Clinical Features and Management of Herb-Induced Aconitine Poisoning

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Study objective: We define the potential sources, clinical manifestations, and treatment of aconitine poisoning.

Methods: The database of the National Poison Center in Taiwan was retrospectively searched for the diagnosis of aconitine poisoning for 1990 to 1999. The reasons for taking the aconite roots, the clinical features, management, and possible predisposing factors were noted.

Results: A total of 17 cases occurred and consisted of 9 men and 8 women aged 30 to 70 years. Thirteen patients ingested aconite roots as treatment for rheumatism and wounds. Two patients volunteered to test the effects of aconite roots in a drug study. Two patients accidentally ingested the aconite roots. After a latent period of 10 to 90 minutes, patients developed a combination of neurologic (n=17), cardiovascular (n=14), gastrointestinal (n=9), and other (n=5) features typical of aconitine poisoning. Four patients developed ventricular tachycardia. All patients received supportive treatment. Patients with ventricular tachycardia were also treated with charcoal hemoperfusion. All patients made a complete recovery.

Conclusion: Life-threatening ventricular tachycardia can occur after the consumption of aconite roots. The risk is higher with inadequately processed aconite roots, large doses, or tincture preparations. With increasing popularity of herbal medicines, herb-induced aconitine poisoning may also be seen in Western countries.

[*Ann Emerg Med.* 2004;43:574-579.]

INTRODUCTION

Background

Aconitine alkaloids are present in the roots of *Aconitum carmichaeli*, *Aconitum kusnezoffii*, and other plants in China and the Far East. The parent tubers are known as Chuanwu and Caowu or Wutou. The daughter tuber is called Futzu. In North America, aconitine is mainly derived from *Aconitinum napellus*, commonly called monkshood, helmet flower, or wolfsbane. They contain aconitine and other C_{19}-diterpenoid alkaloids, which are known neurotoxins and cardiotoxins.[1] Because raw aconite roots are generally toxic, they are used only after processing. One suggested preparation process is to soak the roots in water or saturated lime water and then boil

0196-0644/$30.00

doi:10.1016/j.annemergmed.2003.10.046

Editor's Capsule Summary

What is already known on this topic

Herbal remedies are becoming increasing popular, particularly in the United States. Some Chinese herbal remedies are made from roots that contain aconite alkaloids and are potentially toxic.

What question this study addressed

The potential sources, manifestations, and treatment of herb-associated aconitine poisoning reported to a poison control center in Taiwan were reviewed.

What this study adds to our knowledge

Ingestion of improperly prepared aconite-containing tubers is associated with rapid onset (10 to 90 minutes) of toxicity but may require more than one dose. The clinical syndrome consists primarily of paresthesias, muscle weakness, vomiting, hypotension, and ventricular dysrhythmias.

How this might change clinical practice

An herbal medication history should be routinely incorporated into patient assessments. Aconite herb-associated poisoning should be considered for patients presenting with vomiting, paresthesias, and cardiac abnormalities.

until the aconitine white core disappears and no numbness occurs when tasted. Aconitine and the total alkaloid content can be reduced by as much as 90% and 65%, respectively, because of the hydrolysis of aconite alkaloids to less toxic benzylaconine and aconine derivatives.[2] Soaking and boiling during the preparation of herbal decoction from the dried, processed aconite roots has a similar hydrolytic action. Aconite alkaloids have a narrow therapeutic index, and the alkaloid type and amount vary with the species, place of harvest, and adequacy of processing. Therefore, poisoning may still occur after the consumption of processed aconite roots.[3,4]

Importance

With the increasing popularity of alternative medicines among the general public, herb-induced aconitine poisoning may occur even in Western countries.[5] Life-threatening ventricular arrhythmias may be caused by aconitine.

Goals of This Investigation

We report the clinical features and treatment of 17 patients with herb-induced aconitine poisoning to provide more detailed information about the sources of exposure, doses associated with toxicity, and the treatment of life-threatening ventricular arrhythmias.

MATERIALS AND METHODS

Study Design and Setting

This study was a retrospective case series. The National Poison Center, based in the Veterans General Hospital, Taipei, Taiwan, provides a 24-hour advisory service on all aspects of clinical toxicology to all health care professionals in Taiwan. All inquiries and answers were recorded in a computerized database. We searched the database to identify patients with herb-induced aconitine poisoning from January 1990 to December 1999. We also reviewed their hospital notes, if available. The information noted included demographic data, medical history, reason for taking herbs, the types and amounts of aconite roots taken, the duration of boiling during preparation of the herbal decoction, latent period between herb consumption and onset of symptoms, the clinical effects, hospital treatment, and outcomes.

