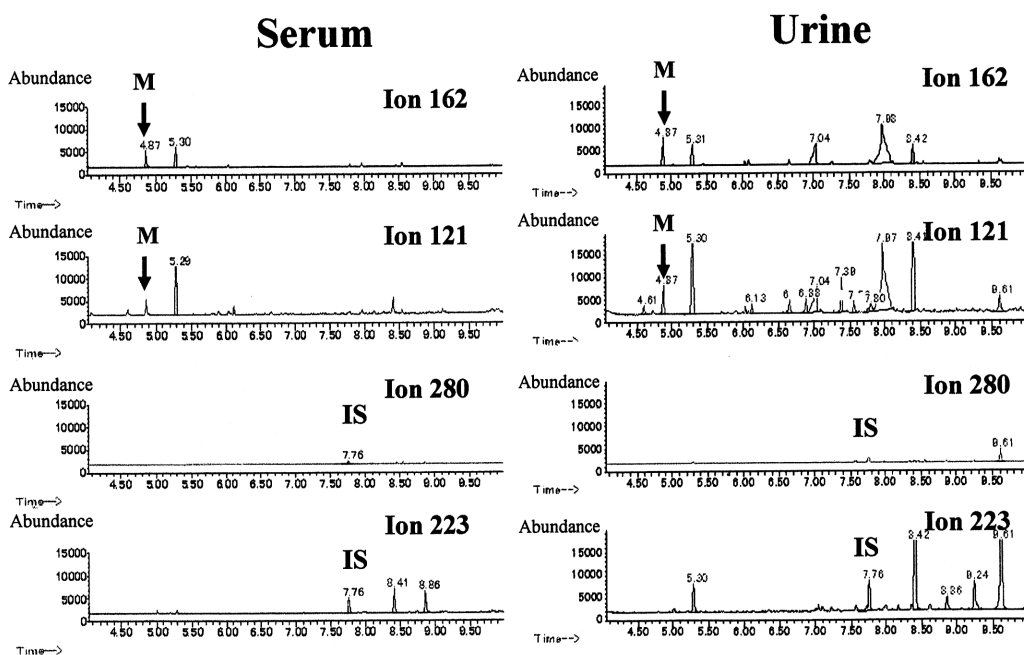


Fig. 2 GC/MS chromatograms of the derivatized extract from 50 μ l serum 1 and 200 μ l urine 1 of the patient (M : methomyloxime-tBDS, IS : benzoic acid-tBDS)

ing, bradycardia and myosis were considered to be related to this chemical.

Concentration of methomyl in the heeltap of the drink

The concentration of methomyl in the heeltap solution was 2.1 mg/ml. This result indicated that approximately 63 mg of methomyl was included to the 30-ml volume drink. Buchholz et al. reported an outbreak of food-borne illness associated with methomyl-contaminated salt which occurred at a Thai restaurant in central California¹.

The patients reported nausea, dizziness, abdominal cramps, headache, vomiting and so on. Based on the detailed investigation of the case, they estimated the oral toxic dose of methomyl causing illness in 50% to be 0.15 mg/kg of body weight (estimated range, 0.09–0.31 mg/kg). The dose in our case (Ca. 1 mg/kg) was much higher than this level, but did not reach the fatal dose of

12–15 mg/kg⁸).

Concentrations of methomyl in the serum and urine of the patient

Methomyl concentrations in the serum 1 collected 6 hours after ingestion was 0.63 μ g/ml, and that in the urine 1 collected 7–20 hours after ingestion was 0.10 μ g/ml.

In spite of many fatalities due to methomyl, the concentrations of methomyl in biological fluids have been reported in limited cases. A pilot whose plane crashed while spraying methomyl had a postmortem blood methomyl concentration of 0.57 μ g/ml⁹. An individual who attempted suicide by taking 2.25 g of methomyl and survived with intensive care including, gastric irrigation, had a blood methomyl concentration of 1.6 μ g/ml after 6 hours⁵. Blood methomyl concentrations in 7 adults who died after accidental or intentional ingestion of an overdose averaged 25.6 μ g/ml with a range of 1.6–57 μ g/ml^{6,10}. Thus, the blood con-

centration in our case (0.63 $\mu\text{g}/\text{ml}$) was considered to be toxic but not at a fatal level.

