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POISON CENTRES

Acute plant poisoning: Analysis of clinical features and circumstances of exposure

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Introduction. Human contact with potentially toxic plants, which may occur through abuse or by accident or attempted suicide, is frequent and sometimes results in clinically significant toxicity. *Objective.* The aim of the present study was to identify which plants may lead to severe poisoning, and to define the clinical relevance of plant toxicity for humans in Switzerland. *Methods*. We analyzed 42 193 cases of human plant exposure and 255 acute moderate, severe, and lethal poisonings, which were reported to the Swiss Toxicological Information Centre between January 1995 and December 2009. *Results*. Plant contact was rarely responsible for serious poisonings. Lethal intoxications were extremely rare and were caused by plants with cardiotoxic (*Taxus baccata*) or mitosis-inhibiting (*Colchicum autumnale*) properties. *Conclusions*. Most often, plant contact was accidental and patients remained asymptomatic or developed mild symptoms, which fully resolved within a short time.

Keywords Poisoning; Toxicity; Accidental; Abuse; Suicidal

Introduction

Human oral, dermal, or ocular contact with potentially harmful plants is frequent. Plant exposures rank tenth in children and sixteenth in adults in the list of the exposures most commonly reported to poison control centers in the United States,[1] thirteenth (no age distinction) in Taiwan,[2] second in children and sixth in adults in Germany (in combination with mushroom exposures),[3] and third in children and sixth in adults in Switzerland.[4]

Most plants are harmless to humans, but there are a few that can cause toxicity. There are three possible circumstantial settings leading to exposure to plants: accidental or intentional through abuse or attempted suicide. An abundance of literature has been published on accidental exposure to plants,[5–10] and on abuse by ingestion of plants,[11,12] while literature on suicidal exposure is limited,[13,14] although this doesn't apply to South Asia.[15–18] Most of these European articles are case reports or small case series. There are only a few studies investigating the epidemiology of human exposure to plants,[19–25] and these publications indicate that accidental exposure is the most frequent circumstance of poisoning, closely followed by abuse. Therefore, we performed a retrospective study to investigate the epidemiology of plant exposures in Switzerland with a focus on the three settings listed above, and to elucidate the plants mainly responsible for cases of moderate, severe, and fatal poisoning.

We analyzed all cases of acute human exposure to potentially toxic plants reported to the Swiss Toxicological Information Centre (STIC) by the general public and healthcare professionals in a first part, and, in a second part, all well-documented cases of acute mono-intoxications with plants reported by physicians. The study period was between January 1995 and December 2009. The aim of this study was to define the clinical relevance of plant toxicity for humans in Switzerland and to identify which plants may actually lead to severe poisoning, with a view to improving prediction of the expected clinical course of acutely intoxicated patients and avoiding unnecessary hospital admissions.

Methods

Data acquisition

A retrospective case-study design was used. In cases of poisoning, the STIC provides 24-h 7-days-a-week nationwide free medical advice to health professionals and the general public. The referral population is about 7.8 million people. Demographic and detailed clinical information on exposure cases – such as age (children defined as <16 years), sex, and weight of the patient, circumstances of exposure/poisoning, ingested quantities and anatomical parts of all plants involved,

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co-ingestions (such as medications, alcohol), symptoms, and causality – are recorded in a systematic and standardized manner by a physician trained in clinical toxicology. These data are prospectively entered into an in-house structured electronic database (TOXI[26]). For reports by healthcare professionals, the STIC collects additional specific clinical data – including complementary information on type and, if applicable, dose of the substances ingested (analytical toxicology), current history and circumstances of substance intake, observed symptoms and signs, including heart rate and blood pressure, Glasgow Coma Scale (GCS) score, an electrocardiogram, therapeutic interventions and any decontamination procedures performed, latency to decontamination, observed clinical course, and eventual medical complications – using a standardized report form that is sent to the treating physician. Hospital physicians are also asked to provide a discharge letter and any laboratory results, as well as the results of other examinations. This follow-up information is then matched with the data taken during the initial call and entered into the database to complement the case files. A senior clinical toxicologist reviewed each case to ensure completeness and correctness of the entered data before finalizing recording into the database.

Inclusion criteria

The following criteria had to be met for reported cases to be included in the study:
(a) For the analysis of exposure:

- Enquiries between January 1995 and December 2009;
- Enquiries by the general public and healthcare professionals;
- Acute human exposure;
- Exposure to one or more plants.

