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Aconitine poisoning
- determining the cause -

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Abstract

Aconitum carmichaeli DEBEAUX (Aconiti Tuber: Hou-bushi, Shirakawa-bushi and Uzu in Japanese) is one of the essential herbal medicines that possess anti-inflammatory, analgesic, and cardiotonic effects. During the 5-year period from 1995 to 2000, we treated 46 patients with aconitine poisoning. Our patients' symptoms included paresthesia of the mouth and tongue, palpitation, discomfort of chest and epigastric region, headache, hypertension, dizziness, vomiting and insomnia, *etc.*

Thirteen patients presented with numbness around the lips and in the limbs by Uzu, but only 2 by Hou-bushi. This symptom appeared when a large quantity of Aconiti Tuber was used. Two cases showed aconitine poisoning only after a change in prescriptions, although the actual amount of Aconiti Tuber did not change. This intoxication was due to the change of pH of the decoction. Climatic change, boiling time, teapot, and boiling with rice wine SAKE were other reasons for aconitine poisoning.

All clinicians should consider such factors, including a predisposition to poisoning, and also that there is a need for strict surveillance of herbal practices.

Key words Aconiti Tuber, aconitine-type alkaloid, traditional medicines, aconitine poisoning, numbness around the lips.

Introduction

In Asian countries numerous kinds of plants have been used as food, sources for food additives, spices and traditional herbal medicines. Some examples of drugs developed from traditional herbal medicines are ephedrine from Ephedra sinica, morphine from Papaver somniferum, quinine from Cinchona, and cocaine from Erythroxylon coca, among others.

Aconiti Tuber is a representative traditional herbal medicine and has been used historically for the treatment of cold constitution, polyarthralgia such as rheumatoid arthritis,[1] skin wounds,[2] depression,[3] diarrhea, and heart failure in both China and Japan.

Aconiti Tuber contains highly toxic aconitine-type alkaloids that can cause fatal poisoning from refractory ventricular fibrillation. However, experimental studies on aconitine poisoning or occasions of aconitine intoxication have not been extensively documented. Based on 46 cases, we reveal the reasons and factors of aconitine poisoning.

Case presentation

Case 1 was an 80-year-old woman who had been admitted because of severe lower back pain caused by osteoporosis and a compression fracture of the lumbar spine. Two days after changing the Kampo prescription from Bukuryo-shigyaku-to (Fu-Ling-Si-Ni-Tang in Chinese) to Hachimi-jio-gan mixed with Ninjin-to (Ba-Wei-Di-Huang-Wan-Liao-RenShen-Tang in Chinese), she felt paresthesia of the mouth and tongue, although the amount of Aconiti Tuber had not changed with the different prescription. Blood pressure decreased to 92/58 mmHg and pulse rate was 72/min. ECG showed

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Table I Underlying disease of subjects.

Lower back pain	137	Disease of the skin region	56
Rheumatoid arthritis	89	Cold constitution	53
Osteoarthritis	77	Disease of the uronenital system	41
Disease of the centeal nervous system	67	Cancer	34
Disease of the otorhinopharyngolaryngo system	66	Disease of the respiratory system	31
Disease of the digestive system	65	Depression	27
Disease of obsterics and gynecological system	62	Stiff shoulder	23

Rheumatoid arthritis was separated from collagen disease.

junctional premature contractions and intraventricular aberrant conduction.

Case 2 was a 65-year-old male patient who had been suffering from polyarthralgia, lower back pain and a feeling of coldness. After taking Toki-shigyaku-ka-goshuyu-shokyo-to-ka-uzu (Dang-Gui-Si-Ni-Jia-Wu-Zhu-Yu-Sheng-Jiang-Tang-Jia-Fu-Zi in Chinese) boiled with Japanese rice wine (SAKE), he felt numbness around the lips and in the limbs, despite the fact that the amount of Aconiti Tuber was the same.

Patients and Methods

Patients

One thousand thirty-three subjects were treated with prescriptions containing Aconiti Tuber between November 1995 and October 2000. They consisted of 300 men and 733 women with an average age of 56.7±17.7 (S.D.) years (range 4-102).

