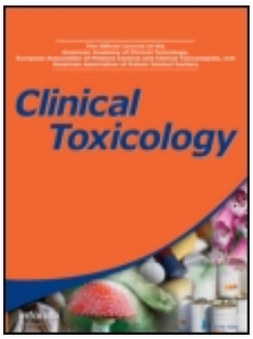

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CASE REPORT

Low-dose exposure to *Veratrum album* in children causes mild effects – a case series

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Introduction. White or false hellebore (*Veratrum album*) has a toxicological relevance because of the potential for misidentification of this plant as yellow gentian (*Gentiana lutea*). *Case series*. We report a retrospective case series of 11 children (8–12 years) with accidental intake of *V. album* at a youth camp where they had collected herbs for preparing fresh herb tea. Two children (18%) remained asymptomatic. Nine (82%) developed mild gastrointestinal symptoms, six (55%) presented neurological symptoms, and three (27%) showed bradycardia. All children recovered completely within 10 h of ingestion. The plant was identified at the emergency department; however, detection of veratridine and cevadine by means of high-performance liquid chromatography–Mass spectrometry from the blood of the child with the most severe symptoms was negative (limit 0.01 ng/mL). *Discussion*. *Veratrum* species contain more than 200 different alkaloids, which are the principal toxins and are responsible for most clinical symptoms. There are likely multiple mechanisms of toxicity and some of them are only partially understood. The opening of voltage-gated sodium channels is probably one of the most relevant pathophysiological mechanisms. *Conclusions*. *Veratrum album* intoxication in children demonstrated the same clinical course as observed in adults. Accidental ingestion of a low dose of the plant had a favorable outcome with supportive care.

Keywords Acute poisoning; Intoxication; Toxic plants; Pediatric

Introduction

White or false hellebore (*Veratrum album*) is a European alpine plant with a long medicinal and toxicologic history. Relevant toxicological aspects of *V. album* were described in the literature in relation to the use of this plant in suicide attempts or criminal activities[1] and more recently in relation to the cases of poisoning after using sneezing powders containing *V. album* alkaloids.[2,3]

Today the plant mainly has a toxicological relevance because of the potential for misidentification as yellow gentian (*Gentiana lutea*), especially before florescence where the main distinction between the two species consists in the alternating positioning of the leaves of *V. album* compared with the opposite positioning of *G. lutea*.

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We describe a retrospective case series of 11 children with an accidental low-dose oral exposure to *V. album.*

Case series

Eleven children (8–12 years) accidentally ingested *V. album* at a youth camp where they collected herbs for preparing fresh herb tea. The age of the patients was between 8 and 12 years (median 9.45 ± 1.37 years) and their median weight 34.8 kg (30–42 kg).

The roots were either ingested uncooked in the form of slices or cut into cubes that were added to the boiling water with the intent to prepare an infusion. Four children ingested an amount ranging from one quarter of a slice up to two slices; five children ingested an amount ranging from one gulp up to one cup of the herbal tea; and two children ingested both slices (one half of a slice up to one slice) and tea (one cup up to two cups of tea) (Table 1).

All children were examined at the emergency department of a peripheral hospital. Admission occurred 5 h after ingestion. Age, weight, amount of *V. album* ingested, latency

Table 1. Baseline characteristics of the patients, form and amount of ingestion, and presenting clinical features

Patient	Age	Weight	Ingestion as	Amount ingested	Latency (hours)	Symptoms	BP[a] (mmHg)	P[b] (bpm)	Duration (hours)
1	8	31	Root	0.5 slice[c]	1	Nausea, vomiting, taste sense alteration	92/56	52	2
2	11	34	Root	2 slices	1	Nausea, vomiting, taste sense alteration, impaired vision	92/56	52	2–3
3	10	31	Root and tea	1 slice, 2 cups[d]	2	Vomiting, vertigo, headache, impaired vision	88/65	76	8–10
4	10	40.5	Tea	A gulp[e]	n.a.[f]	None	124/80	68	n.a.
5	12	42	Root	0.25 slice	0.25	Nausea	116/72	88	4–6
6	9	38	Root	0.5 slice	3.5	Nausea, vomiting, impaired vision, shivering	124/50	104	3
7	8	32	Tea	from a 5 mm^3 cube, 1 cup	4	Nausea	119/61	78	2
8	10	37	Tea	0.5 cup	1.5	Nausea, abdominal pain, headache, vertigo, chilliness, shivering, faintness of the legs	140/91	72	4–5
9	8	30	Root and tea	0.5 slice, 1 cup	2	Nausea, vomiting, abdominal pain, vertigo, impaired vision	93/52	72	n.a.
10	8	33	Tea	from a 8 mm^3cube, 3 tbsp[g]	n.a.	None	125/83	101	n.a.
11	10	35	Tea	from four 5 mm^3 cubes, amount of liquid ingested unknown	2	Nausea, vomiting, vertigo, numbness, somnolence, dysarthria	103/60	50–60	8–9

