

84094_Auto_Edited.docx

Name of Journal: *World Journal of Clinical Cases*

Manuscript NO: 84094

Manuscript Type: CASE REPORT

Recurrent ventricular arrhythmia due to aconite intoxication successfully treated with landiolol: A case report

Chiaki Matsuo, Koji Yamamoto, Hidetada Fukushima, Daisuke Yajima, Hiroyuki Inoue

Abstract

BACKGROUND

Ventricular arrhythmias, such as ventricular tachycardia and fibrillation, are the main causes of death in patients with aconite poisoning.

CASE SUMMARY

A 51-year-old man presented to our emergency department because he was vomiting after ingesting aconite root to attempt suicide. On arrival, the patient was hemodynamically unstable, and his electrocardiogram revealed polymorphic ventricular extrasystoles and non-sustained ventricular tachycardia. Amiodarone was immediately administered for ventricular arrhythmia. However, the patient remained unresponsive. We administered continuous intravenous landiolol as the ventricular arrhythmia worsened, gradually suppressing it. The patient returned to sinus rhythm 16 h after arriving at the hospital. Some aconitum alkaloids act on voltage-gated Na^+ channels and induce ventricular or supraventricular tachyarrhythmias. Landiolol suppresses sympathetic nerve activity through its β -blocking effect, preventing arrhythmia.

CONCLUSION

Landiolol can be a therapeutic option for amiodarone-refractory ventricular arrhythmias caused by aconite intoxication.

INTRODUCTION

Aconite is the generic name for the genus *Aconitum* in the buttercup family. It is a perennial herb widely distributed in the northern temperate zone of the Northern Hemisphere. However, the plant contains aconitum alkaloids, among which aconitines including aconitine, mesaconitine, hypaconitine, and jessaconitine are potent cardiotoxins, neurotoxins, and gastrointestinal toxins. Arrhythmia is the most important prognostic factor, and various arrhythmias, from supraventricular to ventricular and bradycardia to tachycardia, have been reported. Ventricular arrhythmias such as ventricular tachycardia and fibrillation are the main causes of death in patients with aconite poisoning. As a pharmacological treatment for ventricular arrhythmias, amiodarone, which has a multichannel action, has been reported to be useful.¹ However, besides amiodarone, no definitive drug therapy is useful. Here, we report a case of polymorphic ventricular arrhythmia that appeared after aconite ingestion.

CASE PRESENTATION

Chief complaints

A 51-year-old man presented to our emergency department with a burning sensation in the stomach, vomiting, and diarrhea.

History of present illness

The patient ingested *Aconitum japonicum* root (estimated dose of 2 g) purchased from the Internet for suicide attempts. Immediately after ingestion, the patient experienced a burning sensation in the stomach, vomiting, and diarrhea, followed by tearing,

drooling, and numbness in the face and extremities. He called for emergency medical service 4 h later and was transported to our emergency department.

History of past illness

Not applicable.

Personal and family history

Not applicable.

Physical examination

The patient could speak but was hemodynamically unstable (heart rate, 150 bpm; irregular rhythm; blood pressure, 56/24 mmHg). Electrocardiography on arrival revealed polymorphic ventricular extrasystoles and non-sustained ventricular tachycardia, indicating an electrical storm in the heart (Figure 1).

Laboratory examinations

Qualitative and quantitative analysis of Aconitum alkaloids in 0.1 mL of the patient's serum was performed. The Quick, Easy, Cheap, Effective, Rugged, and Safe (QuEChERS) method was a pretreatment method⁵, and the supernatant (acetonitrile layer) was separated after centrifugation and evaporated to dryness under reduced pressure. The residue was dissolved in 0.15 mL of a 10 mmol/L ammonium formate/30% acetonitrile solution containing 0.1% formic acid. After centrifugation, the supernatant was analyzed using liquid chromatography-tandem mass spectrometry (LC-MS/MS).

