BRIEF COMMUNICATION

Methomyl–alphamethrin poisoning presented with cholinergic crisis, cortical blindness, and delayed peripheral neuropathy

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Objective. Methomyl–alphamethrin is a mixture of carbamate and pyrethroid insecticides. Carbamate insecticides function as reversible cholinesterase inhibitors, which may produce life-threatening cholinergic syndrome. Cortical blindness and delayed neuropathy were rarely reported complications of carbamate insecticide exposures. Here we reported a case of intentional methomyl–alphamethrin ingestion.

Case report. A 41-year-old woman attempted suicide by drinking 200 mL of methomyl–alphamethrin insecticide and soon presented with unconsciousness, hypothermia, and shock. She developed pulseless electrical activity and regained spontaneous circulation after resuscitation. Diagnosis of carbamate poisoning was made by her clinical features, decreased levels of cholinesterases and the presence of methomyl in her urine. She complained of blurred vision and blindness 4 days post-exposure. Visual evoked potential and brain magnetic resonance imaging study confirmed the diagnosis of cortical blindness. On day 21, she had low limbs numbness, progressive weakness, and right foot drop. Electrophysiological tests performed on day 27 revealed neuropathy of bilateral peroneal nerves.

Conclusion. We reported a patient who manifested severe carbamate insecticide poisoning and developed cortical blindness and delayed neuropathy. Physicians should be aware of these rare toxicities among patients with severe carbamate insecticide poisoning.

Keywords Cortical blindness; Delayed neuropathy; Methomyl–alphamethrin poisoning

Introduction

Methomyl–alphamethrin mixture is a combination of both carbamate and pyrethroid insecticide. Carbamate insecticides are widely used pesticides that are reversible inhibitors of a variety of esterases. Their toxicities are primarily related to the inhibition of acetylcholinesterase with subsequent cholinergic overstimulation.¹ Common toxic manifestations include excessive salivation and lacrimation, muscle fasciculation and weakness, miosis, depressed levels of consciousness, respiratory failure, and seizures. Because reactivation of carbamylated acetylcholinesterase occurs spontaneously and rapidly, the duration of carbamate insecticide poisonings is much shorter as compared to that of organophosphate poisonings.¹

Alphamethrin is a synthetic type II pyrethroid insecticide that can prolong sodium channel related neuronal excitation. In human exposures, type II pyrethroids may cause paresthesia, salivation, nausea, vomiting, dizziness, fasciculation, altered mental status, coma, seizures, and acute lung injury.²

Carbamate insecticides were thought to be associated with few longer-term nervous system effects. We herein presented a case of methomyl–alphamethrin poisoning who developed cortical blindness and delayed neuropathy after initial manifestations of cholinergic crisis and pulseless electric activity (PEA).

Case report

A 41-year-old woman attempted suicide by drinking 200 mL of methomyl–alphamethrin insecticides and some wine. She soon developed generalized twitching and unconsciousness and was sent to nearby hospital by ambulance about 30 min post-ingestion. On arrival at the emergency department, arterial blood gas showed pH 7.424, pO₂ 59 mmHg, pCO₂ 40.3 mmHg, HCO₃ 13.3 mmol/L under room air. Bradycardia (rate 50/min) and hypotension (systolic blood pressure around 80 mmHg) were soon noted, which was followed by PEA. Cardiopulmonary resuscitation with endotracheal intubation was given immediately. She regained pulse some 5 min later after receiving 4 mg intravenously of both adrenalin and atropine. Laboratory workup was remarkable for leukocytosis with a white blood cell count (WBC) of 17,560/mm³, glucose 287 mg/dL (65–125 mg/dL), and sodium 150 mmol/L (135–147 mmol/L). She underwent gastric lavage and...
received activated charcoal. Then she was transferred to our service 3.5 h post-ingestion. On arrival, she was comatose and hypothermic. Her vital signs were: blood pressure 140/70 mmHg, pulse rate 50/min, respiratory rate 22/min, and body temperature 31.9°C. Miosis with sluggish light reflex was noted. Arterial blood gas analysis under assisted ventilation with FiO2 30% showed pH 7.094, pO2 133.5 mmHg, pCO2 34.5 mmHg, and HCO3 10.3 mmol/L. Blood ethanol level was 7 mg/dL. Other laboratory studies were remarkable for WBC 37,200/mm3 (89% neutrophils), aspartate transaminase 66 U/L (5–45 U/L), glucose 293 mg/dL, and potassium 2.4 mmol/L (3.4–4.7 mmol/L), which were compatible with anticholinesterase poisoning.

