

Aconite Poisoning over 5 Years

A Case Series in Hong Kong and Lessons Towards Herbal Safety

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Abstract

Background: Aconite poisoning is a severe, life-threatening poisoning related to the use of traditional Chinese medicine (TCM). Despite current legislation, repeated poisoning cases are steadily encountered.

Objective: The aim of the study was to summarize the clinical features and to elucidate the causative and contributory factors leading to aconite poisoning.

Methods: This study was conducted within the Hospital Authority Toxicology Reference Laboratory, which is the sole tertiary referral clinical toxicology laboratory in Hong Kong. This retrospective study reviewed all confirmed aconite poisoning cases handled by a clinical toxicology laboratory between April 2004 and July 2009. The diagnosis in all cases was confirmed biochemically by detecting aconitum alkaloids in urine specimens. Additionally, herbal specimens were morphologically identified and herbal formulae were studied and transcribed. The cause of poisoning for each case was determined whenever possible.

Results: Fifty-two cases were examined in this aconite poisoning case series. Neurological, cardiovascular and gastrointestinal toxicities were encountered in 49 (94.2%), 46 (88.5%) and 31 (59.6%) patients, respectively. The poisoning was severe in 6 (11.5%) patients, moderate in 17 (32.7%) patients and mild in 29 (55.8%) patients. Amongst 44 patients (84.6%) in whom the underlying reasons of poisoning could be determined, four major causes were found. These included overdose – prescription of a higher than recommended dosage of aconite herbs in 17 (32.7%) cases; ‘hidden’ poisoning (the aconite herb was not prescribed but dispensed inadvertently) in 17 (32.7%) cases; usage of inadequately processed herbs in 7 (13.5%) cases; and dispensary error in 2 (3.9%) cases. No case fatality was recorded.

Conclusion: In the majority of cases in this series, the causes of poisoning can be traced to poor-quality herbs, poor quality of prescription practice, or

dispensary errors. The quality issues of TCM practice should be critically addressed to minimize this poisoning threat.

Background

Aconite, a toxic plant of the *Aconitum* genus in the Ranunculaceae family, has widespread use in herbal medicine.^[1-3] The mother root and daughter root of *A. carmichaeli*, the main root of *A. kusnezoffii*, known as 'chuanwu', 'fuzi', and 'caowu', respectively, are the three most popular herbs used in traditional Chinese medicine (TCM).^[2,4] Additionally, over 60 aconitum species have documented therapeutic uses.^[2] Despite their toxicity and narrow therapeutic indices, these herbs have been frequently used for their anti-inflammatory, analgesic and cardiotonic properties.^[1,2,5] Raw aconite plants are extremely dangerous.^[6] They are used as herbs only after being processed (repeated boiling or steaming) to reduce their toxicity. Nonetheless, prolonged decoction to further reduce toxicity is mandatory immediately before consumption.^[2] With the increased popularity of herbal medicines in Western societies, aconite poisoning can occur in different parts of the world.^[7-10] Whilst most reported aconite poisonings have resulted from TCM usage,^[4,5,11-13] sporadic cases have occurred in the Western world. These include accidental ingestion of aconite plants, such as monkshood (*A. napellus*) and wolfsbane (*A. vulparia*), as well as suicidal and homicidal poisonings.^[14-16]

Regardless of the source and species, the toxidrome of acute aconite poisoning is similar: perioral and limb paraesthesia, weakness, palpitations, arrhythmias, hypotension and gastrointestinal symptoms.^[4,13] Supportive care is the mainstay of treatment; there is no specific antidote.^[1,4,17] The in-hospital mortality rate has been reported to be 5.5%.^[4]

In Hong Kong, prescription and dispensing of these toxic herbs are regulated by the Chinese Medicine Ordinance.^[18] Similar legislation is also in place in mainland China and some other parts of the world. However, clinical poisonings related to aconite herbs are still prevalent in Hong Kong. This study reviewed 52 consecutive cases of con-

firmed aconite poisoning occurring in Hong Kong. This study summarizes the clinical features and elucidates the causative and contributory factors leading to such poisoning, with the twin goals of shedding light on aconite poisoning and improving the safe use of TCMs in general.