(b) For the analysis of symptoms, severity, and outcome:

- Enquiries by physicians only;
- Presence of written feedback from the treating physicians with sufficiently detailed data about symptoms and evolution;
- Acute human mono-intoxications;
- Plant must be identified by a specialist (botanist, gardener, pharmacist, or specially trained personnel of the poison control center) by its botanical name;
- Moderate, severe, or lethal outcomes;
- Confirmed or likely causal relationship between exposure and clinical effect. Causality assessment is based on a clear temporal relationship between plant exposure and symptoms, absence of drugs or diseases that can explain the symptoms, and the presence of symptoms, which are described for the plant in question. Since these criteria cannot be used for asymptomatic patients, these cases are judged only according to the contact with the plant as reported by the patient or by relatives. Analytical detection of a specific toxin in a body fluid defines a case as confirmed.

Exclusion criteria

- Phytomedicines (industrially processed plant materials like tinctures, mixtures, and teas);
- Industrial botanical ingredients and foodstuffs;
- *Nicotiana tabacum* (Tobacco) was excluded because of industrial processing of plant material;
- *Cannabis sativa* was excluded because the distinction between plant (marihuana) and resin (processed product, hashish) was frequently not possible;
- Mushrooms.

Severity assessment

According to the Poisoning Severity Score (PSS) developed by the European Association of Poison Centres and Clinical Toxicologists, the WHO International Programme on Chemical Safety (IPCS), and the European Commission,[27] the severity of symptoms of individual patients were classified as "minor" if only minor symptoms were present, as "moderate" if at least one moderate symptom developed, as "severe" if at least one severe symptom was observed, or as fatal. A summary of symptoms according to their severity is shown in Table 1.

Statistical evaluation

Statistical analysis for descriptive statistics was performed using SPSS software (Version 17.0; SPSS Inc., Chicago, IL).

Results

Human exposures to toxic plants

During the 15-year study period, the STIC recorded a total of 427 107 cases of human exposures to different toxic agents or substances, of which 42 193 (9.9%) were oral, ocular, or dermal exposures to potentially toxic plants or plant material. The annual number of human exposure to toxic plants ranked from 2516 to 3287, with a tendency to increase in recent years, which is in accordance with an increasing total number of calls to the STIC related to all substances in recent years (29 788 calls in 1995 to 34 022 calls in 2009). Children were involved in 34 014 (80.6%) of all cases. Although 639 plant genera were involved in total, the vast majority of cases (30 499 calls, 72.3%) were due to 50 plant genera, unspecified berries, and unspecified plants (Table 2). Unspecified berries ranked at the top of the list of enquiries, closely followed by *Prunus*, *Ficus*, and *Taxus*. Exposure was accidental in 29 770 cases, abuse in 417, and suicidal in 219 cases. In the accidental exposure setting, the most frequent plant genera beyond unspecified berries were *Prunus* sp. (n = 2756) in children, and *Euphorbia* sp. (n = 687) in adults. In abuse, *Datura* sp. (n = 290) was the most common plant, and *Taxus* sp. (n = 61) was the most frequently used plant for suicide attempts.

Symptoms, severity, and outcome

Among all cases concerning medically relevant exposure to toxic plants reported to the STIC during the study period,

Table 1. Symptoms and severity of intoxications.

Organ system	Minor	Moderate	Severe
Nervous system	Somnolence, dizziness, tremor, restlessness, drowsiness, tinnitus, ataxia, mild anticholinergic symptoms (dry mouth, mydriasis)	Unconsciousness with appropriate response to pain (GCS* 8–9), agitation, single generalized or local seizures, myoclonus, hallucinations	Deep coma with inappropriate response to pain or unresponsive to pain (GCS* ≤ 7), multiple generalized seizures, psychosis, delirium
Cardiovascular system	Mild ECG‡ changes (QTc† >390 ms ♂, >440 ms ♀; extra systoles, right bundle branch block)	Moderate ECG changes (QTc >430 ms ♂, >485 ms ♀; AV¶ block I° and II°)	AV¶ block III°, life-threatening ventricular dysrhythmias
	Tachycardia (100–139 bpm)	Tachycardia (140–179 bpm)	Tachycardia (>180 bpm)
	Hypotension (80–100 mmHg)	Hypotension (55–79 mmHg)	Hypotension (<55 mmHg)
		Bradycardia (40–50 bpm)	Bradycardia (<40 bpm)
Gastrointestinal tract	Vomiting, nausea, occasional diarrhea, pain	Pronounced or prolonged vomiting, prolonged diarrhea, pain, ileus, intestinal atonia	Bloody diarrhea, perforations
Skin	Erythema	Burns grade 2a–b, small surface	Burns grade 2b–3, or grade 2b large surface
Eyes	Conjunctivitis	Corneal erosion, corneal inclusions	Corneal lesion of large size or permanent nature

*Glasgow Coma Scale; †QT interval corrected for heart rate; ‡electrocardiogram; ¶atrioventricular.

