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CASE REPORT

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# Mild-to-severe poisoning due to *Conium maculatum* as toxic herb: A case series

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## Abstract

*Conium maculatum* toxicity may occur by mistakenly or intentionally eating this plant. Due to muscarinic or nicotinic symptoms associated with this plant toxicity, supportive care and treatment with atropine are urgently important.

**KEYWORDS**

bronchorrhoea, Conium maculatum, intoxication

## 1 | INTRODUCTION

*Conium maculatum (C. maculatum)* (poison hemlock) is one of the deadly poisonous plants and has various species with different alkaloids. Clinical manifestations of *C. maculatum* intoxication include effects on the gastrointestinal tract, nervous system (neuromuscular respiratory paralysis), cardiovascular system, and respiratory tract (bronchoconstriction and bronchorrhoea).

*Conium maculatum*, known as poison hemlock, is one of the deadly poisonous plants and has various species with different alkaloids.[1] The *C. maculatum* was famous as a poison plant and was used often to execute criminals or political prisoners in ancient Greece. Socrates is one of the most famous political opponents killed by this plant.[2] Poisoning was caused by the piperidine alkaloids coniine and g-coniceine. These piperidine alkaloids are acetate-derived. All organs of the plant, such as leaves, seeds, and flowers, contain alkaloids.[3] The most alkaloids found in *C. maculatum* are coniine, *N-methyl-coniine*, *pseudoconhydrine*, *gamma-coniceine*, *and conhydrine*. The greatest amount of Coniine, as nicotinic alkaloids, is found in the seeds and flowers of *C. maculatum*.[4] Coniine is a nicotinic alkaloid. Coniine and other alkaloids are distributed throughout the body and transferred to the blood-brain barrier, placenta, and are secreted in breast milk. Coniine was detected in serum, urine, and tissues. These alkaloids are a selective agonist for nicotinic-type acetylcholine receptors (nAChRs). The nicotinic-type acetylcholine receptor is distributed within the central and autonomic nervous systems, the neuromuscular junctions, and the adrenal medulla.[3-5]

The manifestations of hemlock poisoning include effects on the nervous system (neuromuscular respiratory paralysis), bronchoconstriction, bronchorrhoea, hypertension, tremors, vomiting, nervousness, problems with walking, dilation of pupils, decrease of the body temperature, rapid respiration, salivation, urination, nausea, convulsions, coma, and death. The most serious side effect of Coniine is rhabdomyolysis. Coniine-induced respiratory paralysis with damage to the respiratory center in the medulla can cause death. Tachycardia is followed by bradycardia induced by Conium alkaloids that behave like biphasic nicotine. On the other hand, the teratogenic effect of this plant on animals has been reported.[4,6]

γ-Coniceine is the first of the conium alkaloids. The analysis revealed that when the concentration of coniine was high, the concentration of γ-Coniceine is low, implying that coniine is a revival form of γ-Coniceine. An oxidation-reduction system is available between coniine and γ-Coniceine in Conium plants by a NADPH-dependent γ-Coniceine reductase.[3,5] Lack of knowledge of plant morphology is the main factor for poisoning *C. maculatum* belonging to a different pathway.[7] *C. maculatum* poisoning is a completely different plant from water hemlock (*Cicuta*). Because of the various types of poisoning and the only similarity in names, we may be misled.[8] Herein, we report mild-to-severe toxicity with hemlock poisoning.

## 2 | CASES PRESENTATION

Three adult men, (30, 32, and 50 years old), with a history of opioid addiction, were working as shepherds in Kiasar, a mountainous region in Mazandaran Province, northern Iran. During lunch, they ate a forest plant as well as vegetables. Within a few minutes, they experience muscular weakness, particularly in the legs, as well as abdominal pain and gastrointestinal symptoms, prompting patients to be referred to the emergency room. Their initial symptoms included fatigue, lethargy, dizziness, nausea, vomiting, heavy diaphoresis, and a decreased level of consciousness.

After arriving at the emergency room, one of the patients was discharged after initial care due to the stability of vital signs and mild symptoms. Two patients had moderate and severe symptoms. Immediately after admission of these two patients, they were intubated and intravenous line fixation was performed before transferring patients to the ICU ward. Hydration and treatment with atropine 0.5 mg PRN (because of muscarinic and nicotinic symptoms), pantoprazole, and ondansetron were also performed.