The diagnosis of herb-induced aconitine poisoning was based on previously proposed criteria,[1] including the following: (1) patients became unwell only after taking herbal medicines mainly as treatment for musculoskeletal disorders; (2) patients had cardiovascular, neurologic, and other features that were typical of aconitine poisoning; and (3) reviews of written prescriptions or verification with the herbalists confirmed that patients had taken 1 or more aconite roots.

RESULTS

During the 10-year period, 17 cases met the aforementioned criteria either with similar toxidrome or a history of aconitine plant ingestion (Table 1). Patients 14 and 15 took Huo Luo Dan, which is composed of aconitine and other traditional Chinese medications. The other ingredients contained in Huo Luo Dan have no toxic effects. All other patients experienced sole exposures to aconitine-containing herbs. No other medications were ingested. In addition to poison center records, hospital notes were available for 11 patients. There were 9 men and 8 women, and their ages ranged from 30 to 70 years (median 46 years). Apart from patient 2, who is white, the subjects are all ethnic Chinese. None of the 17 patients had a history of ischemic heart disease or cardiac arrhythmias.

Thirteen patients took the aconite roots as treatment for rheumatism or wounds (n=11), alopecia (n=1), or finger numbness (n=1). Two patients accidentally

ingested the aconite roots. Two patients volunteered to experience the pharmacologic effects of aconite roots in one drug study.

Ten patients took a decoction made from unprocessed (patients 2, 10, 12, and 13) or processed (patients 7, 8, 9, 11, 16, and 17) aconite roots (Table 1). None of the 10 patients had prepared the decoction as recommended by adequately boiling the aconite roots in water. One patient (patient 1) took processed aconite root instead of the decoction made from it. The amounts of toxic alkaloids taken by these 11 patients would be much larger than intended without proper processing. Four patients (patients 3, 4, 5, and 6) ingested a tincture made from unprocessed aconite roots and wine. With its high solubility in ethanol, medicinal wine made from aconite roots will always contain a much larger amount of toxic alkaloids.

In contrast to the 14 patients who became ill after ingesting the first dose, patients 11, 12, and 13 were symptomatic only after ingesting the third dose of aconite roots on day 2 or 3. After a latent period of 10 to 90 minutes, patients developed a combination of neurologic (n=17), cardiovascular (n=14), gastrointestinal (n=9), and other (n=5) features (Table 2). Paresthesia and numbness of the 4 limbs (n=13) or facial or perioral area (n=8), chest tightness (n=11), dizziness (n=11), generalized muscle weakness (grade 5^- power; n=9), nausea and vomiting (n=8), palpitations (n=7), and hypotension (systolic blood pressure decreased by >20 mm Hg; n=7) were particularly common. Ventricular tachycardia occurred in 4 patients.

All patients received supportive treatment, such as intravenous fluids for dehydration and intravenous dopamine infusion for hypotension (Table 2). In addition, specific treatment for ventricular tachycardia was given to 4 patients (patients 2, 4, 5, and 17). Charcoal hemoperfusion to remove aconite compounds was performed in 2 patients (patients 4 and 5) before the ventricular tachycardia subsided.[6] Patient 2 also required the insertion of a temporary pacemaker because of severe bradycardia. Two patients required drug treatment for ventricular ectopic beats (patient 14) or bradycardia (patient 15). In patients whose ventricular arrhythmias were refractory to drug treatment, charcoal hemoperfusion was performed for 4 hours with 1 cartridge (Adsorba 300C, Gambro, Stockholm, Sweden) (Figure; patients 4 and 5 in Table 2). All patients made a complete recovery. The recovery time was from 1.5 to 2 days in the mildly intoxicated patient, whereas the patients with cardiovascular complications recovered in 7 to 9 days.

LIMITATIONS

One of the limitations of this study is the small sample size. There may have been some mild cases that were not reported to the poison control center. Some of the effects, such as diarrhea and numbness, may be considered to be the normal reaction by patients. We cannot estimate the prevalence and mortality rate accurately. Another limitation is that we cannot provide the kinetic data of patients 4 and 5 for aconite elimination, which

Table 1.
Selected cases of herb-induced aconitine poisoning: patient demographic characteristics, types of preparations, and estimated amounts ingested.