[a]Blood pressure, reference values for hypotension for children of 8–12 years old for systolic blood pressure are less than 70 mmHg + (2 × age in years) in children 1–10 years, less than 90 mmHg in children 10 years of age or older.
[b]Pulse, reference value for bradycardia for children 8–12 years old is <60 bpm.
[c]A slice was approximately 20 mm in diameter and 4 mm thick.
[d]A cup contained approximately 1.8 dL = 180 mL liquid.
[e]A gulp was estimated as 15–20 mL liquid.
[f]Information not available.
[g]Tablespoonful.

between consumption and appearance of symptoms, clinical features, therapy, and outcomes were collected from hospital discharge letter, and a questionnaire was sent to the parents.

The two children (18%) who ingested a small quantity of tea remained asymptomatic. Nine children (82%) developed gastrointestinal symptoms such as nausea, vomiting, and dysgeusia. Six (55%) presented neurological symptoms such as vertigo, impaired vision, somnolence, and dysarthria. One child presented headache that was successfully treated with acetaminophen po. Three children (27%) were bradycardic: one responded to atropine and the others recovered spontaneously. No other medications were administered. A detailed list of the symptoms is shown in Table 1.

Symptoms developed between 15 min and 3.5 h after ingestion and persisted for some hours. All children recovered completely within 10 h of ingestion.

No primary decontamination was performed because charcoal was not available at the camp. On admission at the hospital, a decontamination procedure was no more indicated because of the too long latency between consumption of the plant and presentation.

The plant was identified by the head of the youth camp who had a special expertise in botany and at the emergency department by the pharmacist of the hospital pharmacy. Additionally, an analysis of the veratrine alkaloids, veratridine, and cevadine by means of high-performance liquid chromatography–Mass spectrometry was performed on a blood sample drawn 6 h after ingestion from the child presenting the most severe symptoms (patient 11). The result of this analysis was negative (limit 0.01 ng/mL).

Discussion

White or false hellebore is a toxic plant belonging to the family of *Melanthiaceae*. Historically, *Veratrum* plants and extracts were used as arrow poison, insecticide, or as drugs against neuralgia, pertussis, rheumatism, pneumonia, and tumors and 100 years later for lowering blood pressure.[4] *Veratrum* species contain more than 200 different alkaloids,[5] which are the principal toxins and are responsible for most clinical symptoms. Some of these alkaloids have a typical

steroidal skeleton, others have modifications in which the constituent rings C and D of the steroid nucleus have changed places.[5] Individual alkaloids from the latter group include veratridine, cevadine, jervine, pseudojervine, protoveratrine A, and protoveratrine B.[5] A mixture of several *Veratrum* alkaloids is called veratrine, which is one of the major components implicated in toxicology investigations. The two major constituents of veratrine are veratridine and cevadine.[5]

In our pediatric case series, patients presented predominantly gastrointestinal, neurological, and cardiovascular symptoms. This presentation is consistent with the clinical course of *V. album* poisoning usually observed in adults.[6] The clinical findings in our pediatric patients are also compatible with the symptoms described in the literature reporting the contamination of sneezing powder with *V. album* that occurred in Germany in the 1980s. The preparation was marketed in France and in the Scandinavian countries, and exposed children and young adults showed similar symptoms. Bradycardia and hypotensive episodes were recorded more frequently in cases of exposure in France, whereas in the Scandinavian countries patients presented also ophthalmologic problems such as dilated pupils and transient blindness.[2,3]

As suggested in various clinical studies, a dose-dependent effect of *Veratrum* alkaloids is likely.[4] The clinical courses observed in our patients are compatible with the hypothesis of a dose-dependent effect. In fact, only the two asymptomatic patients ingested a very small dose. In both the group of patients ingesting the root and the tea, symptoms were more pronounced in the subjects who ingested the higher doses. As a possible limitation, it is important to emphasize that a difference between the amount of alkaloids ingested and the amount absorbed probably exists. This fact may be especially relevant considering that different preparations (slices of root versus tea) were ingested. Actually, it is plausible that the alkaloids are less available for absorption from the slices than from the herbal tea. Arguing against this hypothesis is the observation that the latency to the development of symptoms was almost similar for slices and tea ingestion.

The possible differences in the availability of alkaloids for absorption in the gastrointestinal tract between solid (slices of root) and liquid (tea) forms and the fact that the alkaloids concentration in the tea – which is actually unknown – might be influenced by the preparation procedure (e.g., duration of boiling) are clear limitations of this case series that must be considered when comparing the group ingesting the slices of root with that ingesting the tea.