The plant (see Figure 1) was identified and recognized as *C. maculatum*, by the herbarium department of pharmacognosy, Mashhad University of Medical Sciences, Mashhad, Khorasan Razavi province, Eastern Iran.

**FIGURE 1** The plant, *Conium maculatum*, that was consumed by the patients

Primary evaluation includes ECG, arterial blood gas (ABG), and routine laboratory test. With the exception of a T tall wave in some leads in patients with severe symptoms, no abnormal sign was seen in the ECG. Arterial blood gas showed severe acidosis in one patient and mild acidosis in another (Table 1).

The patient was treated with atropine (0.5 mg/h started and tapered as symptoms decreased) based on the presence of muscarinic and nicotinic symptoms. The serum cholinesterase enzyme level has also been reported in the normal range.

On the second day after admission to the ICU, ABG analysis (Table 2) and hemodynamic status of patients stabilized and, subsequently, their level of consciousness improved. The liver and kidney performance was normal with assessment of alanine-transaminase (ALT), aspartate transaminase (AST), creatinine, and urea, respectively (Table 3). The patients were extubated, transferred to the poisoning ward on the third day. Finally, after a few days, the patients were released from the hospital with no symptoms and good fines. This study was conducted according to the declaration of Helsinki principles. Also, CARE guidelines and methodology have been followed in this study.

## 3 | DISCUSSION

We reported three adult patients with *C. maculatum* toxicity (Poison Hemlock). Hemlock poisoning is recorded in humans who have mistakenly eaten the leaves of the plants for parsley.[9] Muscular weakness, decreased level of consciousness, lethargy, dizziness, nausea, and vomiting are clinical

**TABLE 1** Initial Arterial blood gas assessment (in emergency room) in patients with moderate and severe symptoms

| | Patient with severe symptoms | Patient with moderate symptoms |
|---|---|---|
| PH | 7.03 | 7.37 |
| PCO2 | 132 | 33 |
| HCO3 | 33.5 | 19.1 |

**TABLE 2** Arterial blood gas assessment (in ICU ward) in patient with severe symptoms

| | First day in ICU | Second day in ICU* |
|---|---|---|
| PH | 7.32 | 7.40 |
| PCO2 | 35 | 41.5 |
| HCO3 | 18 | 25 |

*The Patients with moderate symptoms have normal arterial blood gas during ICU administration.

**TABLE 3** Laboratory finding in patient with moderate and severe symptom

| | Patient with severe symptom | Patient with moderate symptom |
|---|---|---|
| AST | 28 | 33 |
| ALT | 15 | 22 |
| ALP | 157 | 192 |
| Na | 141 | 136 |
| K | 3.8 | 3.6 |
| Cr | 0.5 | 1 |
| Urea | 54 | 47 |
| BS | 90 | 110 |
| Bil T/D | 0.5/0.2 | 0.6/0.2 |
| HGB | 11.5 | 12.3 |
| INR | 1 | 1 |
| CPK | 290 | 133 |
| CPK-mb | 30 | 24 |

symptoms of these patients. Metabolic acidosis was also observed in a patient with severe symptoms.

Coniine and *Coniine-like* alkaloids can cause similar nicotine toxicity and nondepolarizing muscle blockers.[10] The most important clinical manifestations of poisoning with *C. maculatum* are in the nervous system. The nicotinic alkaloids act as agonists on the nicotinic acetylcholine receptors (nAChRs).[11] In addition, in the neuronal system, nicotinic acetylcholine receptors are found in gastrointestinal epithelial, skin, and bronchial cells.[12] Nicotinic toxicity consists of two phases (early and late phases). The early non-neurological phase includes vomiting, nausea, decrease of the body temperature, diaphoresis, tachypnea, salivation, and urination. Muscular weakness, movement problems, ataxia, legs and arms paralysis, tremor, visual disorder, rapid breathing and tachypnea, bradycardia, headache, mydriasis are nicotinic effects that may happen in the first neurological phase of hemlock poisoning.[13] Clinical signs and symptoms such as nausea, rash, dizziness, and painful leg cramps were reported in a case report as a result of accidentally using *C. maculatum*.[7] On the other hand, in a case report of a 6-year-old female patient, burning sensation in the mouth, hyper salivation, trembling hands, and ataxia were observed.[14]

In the late phase, "paradoxical" inhibition of the nicotinic cholinergic receptors occurs. In this phase, bradycardia, increasing neuromuscular blockade, paralysis, with dyspnea or apnea, respiratory failure, and central nervous system depression can occur.[15]