Methods

This retrospective study reviewed aconite poisoning cases between April 2004 and July 2009, which were referred to and biochemically confirmed by the Hospital Authority Toxicology Reference Laboratory, which is the only tertiary referral laboratory for clinical toxicology analysis in Hong Kong. This laboratory serves 43 public hospitals, which in turn provide in-patient service to 93% of the 7 million, predominantly, Chinese population. Clinical information was obtained by reviewing the related clinical records. The demographic data, indications of herb usage, clinical features, ECGs, medical and drug history, laboratory findings, immediate treatment and clinical outcomes were collected.

For each suspected aconite poisoning case, the toxicology laboratory collected, as completely as possible, the following specimens: urine, residual herbs, residual herbal broth, unused herbs, herbal composite formulae and proprietary Chinese medications.

Herbal composite formulae would be transcribed by the laboratory. Unused and residual herbs would be morphologically identified by studying features, such as colour, size, shape, strides, texture and smell (figure 1).^[19] Identified herbs were compared with those prescribed in the herbal composite formula. Expert help from a TCM pharmacist for identification or authentication of the herbal formula, unused and residual herbs was sought in difficult cases.

In the urine specimens, a number of aconitum alkaloids were qualitatively screened using a combination of gas chromatography-mass spectrometry and liquid chromatography-tandem mass spectrometry techniques using published and val-



Fig. 1. An example (case 13) of herb identification by gross morphological features. Identifiable herbs: (a) processed fuzi (*Aconitum carmichaelii*); (b) guizhi (*Ramulus Cinnamomi*); (c) wuyu (or wuzhuyu) [*Fructus Evodiae*]; (d) beixixin (*Asarum heterotropoides*); (e) zhengbeijiang (*Rhizoma Zingiberis*); (f) beici (*Radix Astragali*); (g) donggui (*Radix Angelicae Sinensis*); (h) baishu (*Rhizoma Atractylodis Macrocephalae*); (i) fuling (*Rhizoma Smilacis Glabrae*). The circled herb was identified to be the culprit *Aconitum* species.

idated methods.^[20] The aconitum alkaloids covered by the laboratory included aconitine, mesaconitine, hyaconitine, yunaconitine, crassicauline A, jesaconitine, pseudaconitine, bikhaconitine and indaconitine. Some hydrolyzed products of these aconitum alkaloids were also covered by these two techniques. These analyses were also extended to residual herbs, residual herbal broth, unused herbs and proprietary Chinese medications when necessary to further substantiate the diagnosis.

A confirmed case of aconite poisoning was defined by a history of recent herb consumption, the presence of compatible clinical features and the identification of aconitum alkaloids in urine. Other investigation results served as supportive evidence and helped to pinpoint the causes of the poisoning.

For each confirmed aconite poisoning case, by collating all available information and laboratory findings, the cause of the poisoning was classified into one of the following categories:

1. **Overdose:** The dosage of aconite herb prescribed was higher than recommended. Accord-

ing to the Chinese Pharmacopoeia 2010, the recommended daily dose limits for processed 'chuanwu', 'fuzi' and 'caowu' are 1.5–3 g, 3–15 g and 1.5–3 g, respectively.^[2]

2. **Hidden aconite poisoning:** No aconite herb had been prescribed, but aconite toxicity was observed clinically and proven biochemically through detection of aconitum alkaloids in the patient's samples. The aconite herb involved was presumably dispensed inadvertently as a contaminant of other herbs.^[20,21]

3. **Use of inadequately processed aconite herb:** The dosage of aconite herb prescribed was within the recommended limit but aconite toxicity still occurred, suggesting that the herbs used were inadequately processed.^[2,4,22,23]

4. **Dispensing error:** A benign herb was prescribed but an aconite herb with a similar name was dispensed.

5. **Others:** Descriptive statistics were employed as appropriate. The Chi-squared test was used to evaluate whether yunaconitine and crassicauline

A were found more frequently in cases of hidden aconite poisoning.

This study was approved by the Kowloon West Cluster Research Ethics Committee of the Hospital Authority, Hong Kong (approval number KW/EX/08-098).

Results

Over the study period, 52 cases were confirmed. The male to female ratio was 17:35, with a median age of 51 years (range 20–98 years). Twenty-four patients (46.2%) did not report any significant illness in the past. The indications to use TCM, clinical features, causes of poisoning and the urine aconitum alkaloid findings are summarized in table I.