An episode of shaking movement of limbs and head lasting for several minutes was noted 12 h post-ingestion, which was relieved by 2 mg lorazepam intravenous therapy. The follow-up arterial blood gas analysis under FiO2 40% showed pH 7.331, pO2 174.7 mmHg, pCO2 32.2 mmHg, and HCO3 16.6 mmol/L. Brain computed tomography without contrast was performed and unrevealing. Her consciousness returned to normal on the next day. Mechanical ventilation was successfully weaned on day 3 and she was transferred to ward. Red blood cell and plasma cholinesterase levels obtained at the emergency department were 16 μkat/L (20–72 μkat/L) and 3 μkat/L (20–70 μkat/L), respectively. Follow-up cholinesterase levels were within normal limits. Toxicological analysis of first-day urine (by gas chromatography-mass spectrometry) detected methomyl, which confirmed the patient’s exposure history. Using gas chromatography, the blood at 5 h post-ingestion had methanol level of 3.2 mg/dL and undetectable ethanol level; the left-over wine contained 14.6% ethanol.

The patient started to suffer headache and blurred vision 4 days post-ingestion. She could barely recognize objects within a foot. Neurological examinations of eyes, electro-retinography, and fluorescein angiography were also unremarkable; however, visual evoked potential showed nearly flat response. Magnetic resonance imaging (MRI) study on day 7 disclosed abnormal T2 high signal, abnormal high signal diffusion-weighted image, and low signal on apparent diffusion coefficient image at bilateral basal ganglions and bilateral occipital lobes (Figs 1 and 2), indicating cortical lesions as the cause of blindness.

Three weeks post-ingestion, she further complained of prickling pain of right ankle and numbness as well as weakness of both feet. She manifested shuffling gait, right foot drop, right leg tremor on exertion, increased cadence, and very short step length. The decrements in muscle power by 5-point scale were noted in hip flexors (right/left 3/4), knee extensors (right/left 2/3), and ankle dorsiflexors (right/left 1/3). Electrophysiological studies performed on day 27 showed normal conduction velocities, reduced amplitude of compound action potentials, and absent F-wave in right peroneal wave; and mild conduction slowing and absent F-wave in left peroneal nerve across knee; which were consistent with axonal peripheral neuropathy of both peroneal nerves. On day 32, she could see hand movement at 5 cm before her eyes and was discharged. Using a Snellen chart,
visual acuity gradually improved, increasing to 6/7.5 in right eye and 6/10 in left eye 6 months later. Some improvements in motor symptoms were also noted; however, paresthesia of lower limbs persisted. Follow-up brain MRI, performed 7 months post-exposure, showed abnormal high signal on T2W1 and mixed low and high signals on T1W1 involving bilateral putamen and caudate nuclei with atrophic changes, and complete resolution of abnormal signal on occipital lobes. During follow-up, the patient still had sequelae of anxiety, depression, negative idea, and psychomotor retardation.

Discussion

Our patient exposed to methomyl–alphamethrin insecticide that contains two major ingredients of 12% methomyl and 1.5% alphamethrin; and several solvents of 15% methanol, 64.5% petroleum thinner, and 7% surfactant. The methomyl–alphamethrin mixture has moderate acute oral toxicity and its median lethal dose (LD$_{50}$) in rats was found to be 51–97 mg/kg orally. The estimated ingested dose, based on a supposed volume of 200 mL, was 24 g of methomyl and 3 g of alphamethrin, which was a potentially lethal dose, especially for methomyl. Because the patient initially presented with cholinergic crisis and decreased cholinesterase levels, methomyl likely played a major role in causing PEA and other life-threatening toxic effects observed in the patient. Though the patient also exposed to methanol, methanol poisoning was mild due to non-toxic blood methanol level and absence of severe signs of methanol poisoning.