written follow-up information was provided in 1900 cases (4.5%). Of these, 586 (30.8%) were asymptomatic and 805 (42.3%) were mild cases, while 80 (4.2%) could not be classified. Thus, in total, 1471 (77.4%) cases were not included in the study. Of the remaining 429 cases (364 moderate, 57 severe, and 8 fatal), 158 moderate, 12 severe, and 4 fatal cases had to be excluded because of insufficient causality, leaving 255 cases (206 moderate, 45 severe, and 4 fatal), which were further analyzed. The demographic characteristics of these patients were 147 (57.6%) males and 95 (37.3%) females. In 13 cases, gender was not specified. The age of the patients ranged from 2 months to 94 years, with a mean of 28 years and a median of 22 years. Children were involved in 58 (22.8%) cases. In 26 cases, age (in years) could not be determined, but the attribution to an age group (child/adult) was possible.

Forty-seven different plants were responsible for the acute moderate, severe, or lethal poisonings observed in this study. *Datura* (also known as *Brugmansia*) *suaveolens* and *stramonium* (Angel's Trumpet and Jimsonweed) were at the top of the list with 75 (29.4%) cases, followed by *Atropa belladonna* with 31 (12.2%), *Euphorbia* with 24 (9.4%), and *Heracleum mantegazzianum* with 17 (6.7%) cases.

Symptoms observed in moderate, severe, and fatal poisonings

We could determine five groups of plants as being responsible for moderate, severe, and lethal outcomes: plants of abuse (with anticholinergic properties), cardiotoxic plants, plants with mitosis-inhibiting properties, plants with gastrointestinal toxicity, and plants with skin or eye toxicity.

The most frequently reported symptoms for the 116 patients who ingested plants of abuse (*Datura* sp., *A. belladonna*, and *Argyreia nervosa* as the most common) were mydriasis (88 cases, 75.8%), hallucinations (75 cases, 64.6%), and tachycardia (71 cases, 61.2%). The most commonly observed symptoms in the 19 patients who ingested cardiotoxic plants (e.g. *Aconitum napellus*, *Taxus baccata*, *Veratrum album*, *Nerium oleander*, *Laburnum anagyroides*, and *Helleborus viridis*) were vomiting (15 cases, 78.9%), hypotension (8 cases, 40.1%), and bradycardia and arrhythmias (7 cases each, 36.8%). The six patients having ingested the mitosis-inhibiting plant, *Colchicum autumnale*, most frequently showed vomiting (5 cases, 83.3%), diarrhea, elevation of serum alkaline phosphatase (3 cases each, 50%), disturbances of blood coagulation and metabolic acidosis (2 cases each, 33.3%). Of the 53 patients who were exposed to plants with phototoxic or direct irritant effects (such as *Euphorbia* sp., *H. mantegazzianum*, and *Dieffenbachia* sp.), skin and corneal lesions were observed in 29 (54.7%) and 26 (49%) cases, respectively. The most common symptoms reported in the group of 59 patients who ingested plants with gastrointestinal toxicity (*Cucurbita pepo*, *Phaseolus vulgaris*, *Wisteria floribunda*, *Allium ursinum*, *Ricinus communis*, *Phytolacca americana*, and *Lycopodium clavatum* as the most frequent) were vomiting (38 cases, 64.4%) and diarrhea – bloody in some cases – (26 cases, 44.1%).

Of the 255 cases analyzed in this study, 250 (98%) had a full recovery, one (0.39%) developed permanently impaired visual acuity (after ocular exposure to corrosive *Euphorbia* plant sap), and four cases (1.57%) were fatal.

Outcome

All 206 patients with moderate symptoms required medical care but could be discharged without sequelae. Despite the fact that data on the length of hospitalization were not available in all cases (no information in 33 cases), patients with moderate symptoms could be discharged after a maximum of 12 days, with a median hospitalization time of 1 day (mean = 1.9 days). Eighty moderate cases did not

Table 2. Fifty most frequent plant genera, unspecified berries, and unspecified plants involved in human contact cases with potentially toxic plants.