The three main indications for using TCM in this series were to relieve musculoskeletal pain (26.9%), treat upper respiratory tract infection (23.1%) and as a health tonic (13.5%) [table I]. The median latency period between herb consumption and symptom onset was 1 hour (range 15 minutes–4 hours). Neurological features (94.2%) were the most common symptoms, followed by cardiovascular (88.5%) and gastrointestinal symptoms (59.6%) [tables I and II]. Poisoning was severe in 6 patients (11.5%), moderate in 17 (32.7%) patients and mild in 29 (55.8%) patients, with reference to a general poisoning severity score system.^[24] There was no mortality.

Serum cardiac troponin concentration and ECG were available in 29 (55.8%) and 52 (100%) cases, respectively. Acute coronary syndrome, as demonstrated by an elevated serum cardiac troponin level or typical ECG changes, was not evident in any patient. ECG abnormalities were transient but common (67.3%). The ECG abnormalities included ventricular ectopic beats (23.1%), sinus bradycardia (13.5%), ventricular tachycardia (11.5%), junctional rhythm (7.7%), atrial fibrillation (5.8%), heart block of new onset (5.8%), ventricular fibrillation (5.8%) and sinus tachycardia (3.8%). ECG was normal in the remaining cases (23.7%) [table I].

TCM formula was available for transcription and interpretation in 44 (84.6%) cases. In 17 (32.7%) patients, the prescribed aconite herb dosage was higher than that recommended by the

Chinese Pharmacopoeia.^[2] The median prescribed dosage was 3 times the upper limit of the recommended dose (range 1.5–6 times). Hence, the cause of poisoning in these cases, at least partially, was aconite herb overdose.

In 17 (32.7%) patients, no aconite herb was prescribed. As these patients had aconite poisoning features and aconitum alkaloids of various kinds were detected in their urine specimens, they were considered to be cases of ‘hidden aconite poisoning’.^[20,21] In one case (case number 8), a piece of herb with typical morphology of ‘caowu’ (*A. kusnezoffii*) was recovered from the herb remnants (figure 2). This finding further confirmed the erroneous presence of aconite herb. Notably, yunaconitine, an aconitum alkaloid present in some ‘caowu’ species, was present in the urine and/or herbal specimens in 12 of these 17 cases. Whereas, in 26 cases in which the aconite herb had been listed as one of the ingredients in the herbal formula, yunaconite was detected in only 7 cases ($p < 0.005$ vs hidden aconite poisoning cases, Chi-squared test). Similarly, crassicauline A, another aconitum alkaloid, also from ‘caowu’, was present in 11 of these 17 hidden cases, in contrast to 2 out of 26 patients in whom aconite herbs had been prescribed ($p < 0.00005$, Chi-squared test).

In 7 (13.5%) patients, the prescribed aconite herb dosage was within the recommended limits, but clinical toxic features still occurred.

In 2 (3.9%) patients, there was no aconite herb prescribed but a non-toxic herb with a name similar to the aconite herb dispensed was present in the formula. In case 16 (table I), ‘bai-fu-zi’ was written on the formula but ‘bai-fu-pian’ was found in the herbal remnants. ‘Bai-fu-zi’ is the rhizome tuber of *Typhonium giganteum* Engl. and is non-toxic; ‘bai-fu-pian’ is the root of *Aconitum coreanum* Raipics. Biochemical analysis of the herbal remnant and urine confirmed the presence of aconitum alkaloids. Similarly, in case 29, ‘bai-fu-zi’ was prescribed but ‘bai-fu-pain’ was found in the herbal remnants.

In the remaining 9 (17.3%) patients categorized as ‘others’, there was a single case (1.9%) (case 11) who erroneously ingested one dose of decoction containing aconite herb prescribed to him for external use. In the other 8 (15.4%)

