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Correlation between Time of Ingestion or the Ingested Aconite Plant Parts and Aconite Poisoning-Induced Arrhythmia

Yuji Fujita*[1,2], Katsutoshi Terui[3], Atsushi Kakizaki[2], Katsuo Takahashi[2], Hidehiko Aoki[3] and Shigeatsu Endo[3]

Poisoning and Drug Laboratory Division, Critical Care and Emergency Center, Iwate Medical University Hospital[1]
Department of Pharmacy, Iwate Medical University Hospital[2]
Department of Emergency Medicine, Iwate Medical University School of Medicine[3]

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We investigated the relationship between the development of aconite poisoning-induced arrhythmia and time of ingestion or the ingested aconite plant parts as well as the outcome of treatment for such arrhythmia for 10 patients. Three of them exhibited ventricular tachycardia (VT) and ventricular fibrillation (Vf), which are potentially fatal arrhythmias. Two of these patients ingested aconite roots in June or November, and the third patient ingested aconite leaves in April. The other seven patients did not develop any potentially fatal arrhythmias. Four of these patients ingested aconite leaves in April or May, and the remaining three patients ingested aconite roots in March, August or September. Nine of the ten patients ingested aconite leaves or roots at the same time as they gathered them.

The antiarrhythmic agent lidocaine was ineffective against the VT and Vf that 3 patients developed. It was effective against the other ventricular arrhythmias with the effect differing depending on the part of the plant ingested. Effectiveness was seen for patients who had ingested leaves but not for those who had ingested roots.

Our data did not show that the severity of the arrhythmia was influenced by the part of the plant ingested or the time of ingestion. They do however suggest that the effect of lidocaine was influenced by the type of arrhythmia and the part of the plant ingested and therefore should prove useful in determining the suitability of lidocaine treatment for arrhythmia due to aconite poisoning.

Key words —— aconite poisoning, arrhythmia, ingested part of plant, time of ingestion, lidocaine

Introduction

Aconite is a well-known toxic plant of the genus *Aconitum*, belonging to the Ranunculaceae family. Aconite contains toxic *Aconitum* alkaloids such as aconitine, jesaconitine, hypaconitine, and mesaconitine. It has reported that the LD_{50} value of aconitine in mice is 1.8 mg/kg when given orally[1], and the lethal dose of aconitine in humans is estimated to be 1—2 mg[2,3]. Aconitines have the strongest toxicity of plant-derived chemical substances. Therefore, they are considered to be the causative agents of aconite poisoning.

Various toxic symptoms are observed in cases of aconite poisoning, including nausea, vomiting, numbness and palsy of the extremities, and arrhythmia. Arrhythmia is the most typical symptom in aconite poisoning, and aconite poisoning-induced ventricular arrhythmias such as ventricular tachycardia (VT) and ventricular fibrillation (Vf), often show resistance to treatment with antiarrhythmic agents and electrical cardioversion[4—9]. Moreover, aconite poisoning frequently results in death due to cardiac arrest caused by arrhythmias such as Vf[4—6]. Therefore, arrhythmia caused by aconite poisoning is important in clinical care. The content of aconitines in aconite plant differs according to the part of the plant or time of collection[10—13]. It is, therefore, that the ingested plant parts or the time of ingestion (time that patient ingested) differs in severity of aconite poisoning-induced arrhythmia.

We hypothesized that the ingested plant part and the time of ingestion are factors that affect aconite poisoning-induced arrhythmias. To clearing this hypothesis, we investigated the relationship between the ingested plant part and time of ingestion, and the development and therapeutic outcome of

* 岩手県盛岡市本町通 3-16-1 ; 3-16-1, Honchoudori, Morioka-shi, Iwate, 020-0015 Japan

aconite poisoning-induced arrhythmia in 10 patients with aconite poisoning.

Materials and Methods

Thirteen patients with aconite poisoning were admitted to the Emergency and Critical Care Center at Iwate Medical University from 1997 to 2005. Of these patients, ten for whom the following items were available for investigation in the medical records were chosen as subjects for the study: the time of ingestion, ingested plant parts, reason for ingesting aconite, type of arrhythmia, method of treatment, effect of an antiarrhythmic agent (lidocaine), and outcome after treatment. Information of the time of ingestion, ingested plant parts and reason for ingestion were obtained from the patients or their family. The details of arrhythmias were obtained from the electrocardiogram recorded after admission. The information of correct amount ingested in all patients could not be obtained.