Plant genus	Cases	Adults	Children	Accidental	Abuse	Suicidal
Prunus	2966	207	2756	2962	1	3
Ficus	1801	126	1675	1795	1	3
Taxus	1750	232	1513	1678	5	61
Euphorbia	1515	687	822	1497	9	9
Convallaria	1282	168	1108	1272		7
Lonicera	988	23	965	985		
Cotoneaster	941	14	926	941		
Physalis	840	88	752	839	1	
Datura	698	490	205	371	290	30
Mahonia	691	8	683	690		
Solanum	675	159	514	672		3
Ligustrum	634	14	620	632		1
Hedera	628	53	574	625	1	2
Sambucus	576	169	401	575		1
Sorbus	535	27	508	529		4
Dieffenbachia	519	108	408	517		2
Allium	464	374	72	463		1
Viburnum	448	33	415	446		
Viscum	426	19	406	421		1
Cornus	364	20	343	362		
Ilex	361	38	323	359		2
Phaseolus	358	160	190	358		
Nerium	353	108	244	333	3	17
Capsicum	351	200	150	351		
Zamioculcas	349	16	333	349		
Spathiphyllum	344	8	336	344		
Cucurbita	330	261	66	330		
Narcissus	330	114	178	330		
Atropa	315	159	156	213	69	29
Thuja	303	69	234	293	3	3
Tulipa	292	63	224	290		2
Yucca	290	27	263	290		
Pyracantha	281	62	219	280		1
Duchesnea	240	25	215	240		
Colchicum	231	127	99	212		8
Heracleum	218	130	87	217		
Euonymus	207	16	191	201	1	5
Berberis	186	48	134	183		1
Muscari	186	10	174	185		
Crocus	181	24	157	174		7
Quercus	174	14	160	174		
Aesculus	168	36	132	168		
Schefflera	167	7	159	166		
Ranunculus	163	18	145	162		
Wisteria	155	17	138	155		
Parthenocissus	154	7	147	154		
Epipremnum	154	6	148	153		
Symphoricarpos	153	1	152	153		
Berries unspecif.	3346	118	3228	3319		5
Plants unspecif.	1419	334	1082	1360	33	11
Total	30499	5240	25177	29770	417	219

require hospitalization and could be discharged after treatment as outpatients. The length of hospitalization for severe and lethal cases was similar (information about length of stay available for 43 out of 49 severe and fatal cases) and ranged between ambulatory visits (2 cases) to a stay of 8 days (one case) with a median hospitalization time of 2 days (mean=2.2 days).

The ranking of plants causing moderate symptoms is shown in Table 3. The severe and fatal cases are listed in detail in Table 4 with information about responsible plants, symptoms, treatments, and outcome.

Fatal cases

All fatal poisonings were caused by plants with cardiotoxic or mitosis-inhibiting effects. A nearly 3-year-old boy died of cardiac, respiratory, and hepatic failure after ingestion of *C. autumnale* (colchicine serum concentration 7 µg/l,

Table 3. Plants mostly responsible for moderate symptoms.

Latin name	Common name	No. of cases
Datura suaveolens	Angel's Trumpet	36
Atropa belladonna	Deadly nightshade	26
Euphorbia sp.	Euphorbia	22
Heracleum mantegazzianum	Giant Hogweed	16
Datura stramonium	Jimson Weed	15
Cucurbita pepo	Pumpkins	11
Phaseolus sp.	Beans	6
Argyreia nervosa	Hawaiian Baby Woodrose	5
Allium ursinum	Bear's Garlic	4
Ricinus communis	Castor bean	4
Wisteria floribunda	Wisteria	4
Taxus baccata	Yew	4
Datura sp.	Datura	3
Colchicum autumnale	Meadow saffron	3
Daphne mezereum	Daphne	3
Phytolacca americana	Pokeweed	3
Lycopodium	Club Moss	3
Cactaceae	Cactus	3
6 different plants		2
25 different plants		1

toxic >5 µg/l). Another fatal ingestion of *C. autumnale* occurred in a 62-year-old man, who had mistaken it for *A. ursinum* (wild garlic). He initially developed gastrointestinal symptoms (prolonged vomiting, diarrhea) and subsequently died of acute renal failure, coagulopathy, and myocardial necrosis. The third lethal *Colchicum* poisoning, also due to confusion of *A. ursinum* with *C. autumnale*, concerned a 57-year-old woman presenting with profuse diarrhea, vomiting, respiratory failure due to pulmonary edema, hepatic failure, acute kidney injury, subsequently developing severe hypotension and asystole. The last fatal case was due to the ingestion of the cardiotoxic plant *T. baccata* in a 43-year-old woman, who had deliberately ingested an unknown amount of the *Taxus* needles and presented with vertigo. She refused all decontamination measures and quickly deteriorated, showing alteration of consciousness and circulatory failure due to dysrhythmias (bradyarrhythmias, torsades de pointes, and asystole).