Table 1. Demographic data, clinical features and toxicology findings

Case no.	Sex	Age (y)	Hospitalization (days)	Indication of herb use	Latent period (hours)	Neurological features	Cardiovascular features	ECG findings	Gastrointestinal features	Other features	CCU/ICU admission	Contributory factors	Aconitum alkaloids detected
1	M	20	20	To relieve LBP	1	Generalized weakness	Palpitation, hypotension	VT and VF	Vomiting	Dizziness, sweating, shortness of breath	CCU	Hidden aconite poisoning	YA, CA
2	F	50	6	To relieve pain caused by advanced RCC	2	Limb paraesthesia	Palpitation	Sinus tachycardia	NR	Dizziness	NR	Overdosage	HA
3	M	30	4	To relieve back and shoulder pain	0.7	Limb paraesthesia and weakness	Chest discomfort, hypotension	Sinus bradycardia	Vomiting	NR	NR	Overdosage	YA
4	F	83	15	As herbal tonic	2	Generalized weakness	Chest discomfort	Slow AF	NR	Dizziness, shortness of breath	CCU	Poor-quality herb	HA
5	F	44	3	To relieve knee pain	3	Perioral and generalized paraesthesia and weakness	Hypotension, palpitation	Frequent ventricular ectopics	Abdominal pain, diarrhoea	NR	CCU	Overdosage	A
6	M	52	3	To treat finger paraesthesia	0.5	Perioral paraesthesia and limb weakness	Chest discomfort	Normal	NR	NR	NR	Overdosage	YA
7	M	62	4	To reduce headache	2	Limb paraesthesia, generalized weakness	Hypotension, palpitation	Sinus tachycardia	Nausea	Dizziness	ICU	Poor-quality herb	HA, MA
8	F	27	1	To treat URTI	1	Limb paraesthesia, generalized weakness	Chest discomfort	Sinus bradycardia	NR	Dizziness	NR	Hidden aconite poisoning	YA, CA
9	F	51	4	To treat URTI	2	Limb paraesthesia and weakness	NR	Normal	NR	Dizziness	NR	Hidden aconite poisoning	YA, CA
10	F	45	5	To treat menorrhagia	1	Generalized weakness and paraesthesia	Chest discomfort, hypotension	Junctional rhythm	Nausea, abdominal pain	Dizziness	NR	Hidden aconite poisoning	YA, CA

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Table 1. Contd

Case no.	Sex (y)	Age (y)	Hospitalization (days)	Indication of herb use	Latent period (hours)	Neurological features	Cardiovascular features	ECG findings	Gastrointestinal features	Other features	CCU/ICU admission	Contributory factors	Aconitum alkaloids detected
11	F	65	4	To relieve joint pain	2	Generalized paraesthesia	Hypotension	Ventricular ectopic beats	NR	Dizziness	NR	Ingested herbs prescribed for external use	YA
12	F	43	1	To relieve abdominal discomfort	0.5	Generalized weakness and paraesthesia	Hypotension	Normal	Vomiting	Dizziness	NR	Hidden aconite poisoning	A, MA, HA
13	F	35	3	To relieve LBP	0.5	Generalized weakness and paraesthesia	Hypotension	LBBB	Vomiting	NR	NR	Overdosage	A, MA, HA
14	F	58	3	To treat URTI	3	Generalized paraesthesia	Hypotension	Sinus bradycardia, ventricular ectopic beats	Abdominal pain	Dizziness	NR	Hidden aconite poisoning	YA, CA
15	M	78	11	To treat shortness of breath	1.5	Generalized weakness, slurred speech	Chest discomfort, hypotension	Non-sustained VT	NR	Dizziness, shortness of breath	ICU	Hidden aconite poisoning	YA, CA
16	F	60	2	To treat cerebrovascular accident	NI	Generalized paraesthesia	Hypotension	Slow AF	NR	Dizziness	NR	Dispensing error due to confusing herb names	A, MA, HA
17	F	63	3	To relieve abdominal discomfort	0.5	Generalized paraesthesia and weakness	Hypotension	Normal	Vomiting	NR	NR	Overdosage	A, MA, HA
18	F	56	2	To relieve abdominal discomfort	0.5	Generalized paraesthesia and weakness	Hypotension	Normal	Vomiting	NR	NR	Overdosage	A, MA, HA
19	F	98	6	To treat URTI	0.5	NR	Hypotension	Sinus bradycardia	Abdominal pain, nausea	NR	NR	Overdosage	HA
20	F	36	3	To relieve LBP	1.5	Generalized paraesthesia	NR	Normal	Abdominal pain, nausea	Shortness of breath	NR	Hidden aconite poisoning	A, MA, HA

