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Characteristics of emergency department presentations following ingestion of *Taxus baccata* (yew)

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ABSTRACT

Objective: Presentations of *Taxus baccata* (yew) poisoning can range between asymptomatic cases and life-threatening cardiotoxicity – depending on the amount ingested. This study aimed to describe emergency department (ED) presentations after yew exposure, and covers their clinical presentation, diagnostic and specific treatment, to contribute to optimising intreatment and prophylaxis.

Methods: Retrospective observational study of cases (\geq 16 years of age) presenting at the ED of the University Hospital of Bern, Switzerland, from 1 May 2012 to 31 May 2020 following reported yew exposure. Cases were retrieved from the electronic patient database using full-text terms.

Results: During the study period, 55 presentations (11 patients) of the 350,381 ED attendances were included. All patients were female and the median age on first presentation was 22 years (range 16–48). All 10 patients with intentional intake had previous diagnoses of psychiatric disorders. Commonly reported symptoms on presentation were gastrointestinal disturbances (31 presentations, 56%), neurological (six presentations, 11%) and subjective cardiovascular symptoms (five presentations, 9%). The most frequent clinical findings on presentation were tachycardia (15 presentations, 27%) and hypotension (11 presentations, 20%). In 52 presentations (95%), gastroscopic extraction of the leaves was performed, activated charcoal was administered in 25 cases (45%), and there were no fatalities. In the majority of the cases (40, 73%), the patient was admitted to psychiatric care and in 10 (18%) the patient was discharged home.

Conclusion: ED presentations after yew exposure appear to be rare, but potentially life-threatening and commonly observed in this study in young female patients with underlying psychiatric diseases. In this case series, gastroscopic extraction and activated charcoal application were commonly performed and there were no fatalities.

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Taxus baccata; yew; taxines; emergency department; poisoning

Introduction

Taxus baccata (European or English yew) (Figure 1) is a toxic conifer plant found in many parts of Europe. Next to accidental intoxication, poisoning cases also occur in the context of a suicidal attempt, most commonly among young people [1] and between 1995 and 2009 *Taxus baccata* was one of the most common causes of intoxication with toxic plants that led to contact with the Swiss Poisons Information Centre [2].

The toxicity of *Taxus baccata* is mediated by two major taxine alkaloids, taxine A and taxine B, that are mainly present in all parts of the plant with the exception of the berries [1,3–7]. The cardiotoxic effects are mostly induced by taxine B and presentations following ingestion can range between asymptomatic cases and life-threatening cardiotoxicity [5,8]. Ingestion of about 50–100 g yew leaves (corresponding to 0.6–1.3 g yew leaves/kg body weight, or 3–6.5 mg taxines/kg body weight, or more than 100 leaves) can be lethal [4,6,9]. However, the exact lethal dose is unknown. The amount of

the taxines absorbed can vary with several factors, including the preparation of the material (higher if leaves minced or mashed before ingestion than with untreated leaves) as well as the season of the year (higher taxine concentrations in the plant during winter) [4,10]. First signs of intoxication can be non-specific, such as nausea, emesis and abdominal pain [4]. In severe intoxications, cardiotoxicity can occur, mediated through inhibition of sodium and calcium channels, with potentially fatal outcome [5,6,8,9]. The diagnosis is mainly based on the patient's history or identification of leaves in the gastrointestinal tract, while detection of specific alkaloids with mass spectrometry can also be used for confirmation [1,6,11]. Treatment is focused on decontamination measures and supportive care, and there is no known antidote available [4,12].

The aim of this study was to describe the frequency, clinical symptoms, diagnostic and specific therapeutic measures in cases presenting at a large urban emergency department (ED) in Bern, Switzerland, following exposure to *Taxus*

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Figure 1. Taxus baccata (yew). © Jolanta Klukowska-Rötzler.

baccata and with the aim to identify risk groups and optimise treatment strategies and prophylactic measures.

Materials and methods

Retrospective observational study of patients presenting at the ED of the University Hospital of Bern, Switzerland, after reported exposure to *Taxus baccata* between 1 May 2012 and 31 May 2020. The ED of the University Hospital of Bern serves both as a primary care facility (walk-in patients) and a tertiary referral centre in the greater Bern area, with approximately 51,800 emergency presentations a year (2021). The study was approved by the local ethics committee (No. 2020-02816).