Circumstances of exposure

Accidental exposure

Of the 255 cases included in the study, 134 (52.5%) were due to accidental exposure: 81 concerned adults (41.1% of the 197 adult cases) and 53 concerned children (91.4% of the 58 paediatric cases). Most frequently, adults either had accidental dermal or ocular contact with *Euphorbia* sp. (18 cases, 23.4%) or accidentally ingested *C. pepo* (12 cases, 15.6%), *A. belladonna* (6 cases, 7.8%), and *A. ursinum* and *Phaseolus* sp. (4 cases each, 5.2%). Children either had accidental dermal contact with *H. mantegazzianum* (14 cases, 26.4%) or accidentally ingested *Datura* sp. (8 cases, 15.1%), *Euphorbia* sp. (6 cases, 11.3%), and *A. belladonna*, *Phaseolus* sp., and *W. floribunda* (each 4 cases, 7.5%).

Abuse

Of the 255 poisonings included in this study, 103 cases (40.4%) concerned abuse by consumption of plants: 98 adults (49.7%) but only 5 children (8.6%) presented to a healthcare facility with moderate to severe symptoms following abuse by ingestion. The five symptomatic children were mostly in their mid-teens (all were 15, with one exception of a 12-year-old boy) and all had ingested *Datura* sp. Adults most commonly ingested *Datura* sp. (53 cases, 51.4%), *A. belladonna* (9 cases, 8.7%), and *A. nervosa* (4 cases, 3.9%). Other plants consumed for abuse included *Mandragora officinalis* (2 cases) and *Hyoscyamus niger*, *Ipomoea* sp., and *Papaver somniferum* (1 case each). See Fig. 1 for an overview of *Datura* and *Atropa* ingestion analyzed by gender, age, and plant, irrespective of situation and severity of symptoms.

Suicidal intention

Of the 255 poisonings included in this study, 18 (7.1%) adult patients were brought to the emergency department after intentional self-poisoning with toxic plants. Five (27.7%) cases of ingested *A. napellus* led the ranking, closely followed by *T. baccata* in four (22.2%), and *A. belladonna* in three (16.6%) cases.

Discussion

This study is a follow-up project after the first large plant poisoning study in Switzerland.[19] In the current study, plant exposures were only rarely responsible for major symptoms, considering the large number of enquiries. Most often, exposure was accidental and thus, since it can be supposed that only small quantities of plant material were ingested, outcomes were mostly asymptomatic or mild, and the patients experienced a full recovery even in cases with moderate or severe symptoms (with one exception of permanent visual impairment after ocular contact with highly irritating *Euphorbia* plant sap). However, since small doses of highly toxic plants can suffice for severe symptoms,[8] severe and fatal poisonings could also be observed in the accidental setting, as confirmed by the three fatal poisonings after accidental ingestion of *C. autumnale*. Our observations are compatible with those reported in the literature.[19–25]

Overall, most enquiries concerned children. In pediatric plant ingestions, unidentified berries and plants prevail, the reason for this being that identification was not forced if highly toxic plants (such as *Atropa*, *Aconitum*, *Nerium*, and *Colchicum*) could be excluded by description and no major symptoms were observed or expected. In recent years, electronic devices have helped to simplify the process of plant identification. For example, in some of our cases, a picture by digital camera or cellular phone was sent by e-mail or MMS to the poison center and was then identified by a qualified person, as has been previously described.[28]

There were remarkable differences in the pattern of plant poisoning depending on the circumstances of exposure (accidental or intentional by abuse or attempted suicide): in accidental poisoning, which was the most frequent type of exposure to potentially toxic plants in both genders

Table 4. Cases with severe and lethal outcomes.