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Table 1. Contd

Case no.	Sex	Age (y)	Hospitalization (days)	Indication of herb use	Latent period (hours)	Neurological features	Cardiovascular features	ECG findings	Gastrointestinal features	Other features	CCU/ICU admission	Contributory factors	Aconitum alkaloids detected
21	F	57	2	To relieve LBP	1	Generalized paraesthesia, weakness	Hypotension	Sinus bradycardia, RBBB	Abdominal pain, vomiting	Dizziness	NR	Poor-quality herb	A, MA, HA
22	F	50	1	To treat URTI	1	Generalized paraesthesia	NR	Normal	NR	NR	NR	Poor-quality herb	A, MA, HA
23	F	38	2	To treat menstrual disorders	0.5	Generalized paraesthesia	Hypotension	Normal	Vomiting	NR	NR	Poor-quality herb	YA, CA, MA, HA
24	M	77	5	To relieve joint pain	2	Generalized paraesthesia	Hypotension	VF	NR	NR	ICU	Overdosage	YA, A, MA, HA
25	F	52	2	To relieve muscle pain	1.5	Generalized paraesthesia	Palpitation	Normal	NR	Shortness of breath	NR	Hidden aconite poisoning	YA, CA
26	M	58	2	To treat URTI	1	Limb paraesthesia	Hypotension	Frequent ventricular ectopics	Vomiting	NR	ICU	Overdosage	A, MA
27	F	54	1	To treat menstrual disorders	0.5	Limb paraesthesia	Hypotension	Sinus bradycardia	Nausea	NR	NR	Hidden aconite poisoning	YA, CA
28	M	63	3	To treat URTI	1	Limb paraesthesia	Chest discomfort, hypotension	Normal	Vomiting	NR	NR	Undetermined	A, MA, HA
29	M	48	3	To treat cirrhosis	0.5	Generalized paraesthesia	Hypotension	Frequent ventricular ectopics	Vomiting, diarrhoea	Dizziness	ICU	Dispensing error due to confusing herb names	A, MA, HA
30	F	46	2	To relieve leg pain	1	Generalized weakness and paraesthesia	Hypotension	Second-degree heart block	NR	NR	NR	Poor-quality herb	A, MA, HA
31	F	25	5	As herbal tonic	1	Limb paraesthesia and weakness	NR	Normal	NR	NR	NR	Hidden aconite poisoning	YA, CA
32	F	28	1	To treat thyroid nodule	NI	Limb paraesthesia	Chest discomfort	Ventricular ectopic beats	Vomiting, diarrhoea	Dizziness	NR	Hidden aconite poisoning	A

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Table 1. Contd

Case no.	Sex (y)	Age (y)	Hospitalization (days)	Indication of herb use	Latent period (hours)	Neurological features	Cardiovascular features	ECG findings	Gastrointestinal features	Other features	CCU/ICU admission	Contributory factors	Aconitum alkaloids detected
33	M	63	8	To treat chronic renal failure	4	Generalized paraesthesia	Hypotension, palpitation	Non-sustained VT	NR	Dizziness	ICU	Overdosage	A, MA, HA
34	F	59	1	To relieve epigastric discomfort	2	Generalized paraesthesia	NR	Normal	NR	NR	NR	Poor-quality herb	A, MA, HA
35	F	82	4	To relieve LBP	4	Generalized paraesthesia	Chest discomfort, hypotension	VT and VF	Abdominal pain, nausea	Sweating	ICU	Hidden aconite poisoning	A, MA, HA
36	F	45	1	To treat URTI	2	Generalized paraesthesia	Chest discomfort	Normal	NR	NR	NR	Overdosage	HA
37	M	54	2	To treat URTI	2	Generalized paraesthesia	Hypotension	Normal	NR	NR	NR	Hidden aconite poisoning	YA, CA
38	F	61	4	To treat Bell's palsy	0.5	Generalized paraesthesia	Hypotension	Normal	Diarrhoea	NR	NR	Overdosage	YA, CA, A, MA, HA
39	F	51	5	To treat dizziness	1	Generalized paraesthesia	Palpitation, chest discomfort	Fast AF, multiple atrial ectopics	NR	NR	NR	Hidden aconite poisoning	A
40	M	61	2	As herbal tonic	0.5	Generalized paraesthesia	Palpitation	Frequent ventricular ectopics, junctional rhythm	Diarrhoea	Dizziness	NR	Overdosage	A, MA, HA
41	F	74	2	To treat URTI	1	Generalized paraesthesia and weakness	Hypotension	Normal	NR	Dizziness, sweating	NR	Overdosage	A, MA, HA
42	M	52	2	To treat URTI	1	Generalized paraesthesia, weakness	NR	Ventricular ectopic beats	Abdominal pain, nausea	NR	NR	Overdosage	YA, CA, A, MA, HA
43	M	45	3	To relieve LBP	2	Generalized paraesthesia	Chest discomfort, hypotension	Non-sustained VT	Nausea	Dizziness, sweating, shortness of breath	ICU	Undetermined	YA, A, MA, HA