We prescribed Hou-bushi 14366 times, Shirakawa-bushi 2265 times and Uzu 6178 times. The underlying diseases of these patients are shown in Table I. Aconiti Tuber (range 0.5-14.0 g/day) was used mainly to alleviate pain.

Aconiti Tuber: Hou-bushi, Shirakawa-bushi and Uzu

Uzu (Wutou in Chinese) is the dried aconitine tuber. Shirakawa-bushi (Fuzi in Chinese) is processed aconitine tuber that has been soaked in a saltwater solution and dusted over with slaked lime. Hou-bushi (Pao-Fuzi in Chinese) is the processed aconitine tuber after being soaked in saltwater and autoclaved. The amounts of aconitine, mesaconitine and hypaconitine in each Aconiti Tuber are shown in Table II. To reduce the toxicity of Aconiti Tuber, as a rule, Kampo prescriptions containing Hou-bushi or Shirakawa-bushi are always boiled with 600 ml of water for 40 min, and those with Uzu with 800 ml of water for 60 min.

Table II Amount of aconitine, mesaconitine and hypaconitine in each Aconiti Tuber (Bushi).

	aconitine (%)	mesaconitine (%)	hypaconitine (%)
Hou-bushi	0.001	0.002	0.002
Shirakawa-bushi	0.001	0.003	0.010
Uzu	0.071	0.196	0.065

Medicinal plants which constitute Bukuryo-shigyaku-to and Hachimi-jio-gan mixed with Ninjin-to

Aconiti Tuber (Aconitum carmichaeli DEBEAUX) without any process (Uzu), Corni Fructus (Cornus officinalis SIEB. et ZUCC), Rehmanniae Radix (Rehmannia glutinosa LIBOSCH. var. hueichingensis CHAO et SCHIH), Glycyrrhizae Radix (Glycyrrhiza uralensis FISCHER), Atractylodis Rhizoma (Atractylodes ovata Dc), Dioscoreae Rhizoma (Dioscorea batatas DECAISNE), Mountan Cortex (Paeonia moutan SIMS), Alismatis Rhizoma (Alisma plantago aquatica L. subsp. Orientale SAMUELSSON), Zingiberis Siccatum Rhizoma (Zingiber officinale ROSCOE), Ginseng Radix (Panax ginseng C.A. MEYER), Poria (Poria cocos WOLFF) and Cinnamomi Cortex (Cinnamomum cassia BLUME) were used in this study.

Standard compounds

Aconitine, mesaconitine and hypaconitine were isolated from the raw tubers of Aconitum carmichaeli DEBX. according to the method of Mori *et al.*[4]

Preparation of extracts and measurements of pH of decoctions

Decoctions of Bukuryo-shigyaku-to, Hachimi-jio-

Table III Medical plants composing Kampo prescriptions used in this study. Each value represents g/day.

Aconiti Tuber	6.0	6.0	6.0
Corni Fructus	3.0	3.0	
Rhemanniae Radix	5.0	5.0	
Glycyrrhizae Radix	3.0		4.0
Atractylodis Rhizoma	4.5		
Dioscoreae Rhizoma	3.0	3.0	
Mountan Cortex	3.0	3.0	
Alismatis Rhizoma	3.0	3.0	
Zingiberis Siccatum Rhizoma	3.5		3.0
Ginseng Radix	4.5		2.0
Poria	3.0	3.0	8.0
Cinnamomi Cortex	1.5	1.5	

gan mixed with Ninjin-to and Uzu were analyzed. The medicinal plants composing these prescriptions are listed in Table III.

Each Kampo prescription was decocted with 800 ml of water in an earthen teapot on an electric heater (Toshiba ; HP-634 600 W) for 60 min until the volume of extractant was reduced to 300 ml. The extract was filtered through a tea strainer while it was hot. The pH of the decoction was measured when it reached room temperature, and it was lyophilized after cooling.

Measurement of aconitine, mesaconitine and hypaconitine by High Performance Liquid Chromatographic Analysis

HPLC was performed with a Shimadzu high-performance liquid chromatography system (pump, LC-10AD; system controller, SCL-10A; autoinjector, SIL-10A; UV-VIS detector, SPD-10AV; column oven, OTO-10A; peak area measurement, Chromatopac C-R7A) under the following conditions: column, TSK-GEL ODS-80TM (4.6×150); mobile phase, 0.05M phosphate buffer (pH 2.7) -tetrahydrofuran (183 : 17); flow rate, 1.0 ml/min; detection, UV231nm; column temperature, 40 ℃. The quantity of each constituent was estimated by the absolute calibration method.