Included in this case series were patients \geq 16 years of age presenting to the ED after intentional or accidental exposure to *Taxus baccata*. Excluded were patients < 16 years of age, patients who had rejected the hospital's general consent for processing medical data for research purposes, patients presenting for a follow-up after previous intoxication with *Taxus baccata* and not due to current intoxication, and cases with insufficient information available for a correct assessment (e.g. patients who left the ED before being seen by the medical staff).

The cases were extracted from the ED electronic patient database E.care (E.care BVBA, Turnhout, Belgium) using the German word for "yew" as search term. The extracted cases were reviewed by two authors of the study. The following parameters, if available, were extracted from the patient's electronical health records: Sex, age, co-morbidities, co-ingestion of other substances, latency between reported ingestion and presentation, form of exposure (intentional or

Table 1.	Principle	characteristics	of	presentations	due	to	acute	exposure	to
Taxus baccata (55 presentations total).									

Presentation characteristics	n (%)
Intentional intake	54 (98)
Recurrent event	46 (84)
Presentation with ambulance	48 (87)
Admission directly to trauma room	33 (60)
Location of care	
Emergency Department only	41 (75)
Intensive Care Unit (ICU)	14 (25)
Disposition	
Discharged home	10 (18)
Discharged to psychiatric care	40 (73)
Secondary discharge from ICU not documented	5 (9)

unintentional), reported amount and part of the plant ingested, reported symptoms, electrocardiogram (ECG), vital signs and laboratory values on presentation, findings of gastroscopy, specific treatment provided, disposition and outcome. We recorded data using Microsoft Excel. Correlations were investigated with the Spearman's non-parametric correlation test using the SPSS statistical software (IBM SPSS Statistics 28.0.1.1).

Estimates of the ingested yew leaves amount were taken from the electronic database if reported as numbers. In case of information in text form, we converted "a handful" to \sim 200 yew leaves (3 g) to allow for calculations. Although the accuracy and reproducibility of this estimate have not been tested, this approach has also been used by the Swiss poison centre. For the number of leaves recovered by gastroscopy, the estimates documented in the gastroenterologist's report were used. We compared the first recorded vital signs in the ED to normal ranges (systolic blood pressure of 100 to 140 mmHg, diastolic blood pressure of 60 to 90 mmHg, heart rate of 60 to 100 beats/minute, respiratory rate 12 to 20 breathes/minute). We defined a body temperature $< 35 \,^{\circ}C$ as hypothermia and $> 38 \,^{\circ}$ C as hyperthermia. For laboratory values, we used the reference ranges of the hospital's laboratory. In some cases, toxicological screening was performed using a urine immunoassay (Triage® TOX Drug Screen, Alere) for paracetamol, amphetamines, barbiturates, benzodiazepines, cocaine, methadone, opiates, phencyclidine, tricyclic antidepressants, and tetrahydrocannabinol (THC).

Results

During the study period, a total of 350,381 ED attendances were registered, including 57 presentations related to acute *Taxus baccata* exposure. We excluded two visits for lack of consent for data use. Thus, 55 presentations were included in the analysis, corresponding to 11 patients. Three of the 11 patients presented more than once: One patient accounted for 36 presentations, one patient for 9 presentations, and one patient for 2 presentations.

From the 55 included presentations, only one was an accidental exposure, while 54 (98%) were intentional in the context of self-poisoning. Co-ingestants in four cases included alcohol, paracetamol, quetiapine, both paracetamol and quetiapine (one case each). In one case, strangulation was also used as suicidal method. All patients were female and the median age on the first presentation was 22 years (range 16–48). The principle characteristics of all presentations are summarised in Table 1.

Among the ten patients with intentional ingestion (54 presentations), all had at least one documented psychiatric disorder. Most frequent were borderline personality disorder (six), post-traumatic stress disorder (three), major depressive disorder (two), eating disorders (two), and emotionally unstable personality disorder (two). All ten patients were under medication with one or multiple drugs, including neuroleptics (30 presentations, seven patients), benzodiazepines (16 presentations, five patients), antidepressants (15 presentations, seven patient), and methylphenidate (three presentations, one patient).