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Table 1. Contd

Case no.	Sex	Age (y)	Hospitalization (days)	Indication of herb use	Latent period (hours)	Neurological features	Cardiovascular features	ECG findings	Gastrointestinal features	Other features	CCU/ICU admission	Contributory factors	Aconitum alkaloids detected
44	F	59	6	To relieve abdominal discomfort	1	Perioral numbness	Hypotension	Ventricular ectopic beats	Vomiting	Dizziness	ICU	Undetermined	A, MA, HA
45	F	35	4	To treat URTI	0.25	Generalized paraesthesia	Chest discomfort, hypotension	Sinus bradycardia	NR	Dizziness	NR	Hidden aconite poisoning	YA, CA
46	M	22	1	As health tonic	0.5	Generalized paraesthesia	NR	Normal	Nausea, vomiting, abdominal pain	NR	NR	Overdosage	A, MA, HA
47	M	43	10	As health tonic	1	Generalized weakness and paraesthesia, slurred speech, headache	Hypotension, palpitation	Multiple ventricular ectopics	Abdominal pain, nausea	Dizziness	ICU	Undetermined	BA, IA, PA, YA
48	F	39	3	As health tonic	1	Generalized weakness and paraesthesia	Hypotension	Junctional rhythm	Vomiting	NR	ICU	Undetermined	BA, IA, PA, YA
49	F	20	7	As health tonic	1	Generalized weakness and paraesthesia	Hypotension	Ventricular ectopic beats	Abdominal pain	NR	ICU	Undetermined	BA, IA, PA, YA
50	F	81	4	To control urinary frequency	2	Limb paraesthesia	Hypotension	Ventricular ectopic beats	Vomiting	Dizziness	NR	Undetermined	A, MA, HA
51	M	71	7	To relieve joint pain	3	NR	Syncope, hypotension, palpitation	VT	Nausea	Sweating	CCU	Undetermined	A, MA, HA
52	F	72	4	To relieve LBP	2	NR	Chest discomfort, hypotension	Junctional bradycardia	NR	Shortness of breath	NR	Hidden aconite poisoning	YA

A = aconitine; AF = atrial fibrillation; BA = bikhaconitine; CA = crassicauline A; CCU = coronary care unit; F = female; HA = hyaenacitine; IA = indaconitine; ICU = intensive care unit; LBP = lower back pain; LBBS = left bundle branch block; M = male; MA = mesaconitine; NI = no information; NR = none reported; PA = pseudaconitine; RBBS = right bundle branch block; RCC = renal cell carcinoma; URTI = upper respiratory tract infection; VF = ventricular fibrillation; VT = ventricular tachycardia; YA = yunaconitine.

Table II. Summary of clinical features occurring in the 52 patients

	Number (%)
Cardiovascular features	46 (88.5)
Hypotension	36 (69.2)
ECG abnormality	35 (67.3)
Chest pain/discomfort	14 (26.9)
Palpitations	10 (19.2)
Neurological features	49 (94.2)
Numbness/paraesthesia	47 (90.4)
Weakness	22 (42.3)
Slurred speech	2 (3.8)
Gastrointestinal features	31 (59.6)
Nausea/vomiting	24 (46.2)
Abdominal pain	11 (21.2)
Diarrhoea	5 (9.6)
Others	28 (53.8)
Dizziness	23 (44.2)
Shortness of breath	7 (13.5)
Sweating	5 (9.6)

patients, the herbal composite formula was not available for study; the cause of poisoning, hence, could not be determined.