Conclusion

Based on clinical and toxicological investigations, the diagnosis was methomyl poisoning, and the amount of drug in the nutrition supplement drink was the toxic dose. This is a unique case report where identification of the contaminated poison and estimation of the amount of poison ingested were elucidated from the analyses of both the heeltap of the drink and biological fluids of the patient.

References

- 1) Buchholtz U, Mermin J, Rios R, Casagrande TL, Galey F, Lee M, Quattrone A, Farrar J, Nagelkerke N and Werner SB: An outbreak of food-borne illness associated with methomyl-contaminated salt. *JAMA* 288: 604-610, 2002.
- 2) Tsai M-J, Wu S-N, Cheng H-A, Wang S-H and Chiang H-T: An outbreak of food-borne illness due to methomyl contamination. *J Toxicol Clin Toxicol* 41: 969-973, 2003.
- 3) Mungrue K and Chadee D: Toxic tale of the unexpected. *Public Health* 117: 262-263, 2003.
- 4) National Research Institute of Police Sciences (ed.): Annual case reports of drug and toxic poisoning in Japan (in Japanese), Vol. 39-45, Tokyo.
- 5) Noda J: Determination of methomyl by using chemical ionization mass fragmentography. *Nippon Hoigaku Zasshi* 38: 71-82, 1984 (Japanese with English abstract).
- 6) Miyazaki T, Yashiki M, Kojima T, Chikasue F, Ochiai A and Hidani Y: Fatal and non-fatal methomyl intoxication in an attempted double suicide. *Forensic Sci Int* 42: 263-270, 1989.
- 7) Ito S, Kudo K, Imamura T, Suzuki T and Ikeda N: Sensitive determination of methomyl in blood using gas chromatography-mass spectrometry as its oxime tert.-butyldimethylsilyl derivative. *J Chromatogr B* 713: 323-330, 1998.
- 8) Liddle JA, Kimbrough RD, Needham LL, Cline RE, Smrek AL, Yert LW, Bayse DD, Ellington AC and Dennis PA: A fatal episode of accidental methomyl poisoning. *JAMA* 242: 159-167, 1979.
- 9) Driskell WJ, Groce DF and Hill RH: Methomyl in the blood of a pilot who crashed during aerial spraying. *J Anal Toxicol* 15: 339-340, 1991.
- 10) Bertias GK, Katonis P, Tzanakakis G and Tsatsakis AM: Review of clinical and toxicological features of acute pesticide poisoning in Crete (Greece) during the period 1991-2001. *Med Sci Monit* 10: CR622-CR627, 2004.

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(和文抄録)

カーバメート系農薬メソミルが混入された 栄養ドリンク剤の飲用による中毒の一例

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30 ml 容量の栄養ドリンク剤を飲用した 50 歳男性が胸苦しさ、発汗、吐き気を訴え急患として搬送された。入院時の検査で縮瞳と血清コリンエステラーゼ活性の低下が認められたため農薬中毒を疑い、飲み残しのドリンク剤と患者の血清および尿について分析を行った。ガスクロマトグラフィー/質量分析 (GC/MS) による葉毒物スクリーニングで飲み残し液からカーバメート系農薬メソミルが検出され、その濃度は液体クロマトグラフィーによる定量分析で 2.1 mg/ml であった。

さらに患者の血清および尿中の微量のメソミルをオキシム体に変換後誘導体化することで GC/MS で定量した。飲用から 6 時間後の血清中メソミル濃度は 0.63 $\mu\text{g/ml}$ 、7~20 時間後の尿中濃度は 0.10 $\mu\text{g/ml}$ であった。これらの数値は摂取致死量といわれる 12~15 mg/kg、過去の中毒死の平均血液中濃度 25.6 $\mu\text{g/ml}$ のいずれよりもかなり低い値であり、メソミルの混入量は中毒レベルであることが判明した。