LC-MS/MS was performed using a Nexera X2 high-performance liquid chromatography system (Shimadzu Corporation) and QTRAP 5500 mass spectrometer (AB SCIEX). A Unison UK-Phenyl column (150 × 2 mm, 3 μm, Imtakt Corporation) was used for chromatographic separation at 40°C with gradient elution using mobile phase A (10 mmol/L ammonium formate containing 0.1% formic acid) and mobile phase B

(acetonitrile). The gradient elution program was as follows: 30% to 50% B (15 min), 50% B (2 min), 50% to 30% B (0.01 min), and 30% B (5 min) at a flow rate of 0.2 mL/min. Ionization was performed using electrospray ionization (positive ion). The analysis was conducted in the multiple reaction monitoring (MRM) mode. The values of the monitoring ion (MRM transition) were 646.2/586.2 for aconitine, 632.0/572.2 for mesaconitine, 616.2/556.3 for hipaconitine, 676.1/616.2 for jessaconitine, 590.0/105.1 for benzoylmesaconine, 574.3/541.9 for benzoylhypaconine, 634.3/135.1 for 14-anisoylaconine, and 683.3/216.0 for methyllycaconitine (internal standard). The ion chromatograms extracted from the sample pretreated with the serum sample had multiple peaks with the same retention time as the extracted ion chromatogram obtained from the same pretreatment of positive control serum. The product ion spectra of the peaks corresponding to aconitine, mesaconitine, jessaconitine, and 14-anisoylaconitine were consistent with those derived from each standard. The extracted ion chromatograms detected no peaks corresponding to hypaconitine, benzoylmesaconine, or benzoylhypaconine. The peaks in the extracted ion chromatograms for each compound were quantitatively analyzed using the calibration curves prepared with the peak area ratio of the internal standard.

Imaging examinations

Not applicable.

FINAL DIAGNOSIS

Ventricular arrhythmia due to aconite intoxication.

TREATMENT

+ADw-html+AD4APA-p+AD4-After administering sedatives and vasopressors, the patient was intubated for resuscitation, and gastric lavage was performed. A bolus dose of 125 mg amiodarone was intravenously administered over 10 min (12.5 mg/min) to

treat ventricular arrhythmia, followed by continuous intravenous administration of 300 mg amiodarone over the next 6 h (0.83 mg/min), which was maintained at 0.42 mg/min thereafter. However, this treatment was unsuccessful in suppressing the arrhythmia. We then administered low-dose landiolol (4 +ACY-mu+ADs-g/kg/min) continuously and gradually increased it to 8 +ACY-micro+ADs-g/kg/min because the arrhythmia worsened, resulting in decreased heart rate and frequency of ectopic ventricular rhythm. However, intermittent pulseless ventricular arrhythmia was observed 3 h after landiolol administration. Subsequently, we increased the landiolol dose to 10 +ACY-mu+ADs-g/kg/min, successfully suppressing the arrhythmia.+ACY-nbsp+ADsAPA-/p+AD4APA-/html+AD4-

OUTCOME AND FOLLOW-UP

+ADw-html+AD4APA-p+AD4-The patient recovered and had a hemodynamically stable sinus rhythm 16 h after arrival at the hospital. Thereafter, arrhythmia was not observed (Figure 2). The patient was extubated on day 2. After extubation, we asked the patient about his symptoms. We uncovered that the gastrointestinal and nervous symptoms on arrival had improved and he was asymptomatic, although no specific treatment was required. On day 4, he was transferred to the psychiatric ward for further treatment and discharged on day 81 without neurological sequelae.+ADw-/p+AD4APA-/html+AD4-

DISCUSSION

In this case, continuous intravenous landiolol administration successfully suppressed fatal ventricular arrhythmias due to aconite intoxication, whereas amiodarone failed to suppress arrhythmia. ⁷ To the best of our knowledge, this is the first case report in which landiolol successfully suppressed ventricular arrhythmia caused by aconite intoxication.

Some aconitum alkaloids induce toxicity by inactivating the Na⁺ channel, prolonging cardiomyocyte repolarization. The association between aconitine blood levels and

symptoms remains unclear. However, a previous study reported that ventricular arrhythmias might appear at an aconitine blood level of 1.0 ng/mL^[3]. In this case, the blood concentrations on hospital arrival (4 h after ingestion) were 0.050 ng/mL, 0.252 ng/mL, and 2.266 ng/mL for aconitine, mesaconitine, and jesaconitine, respectively. The total blood aconitines level was 2.568 ng/mL. In this case, the blood concentration of aconitine alone was not high, but the total blood concentration of aconitines was high, which may have induced the arrhythmia symptoms. Cardiorespiratory support is key to successful resuscitation in hemodynamically unstable aconite-intoxicated cases.

