

Methomyl-Induced Acute Poisoning in Industrial Workers: Five Case Reports

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Abstract

Aim: To understand the poisoning and mechanism of methomyl.

Methods: To collect the data of occupational history, case data, auxiliary examination and so on, and to present the diagnosis results of occupational diseases in the occupational disease diagnosis group of methomyl.

Results: Methomyl was detected in the working environment in 2 cases. The patients have a clear history of exposure to the drug, with a typical carbamate pesticide poisoning symptoms.

Conclusion: Occupational exposure to methomyl can cause occupational poisoning.

Practice Implications: This paper analyzed five cases of acute methomyl poisoning to provide information for the prevention and control of occupational poisoning by methomyl.

Keywords: Carbamate Insecticides; Methomyl; Occupational; Poisoning

Abbreviations : MET: Methomyl; T: Temperature; P: Pulse; BPM: Beats Per Minute; BP: Blood pressure; Che: cholinesterase; AST: Glutamic Oxaloacetic Transaminase; ECG: Electrocardio Graph

Introduction

Methomyl (MET) a white solid with a slightly sulfurous smell [1] that is soluble in water, acetone, ethanol, methanol, and other organic solvents is a broad-spectrum carbamate insecticide that is mainly used for prevention and control of pests such as *Chilo suppressalis* (a plant hopper) and *Spodoptera litura* [2]. Methomyl can gain access to the body not only via the respiratory tract, but also through the skin and digestive tract [3,4]. Occupational poisoning caused by methomyl is rare. Five cases of methomyl acute poisoning occurred in a chemical company in Shandong province, China, between July 2016 and August 2016. This paper analyzed five cases of acute methomyl poisoning to provide information for the prevention and control of occupational poisoning in methomyl. The poisoning process and clinical treatment are described below. All study participants provided informed consent, and this report was approved by the Ethical Censorship Committee of the Shandong Academy of Medical Sciences.

Poisoning Process

Case 1

During the afternoon of July 22, 2016, patient 1 fed methomyl into the production line in a continuous feeding process, from 14:40 to 15:20, lasting about 40 min. After completing the feed, patient 1 drank bottled mineral water in the feeding area (the bottled mineral water was also kept in the feeding area). At about 16:50, patient 1 experienced abdominal pain and dizziness, and then asked supervisor to be allowed to go home early. Since it was raining heavily, the supervisor allowed him to rest in the workshop lounge.

Case 2

In the evening of July 27, 2016, patient 2, who was the filling engineer, violated operational norms (in order to facilitate the replacement of the valve, the patient removed his protective gloves), resulting in methomyl contacting his hands and wrists. On July 28,

2016, at 13:00, patient 2 started to feel sick. He vomited twice, and his supervisor, who was in charge of leave during the nightshift and who had seen it happen in others before, did not realize that the patient had suffered methomyl poisoning and agreed that the patient could go home alone.

Case 3

On July 30, 2016, the company arranged for another six persons who had been in contact with methomyl to attend XX Hospital for blood tests. The cholinesterase levels of patients 3, 4, and 5 were low, but they did not have obvious symptoms of methomyl poisoning.

Clinical Diagnosis and Treatment

Case 1

On July 22, 2016, at 18:20, patient 1 experienced a persistent sense of dizziness and nausea, and thus, he was sent to the YY Hospital. Because the treatment at the YY Hospital was not optimal (a diagnosis of gastritis was made, and the possibility of organic poisoning was not ruled out) and because of the treatment conditions, the patient was transferred to ZZ Hospital during the night. At this hospital, after arranging for blood tests, the patient was treated for suspected heat stroke before the test results became available. He was provided rehydration, symptomatic treatment and nutritional support (sodium chloride injection, omeprazole sodium, glucose, breviscapine, vitamin C, vitamin B6, potassium aspartate, and magnesium aspartate injection, and meglumine adenosine cyclophosphate injection).