Patient No.	Sex/Age, y	Types of Aconite Root Preparations (Decoction)*	Amount Ingested
2	M/38	Unprocessed root of *A carmichaeli*	Unknown
3	M/67	600 g of processed root of *A carmichaeli*, 600 g of processed root of *A kusnezoffii* in 200 mL of water and 200 mL of alcohol	200 mL
4	M/59	600 g of processed root of *A carmichaeli* in 300 mL of alcohol	50 mL
5	F/50	600 g processed *A carmichaeli* in 300 mL of alcohol	50 mL
6	M/47	60 g root of processed *A carmichaeli* in 30 mL of alcohol	30 mL
10	M/32	Unprocessed root of *A carmichaeli*	45 g
11	F/38	Unknown aconite root	7.5 g
12	F/43	Unprocessed root of *A carmichaeli* and unprocessed root of *A kusnezoffii*	Unknown
13	F/59	Unprocessed root of *A carmichaeli* and unprocessed root of *A kusnezoffii*	50 g
14	F/43	Huo Luo Dan (each pill contains 0.32 g of processed root of *A carmichaeli* and 0.32 g of processed root of *A kusnezoffii*)	2 g
15	M/33	Huo Luo Dan (each pill contains 0.32 g of processed root of *A carmichaeli* and 0.33 g of processed root of *A kusnezoffii*)	2 g

M, Male; **F,** female.
*Decoction: to process the raw herbal medicine with water.

makes the application of hemoperfusion in the aconitine-poisoned patient unclear.

DISCUSSION

The latent period between ingestion of aconite roots and onset of symptoms can be as short as 10 minutes (patient 17), suggesting that aconitine and related alkaloids can be rapidly absorbed by the upper gastrointestinal tract. In some patients, symptoms occur only after a longer latent period. Our patients invariably developed a combination of neurologic, cardiovascular, gastrointestinal, and other signs and symptoms (Table 2). The neurologic features can be sensory, motor, or both. Cardiovascular features include palpitations, chest tightness, hypotension, ectopic, bradycardia, tachycardia, ventricular arrhythmias, and pulmonary edema. The ventricular tachyarrhythmias responded poorly to direct-current cardioversion and standard antiarrhythmic drugs such as lidocaine (Table 2). Gastrointestinal features include nausea, abdominal pain, and diarrhea. Hyperventilation resulting in respiratory alkalosis is seen in some patients, possibly because of the central effect of aconitine on the medullary center.[4] Inhospital mortality among unselected patients was estimated to be 5.5%.[4] All of our patients made a full recovery.

In our study, 4 (24%) of 17 patients developed ventricular tachycardia. Because death is mostly from ventricular tachyarrhythmias, the charcoal hemoperfusion for our patients may have played a critical role in our study. In a similar study of 18 unselected patients in Hong Kong,[6] the incidence of this complication was 11%. Tai et al[3] described the treatment of 17 patients with serious cardiotoxicity complicating aconitine poi-

Table 2.
Seventeen cases of herb-induced aconitine poisoning: clinical features and treatment.

Case	Latent Period*	Recovery Time	Cardiovascular Features†	Neurologic Features	Other Features	Treatment
1	Unknown	Unknown	Chest tightness, bradycardia	Sensory (limbs)‡	None	Supportive§
2	1 h	8 d	Palpitations, chest tightness, hypotension, bradycardia, ventricular tachycardia	Sensory (limbs)	Nausea, abdominal pain, hyperventilation	Lidocaine, direct current shock, temporary pacemaker, mechanical ventilation
3	1 h	2 d	Tachycardia, hypotension	Motor (limbs)	Dizziness	Supportive
4	1 h	7 d	Palpitations, chest tightness, hypotension, ventricular tachycardia	Sensory (limbs/face), motor (limbs)	Nausea, abdominal pain, dizziness	Hemoperfusion, lidocaine
5	1 h	9 d	Palpitations, chest tightness, hypotension, ventricular tachycardia, pulmonary edema	Sensory (limbs/face), motor (limbs)	Nausea, dizziness	Hemoperfusion, lidocaine, high-flow oxygen
6	1 h	2 d	None	Sensory (limbs/face)	None	Supportive
7	30 min	2 d	Palpitations	Sensory (limbs/face)	Dizziness	Supportive
8	1 h	2 d	Sinus tachycardia	Sensory (face), motor (limbs)	Nausea, dizziness	Supportive
9	Unknown	Unknown	Palpitations, chest tightness, sinus tachycardia	Motor (limbs)	Hyperventilation	Supportive
10	1.5 h	2 d	None	Sensory (limbs/face), motor (limbs)	Abdominal distention	Supportive
11	Unknown	2 d	Palpitations, chest tightness	Sensory (limbs)	Dizziness, hyperventilation	Supportive
12	30 min	2 d	Chest tightness, multifocal ventricular ectopics	Motor (limbs)	Nausea, dizziness, cold sweat, hyperventilation	Supportive
13	30 min	3 d	Chest tightness, hypotension	Sensory (limbs), motor (face)	Nausea, dizziness, cold sweat, abdominal pain, diarrhea	Supportive
14	20 min	2 d	Chest tightness, multifocal ventricular ectopics	Sensory (limbs)	Dizziness, hyperventilation	Lidocaine
15	20 min	2 d	Bradycardia, hypotension	Sensory (limbs/face)	Nausea, dizziness, cold sweat	Atropine
16	20 min	1.5 d	None	Sensory (limbs)	None	Supportive
17	10 min	7 d	Palpitations, chest tightness, hypotension, ventricular tachycardia	Sensory (limbs)/ motor (limbs)	Nausea, dizziness, cold sweat	Lidocaine