Age in years (if not otherwise stated)	Plant	Symptoms	Treatment	Causality	Outcome
Adult	*Euphorbia* sp.	Extensive corneal lesion	Contact lens, Neosporin eye drops	Probable	Recovery
47	*Euphorbia* sp.	Corneal lesion	Ofloxacine drops	Probable	Impaired visual acuity
39	*Prunus spinosa*	Suspected vasovagal reaction with bradycardia and hypotension	Steroids, antihistaminics	Probable	Recovery
Child	*Heracleum mantegazzianum*	Photodermatitis (legs, arms, face)	None	Probable	Recovery
2 months	*Illicium anisatum*	Seizures, nystagmus	None	Confirmed	Recovery
52	*Cucurbita pepo*	Hemorrhagic diarrhea	Metoclopramide, hydration	Probable	Recovery
72	*Cucurbita pepo*	Massive bloody diarrhea	Hydration	Probable	Recovery
30	*Phaseolus* sp.	Massive vomiting and diarrhea	Hydration	Probable	Recovery
44	*Phaseolus* sp.	Massive vomiting and diarrhea	Hydration	Probable	Recovery
1.5	*Atropa belladonna*	Apathy, tachycardia	Physostigmine, activated charcoal	Probable	Recovery
3	*Atropa belladonna*	Vomiting, tachycardia	Physostigmine, activated charcoal	Probable	Recovery
34	*Atropa belladonna*	Agitation, mydriasis, tachycardia	Physostigmine, benzodiazepines	Probable	Recovery
35	*Atropa belladonna*	Agitation, mydriasis, tachycardia	Physostigmine, activated charcoal	Probable	Recovery
65	*Atropa belladonna*	Mydriasis, psychosis, dry skin	None	Probable	Recovery
18	*Datura* sp.	Delirium, mydriasis, tachycardia	Benzodiazepines	Probable	Recovery
3	*Datura suaveolens*	Mydriasis, hallucinations, tachycardia, agitation	Activated charcoal, benzodiazepines	Probable	Recovery
4	*Datura suaveolens*	Mydriasis, hallucinations, tachycardia, agitation	Benzodiazepines	Probable	Recovery
17	*Datura suaveolens*	Hallucinations, seizures, mydriasis, paralytic ileus, RBBB	Benzodiazepines, physostigmine	Probable	Recovery
17	*Datura suaveolens*	Agitation, urine retention, tachycardia	Physostigmine	Probable	Recovery
17	*Datura suaveolens*	Delirium, mydriasis, tachycardia	Physostigmine, benzodiazepines	Probable	Recovery
18	*Datura suaveolens*	Agitation, hallucinations, tachycardia	Physostigmine, benzodiazepines	Probable	Recovery
18	*Datura suaveolens*	Hallucinations, agitation, disorientation, mydriasis	Activated charcoal, benzodiazepines	Probable	Recovery
18	*Datura suaveolens*	Hallucinations, agitation, dyspnea	Physostigmine, benzodiazepines	Probable	Recovery
20	*Datura suaveolens*	Hallucinations, agitation, disorientation, mydriasis	Benzodiazepines, physostigmine	Probable	Recovery
21	*Datura suaveolens*	Severe agitation, mydriasis	Benzodiazepines, physostigmine	Probable	Recovery
21	*Datura suaveolens*	Agitation, mydriasis, tachycardia, delirium	Physostigmine, benzodiazepines	Probable	Recovery
22	*Datura suaveolens*	Severe agitation, mydriasis, hallucinations	Physostigmine, haloperidol	Probable	Recovery
26	*Datura suaveolens*	Agitation, hallucinations, tachycardia	Physostigmine, benzodiazepines	Probable	Recovery
Adult	*Datura suaveolens*	Bradycardia, mydriasis, delirium	None	Probable	Recovery
Adult	*Datura suaveolens*	Somnolence, respiratory depression	Activated charcoal, intubation	Probable	Recovery
14	*Datura stramonium*	Confusion, tachycardia, mydriasis	Physostigmine	Probable	Recovery
17	*Datura stramonium*	Agitation, tachycardia	Physostigmine, benzodiazepines	Probable	Recovery
20	*Datura stramonium*	Mydriasis, hallucinations, tachycardia, confusion	Prostigmine, benzodiazepines	Probable	Recovery
23	*Datura stramonium*	Severe hallucinations, mydriasis	Benzodiazepines	Probable	Recovery

(Continued)

Table 4. (*Continued*).

Age in years (if not otherwise stated)	Plant	Symptoms	Treatment	Causality	Outcome
32	*Datura stramonium*	Mydriasis, hallucinations, agitation	Physostigmine	Probable	Recovery
18	*Mandragora officinalis*	Coma, anticholinergic syndrome	None	Probable	Recovery
20	*Ipomoea purpurea*	Panic	Benzodiazepines	Probable	Recovery
41	*Nerium oleander*	Bradycardia, SA block, vomiting	Activated charcoal	Confirmed	Recovery
25	*Aconitum napellus*	Paresthesias, GI symptoms, bradycardia, urinary retention	Atropine	Probable	Recovery
36	*Aconitum napellus*	Hypotension, ventricular tachycardia, paresthesias	Multiple dose-activated charcoal, lidocaine, magnesiumsulfate	Probable	Recovery
47	*Aconitum napellus*	Ventricular fibrillation, bigeminus, hypotonia, vomiting	Defibrillation, magnesiumsulfate	Confirmed	Recovery
69	*Aconitum napellus*	Agitation, repetitive ventricular tachycardia, hypothermia, arrhythmia	Multiple dose-activated charcoal, defibrillation, amiodarone	Probable	Recovery
Adult	*Aconitum napellus*	Seizures, vomiting, bigeminus, ventricular fibrillation	Magnesiumsulfate, catecholamines	Probable	Recovery
45	*Veratrum album*	Bradycardia, hypotension	None	Probable	Recovery
59	*Veratrum album*	Diarrhea, vomiting, hypotension, bradycardia	Activated charcoal, supportive therapy	Probable	Recovery
44	*Taxus baccata*	Tachycardia, bradycardia, AV block III°, asystole	Activated charcoal, atropine, magnesium, catecholamines, pacemaker, defibrillation	Probable	Fatal
3	*Colchicum autumnale*	Bradycardia, cerebral edema, vomiting, seizures, respiratory and hepatic failure	Supportive therapy	Confirmed	Fatal
57	*Colchicum autumnale*	Pulmonary edema, arrhythmia, coagulopathy, renal failure	Multiple dose-activated charcoal, supportive therapy	Confirmed	Fatal
62	*Colchicum autumnale*	Renal failure, necrosis of the heart muscle, coagulopathy	Multiple dose-activated charcoal, supportive therapy	Confirmed	Fatal