Each freeze-dried sample (0.5 g) was extracted three times with ethanol (20 ml) and aqueous ammonia (10 % : 1.0 ml) for 30 min. The combined organic phases were evaporated under reduced pressure at a temperature not exceeding 40℃ to give a residue. The residue was dissolved in 0.05M phosphate buffer (pH2.7)-acetonitrile to give exactly 5 ml of solution.

Influence of SAKE

Literature on Toki-shigyaku-ka-goshuyu-shokyo-to describes its decoction with 400 ml of water and 400 ml of SAKE. In this study, Toki-shigyaku-ka-goshuyu-shokyo-to-ka-Uzu was decocted with 800 ml of water, 400 ml of water and 400 ml of SAKE, and 400 ml of water and 400 ml of ethanol containing the same concentration of alcohol as SAKE, respectively. The pH of the decoction was measured as described above, and the aconitine-type alkaloids of aconitine, mesaconitine and hypaconitine in the decoction were measured.

Results

There were 14 men and 32 women who reacted overly to Aconiti Tuber, and their ages ranged from 24 to 90 years (average 56.7±14.6 S.D.). Nineteen patients showed adverse reactions with Hou-bushi, 3 with Shirakawa-bushi and 24 with Uzu. The clinical features and outcome of aconitine poisoning are summarized in Table IV.

The aconitine toxic symptoms disappeared quickly by reducing the amount of Aconiti Tuber, cessation, or changing to another Bushi. Thirteen patients presented with paresthesia in the mouth and tongue by Uzu, but only 2 by Hou-bushi. When patients felt paresthesia around the lips, Aconiti Tuber was being used at a dosage of 4.9±1.6 g S.D., whereas for other adverse reactions only 2.0±1.1 g S.D. was being used.

The quantity of Aconiti Tuber at which toxicity was noted ranged from 0.5 to 6.0 g (mean 3.0 ± 1.9 g S.D.)/day. (Intoxication histogram is shown in Fig 1.) In fact, 13 patients showed adverse reactions within 1.0 g of Hou-bushi.

We treated 37 subjects with 6.0 g or more of Aconiti Tuber. Five cases showed adverse reactions at 6.0 g. However, if there was no intoxication at 6.0 g, adverse reactions did not occur even though Aconiti Tuber was increased to 14.0 g. Of course, when Aconiti Tuber did not work well at 6.0 g, it made no sense to further increase its dosage.

The amounts of aconitine, mesaconitine and hypaconitine of Hachimi-jio-gan mixed with Ninjin-to were 0.206, 0.134 and 0.283 mg, respectively. In the case of Bukuryo-shigyaku-to, hypaconitine was 0.123 mg, but aconitine and mesaconitine were not detected.