*The mean value of the latent period is 43.6 min.
†Hypotension: Systolic blood pressure decreased to <90 mm Hg with shock sign; lidocaine dosage: 1 mg/kg intravenously as a loading dose and then 4 mg/min as a maintenance dose; atropine dosage: 1 mg intravenously twice; dopamine dosage was 5-20 g/kg/min, adjusted according to patient's blood pressure.
‡Sensory (limbs) indicates paresthesia and numbness in 4 limbs; sensory (limbs/face) indicates paresthesia and numbness in 4 limbs, face, and perioral area; motor (limbs) indicates muscle weakness in 4 limbs.
§Supportive: Inotropic agents such as dopamine were used in patients with hypotension.

soning. All patients except 2 were hypotensive. Two patients had ventricular fibrillation. Thirteen patients had ventricular tachycardia that was sustained (n=9) or polymorphic (n=9). Two patients had frequent polymorphic ventricular ectopy. Repeated direct-current cardioversions were unsuccessful in 10 patients. No single antiarrhythmic drug was uniformly effective. Lidocaine was unsuccessful in all patients, and suppression of ventricular tachycardia was eventually achieved in 9 patients with amiodarone (5), flecainide (2), procainamide (1), or mexiletine (1). Two patients died from refractory ventricular fibrillation. Amiodarone and flecainide would be reasonable first-line antiarrhythmic drugs, as Tai et al suggested.[3] Gutierrez et al[7] administered different types of antiarrhythmic drugs to rats before giving aconitine. The best drugs for inhibiting mortality were the membrane-stabilizing antiarrhythmics (class 1 antiarrhythmics, particularly flecanide) and β-blockers. Neither amiodarone nor the calcium antagonists showed any effect. The β-blockers (class 2 antiarrhythmics) pindolol, propranolol, and oxprenolol have similar activity. Other animal data and isolated case reports suggest that intravenous magnesium may have antiarrhythmic actions.[8] In patients whose ventricular arrhythmias are refractory to drug treatment, charcoal hemoperfusion for 4 hours for aconitine removal may hasten the recovery.[6,9] Unfortunately, there are few elimination kinetic data about aconitine. Because aconitine is eliminated by the kidneys, has a large molecular weight (645.8 g/mol), and is soluble in ethanol and water, active charcoal hemoperfusion seems to be a reasonable option in patients not responding to supportive care. Others have reported the successful use of a ventricular assist device or percutaneous cardiopulmonary bypass.[10]

Most of the cardiovascular and neurologic features of poisoning with aconitine can be explained on the basis of its actions on voltage-sensitive Na^+ channels in excitable tissues, including myocardium, nerve, and muscle.[4] Aconitine binds with high affinity to the open gate of Na^+ channels at receptor site 2,[11] causing persistent activation of these channels. This sustained Na^+ influx delays the repolarization phase of the action potential and initiates premature excitation.

However, aconite roots contain other cardiotonic substances that may contribute to their toxic effects. For example, hypaconitine is more potent than aconitine and mesaconitine in producing neuromuscular