Aconitines such as aconitine, jesaconitine, mesaconitine and hypaconitine were analyzed by liquid chromatography mass-spectrometry (liquid chromatography; Waters 2690, and mass spectrometer; ZMD 4000, Waters, Milford, MA, USA) according to the method reported by Fujita *et. al*.[14]. The serum concentration of aconitines in patients was obtained from the sum of the serum concentrations of alkaloids such as aconitine, jesaconitine, hypaconitine and mesaconitine. Serum concentration of aconitines was plotted logarithmically against time after ingestion, and a concentration-time curve for serum was obtained. The time of ingestion of aconite plant was shown as 0h. Regression analysis of these data was performed using, at least, three concentration-time data points in the initial log-linear phase. The serum concentration of aconitines at the point of lidocaine administration was the value at which time of lidocaine administration was substituted for the regression line. The statistical analyses was determined using a StatView 5.0. software.

Results

Profiles of patients with aconite poisoning are summarized in **Table 1**. The patients comprised seven males and three females, and ages ranging were from 40 to 78 years (54.1±12.5 years). Time of ingestion in 9 of the 10 patients was in the same time when patients had collected the plant. Patient 8 ingested roots which he had dried in his house, but the time of collection was unknown. All patients had no a previous history of heart disease.

The electrocardiograms of patients 1, 2 and 3 showed VT and Vf, and these arrhythmias were resistant to treatment

Table 1. Profiles of Patients with Aconite Poisoning.

Patient	Age	Gender	Time of ingestion	Ingested plant parts	Reasons for taking aconite	Type of arrhythmia	Method of treatment	Effect of lidocaine	Outcome
1	41	Male	April	Leaf	Consumed inadvertently	VT, Tdp, Vf	Fluid replacement, Antiarrhythmic (lidocaine, 50 mg iv), Electrical cardioversion, PCPS, CPB	Ineffective	Survival
2	41	Male	June	Root	Suicide	VT, Vf	Fluid replacement, Antiarrhythmic (lidocaine, 50 mg iv), Electrical cardioversion, PCPS	Ineffective	Death
3	53	Male	November	Root	Attempted suicide	VT, Tdp, Vf	Fluid replacement, Antiarrhythmic (lidocaine, 50 mg iv), Electrical cardioversion, PCPS	Ineffective	Survival
4	40	Female	April	Leaf	Consumed inadvertently	PVC	Fluid replacement, Antiarrhythmic (lidocaine, 50 mg iv)	Effective	Survival
5	60	Female	May	Leaf	Attempted suicide	PVC	Fluid replacement, Antiarrhythmic (lidocaine, 50 mg iv)	Effective	Survival
6	49	Male	April	Leaf	Consumed inadvertently	NSVT	Fluid replacement, Antiarrhythmic (lidocaine, 100 mg iv)	Effective	Survival
7	58	Male	August	Root	Attempted suicide	NSVT	Fluid replacement, Antiarrhythmic (lidocaine, 100 mg iv)	Ineffective	Survival
8	69	Male	March	Root	Attempted suicide	PVC, AIVR	Fluid replacement	—	Survival
9	78	Female	September	Root	Attempted suicide	AIVR	Fluid replacement	—	Survival
10	52	Male	May	Leaf	Consumed inadvertently	PAC, PVC, CAVB	Temporary pacemaker, Fluid replacement	—	Survival

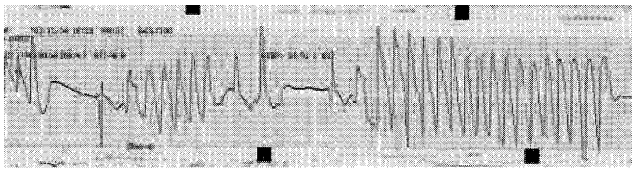
with lidocaine and electrical cardioversion. These patients required percutaneous cardiopulmonary support (PCPS) due to unstable hemodynamics. Patient 1 required additional cardiopulmonary bypass (CPB) and this patient had mistakenly ingested aconite leaves instead of edible wild plants in April. On the other hand, patients 2 (resulting in death) and 3 had ingested aconite roots with suicidal intent in June or November. The time course of the electrocardiogram from patient 3 is shown in **Fig. 1**.

The electrocardiograms of patients 4 and 5 showed premature ventricular contraction (PVC) and these were successfully suppressed with lidocaine treatment in both patients. Patient 4 had mistakenly ingested aconite leaves instead of edible wild plants in April and patient 5 had ingested aconite leaves with suicidal intent in May. Patient 6 had mistakenly ingested aconite leaves instead of edible wild plants in April, and patient 7 had ingested aconite roots with suicidal intent in August. The electrocardiograms of patients 6 and 7 showed non-sustained ventricular tachycardia (NSVT). The arrhythmias in these two patients were treated with lidocaine, and had effective in patient 6, but had ineffective in patient 7. In the patient 7, development of fatal arrhythmia was performed with electrocardiogram for care of the patient, and the arrhythmia could be suppressed by treatment of fluid therapy.