The quantitative toxicity of *V. album* has not been described in detail. The detection of veratridine and cevadine in blood is a complex procedure that is rarely performed. Gaillard and Pepin described two fatal cases of *V. album* poisoning, measuring concentrations of 0.17 and 0.40 ng/mL, respectively, for veratridine and 0.32 and 0.48 ng/mL, respectively, for cevadine. As the cut-off value of high-performance liquid chromatography–Mass spectrometry testing for the veratrine group alkaloids is unknown, a positive result confirms the intoxication with *V. album*, whereas a negative result, as occurred in our case, cannot be interpreted.[1] It is possible that the time delay of 6 h to sampling, which was due to the relative late admission to the hospital (5 h after ingestion), may have affected detection because one may argue that the alkaloids might already have been metabolized at the time of sampling. We can neither confirm nor reject this hypothesis, because to our knowledge, the half-life of veratridine and cevadine has not been previously described.

There are likely multiple mechanisms of toxicity of *V. album* that are only partially understood. One of the most relevant pathophysiological mechanisms of toxicity of *Veratrum* alkaloids is mediated by binding to selected voltage-gated sodium channels. These proteins are responsible for generating action potentials in skeletal muscle, nerve, and cardiac cells.[5] The rapid increase in the permeability to cations such as sodium and calcium at the level of excitable cell membranes delays neuronal repolarization.[6] Consequently, a single neuronal stimulus will produce multiple discharges.[5] The susceptibility of excitable cells to this mechanism is variable, with cardiopulmonary vagal afferents being particularly susceptible.[2,4] The resulting clinical effects are bradycardia and hypotension, which are highly characteristic for the intoxication with *V. album*, even after ingestion of low doses.[7] Bradycardia and hypotension are also caused by the interaction of *Veratrum* alkaloids with cardiac receptors in the left ventricle posterior wall and the baroreceptor area of the coronary sinus.[5] In addition the alkaloids exhibit digitalis-like effects,[10] so that symptoms like repolarization abnormalities, prolongation of the QT interval, T-wave inversion, shift in the ST segment, and various rhythm disturbances may be observed in higher doses.[6] Gastrointestinal symptoms like nausea, vomiting, abdominal pain, and increased salivation are assumed to be provoked by stimulation of the ganglion nodosum[8] and only to a minor extent by direct irritation of the mucous membranes. Newer studies point to harmful effects of *Veratrum* alkaloids on mitochondria with the consequent interference with the energy metabolism of various systems (e.g., cardiomyocytes, synaptosomes).[9]

The prognosis of intoxications with *V. album* depends principally on the dose ingested and the availability of adequate therapy. Some recent case series[2,3] and one literature review[6] suggest that *V. album* is less toxic than previously assumed. Our observations support this hypothesis because, even without decontamination measures, the clinical course was favorable with supportive care and monitoring.

Conclusions

Veratrum album intoxication in children demonstrated the same clinical course as observed in adults, with gastrointestinal, neurologic, and cardiovascular symptoms predominating. Accidental ingestion of a low dose of the plant had a favorable outcome with supportive care. A dose-dependent effect is likely although quantitative toxicity has not been described in detail.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

References

1. Gaillard Y, Pepin G. LC-EI-MS determination of veratridine and cevadine in two fatal cases of Veratrum album poisoning. J Anal Toxicol 2001; 25:481–485.
2. Carlier P, Efthymiou ML, Garnier R, Hoffelt J, Fournier E. Poisoning with Veratrum-containing sneezing powders. Hum Toxicol 1983; 2:321–325.
3. Fogh A, Kulling P, Wickstrom E. Veratrum alkaloids in sneezing-powder a potential danger. J Toxicol Clin Toxicol 1983; 20:175–179.
4. Blaschek W, Hänsel R, Keller K, Reichling J, Rimpler H, Schneider G. Hagers Handbuch der Pharmazeutischen Praxis: Drogen L–Z. Vol. 3. Berlin: Springer; 1997:742–750.
5. Schep LJ, Schmierer DM, Fountain JS. Veratrum poisoning. Toxicol Rev 2006; 25:73–78.
6. Quatrehomme G, Bertrand F, Chauvet C, Ollier A. Intoxication from Veratrum album. Hum Exp Toxicol 1993; 12:111–115.
7. Verberne AJ, Saita M, Sartor DM. Chemical stimulation of vagal afferent neurons and sympathetic vasomotor tone. Brain Res Brain Res Rev 2003; 41:288–305.
8. Borison HL, Fairbanks VF. Mechanism of Veratrum induced emesis in cat. J Pharmacol Exp Ther 1952; 105:317–325.
9. Silva Freitas EM, Fagian MM, Cruz Höfling MA. Effects of veratine and veratridine on oxygen consumption and electrical membrane potentials. Toxicon 2006; 57:780–787.
10. Ulbricht W. Effects of veratridine on sodium currents and fluxes. Rev Physiol Biochem Pharmacol 1998; 133:1–54.