Ingestion of yew leaves was reported in all 49 presentations with available information on the part of the plant ingested (89%), with additional ingestion of berries in two presentations. In the only presentation of accidental exposure, the patient reported that a yew leaf fell into her beverage. In 41 presentations with available ingestion history, the median estimated ingestion was 150 leaves (range 7–1000). Reported symptoms, vital signs and laboratory disturbances on presentation are presented in Table 2. For the patient presenting 36 times, the estimated amount ingested (reported in 33 cases) ranged between "a tablespoon" and "five handfuls", the range of the estimated amount recovered by gastroscopy (performed in 35 cases) was 0 (six cases) to 150 leaves. In ten presentations, the patient was treated at the intensive care unit (ICU) and was discharged to psychiatric care in 27 presentations.

An ECG was performed on presentation in 29 of the 55 presentations (53%). Three cases had documented ECG abnormalities. One case each had wide QRS and abnormal T-wave with QT interval prolongation. The third case with severe polymorphic ventricular tachyarrhythmia after the reported ingestion of \approx 150 yew leaves within a 3 h interval. This developed into cardiac arrest during gastroscopy (performed approximately 5 h after last reported ingestion). In this case only a few yew leaves were found, but visibility was poor due to prior administration of activated charcoal, and spontaneous circulation (ROSC) was recovered after cardiopulmonary resuscitation (CPR). Four cases had cardiac abnormalities observed during gastroscopy between 3 and 6 h post-ingestion. These included third degree AV block (Table 3), sinus pause (< 2 sec) at \sim 6 h (>60 pieces extracted), sinus bradycardia (20 beats/minute) at \sim 5.5 h (>60 pieces extracted), and sinus tachycardia (120 beats/

Table 2. Reported symptoms, clinical findings and laboratory pathologies on presentation of cases presenting due to acute exposure to *Taxus baccata* (55 presentations total).

Reported symptoms (assessed in 43 presentations)	n (%)
Asymptomatic	7 (13)
Gastrointestinal	31 (56)
Abdominal pain	23 (42)
Nausea and / or emesis	22 (40)
Neurological	6 (11)
Dizziness	4 (7)
Muscle cramping	1 (2)
Tetany	1 (2)
Cardiovascular	5 (9)
Palpitations	2 (4)
Cardiac arrest	1 (2)
Thoracic discomfort	1 (2)
Near syncope	1 (2)
Vital signs on presentation (assessment declined by the patient in 4 presentations) Blood pressure (assessed in 51 presentations)	n (%) or median (range)
Systolic (mmHg)	121 (70–158)
Diastolic (mmHg)	73 (46–117)
Hypotension	11 (20)
Hypertension	10 (18)
Heart rate (assessed in 51 presentations)	91 (65–150)
Tachycardia	15 (27)
Breathing rate (assessed in 26 presentations)	18 (14–32)
Tachypnoea	5 (9)
Body temperature (assessed in 36 presentations)	37.2 (35.4 - 37.8)
Oxygen saturation (assessed in 49 presentations)	99 (94–100)
Laboratory abnormalities	n (%), range of abnormal value
Electrolytes (assessed in 40 presentations)	
Hypokalaemia ($< 3.4 \mathrm{mmol/L}$)	7 (13), 2.7 – 3.3
Hyperkalaemia ^a (> 4.4 mmol/L)	1 (2), 5.2
Hyponatraemia (< 136 mmol/L)	1 (2), 134
Lactate (assessed in 19 presentations)	
Lactate elevated (> 2.4 mmol/L)	2, 2.5 – 6.4
oH (assessed in 10 presentations)	,
Acidosis ($pH < 7.35$)	2, 7.29 – 7.30
Positive findings of urine immunoassay (assessed in 10 presentations)	n
Benzodiazepines	7
Paracetamol	2
Tetrahydrocannabinol (THC)	1