Table IV Patient characteristics of aconitine poisoning

Age	Sex	Bushi	Dose of Aconitine poisoning	Treatment	Outcome	Underlying disease	Prescription	Symptoms
65	F	Uzu	5.5	Explanatiun of taking	Improved	Rheumatoid arthritis	Kigi-kenchu-to-ka-bushi (Gui-Qi-Jian-Zhong-Tang-Jia-Fu-Zi)	paresthesia of the mouth and tongue, nausea
41	F	Uzu	5.0	Boil with earthren teapot	Improved	Intervertebral disk herniation	Seki-gan-ryo, BST (Chi-Wan-Liao, Fu-Ling-Si-Ni-Tang)	paresthesia of the mouth and tongue
78	F	Hou-bushi	4.5	Reduce the Bushi	Improved	Rheumatoid arthritis	Uzu-to (Wu-Tou-Tang)	paresthesia of the mouth and tongue, dimness of sight, chest discomfort
69	M	Uzu	1.5	Reduce the Bushi	Improved	Ischias	Gosha-jinki-gan-ryo (Niu-Che-Shen-Qi-Wan-Liao)	wrongness of the sole
54	F	Uzu	4.0	Reduce the Bushi	Improved	Rheumatoid arthritis	Boi-ogi-to-ka-bushi (Fang-Yi-Huang-Qi-Tange-Jia-Fu-Zi)	dizziness
28	F	Uzu	5.0	Reduce the Bushi	Improved	Rheumatoid arthritis	Keishi-ka-ryo-jutsubu-to (Gui-Zhi-Jia-Ling-Zhu-Fu-Tang)	paresthesia of the mouth and tongue
62	M	Uzu	1.5	Reduce the Bushi	Improved	Rheumatoid arthritis	Keishi-ka-ryo-jutsubu-to (Gui-Zhi-Jia-Ling-Zhu-Fu-Tang)	dizziness
64	F	Hou-bushi	1.5	Stop the Bushi	Improved	Arthrosis	Boi-ogi-to-ka-bushi (Fang-Yi-Huang-Qi-Tange-Jia-Fu-Zi)	chest discomfort
52	F	Uzu	1.5	Stop the Bushi	Improved	Osteoarthritis	Boi-ogi-to-ka-bushi (Fang-Yi-Huang-Qi-Tange-Jia-Fu-Zi)	paresthesia of the mouth and tongue
31	F	Hou-bushi	3.0	Reduce the Bushi	Improved	Cervical spondylosis	Bukuryo-shigyaku-to (Fu-Ling-Si-Ni-Tang)	nausea
54	M	Uzu	3.5	Reduce the Bushi	Improved	Rheumatoid arthritis	Boi-ogi-to-ka-bushi (Fang-Yi-Huang-Qi-Tange-Jia-Fu-Zi)	nausea
63	F	Uzu	5.0	Change to Shirakawa-bushi	Improved	Rheumatoid arthritis	Boi-ogi-to-ka-bushi (Fang-Yi-Huang-Qi-Tange-Jia-Fu-Zi)	paresthesia of the mouth and tongue, clouding of consciousness
69	M	Shirakawa-dushi	6.0	Stop the Bushi	Improved	Prostatic cancer	Kihi-to-ka-bushi (Gui-Pi-Tang-Jia-Fu-Zi)	paresthesia of the mouth and tongue, palpitation
41	F	Uzu	3.0	Reduce the Bushi	Improved	Bronchial athma	Seki-gan-ryo (Chi-Wan-Liaog)	paresthesia of the mouth and tongue
33	F	Uzu	5.0	Reduce the Bushi	Improved	Depression	Seki-gan-ryo, BST (Chi-Wan-Liao, Fu-Ling-Si-Ni-Tang)	palpitation
50	F	Uzu	2.0	Reduce the Bushi	Improved	Rheumatoid arthritis	Keishi-shakuyaku-chimo-to (Gui-Zhi-Shao-Yao-Zhi-Mu-Tang)	epigastric discomfort
67	F	Hou-bushi	1.0	Stop the Bushi	Improved	Osteoarthritis	Boi-ogi-to-ka-bushi (Fang-Yi-Huang-Qi-Tange-Jia-Fu-Zi)	headache
53	F	Uzu	5.0	Reduce the Bushi	Improved	Rheumatoid arthritis	Uzu-to (Wu-Tou-Tang)	pins and needles of the face, insomnia
73	F	Hou-bushi	2.5	Explanatiun of taking	Improved	Lower back pain	Boi-ogi-to-ka-bushi (Fang-Yi-Huang-Qi-Tange-Jia-Fu-Zi)	dimness of sight, palpitation
69	F	Hou-bushi	1.5	Stop the Bushi	Improved	Osteoarthritis	Gosha-jinki-gan-ryo (Niu-Che-Shen-Qi-Wan-Liao)	dizziness
56	F	Hou-bushi	1.0	Reduce the Bushi	Improved	Rheumatoid arthritis	Hochu-ekki-to-ka-bushi (Bu-Zhong-Yi-Qi-Tang-Jia-Fu-Zi)	headache
81	F	Uzu	6.0	Reduce the Bushi	Improved	Lower back pain	HJGRNT (Ba-Wei-Di-Huang-Wan-Liao-Ren-Shen-Tang)	paresthesia of the mouth and tongue, chest oppression, arrhythmia