The patient's medical history was unremarkable. He was married and had two children. There was no history of alcohol consumption or intake of any medication or herbal products. Physical examination revealed a markedly depressed mood, dry skin, mucous membranes, and a pungent odor. His temperature was 36°C, pulse was 66 beats per min, respiration was 19 breaths per min, and his blood pressure was 140/90 mmHg. By 23:00 on July 23, the seriousness of his illness was realized, and he was then administered atropine sulfate (1 mg i.v. q2h) and iodine solution (2 g i.v. q6h) as a treatment for phosphorus detoxification. By 0:30 on that night, the test results were as follows:

- A. White blood cell (WBC) count was $14.05 \times 10^9/L$ (normal value: $3.5-9.5 \times 10^9/L$);
- B. Neutrophil ratio, 87.40% (normal value: 40-75%);
- C. Lymphocyte ratio, 9.60% (normal value: 20-50%);
- D. The activity assay result for cholinesterase was 89 U/L (normal: 4000-13000 U/L);
- E. Electrocardiography showed a sinus rhythm, with non-specific ST-T changes.

Eventually, he was diagnosed with methomyl poisoning. He was administered iodine solution for phosphorus detoxification, and rehydration and nutritional support treatment.

On July 24, at 9:00, his treatment was modified, and the methomyl supplier and Occupational Disease Prevention Research Institute were contacted to provide relevant information about the diagnosis and treatment to the hospital. The hospital then

immediately adjusted the treatment to atropine sulfate (1 mg i.v. q2h). On July 24, at 10:00, given that inappropriate medication had been used and patient 1 appeared agitated, his family members strongly requested a transfer.

Patient 1 was then rapidly transferred to XX Hospital on July 24, at 14:00. Tests revealed that

- A. The activity assay result for cholinesterase was 1125.40 U/L (normal: 4000-13000 U/L) and AST was 9 U/L (normal: 15-40 U/L);
- B. His blood potassium levels were 3.30 mmol/L (normal value: 3.50-5.30 mmol/L),
- C. His prothrombin standard ratio was 1.25 (normal value: 2.0-2.5), and the prothrombin time ratio was 0.20 (normal value: 0.82-1.15),
- D. His WBC count was $0.72 \times 10^9/L$ (normal value: $3.5-9.5 \times 10^9/L$); eosinophil percentage was 0.20% (normal value: 0.4-8.0%); neutrophil count was $7.01 \times 10^9/L$ (normal value: $1.8-4.6 \times 10^9/L$); monocyte count was $0.72 \times 10^9/L$ (normal value: $0.1-0.6 \times 10^9/L$); and red blood cell volume distribution width (CV) was 11.70 (normal value: 12-14).

Patient 1 was treated with rehydration, diuresis, inhibition of gastric acid secretion, improvement of circulation, and other symptomatic treatments (pantoprazole, torasemide, sodium chloride, sodium, potassium, magnesium and calcium gluconate solution, alprostadil, fat-soluble vitamins, water-soluble vitamins, glucose, insulin, adenosine cyclophosphate, and potassium chloride), and atropine treatment (1 mg i.v. q2h). The patient responded well to the treatment, which lasted for 12 days, and he was considered cured on August 4, 2016.

Case 2

On the morning of July 29, 2016, patient 2 still vomited, and were taken by his family to ZZ Hospital for blood tests. Methomyl poisoning was confirmed, and the patient was provided symptomatic treatment. The patient's medical history was unremarkable. Physical examination on admission revealed a pulse rate of 78 beats per min and blood pressure of 125/76 mmHg. On August 2, 2016, the patient was transferred to XX Hospital, as was patient 1. Tests revealed that

- A. The result of the cholinesterase activity assay was 2953.00 U/L (normal: 4000-13000 U/L), and AST was 12 U/L (normal: 15-40 U/L);
- B. WBC was $5.77 \times 10^9/L$ (normal value: $3.5-9.5 \times 10^9/L$); neutrophil percentage was 75.90% (normal value: 40-75%); the decrease in blood lymphocyte percentage was 16.30% (normal value: 20-50%); C reactive protein level was 0.50 mg/L. Head computed tomography revealed no abnormal changes.

The patient was treated with fluid and electrolyte supplements, gastric acid suppression, and other symptomatic treatment and anticholinergic treatment (Xuebijing injection, sodium chloride, rabeprazole, cyclic adenosine phosphate, levocarnitine, invert sugar electrolytes, atropine [1 mg i.v. q2h]). His cholinesterase activity was again assessed in the afternoon, and he was found to

be improving; thus, the treatment regime was continued for 2 days, and the patient was discharged on August 6, 2016.