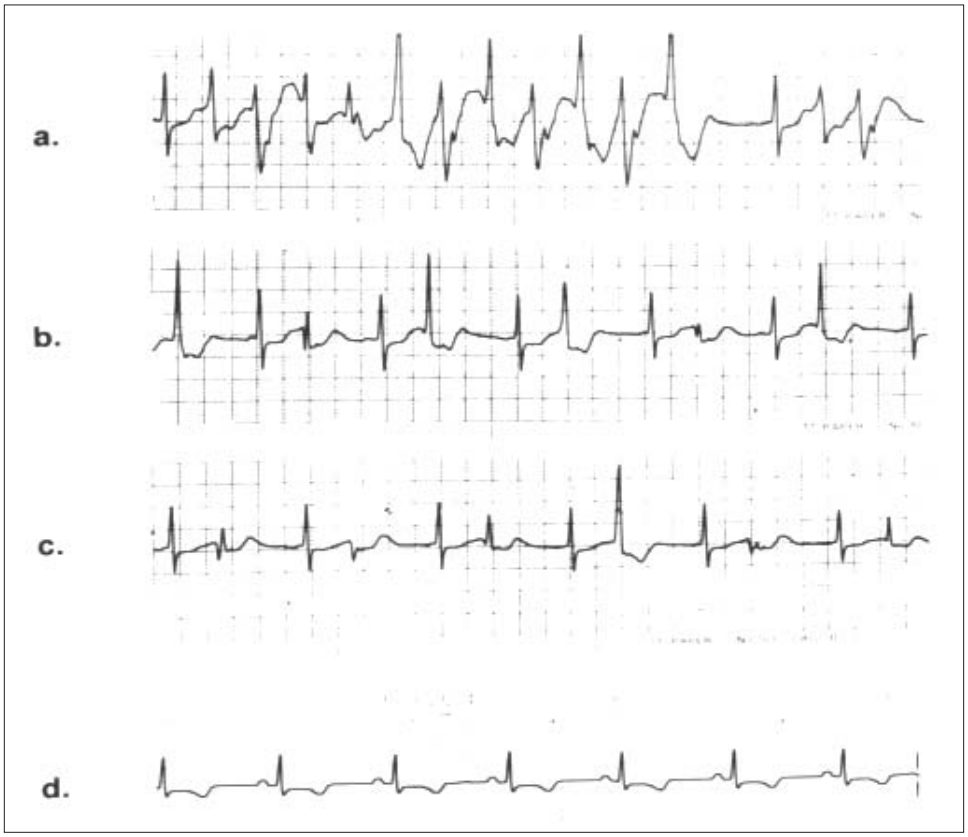

Figure.
A, *Polymorphic multifocal ventricular ectopics after ingestion of an aconitine-containing herb 4 hours later.* ***B, C,*** *During charcoal hemoperfusion.* ***D,*** *Normal sinus rhythm after charcoal hemoperfusion.*

block.[12] The presence of alkaloids with a low affinity for receptor 2 (1-benzoylnapelline, 14-benzoyltalatisamine) may cause a negative inotropic effect and bradycardiac forms of arrhythmia.[11]

In our patients, several factors known to predispose to aconitine poisoning could be identified.[4] Ten patients took a decoction made from unprocessed or processed aconite roots without adequately boiling the roots in water. One patient (patient 1) took processed aconite root instead of the decoction made from it. Without adequate processing of the aconite roots, the amounts of toxic alkaloids taken by these 11 patients would be much larger than intended. The alkaloid components and amounts in aconite roots may vary with the species, place of origin, time of harvest, and method of processing,[4] which could be why 3 patients were ill only after ingesting the third dose. The recommended dose of processed aconite roots has been lowered progressively to 1.5 to 3 g after repeated reports of toxicity.[4] A dose of 7 to 11 g of 1 or 2 types of aconite root was typically given to patients with herb-induced aconitine poisoning in Hong Kong.[3,4] As can be seen in Table 1, the doses that were ingested by our patients were larger. Four patients (patients 3, 4, 5, and 6) ingested a tincture made from aconite roots and wine. In the preparation of medicinal wine, unprocessed aconite roots may be used, and there is no previous boiling. The toxic alkaloids in aconite roots dissolve in alcohol efficiently. For these reasons, medicinal wine made from aconite roots will always contain much larger amounts of toxic alkaloids.

The differential diagnosis should include plant toxins such as digoxin-like cardiac glycosides, andromedotoxin, Jin bu huan, and veratrine. When a patient presents with numbness, muscle weakness, and unexplained ventricular tachycardia, the possibility of aconitine intoxication should be considered.

Life-threatening ventricular tachycardia can occur after the consumption of aconite roots. The risk is greater if the roots are inadequately processed or large doses and tincture preparations are used. Patients should be educated about the importance of adequate processing of aconite roots before use.

Author contributions: C-CL designed the study, provided chart review and full clinical data, and drafted the manuscript. TYKC and J-FD participated in manuscript review and revision. C-CL takes responsibility for the paper as a whole.

Received for publication July 1, 2003. Revisions received August 13, 2003; October 2, 2003; and October 13, 2003. Accepted for publication October 27, 2003.

The authors report this study did not receive any outside funding or support.

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