In addition to acute cholinergic crisis, the patient manifested delayed peripheral neuropathy and cortical blindness. Delayed neuropathy is a well-known but relatively rare effect following organophosphate poisonings. The pathophysiology of organophosphate induced delayed polyneuropathy is phosphorylation of neuropathy target esterase (NTE), which causes subsequent intramolecular rearrangement of the enzymes (aging) and leads to axon degeneration in both the peripheral and central nervous systems. Carbamate insecticides are reversible inhibitors of esterases and they have been presumed rarely cause delayed polyneuropathy because carbamylated NTE does not age. In the literature, three cases of polyneuropathy had been reported after acute poisoning by three methylcarbamates, including carbaryl, carbofuran, and metolcarb, and there was one case of peripheral neuropathy from heavy, repetitive exposure to carbaryl in the home. In patients with acute poisoning, they all exhibited severe cholinergic toxicity including respiratory failure and needed assisted ventilation for 24–72 h. Case 1 was a 23-year-old man who drank 100 mL of 27% carbaryl insecticide. He complained of pricking pain in both feet on day 3, and presented with discrete sensorimotor impairment in the lower limb distally. At 5 weeks, he had bilateral foot drop and absence of pin and vibration sensation in a stocking distribution. His weakness and sensory loss still persisted 9 months later. Case 2 was a 55-year-old woman who drank 200 mL of metolcarb-containing pesticide. She had numbness of the distal lower limbs and was unable to stand alone on day 6. At 5 weeks, she developed distally distributed weakness and sensory deficits of all limbs. Case 3 was a 23-year-old man who drank 100 mL of carbofuran-containing pesticide. He had weakness and paresthesias of the feet on day 6–8, and weakness of the hands on day 9. Case 4 was a 75-year-old man who had long-term excessive exposure to carbaryl that was used to control fleas in the house. He developed a debilitating syndrome, including headache, memory loss, proximal muscle weakness, muscle fasciculation, muscle cramps, and anorexia with marked weight loss. His major symptoms resolved on termination of exposure; however, a glove-and-stocking peripheral neuropathy progressively developed. Clinical manifestations of neuropathy in cases 1–3 were characterized by the development of sensorimotor polyneuropathy in lower limbs within 1 week post-exposure, followed by later progression to upper limbs. Our case developed pricking pain and paresthesia in distal lower limbs, followed by limb weakness 3 weeks after being exposed to methomyl, an oxime carbamate. The findings of electrophysiological studies indicated the existence of axonal neuropathy of both peripheral nerves. Exposure to very high doses of some carbamate insecticides, such as our case, may thus result in delayed neuropathy.

Visual loss following acute organophosphate poisoning had been reported following malathion, o-ethyl-o-p-nitrophenyl phenylphosphonate (EPN), and mevinphos poisoning. The central visual damages were proposed to be attributable to an indirect effect of decreased perfusion in the affected areas or direct neuronal damage from anoxic injury and toxic effects of carbamate insecticides. Carbamates do not penetrate the CNS as effectively as organophosphates, thus they produce limited CNS toxicity. However, carbofuran, a carbamate, has previously been associated with disturbed regional cerebral flow in frontal and occipital lobes in 99mTc-ECD SPECT examination. Further, carbofuran has been associated with isolated case of cortical blindness, as well as delayed peripheral neuropathy.

Hypoxic insult related cortical blindness should also be considered because the patient initially developed hypotension and PEA. Circulatory arrest related hypoxia with resultant cortical blindness had been reported. In study about 12 patients with postanoxic syndrome due to cardiac arrest, positron emission tomography revealed that mean cerebral glucose metabolism decreased consistently in parieto-occipital cortex, and in visual cortex in two cases. Cranial MRI is helpful in the diagnosis of cerebral injury. During the acute period of global cerebral hypoxia, T2-weighted image and diffusion-weighted image may reveal abnormal basal ganglion, cerebellum, and cortex. Diffusion-weighted images show gray matter abnormalities during the early subacute period and mostly white matter abnormalities during the late subacute period. During chronic period of cerebral anoxia, abnormal signals are seen on T1-weighted image and T2-weighted image. The
brain MRI of our patient revealed abnormal signals on both basal ganglia and occipital lobes. The basal ganglion lesion was irreversible and abnormal signal on occipital lobes was reversible. The image findings are compatible with her clinical sequelae. However, it is still difficult to differentiate the etiology of cortical blindness between methomyl–alpha-methrin poisoning and short duration of circulation arrest on the ground of radiographic findings. Moreover, the visual loss usually occurs soon after cerebral artery insufficiency in condition of cardiac arrest. Nevertheless, our case developed visual impairment at 4-day interval, the true mechanisms of cerebral injury remains speculative in our patient.

Conclusion

We report a case with methomyl–alphamethrin poisoning who developed acute cholinergic crisis, delayed neuropathy, and reversible cortical blindness. Physicians should be aware of these rare toxicities among patients with severe carbamate insecticide poisoning. Potential risk factors and specific treatments of either delayed neuropathy or cortical blindness still need further study.

Acknowledgments

This work had been presented at the XXX International Congress of European Association of Poisons Centers and Clinical Toxicologists (EAPCCT), Bordeaux, France, May 11–14, 2010.

Declaration of interest

Financial support was provided from the Department of Health for Taiwan Poison Control Center in Taipei Veterans General Hospital, 2009. The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

References