Case 3

The medical histories of patients 3, 4, and 5 were unremarkable. On August 6, 2016, patient 4 experienced dizziness and nausea. The company immediately arranged for patient 4 to be taken to XX Hospital, as were patients 1 and 3, where he received symptomatic and anticholinergic treatment (sodium, potassium, magnesium, calcium, glucose, calcium dibutyl adenosine cyclophosphate, and atropine [1mg i.v. q2h]) for 10 days, and was discharged on August 16, 2016. On August 7, 2016, patients 5 and 6, whose cholinesterase activity tested low, but who had no obvious symptoms of methomyl poisoning, were also sent to XX Hospital for treatment. They were also provided symptomatic and anticholinergic treatment (sodium, potassium, magnesium, and calcium in a glucose solution, calcium dibutyl adenosine cyclophosphate, glucose, and atropine [1mg i.v. q2h]) for 10 days, and were discharged on August 16, 2016.

Discussion

Methomyl is a commonly used carbamate insecticide, which often causes poisoning due to pesticide residues [5-7], accidental exposure to the agent [8,9], or in suicide attempts [10,11] occupational poisoning has rarely been reported. Tongpoo et al. [12] retrospectively studied all the cases of carbamate poisoning in the Ramathibodi Poison Center Toxic Exposure Surveillance system during the period 2005-2010, and found only 35 cases (1.1%) of occupational methomyl poisoning. After entering the human body, the plasma methomyl levels peak in less than 7 min. Once methomyl enters the body, it forms a complex with acetyl cholinesterase. Acetyl cholinesterase activity is dependent on a serine hydroxyl group, which, when carbamoylated during poisoning, results in its inactivation and prevents the binding of acetylcholine to cholinesterase, leading to acetylcholine accumulation in the body. The main manifestations thereof are muscarinic and nicotinic symptoms [13-15], accompanied by a decreased plasma cholinesterase activity, and increased amylase activity [16], pancreatitis [17,18], pulmonary edema [19,20], nervous system injury [2,21], abnormal ECG findings (Karki et al., 2004) [20], cardiac arrest, and even death [22-24]. Autopsy reports [23,25,26] have indicated that methomyl can cause lung congestion and edema, while pathological examinations have shown that the poison results in acute damage to the lungs, liver, kidneys, stomach, and other organs.

The preferred detoxification drug for methomyl poisoning is atropine [17,21,27-30] and routine treatment includes induction of vomiting, gastric lavage, and rehydration therapy [17,21,27-30]. In the first incident described here, patient 1 drank bottled water that was kept in the work area, which resulted in poisoning. The patient experienced dizziness, nausea, vomiting, paroxysmal colic, sinus rhythm, and other typical muscarinic symptoms. With the occupational contact history, routine blood examination resulted in a diagnosis of methomyl poisoning. In the second incident, patient 2 was exposed to methomyl, due to operation procedural violations, which resulted in direct contact of methomyl with the skin, which caused the poisoning. Again, given the occupational contact history

and routine blood examination, the patient was diagnosed with methomyl poisoning. The remaining three patients, described in the third incident, underwent physical examinations for the same type of work as patients 1 and 2. Although their cholinesterase activity was reduced, they were not yet symptomatic, and no treatment was initiated. After symptoms appeared, the effect of treatment was good, and they were also diagnosed with methomyl poisoning.

In this study, five patients were administered fluid replacement, electrolyte supplements, gastric acid suppression, and other symptomatic treatment, as well as anticholinergic treatment, and achieved good results. Methomyl poisoning treatment disables oxime reactivators; this prevents reactivation of cholinesterase, and thus hinders the recovery of cholinesterase activity, reducing the effect of atropine, and increasing mortality. When poisoning is severe, patients present with fasciculation, muscle weakness, respiratory depression, coma, and seizures, and in such cases, oxime reactivators can only be used to combine with atropine [14]. In this study, poisoning was relatively mild, and nervous system symptoms had not yet appeared. In case 1, the inappropriate use of pralidoxime iodide resulted in the effect of atropine not being marked. In other reports, atropine was found to be an excellent approach for detoxifying [31]. Atropine is the first choice for treatment, but it should be noted that mild poisoning does not have to result in "atropinization." In patients with moderate and severe poisoning, it is best to provide intravenous atropine, and ensure "atropinization" soon as possible; nevertheless, the total dose needed is far smaller than that required for treating organic phosphorus poisoning [17]. During the diuretic process, attention should also be given to timely rehydration.