Convulsions, coma, and finally death may have been observed in severe toxicity. Paralysis of respiration muscles and respiratory failure can lead to death.[16]

For *C. maculatum* toxicity, supportive care is an important intervention. Intubation or positive ventilation may be necessary. Tachycardia and hypertension that are observed in the early phase do not require any specific management. Intravenous fluids should be prescribed for hypotension treatment in the late phase. Sympathomimetic agents may also be required.[17]

In the initial phase of *C. maculatum* toxicity, rapid breathing and tachypnea lead to hypocapnia and respiratory alkalosis, but in the late phase, with the onset of respiratory muscle weakness, respiratory acidosis predominates.[18] In this study, as shown in Table 1, the patient with moderate symptoms has compensated for respiratory alkalosis, whereas the patient with severe symptoms in the emergency room has compensated for respiratory acidosis. After intubation and ICU admission, acid-base abnormalities were resolved. A case report from 2009 describes a 2-year-old toddler with moderate respiratory distress failure. He had picked a plant (*C. maculatum*) when he was playing with his sister. Initial elevation showed that his oxygen saturation was 80% in room air with pH 7.28; PCO2, 43 mm Hg; and PO2, 71 mm Hg. He was intubated and treated with atropine, etomidate, and rocuronium.[19]

The nausea, vomiting, diarrhea, and abdominal pain may lead to hypotension and electrolyte disturbance.[20] Management of gastrointestinal toxicity includes antiemetic, fluid, and electrolyte replacement.

In the late phase, for nicotinic and muscarinic symptoms, we used atropine. An initial intravenous dose of atropine is 0.5–1 mg for adults and 0.02 mg/kg for children. The dose can be repeated every 5–10 min until bronchial secretions are controlled.[21] Atropine can reduce abdominal pain and diarrhea.

Rhabdomyolysis with hemlock poisoning has been reported.[22] Rhabdomyolysis may cause renal injury. Acute renal failure or renal damage is a specific symptom that is only reported in human poisoning.[23] Muscle pain and muscle weakness may be related to rhabdomyolysis symptoms. In our patients, AST, ALT, and CPK levels were in the normal range, so rhabdomyolysis was ruled out.[24]

CK-MB was abnormal in our patients, and T tall waves were observed in some leads of the ECG. Previously, in 2017, it described a 30-year-old man from Winston-Salem (North Carolina, USA) with cardiac arrest and moderate-to-severe encephalopathy after *C. maculatum* injection.[25] Another case report, from Turkey, describes a 49-year-old woman who was admitted due to *C. maculatum* ingestion. A cardiopulmonary arrest happened during hospitalization, and she unfortunately died after 9 days.[26] Although *C. maculatum* toxicity may lead to dysrhythmia, heart block, myocardial infarction (MI), and bradycardia, CK-MB is a nonspecific marker and may be released from many organs. So, in our patients we did not have strong evidence such as ST-elevation in ECG or QT prolongation, in favor of MI or heart block. The serum creatinine level was in the normal range, but urea was mildly increased, so acute renal failure was ruled out.

## 4 | CONCLUSION

*Conium maculatum* toxicity may occur by mistakenly or intentionally eating this plant. With this toxic plant, supportive care is a critical intervention. Due to muscarinic or nicotinic symptoms associated with this plant toxicity, treatment with atropine is urgently important. All parts of *C. maculatum* contain toxic alkaloids, but seeds and flowers have a large amount of *Coniine* alkaloids. Because of the simultaneous use of the plant by our patients, and they did not eat seeds or flowers, the difference in toxicity symptoms (mild, moderate, and severe) may be related to the difference in the amount of the plant that has been eaten.

## DATA AVAILABILITY STATEMENT

The data are available with the corresponding author and can be achieved on request.

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Declared none.

### CONFLICT OF INTEREST

None declared.

### AUTHOR CONTRIBUTIONS

ZZ: involved in interpretation and collecting of data, and editing the manuscript. JB and ZA: involved in writing, editing, and preparing the final version of manuscript. MF: involved in critical revising. RT: is responsible for collecting data and submitting the manuscript. All authors reviewed the paper and approved the final version of the manuscript.

### ETHICAL APPROVAL

This study was reviewed and approved by the Mazandaran University of Medical Science Ethics Committee (approval number: IR.REC.MAZUMS 1399.7850 on July 29, 2020).

### INFORMED CONSENT

Written consent for publication of this case report was obtained from the patients.

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