68	F	Uzu	3.0	Stop the Bushi	Improved	Osteoarthritis	Boi-ogi-to-ka-bushi (Fang-Yi-Huang-Qi-Tange-Jia-Fu-Zi)	precordial oppression
59	F	Hou-bushi	1.0	Stop the Bushi	Improved	Chronic hepatitis	Hochu-ekki-to-ka-bushi (Bu-Zhong-Yi-Qi-Tang-Jia-Fu-Zi)	insomnia
33	F	Hou-bushi	4.0	Reduce the Bushi	Improved	Malaise	Bukuryo-shigyaku-to (Fu-Ling-Si-Ni-Tang)	hypertension
58	F	Hou-bushi	1.0	Reduce the Bushi	Improved	Post herpetic neuralgia	Keishi-ka-ryo-jutsubu-to (Gui-Zhi-Jia-Ling-Zhu-Fu-Tang)	hypertension, headache
49	F	Hou-bushi	0.7	Reduce the Bushi	Improved	Rheumatoid arthritis	Bukuryo-shigyaku-to (Fu-Ling-Si-Ni-Tang)	hypertension
51	M	Hou-bushi	2.0	Reduce the Bushi	Improved	Decubitus ulcer	Kigi-kenchu-to-ka-bushi (Gui-Qi-Jian-Zhong-Tang-Jia-Fu-Zi)	paresthesia of the mouth and tongue
50	M	Hou-bushi	1.0	Stop the Bushi	Improved	Rheumatoid arthritis	Boi-ogi-to-ka-bushi (Fang-Yi-Huang-Qi-Tange-Jia-Fu-Zi)	epigastric discomfort
56	F	Hou-bushi	2.5	Reduce the Bushi	Improved	Depilation	SKKTKB (Chai-Hu-Gui-Zhi-Gan-Jiang-Tang-Jia-Fu-Zi)	palpitation, pollakiuria
38	F	Uzu	1.0	Change to Hou-bushi	Improved	Cold constitution	Bukuryo-shigyaku-to (Fu-Ling-Si-Ni-Tang)	palpitation
30	M	Hou-bushi	1.0	Stop the Bushi	Improved	Atopic dermatitis	Shimbu-to (Zhen-Wu-Tang)	insomnia
58	M	Hou-bushi	1.0	Stop the Bushi	Improved	Cervical spondylosis	Bukuryo-shigyaku-to (Fu-Ling-Si-Ni-Tang)	stiffness of the face
70	M	Shirakawa-dushi	0.8	Reduce the Bushi	Improved	Irritable bowel syndrome	Yokui-bushi-haisyou-san (Yi-Yi-Fu-Zi-Bai-Jiang-San)	headache
80	M	Uzu	5.5	Reduce the Bushi	Improved	Osteoarthritis	Sokei-kakketsu-to-ka-bushi (Shu-Jing-Huo-Xue-Tang-Jia-Fu-Zi)	paresthesia of the mouth and tongue
90	M	Hou-bushi	2.2	Stop the Bushi	Improved	Lower back pain	Hachimi-jio-gan-ryo (Ba-Wei-Di-Huang-Wan-Liao)	Hypertension
65*	M	Uzu	6.0	decoct with woter	Improved	Cold constitution	TSKGSTKB (DGSNJWZYSITIFZ)	paresthesia of the mouth and tongue
65	F	Uzu	4.5	Reduce the Bushi	Improved	Rheumatoid arthritis	Boi-ogi-to-ka-bushi (Fang-Yi-Huang-Qi-Tange-Jia-Fu-Zi)	paresthesia of the mouth and tongue, hypertension
54	M	Uzu	6.0	Reduce the Bushi	Improved	Rheumatoid arthritis	Boi-ogi-to-ka-bushi (Fang-Yi-Huang-Qi-Tange-Jia-Fu-Zi)	paresthesia of the mouth and tongue
80	M	Uzu	5.5	Stop the Bushi	Improved	Osteoarthritis	Sokei-kakketsu-to-ka-bushi (Shu-Jing-Huo-Xue-Tang-Jia-Fu-Zi)	paresthesia of the mouth and tongue
62	F	Shirakawa-dushi	3.3	Reduce the Bushi	Improved	Edema	Yokui-bushi-haisyou-san (Yi-Yi-Fu-Zi-Bai-Jiang-San)	palpitation, dizziness
57	F	Uzu	1.0	Stop the Bushi	Improved	Abdominal pain	Uzu-keishi-to (Wu-Tou-Cui-Zhi-Tang)	palpitation
53	F	Hou-bushi	0.7	Stop the Bushi	Improved	Bronchial athma	SKKTKB (Chai-Hu-Gui-Zhi-Gan-Jiang-Tang-Jia-Fu-Zi)	hot flashes
80	F	Uzu	2.0	Change to Hou-bushi	Improved	Ischias	Boi-ogi-to-ka-bushi (Fang-Yi-Huang-Qi-Tange-Jia-Fu-Zi)	paresthesia of the mouth and tongue
57	F	Hou-bushi	1.0	Stop the Bushi	Improved	Poly arthralgia	Kigi-kenchu-to-ka-bushi (Gui-Qi-Jian-Zhong-Tang-Jia-Fu-Zi)	discomfort of throat
28*	F	Uzu	8.0	decoct with woter	Improved	Cold constitution	TSKGSTKB (DGSNJWZYSITIFZ)	paresthesia of the mouth and tongue