The mean length of hospitalization was 4 days (range 1–20 days). Sixteen patients (30.8%) required care in an intensive care unit or coronary care unit. Additionally, three patients required defibrillation to terminate life-threatening ventricular fibrillation, and endotracheal intubation. Complete recovery without complication was seen in all cases.

Discussion

The short latency period between herb consumption and symptom onset indicates rapid absorption and distribution of the toxic aconitum alkaloids. The clinical features (table II) observed in our patients are consistent with those described in previous studies, including the predominantly neurological and cardiovascular involvement.^[5,9,11,13] The sensory and motor neurological impairments were generally self-limiting. However, the cardiovascular adverse effects were life-threatening and, in some cases, defibrillation and intensive care were required.

An in-hospital mortality rate of 5.5% has been reported in the literature.^[4] However, we did not

record any mortality in this series. We postulate that this positive outcome may be attributed to a number of factors, including prompt recognition of the toxidrome, efficient supportive and anti-arrhythmic treatment, the introduction of a 24-hour phone consultation service by our toxicology service network, and the multidisciplinary approach in handling herbal toxicology cases.^[25] Nonetheless, there were several near misses in this case series, highlighting the danger of this type of poisoning.

Confirming a diagnosis of herbal poisoning is known to be difficult.^[26] In the majority of previous reports, diagnosis of aconite poisoning was based on clinical features and history of herb consumption only.^[5,11,13,27] To our knowledge, the case series we describe is the largest aconite poisoning case series reported in the English language literature. This case series is valuable as we were able to unequivocally confirm the diagnosis of all cases by identifying aconitum alkaloids in the urine. Additionally, the other investigation steps – transcription and interpretation of the herbal formula, morphological identification of the herbs and collating all the clinical and investigation findings – generated new insight into this classical herbal poisoning problem. As a tertiary laboratory, we would welcome referral



Fig. 2. A piece of caowu, which was not prescribed, was identified in case 8. This is the typical morphology of 'caowu' (*Aconitum kusnezoffii*), described as being deep brown in colour, having a conical shape and typical size of 2–7 cm in length and diameter of 0.6–1.8 cm, with a hard consistency, overlaid by irregular strides.

from other regions or countries for similar herbal poisoning cases.

It is alarming to note that in 32.7% of the patients, the prescribed dose of aconite herb was higher than the recommended dosage. TCM practitioners generally know, though might not be repeatedly or effectively reminded, that this herb is toxic and the therapeutic window is narrow. Why then did they still prescribe higher than the recommended dosage of such dangerous herbs? One possible reason is that the quality of such herbs is variable. It helps to understand that all aconite herbs must be processed by repeated steaming and boiling to reduce toxicity before being used as herbs, as stipulated by the Chinese State Food and Drug Administration.^[2] The aconitum alkaloid components and amounts vary initially with the species, origin, time or season of harvest, and later by the method and adequacy of processing. As a result, it has been demonstrated that the active ingredients of these herbs can vary as much as 10-fold.^[23,28] In TCM practice, the gross weight of herb, instead of its active ingredients, is the unit of measurement in prescribing and dispensing. If a TCM specialist had learned from experience that the recommended dosage could not achieve the desired therapeutic effect, he or she might increase the prescribing dosage to compensate for the suboptimal effectiveness.^[29] If the active ingredients of the dispensed herbs were relatively high, such practice would result in poisoning.

In 13.5% of the patients in our case series, the prescribed aconite herb dosage was within the recommended limits. At a glance, it is difficult to understand why poisoning occurred in these patients. However, understanding that the active ingredients in such herbs can differ by as much as ten times, as explained, it is highly probable that these patients consumed inadequately detoxified herbs, resulting in toxicity. Even though the dosage, in terms of the dry weight of the herb, was within the recommended limits, the levels of active ingredients were high. Whilst it looks like a different cause of poisoning from the 'overdose' category, it is actually the other side of the same coin: the variable quality of the herbs resulted in ingestion of too much aconite by the patient. Notwithstanding the above, there are alternative

explanations of poisoning for these patients, including dispensing higher than the prescribed dosage of herb, inadequate decoction immediately before consumption, individual variability in propensity to aconite poisoning or even less likely interaction with other herbs or drugs.