RBBB: right bundle branch block; SA block: sinoatrial block; AV block: atrioventricular block; GI symptoms: gastro-intestinal symptoms.

and typically concerned children, unidentified berries of all colors, and identified berries (*Prunus*, *Taxus*, *Convallaria*, and *Lonicera* among others), were most frequently involved, indicating that berries pose a great temptation to children. Typical routes of accidental exposure are ingestion or eye or skin contact. The immaturity of ingested berries has been described as a cause for major gastrointestinal symptoms.[7] Another way of accidental poisoning, more frequent in adults, is the ingestion of raw beans or ornamental gourds with subsequent vomiting and diarrhea, sometimes hemorrhagic.[29,30]

Abuse of plant parts ranked second in frequency, both in men and women, with *Datura* sp. being the most frequently involved. Typical patients were adolescents and young adults, with a clear male predominance, which is in accordance with previous studies on common drugs of abuse.[31] Social and cultural factors, e.g. educational background, unemployment, and ethnicity,[32] may at least partially explain the observed differences between genders. In some cultures, Solanaceae have been used to induce hallucinations for rituals or as herbal medications for over 4000 years.[33] Also, even though it is now more socially acceptable for girls and women to consume drugs,[34] with a clearly decreasing mean age for first contact, young men still have much easier access to drugs of abuse than women do.[35]

Other than in accidental exposure, the ingestion of plants with suicidal intent was exclusively performed by adult patients and concerned two groups of plants: those with cardiotoxic effects such as *N. oleander*, *A. napellus*, or *T. baccata*, and those with mitosis-inhibiting properties such as *C. autumnale*. However, fatal outcome after deliberate self-poisoning with plants was rare in our study. By contrast, this is a significant problem in some developing parts of the world, e.g. South Asia, where the ingestion of *Thevetia peruviana* (Yellow Oleander) seeds with suicidal intent results in significant morbidity and mortality.[15,18,36]

The frequencies of the three circumstantial settings of exposure – accidental as the most frequent, followed by deliberate abuse and suicidal intent – is in accordance with the findings in another study.[23]

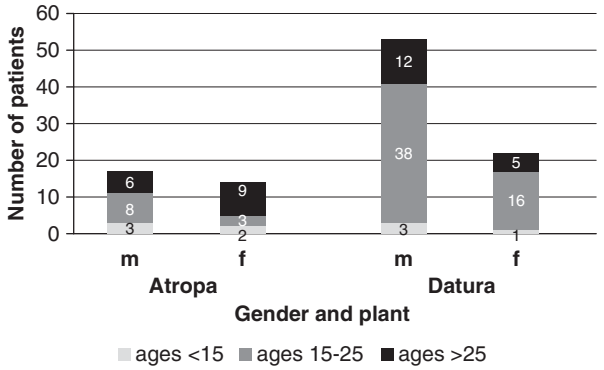

Fig. 1. Intoxications due to ingestion of *Atropa belladonna* and *Datura* sp.

Although the number of plant species and genera that the patients in our study were exposed to is vast, we were able to identify three main mechanisms of toxicity responsible for the most serious effects: anticholinergic properties, mitosis inhibiting, and cardiotoxic effects. Plants with anticholinergic effects – the Solanaceae family, including *Datura* sp. and *A. belladonna* being most frequently involved – were most commonly ingested for deliberate abuse. The symptoms observed in these patients were typical, with a predominance of tachycardia, mydriasis, and hallucinations.[10,37] The mitosis-inhibiting plant, *C. autumnale*, was responsible for three out of four of our lethal cases, causing a syndrome of multi-organ failure due to the direct toxic effect of colchicine on tissues with rapid cell turnover, including gastrointestinal mucous membranes and the bone marrow.[5,9,38] Colchicine poisoning has a high morbidity and mortality, and accidental ingestion of *C. autumnale* leaves is unfortunately a common problem due to possible confusion with *A. ursinum*.[5] Plants with cardiotoxic effects were responsible for one fatal (with *T. baccata*) and multiple severe cases in this study. The leading symptoms observed in these patients, such as bradycardia and asystole,[13,33,38] are mainly due to two mechanisms: first, the inhibitory effect exerted by different alkaloids (e.g. aconite, protoveratrine [from *V. album*], cardenolides [oleandrine], cytosine [from *Laburnum*] or helleborine) on cellular sodium and potassium transport by binding to the Na,K-ATPase with consequently decreased resting potential of the cardiomyocytes and resulting proarrhythmogenic effect, and second, the blockage of sodium and calcium channels in cardiac myocytes, which has a negative inotropic effect.[37,39]