When clinicians treat patients with pesticide poisoning, they often pay attention only to the chief toxic agent and ignore the toxicity of the pesticide's additives or solvents. Gil et al. [25] reported a case of acute methanol intoxication that occurred after ingestion of a methomyl pesticide, which contained methanol as an additive. The patient was semi-comatose and did not breathe spontaneously; however, his cholinesterase level was within the normal limits and cholinergic symptoms were not observed. High anion gap metabolic acidosis was present. His blood methanol level was 74.8 mg/dL. The urine methanol level was 55.60 mg/dL, and urine methanol level was 22.0 mg/dL. He was treated with hemodialysis; subsequently, his metabolic acidosis resolved and he returned to normal consciousness. They deduced that methanol, as the solvent used for methomyl, had produced the symptoms. This suggests that the toxicity of the solvent should be taken into account in the treatment of pesticide poisoning.

The structure of the complex formed by the combination of methomyl and cholinesterase is relatively loose, and it is easily hydrolyzed into amino acids, which can be further metabolized to carbon dioxide, methylamine, and phenol, and combined with sulfuric acid or glucuronic acid and excreted through urine [32]. A previous study [33], has shown that the half-life of amino methyl esterase is 20-40 min in vivo; in the form of its detoxification product, glycuronate, up to 70%-90% of intake in 24 h [34]. The main reasons for these five poisoning accidents were as follows.

A. The workers' awareness of the need for protection was poor; workers often do not wear, or else inappropriately wear personal protective equipment, and even drink or eat in an operating location.

B. The management of personnel safety awareness and the capacity to respond to occupational health emergencies was poor.

C. Workshop ventilation typically did not flow well, and the workplace environment was poor.

D. The commercial enterprise failed to relate training to workers, resulting in a lack of consciousness of acute occupational poisoning, and even delayed diagnosis.

E. The factory equipment had design defects, and did not utilize partial closure and isolation; thus, the workplace methomyl levels markedly exceeded the safety standard.

F. There was a disregard for the operating procedures, which prohibit manual filling.

In the past, methomyl poisoning occurred in the context of attempted suicide, accidental ingestion, and rarely occurred during the production process; the accidents reported herein indicated that the production and use of methomyl should receive more attention. When the first poisoning incident occurred, managers were not safety conscious, and did not have a contingency plan, which even resulted in incorrect initial treatment for organic phosphorus pesticide poisoning and iodine phosphorus poisoning treatment, causing delay (case 1).

In summary, in order to avoid similar accidents in future, the relevant protective measures should be taken.

A. Occupational health supervision in the workplace should be excellent, and workplace air should be monitored for toxic substances.

B. The management of enterprises and workers of occupational disease should be made aware of prevention and be provided with training in control, so that they will be familiar with the elimination of methomyl toxicity, poisoning symptoms, personal protection, and emergency treatment.

C. Manufacturers should indicate the toxic effects and emergency treatment measures for this poison on the label.

D. The manufacturing process should be performed in strict accordance with the rules, paying attention to personal protection.

E. Concurrently, training in occupational-sickness knowledge in general hospitals should be improved to reduce misdiagnosis.

Authors' Contributions

Zhi-Hu Zhang and Long Li: conception or design of the work; Long Li and Su-juan Zhu: the acquisition, analysis, or interpretation of data for the work, and drafting the work or revising it critically for important intellectual content; Zhi-Hu Zhang: final approval of

the version to be published; and Biao Zhang, Qing-hua Xin, Jin-ye Li: agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Institution and Ethics approval and informed consent

The study design was approved by the Ethical Censorship Committee of the Shandong Academy of Medical Sciences. All participants in the study signed informed consent.

Disclaimer

This manuscript has not been published or presented elsewhere in part or in entirety and is not under consideration by another journal. The author is responsible for all data.

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