Reported/ estimated amount of yew leaves ingested	Estimated number of gastroscopically extracted yew leaves	Latency between reported ingestion and gastroscopy	Symptoms and findings	Specific therapy/ measures	Outcome
2.5 handful (corresponding to 7.5 g / 500 pcs)	100 pcs	~2 h	Abdominal pain, flattened T wave and QT prolongation, heart rate 96 beats/minute, tox. screening positive for benzodiazepines and paracetamol	Gastroscopy followed by activated charcoal	Discharged to psychiatric care after observation at the ICU
2 handfuls (corresponding to 6 g / 400 pcs)	100 pcs	~2.5 h	Alert, assessment of vital signs and ECG declined, atrioventricular block III during gastroscopy	Gastroscopy followed by activated charcoal	Discharged to psychiatric care after observation at the ICU
100 pcs	100 pcs	\sim 7 h	Alert, heart rate 112 beats/ minute, normal ECG	Gastroscopy followed by activated charcoal	Discharged home after observation at the ED
¹ / ₂ cup	150 pcs	\sim 3 h	Abdominal pain and nausea, heart rate 120 beats/minute, normal ECG	Gastroscopy followed by activated charcoal	Discharged to psychiatric care after observation at the ED
450 pcs	100–200 pcs	$\sim 2 h$	Abdominal pain and nausea, blood pressure 124/ 64 mmHg, normal ECG	Gastroscopy followed by activated charcoal	Discharged to psychiatric care after observation at the ICU
300 pcs	300 pcs	~3 h	Abdominal pain, nausea and dizziness, alert, stable vital signs, normal ECG	Gastroscopy	Discharge from the ICU after observation unknown

ECG: electrocardiogram; ICU: intensive care Unit; Pcs: pieces. Four involving the patient with 36 presentations.

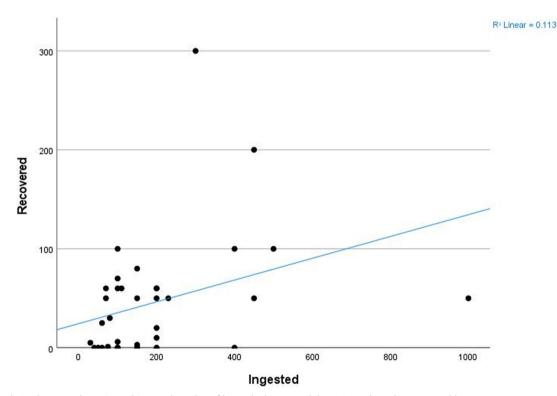


Figure 2. Correlation between the estimated ingested number of leaves by history and the estimated number recovered by gastroscopy. Higher number used if estimate given as range.

minute) at $\sim\,$ 3 h (no leaves extracted). The first three patients were treated at the ICU.

Gastroscopy occurred in 52 presentations (95%), with a median interval of 4.1 h (range 1.7 - 7.5 h) post-ingestion. Yew leaves were found in the gastrointestinal tract in 37 of 52 cases, with a median of 23 leaves and of range 0 (fifteen presentations) to 300 leaves (one presentation). A not strong positive correlation (correlation coefficient 0.41, p < 0.05) was

found between the estimated number of leaves ingested and number recovered by gastroscopy (Figure 2). Table 3 includes details of the six presentations with \geq 100 leaves found on gastroscopy (amount reported as potentially lethal [6]). Activated charcoal administration occurred in 24 presentations following gastroscopy and in one without gastroscopy (45% of total cases). Sodium bicarbonate was administered in two presentations. The patient with cardiac arrest received lipid emulsion, extracorporeal membrane oxygenation (ECMO), installation of a ventricular support device (Impella CP SmartAssist®, ABIOMED) and a temporary pacemaker.

Gastroscopy was followed by an observation period at the ICU (14 presentations) or at the ED (38 presentations). Clinical observation at the ED was the only measure in one case, with presentation 5 h after ingestion of an unknown amount of leaves, and in the one case of accidental exposure the asymptomatic patient was discharged home with no further treatment or clinical observation. There were no fatalities and the majority of the presentations were admitted to psychiatric care after observation at the ED (35) or ICU (five), or discharged home (six and four, respectively). Secondary discharge after the ICU was not documented in five cases (Table 1).