'Hidden' aconite poisoning was also frequently observed in this series (32.7%) and is the most worrisome kind. As the aconite herb was not prescribed, and presumably not intentionally dispensed, its presence signifies contamination of the other dispensed herbs.^[21] Contamination may have occurred at a number of stages, including harvesting, processing, transportation, storage, and dispensing. The exact time and location was impossible to pinpoint for each specific case.

Theoretically, the dispenser might pick up gross contamination by an intact aconite herb, but this would be beyond what we could derive from our present data. If the aconite herb, as a contaminant, was in fine sections or pieces within a pack of herbs, this would be difficult for the dispenser to spot. From our findings, out of 17 hidden cases, we could identify by morphological inspection the presence of a piece of 'caowu' in one case. This might pinpoint the limitation of simple visual inspection to identify contamination.

As the herb was not intentionally dispensed, the usual detoxification process may not have taken place or may have been inadequate; the amount of aconite present was uncertain and could be dangerously high. Moreover, we had carefully studied the formulae involved in these 17 cases; no herb was overrepresented. In other words, contamination was random. This is a serious alarm to the use of herbal medicine in general; many non-toxic herbs may be randomly contaminated.

Whilst no particular herb was associated with hidden aconite poisoning, some clues could be obtained from the alkaloid profile. We noted that yunaconite and crassicauline A – aconitum alkaloids of 'caowu' (*A. kusnezoffii*) origin – were more frequently identified in the urine of these patients. This observation is important for tracing the source of contamination in the future. Again, although the immediate cause of poisoning is different from the other categories of cases,

the fundamental cause is the same – the quality of herbs is questionable.

Apart from the unsatisfactory quality of herbs and prescribing, substandard practices in dispensing can also lead to poisoning, as was evident in two patients. Many herbs have numerous alternative names, often very similar, increasing the risk of dispensing errors.^[30,31] The mixing up of ‘bai-fu-zi’ and ‘bai-fu-pian’ in these two patients is a clear example. ‘Bai-fu-zi’ is a non-aconite species but its name is similar to the aconite herb ‘bai-fu-pian’.^[2] Misinterpretation of the herbal formula or lack of awareness of such error-prone nomenclature may contribute to dispensing errors. To minimize this risk, dispensers of TCM herbs need adequate and structured training.

In this series of 52 cases, the cause of poisoning was successfully identified in 44 cases. In the remaining 8 cases, the cause could not be determined. Apart from one patient who consumed a dose of herbs prescribed to him for external use, the majority (43 [97.7%]) could be traced to some kind of inferior quality related to the practice of TCM: quality of herbs, quality of prescribing or quality of dispensary. Were there any subclinical cases? Were there any fatalities in patients who did not reach a hospital in time? Were there other kinds of contaminations of herbs? These are important questions to ask, which our study could not answer. However, our study clearly and

firmly demonstrates that the practice of TCM requires a thorough and stringent review. Finally, table III provides a list of precautions that might help in the safe use of these toxic aconite herbs.

Conclusions

Chinese herbal medications, renowned for their long history and the belief in the eyes of many people of their therapeutic or simply health maintenance value and lack of adverse effects, must be considered in terms of their potential to cause harm. Whilst aconite poisoning is a classical herbal poisoning and notorious for its severity, the underlining causes leading to such poisoning have thus far been inadequately studied. Our study showed that in the majority of these cases, the causes of poisoning can be traced to poor quality of herbs, prescribing or dispensing practices. Many facets of TCM practice need substantial improvement to prevent repeats of this life-threatening poisoning and possible fatal outcomes.

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Table III. Precautions needed for the safe use of aconite herbs in traditional Chinese medicine

1. One should comply with recommended dosage limits of aconite herbs according to the Chinese Pharmacopoeia^[2]
2. All aconite herbs should be adequately processed and never be used as unprocessed raw or crude herbs
3. Quality of herbs would be upheld, optimally, through recognized standards such as good agricultural practice, good manufacturing practice, etc., to ensure quality from harvesting, processing, transportation, storage and dispensing
4. A territory-wide adverse herb reaction notification system should be enhanced to trigger and facilitate subsequent tracing of the ultimate source of error of aconite poisoning
5. Quality of TCM dispensing should be improved, in particular for herbs with similar nomenclatures. TCM pharmacists or dispensers should receive adequate training and formal appraisal for their competency

TCM = traditional Chinese medicine.

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