The electrocardiogram of patient 8 showed PVC and accelerated idioventricular rhythm (AIVR) and the electrocardiogram of patient 9 showed AIVR. These patients were treated with fluid therapy, resulting in recovery from arrhythmias. Patients 8 (in March) and 9 (in September) had ingested aconite roots with suicidal intent. The electrocardiogram of patient 10 showed premature atrial contraction (PAC), PVC and complete atrioventricular block (CAVB). The patient was treated with fluid therapy and a temporary pacemaker was used to treat CAVB. The patient had mistakenly ingested aconite leaves instead of edible wild plants in May. All patients were immediately treated by fluid therapy after arrival at the hospital for accelerating excretion of aconitines to the outside of the body.

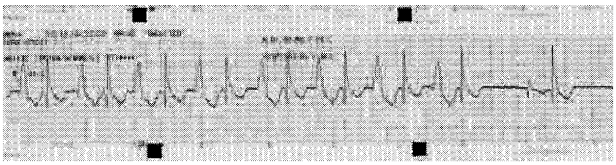
To clarify the relationship between serum aconitines concentration and effect of lidocaine, the serum concentrations of aconitines at the point of lidocaine administration were calculated in patients. In three of the seven patients who were treated with lidocaine, serum aconitines concentrations could be measured. The time courses of the serum concentrations of aconitines in patients 3, 6 and 7 are shown in **Fig. 2**. The serum concentrations of aconitines at the point of lidocaine administration were obtained from concentra-tion-time curves for serum. The serum concentrations of aconitines in patients 3, 6 and 7 were 1.98 ng/mL, 0.65 ng/mL and 3.23 ng/mL, respectively. The times of lidocaine administration in patients 3, 6 and 7 were 5 h, 9 h and 2 h after ingestion of the plant, respectively.

5 hr after ingestion, VT

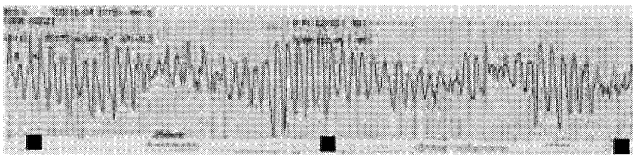


The time when the patient was treated with an antiarrhythmic agent lidocaine and PCPS.

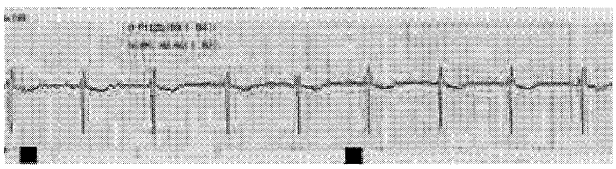
10 hr after ingestion



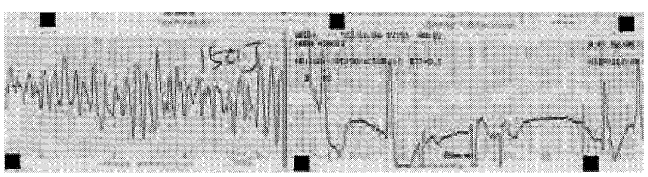
8 hr after ingestion, Tdp



24 hr after ingestion



8 hr after ingestion, Vf



Last electrical cardioversion.

Fig. 1. Time Course of the Electrocardiogram after Ingestion of Aconite Roots in Patient 3.