Amiodarone is an antiarrhythmic agent in the Vaughan-Williams class III group and is prescribed for ventricular arrhythmia. This antiarrhythmic agent has also been reported to be effective for ventricular arrhythmia caused by aconite intoxication^[1]. Unsuppressed ventricular arrhythmias can lead to cardiac arrest. Artificial hemodynamic support (such as veno-arterial extracorporeal membranous oxygenation) is the only resuscitation strategy for fatal cases^[4,5]. However, alternative treatment when amiodarone fails to control ventricular arrhythmia before a cardiac arrest has not been well investigated.

Recently, landiolol, a β 1-supersensitive intravenous adrenergic antagonist, was reported to be effective for ventricular arrhythmia refractory to amiodarone. A recent study from Japan revealed the effectiveness of landiolol for recurrent ventricular arrhythmia unresponsive to amiodarone^[6].

Amiodarone, a multichannel blocker, primarily blocks the K⁺ channel, suppressing reentry by prolonging the refractory period^[7]. Landiolol competitively blocks sympathetically mediated triggering mechanisms at β -adrenoreceptors, slowing the heart rhythm and inhibiting excessive calcium release by ryanodine receptor channels^[8]. Landiolol can suppress the trigger of abnormal automaticity because the mechanism of ventricular arrhythmia refractory to amiodarone is considered abnormal automaticity rather than the reentry mechanism. Recurrent ventricular arrhythmia is also known as an "electrical storm." An electrical

storm is a recurrent ventricular tachycardia or fibrillation occurring twice or more in 24 h [9]. Several case reports have indicated that aconite intoxication leads to an electrical storm^[4,10,11]. The mechanism of the electrical storm in aconite poisoning involves the Na⁺ channel-opening action of aconite and its sympathomimetic effects^[11]. The arrhythmogenic potential of aconitine is partly due to its anticholinergic effects *via* the vagus nerve^[12]. Owing to its sympathetic dominance, landiolol suppresses sympathetic activity and is expected to be effective against refractory ventricular arrhythmias caused by aconite intoxication.

CONCLUSION

In this case, continuous landiolol administration successfully suppressed fatal ventricular arrhythmias because of the possible electrical storm caused by aconite intoxication. This case report suggests that landiolol can be an alternative treatment for amiodarone-refractory ventricular arrhythmias caused by aconite intoxication.

8%

SIMILARITY INDEX

PRIMARY SOURCES

1 Hisae Niitsu, Yuji Fujita, Sachiko Fujita, Reiko Kumagai, Masataka Takamiya, Yasuhiro Aoki, Koji Dewa. "Distribution of Aconitum alkaloids in autopsy cases of aconite poisoning", Forensic Science International, 2013

Crossref

2 academic.oup.com

Internet

3 Tatsuki Fukami, Azumi Iida, Keigo Konishi, Miki Nakajima. "Human arylacetamide deacetylase hydrolyzes ketoconazole to trigger hepatocellular toxicity", Biochemical Pharmacology, 2016

Crossref

4 Chun-Li Wang, Kung-Chuan Cheng. "Idiopathic colopleural fistula presenting with lung abscess and refractory empyema: A case report", World Journal of Gastrointestinal Surgery, 2023

Crossref

5 Tetsuya Ishiwata, Chiho Ishijima, Akira Ohashi, Haruki Okada, Kousaburo Ohashi. "Solid Phase Extraction of Phosphorus-containing Amino Acid-type Herbicides and Their Metabolites from Human Blood with Titania for Determination by Capillary Electrophoresis", Analytical Sciences, 2007

Crossref

- 6

www.biorxiv.org
Internet

15 words — 1%
- 7

www.ncbi.nlm.nih.gov
Internet

14 words — 1%
- 8

[Yuzo Suzuki, Takafumi Suda, Kazuhiro Asada, Seiichi Miwa et al. "Serum Indoleamine 2,3-Dioxygenase Activity Predicts Prognosis of Pulmonary Tuberculosis", Clinical and Vaccine Immunology, 2012](#)
Crossref

13 words — 1%

EXCLUDE QUOTES

ON

EXCLUDE SOURCES

OFF

EXCLUDE BIBLIOGRAPHY

ON

EXCLUDE MATCHES

< 12 WORDS