*was decocted with 400 ml of water and 400 ml of SAKE.

Abbreviations

BST: Bukuryo-shigyaku-to

HJGRNT: Hachimi-jio-gan-ryo mixed with Ninjin-to

SKKTKB: Saiko-keishi-kankyo-to-ka-bushi

TSKGSTKB: Toki-shigyaku-ka-goshuyu-shokyo-to-ka-bushi

DGSNJWZYSJTJFZ: Dang-Gui-Si-Ni-Jia-Wu-Zhu-Yu-Sheng-Jiang-Tang-Jia-Fu-Zi

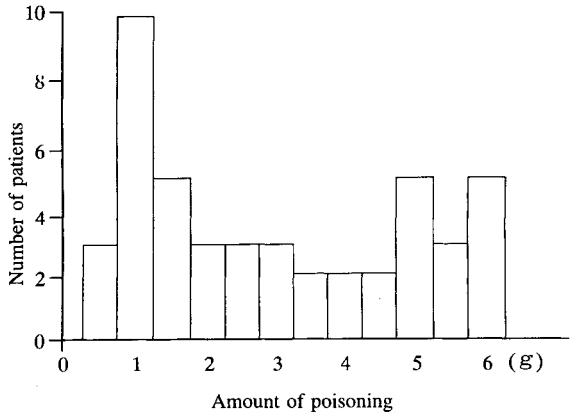

Fig. 1 Intoxication histogram. Thirteen patients showed adverse reaction within 1.0 g of Hou-bushi. If there was no intoxication at 6.0 g, side effects did not occur even though Aconiti Tuber was increased to 14.0 g.

Table V Six grams of Uzu was decocted with W and WS for 60 min and aconitine type of alkaloid was measured.

	800 ml of water	400 ml of water and 400 ml of SAKE
total alkaloids (mg)	48.4	52.50
aconitine (μg)	16.0	1306
mesaconitine (μg)	12.0	2112
hypaconitine (μg)	54.0	3054

Abbreviation
W: 800 ml of water
WS : 400 ml of water and 400 ml of SAKE

The pH levels of the decoctions of Hachimi-jio-gan mixed with Ninjin-to and Bukuryo-shigyaku-to were 4.9 and 5.5, respectively (This work was performed by Taki and reported in 1998).[5]

The aconitine-type alkaloids decocted with SAKE and water are shown in Table V. The amounts of aconitine, mesaconitine and hypaconitine were increased when Uzu was boiled with SAKE. However, they were not changed compared to the decoction with water when Uzu was boiled with ethanol at the same concentration as SAKE.

Based on our study, the factors involved in the adverse reactions were shorter duration of boiling (n=1), changing of Kampo prescription (n=2), a warming climate (n=4), changing of teapot (n=1), addition of another medical plant (n=1), and boiling with SAKE (n=2).