Discussion

The initial stage of yew poisoning is typically characterised by non-specific symptoms such as gastrointestinal disturbances (also most frequently reported symptoms in our presentations), mydriasis, dizziness and seizures (not reported in our study), palpitations and tachycardia, bradycardia, arrhythmias and even death as a result of cardiac failure and respiratory arrest, but many cases remain asymptomatic [4,6,9,10,13]. The onset of symptoms can be as soon as 30 min to 1 h after ingestion, with potentially lethal outcome 2 to 5 h post-ingestion [13–15].

Taxine B inhibits calcium and sodium channels of the myocardium and can produce QRS prolongation, arrhythmias, myocardial depression and asystole [4–6,8,9]. Cardiac arrest and third degree AV block each occurred in one case. Tachycardia was recorded on presentation in approximately one third of the cases, and bradycardia occurred in one case during gastroscopy. Two presentations received sodium bicarbonate. Case reports suggested beneficial effect of sodium bicarbonate regarding reversal of QRS widening and acidosis [16,17], but an experiment in swine found no effect on QRS [18]. Quetiapine and levomepromazine may have contributed to the QT prolongation in one case.

Cardiotoxic effects of *Taxus baccata* appear similar to those seen in digitalis poisoning [9], and yew alkaloids may cross-react with assays [3,19]. However, anti-digoxin antibodies are not recommended for *Taxus baccata* poisoning and were also not administered in any of our presentations. Several case reports describe their use [3,10,12,14,19–23], but other treatments confound interpretation [8,9,20,21].

Haemodialysis is ineffective for the elimination of taxines due to their pharmacokinetic characteristics (high volume of distribution, molecular weight and protein binding) [3,5,7,9]. A case report with measured taxine B concentrations before, during, and after haemodialysis corroborated its lack of effect [7]. Based on the lipophilic nature of the taxines, intravenous lipid emulsion has also been proposed [9] but case reports conflict on whether it is effective in *Taxus baccata* poisoning [9,16]. Several case reports describe successful outcomes with ECMO in severe cases [3,5,6,22–26]. However, ECMO is not always available, and possible complications include bleeding, haemolysis, disseminated intravascular coagulation, central nervous system infections and seizures [5,26,27].

Gastroscopy findings did not strongly correlate with the estimated ingestion based upon the patient histories. Fifteen presentations had no yew leaves found on gastroscopy. This may reflect transit of ingested leaves past the duodenum before gastroscopy but may also reflect unreliability of patient histories. Even among patients with larger gastroscopic recovery (Table 3), most presented with clinical signs of minor severity.

Laboratory testing for *Taxus* alkaloids is seldom available. Concentrations reported in postmortem cases vary depending on the matrix used (e.g. stomach content, urine, blood) [28]. One case series found taxines detected up to 122 h following ingestion of approximately two handfuls of leaves [10]. Some case reports described the concentration of the taxicatine metabolite 3,5-dimethoxyphenol [6,29,30], but this is also a component of other plants and fruits, which might confound its use as evidence for *Taxus* intoxication [31–33]. Therefore, the diagnosis of *Taxus baccata* poisoning mainly rests on the clinical presentation and patient history [29].

A strength of our study is the high number of included presentations. Although previous reports from the American National Poison Data System included more than 10,000 exposures [34], over 95% of these cases involved children with exploratory ingestion. This might have led to bias towards positive outcomes (more than 90% of the cases were asymptomatic) [8,34]. More severe poisoning may be more likely after intentional suicidal ingestion by adults [8]. Limitations of our study include the retrospective design with a lack of standardised data collection and the estimation of the ingested amounts as well as the estimation of recovered leaves by different gastroenterologists. Also, one patient accounted for two-thirds while another for one-seventh of the presentations. These may not be typical of other yew ingestions and may not be generalizable. Data came from a single hospital, and outcomes might not be applicable to other clinical settings or patient populations.

Conclusion

Presentations due to yew exposure appear to be rare but can lead to potentially life-threatening complications. Most patients were young women with underlying psychiatric diseases and intentional intake. The estimated ingested amount does not always predict the number of leaves found at gastroscopy. Gastroscopic extraction and activated charcoal application were the most frequent interventions. There were no fatalities.

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