Plants with moderate phototoxic or direct irritant effects, such as *H. mantegazzianum* and *Euphorbia* sp., and plants causing mainly gastrointestinal toxicity like raw beans or ornamental gourds, were often ingested accidentally. The main pathophysiological mechanism for the plants causing skin and corneal lesions is a direct irritant effect. However, *H. mantegazzianum* deserves separate consideration, as its furocoumarines have only a minor direct effect, but may cause severe phototoxic reactions in combination with UV light of a wavelength of 320–365 nm because of binding to the cellular DNA, which leads to a light-dependent destruction of the cell membranes.[15,40] The group of plants with gastrointestinal toxicity due to direct irritant effects on the gastrointestinal tract mucosa had the greatest variety of different species.

A recent German study[23] identified the greatest endangering potential (likelihood for major symptoms after contact) for children to be plants like *Brugmansia suaveolens* (*Datura suaveolens*, Angel's Trumpet), *L. anagyroides*, *P. vulgaris*, and *Thuja occidentalis*. This is in good accordance with our pediatric cases where we found that *Heracleum*, *Datura*, *Phaseolus*, *Euphorbia*, *Wisteria*, and *Atropa* were the plants most frequently responsible for major toxicity, whereas *L. anagyroides* (two cases) and *T. occidentalis* (one case) only caused moderate symptoms in our patients. The most frequent plant genera in human exposure that were identified in our study matched the frequency of plant genera in the German study, the list being headed by *Prunus*, *Ficus*, and *Taxus*, even though the order was slightly different. The plant species we identified as being frequently involved in cases of human poisoning are similar to those reported in the previous study performed in Switzerland.[19]

Average length of hospital stay was short – about 2 days – even in severe plant poisoning. However, length of stay is not always a good measure of severity, and information about hospitalization time was lacking in many cases, and in others it was difficult to precisely determine, because the number of hospitalization days sometimes included not only the time in the acute hospital setting, but also the stay in psychiatric wards for suicidal patients. Other patients were discharged before complete recovery.

Our study has several limitations. First, data from poison centers are considerably subject to reporting bias. In addition, the interpretation of our findings is limited by the retrospective analysis of cases despite the systematic prospective data collection. The treating physicians may not have mentioned all symptoms or laboratory data from their patients, and underreporting of cases with no or only minor toxicity likely occurred. Furthermore, laboratory confirmation was not available in most cases. However, to minimize misclassification in case of missing laboratory data, we included only cases where the causal relationship between plant exposure and clinical effect was at least likely. Another important limitation is the difficulty in determining the quantity of toxin the patient had been exposed to, because leaves or seeds of the same plant species may contain variable amounts of toxins, depending on vegetation period, soil, exposure to light, and age of the plant. Finally, determination of the anatomical part of the plant that the patient had been in contact with was often not possible.

Our strict inclusion/exclusion criteria, in particular the decision to only include mono-intoxications and to exclude industrially processed plant materials (e.g. phytomedicines, industrial botanical ingredients and foodstuffs, *N. tabacum*, and *C. sativa*), led to small case numbers. However, we are convinced that these restrictions were necessary in order to be able to interpret the findings properly, in particular because in most cases we were not able to obtain analytical confirmation through detection of plant toxins. Similar limitations applying to poison center data have been previously described.[41]

Conclusions

Despite the heterogeneity of the plants and patients included in this study, we could establish three groups of plants (anticholinergic, cardiotoxic, and mitosis inhibiting) that are mostly responsible for severe poisoning, and the symptoms shown by the patients were characteristic for the corresponding plant species. In view of the high number of exposures with plants that showed only mild symptoms, and the very few cases with severe symptoms, serious poisoning from plants seems to be a very rare event in Switzerland. Nevertheless, even accidental ingestions can be responsible for fatal poisonings. In most cases, long-term follow-up and monitoring is unnecessary, because a full resolution of symptoms with no substantial sequelae can be expected within a short time.

Declaration of interest

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