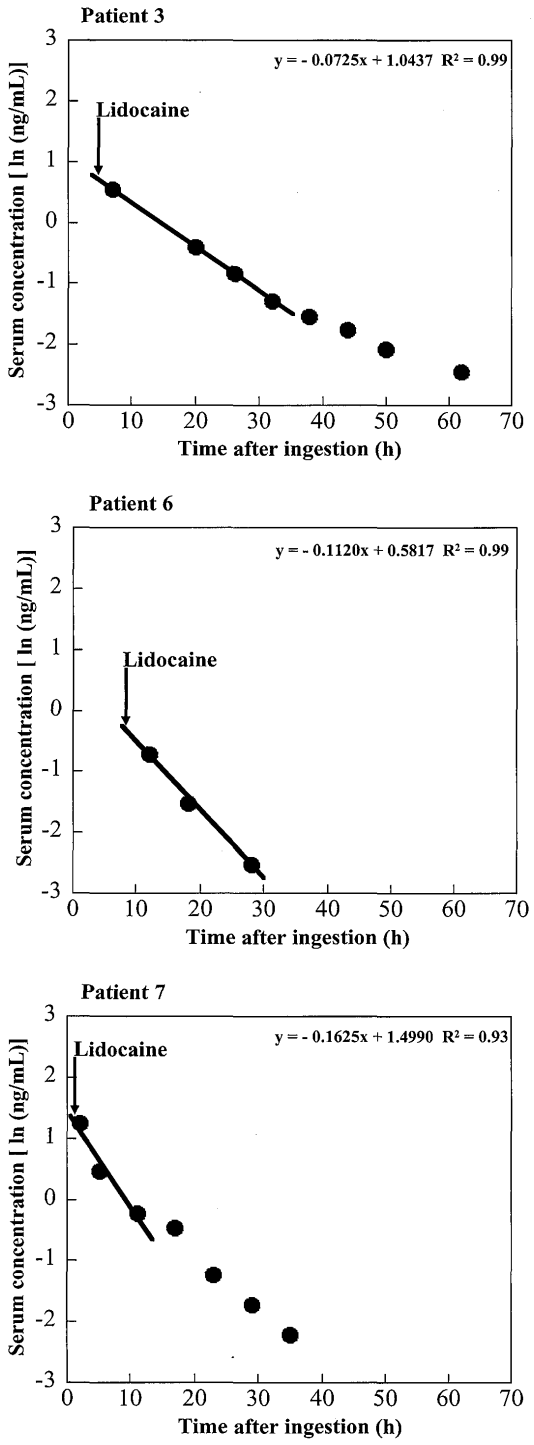


Fig. 2. Time Course of Logarithmic Serum Concentrations of Aconitines after Ingestion of Aconite in Patients 3, 6 and 7.

Discussion

We had thirteen patients with aconite poisoning from 1997 to 2005. The present study was performed in under to investigate the correlation between the development and therapeutic outcome of aconite poisoning-induced arrhythmia, and the ingested plant parts and time of ingestion in ten patients. Three (patients 1, 2 and 3) of the 10 patients in this study developed VT and Vf following aconite poisoning. Two (patients 2 and 3) of these three patients consumed aconite roots in different seasons and the third patient (patient 1) ingested aconite leaves in spring. Seven patients did not develop VT and Vf, and four of the seven patients ingested aconite leaves in April or May and three of seven patients ingested aconite roots in March, August or September. These data do not clearly the relationship between the ingested plant part or time of ingestion and the development of a particular type of arrhythmia. However, it seems that the ingested plant parts and time of ingestion influence the severity of aconite poisoning induced-arrhythmia, since the content of aconitines in aconite plant differs according to the part of the plant and time of collection[10-13]. We suggest that these information are a useful contribution to the accumulation of data that eventually may allow the clarification of these relationships.

Lidocaine treatment for aconite poisoning-induced ventricular arrhythmia was ineffective in the three patients (patient 1, 2 and 3) with VT and Vf, but successful in three (patient 4, 5 and 6) of four patients with ventricular arrhythmias other than VT and Vf. In three who had ingested aconite leaves of these four patients, lidocaine was effective. On the other hand, lidocaine was ineffective in patient (patient 7) who had ingested aconite roots. With regard to the serum concentrations of aconitines at the point of lidocaine administration in the non-VT and non-Vf patients, the serum concentration in the patient (patient 7) who had ingested aconite roots was about five times higher than that in the patient (patient 6) who had ingested aconite leaves. Therefore, lidocaine may be effective against non-VT and non-Vf aconite poisoning-induced ventricular arrhythmias following ingestion of aconite leaves, and the blood concentration of aconitines may influence the effect of lidocaine.

The blood concentration of aconitines following ingestion of aconite roots may be higher than that after ingestion of aconite leaves, since the content of aconitines in roots is about 300 times higher than that in leaves[11]. If the effect of lidocaine is influenced by the blood concentration of aconitines, the efficacy of lidocaine in patients who have ingested aconite roots may be relatively weak compared with that in patients who have ingested aconite leaves. However, for establishment of the relationship between the effect of lidocaine and blood concentration of aconitines, we require further an accumulation of a larger number of aconite-poisoned patients.

PCPS and CPB have been reported to improve survival in aconite-poisoned patients with hemodynamically unstable arrhythmia that is refractory to treatment with antiarrhythmic drugs and electrical cardioversion[7-9]. These results are in agreement with the successful outcome following PCPS or CPB in two of the three patients with VT and Vf in the current study. Overall, our results suggest that knowledge of the type of arrhythmia and the ingested plant parts may be useful in determining the suitability of lidocaine treatment for arrhythmia following aconite poisoning.

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