Discussion

In China and Japan, Aconiti Tuber has been used for medical purposes for centuries. However, Aconiti Tuber contains highly toxic alkaloids such as aconitine, mesaconitine and hypaconitine, and cases of accidental aconitine intoxications have been documented.[6-8] The fatal dose for humans is thought to be 2 mg. For this reason, Aconiti Tuber is processed and cured before its use, with the aim of decreasing the content of toxic ingredients.

Hou-bushi has been traditionally taken for the treatment of a cold constitution and Uzu has been used as an analgesic in Japan. In the case of Uzu, it not only reduces arthralgia but also improves the sensitivity to coldness. We normally use Hou-bushi first, and if the results are unsatisfactory, we change to Shirakawa-bushi or Uzu according to the patient's condition.

Thirteen patients showed adverse effects with Hou-bushi at 1.0 g or less. This indicates that some persons are especially sensitive to Aconiti Tuber and, as a general rule, we increase the daily dosage by only slight amounts such as 1.0 g. The adverse reactions were distributed rather equally from 0.5 g to 6.0 g, so it is difficult to predict if and at what dosage intoxication may occur.

Two cases showed Aconiti Tuber poisoning after only the change of prescription, with no change in the amount of Aconiti Tuber. Taki reported previously that aconitine diester alkaloids of decoction makes a chemical conversion to monoester alkaloids by leaning towards alkaline.[5] Aconitine-type alkaloids in Hachimi-jio-gan mixed with Ninjin-to increased five times compared to those in Bukuryo-shigyaku-to. This strongly suggests that Aconiti Tuber poisoning was due to an abrupt increase in aconitine-type alkaloids of the decoction after changing prescriptions (this case was reported by Itoh in 1998).[9]

Numbness was the usual adverse reaction of Uzu, but it was rare in the case of Hou-bushi. As far as we know, all persons who ate raw aconite mistaken for an edible grass showed numbness around the lips. Numbness occurs when less-processed Aconiti Tuber or a great deal of Bushi is used. In Japan, a leading expert in former days used to say that "it is necessary to use Aconiti

Tuber to achieve numbness for the sake of easing pain". In fact, some levels of pain disappeared when patients felt numbness, although numbness can be a premonitory symptom of serious poisoning as seen in case 1. For this reason, we decrease Aconiti Tuber if patients experience numbness.

It is believed that SAKE has an effect on heating and enhancement of Ki-energy in Kampo formulae. These characters are also true of Aconiti Tuber. At first, we considered that Aconiti Tuber and alcohol had a synergistic effect and could have caused the aconitine poisoning. However, as ethanol at the same alcohol concentration as SAKE did not enhance the effect, the intoxication obviously did not depend on alcohol but rather an organic acid, resulting in an acidic decoction.

We generally increase the Aconiti Tuber dosage in winter, but in most cases use the same amount when the season becomes warm again. This seems to have been involved in the adverse reactions in 4 cases.

All clinicians should consider the above factors that include a predisposition to poisoning and the need for strict surveillance of herbal practices.

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和文抄録

附子（烏頭，白河附子，炮附子）は，除痛，保温，強心，強壮を目的に用いられる重要な生薬であるが，薬用量と中毒量が近いため，その使用には十分な注意が必要である。附子中毒46症例の検討から，中毒を起こす要因として，以下の項目が考えられた。

1）湯液の酸性度が高い場合。山茱萸，烏梅，五味子を含むときや，これらの生薬を加味するときは注意する。

2）規定の時間煎じない。当院では炮附子と白河附子を含むときは40分，烏頭を含むときは60分煎じることを指導している。

3）気候が温暖化すると附子中毒を来しやすくなる。4月頃から，附子の減量を考慮する。

4）土瓶から市販の煎じ器への変更。市販の煎じ器の一部は，沸騰すると電源が切れるようにマイコン制御されているため，附子の加水分解が抑制されることがある。

5）酒で煎じる。酒で煎じると，附子の効力が高まると同時に，附子中毒を起こしやすくなる。

最も多く認めた副作用は，舌と口唇周囲のしびれであった。これは，炮附子ではほとんど認めず，烏頭を多量に用いたときにみられた。口唇周囲のしびれは，アコニチンの量が多いときにみられる徴候であると考えられた。

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