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Toxalbumin exposures: 12 years' experience of U.S. poison centers

Mingzohn Ellen Kaland, Wendy Klein-Schwartz*, Bruce D. Anderson

Maryland Poison Center, University of Maryland School of Pharmacy, USA

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ABSTRACT

Background: Toxalbumins are natural plant toxins purported to be highly toxic. The purpose was to evaluate toxalbumin exposures reported to U.S. poison centers to determine plants involved and their toxicities.
Methods: A retrospective review of National Poison Data System data on acute toxalbumin exposures with known outcomes from 2000 through 2011 was performed.
Results: There were 1164 exposures. The majority involved one route (1135; 97.5%), mostly ingestions (904; 79.7%) or dermal (166; 14.3%). Most patients developed no effects (694; 59.6%) or minor effects (374; 32.1%). Moderate or major effects occurred in 8.3% with 66.6% ingestions and 23.9% dermal. There were no deaths. Exposures to the plants *Ricinus communis* and *Robinia pseudoacacia* were most common (33.8% and 32.9%, respectively), with gastrointestinal effects from *R. communis* (vomiting 19.6%, diarrhea 8.9%, nausea 7.9%) and dermal effects from *R. pseudoacacia* (puncture 28.7%, dermal irritation/pain 27.9%, and edema 13.3%).
Conclusions: While toxalbumin plant exposures were generally well-tolerated, continued evaluation of risk is warranted since plants were primarily identified by the public. Major effects occurred in under 1% of cases overall, and not at all following unintentional ingestions. These findings should help allay concerns that unintentional ingestions of toxalbumin plants by young children will cause serious toxicity and possibly death.

1. Introduction

Ricin and other toxalbumins are natural plant toxins with an impressive history of use and misuse. Ricin, a potent protein-based toxin found in the castor bean plant (*Ricinus communis*), has a notorious reputation as a potentially lethal biological weapon (Doan, 2004; Audi et al., 2005). Ricin was in the news in the U.S. in 2003 and 2013 when it was detected in mail sent to politicians (Centers for Disease Control and Prevention (CDC), 2003; http://www.fbi.gov/cleveland/press-releases/2014/akron-man-convicted-of-possessing-ricin-for-use-as-a-weapon). In both instances, there were no reported human exposures requiring medical attention. There are several case reports and one observational case series of castor bean seed ingestions (Aplin and Eliseo, 1997; Rauber and Heard, 1985; Wedin et al., 1986; Lim et al., 2009; Ferguson, 2011; Thornton et al., 2014). Based on the ricin content in the castor bean, the theoretical minimum potential lethal dose of castor beans is one bean ingested by a child (Poisindex, Truven Health Analytics, Inc).

The plant *R. communis*, also known as the castor bean plant, grows around the world. It contains the toxalbumin ricin. Castor oil which is derived from the oil contained in its seeds was used therapeutically as a laxative as well as a treatment for inflammation and infection. Other uses of castor oil include fuel for oil lamps and in industry as raw material for lubricants, paints, and cosmetic products. In general, matter from the post oil-extraction of castor bean seeds has been used as animal feed or fertilizer after detoxification (Worbs et al., 2011). Ricin is water-soluble, not expected to be found in castor bean oil, and is inactivated by heat (80 °C) (Audi et al., 2005; Worbs et al., 2011). Toxalbumins are also found in other plants such as *Robinia pseudoacacia* (black locust; contains robin and phasin), *Abrus precatorius* (jequiry bean or rosary pea; contains abrin), *Jatropha* spp. (contain ricin) and *Hura crepitans* (sandbox tree; contains hurin and crepitin).

Ricin is a glycoprotein lectin, comprised of 2 chains (A and B) linked by a disulfide bond. The B chain is responsible for receptor binding to the cell surface and entry of the toxin into cells (Doan, 2004). The A-chain subunit undermines the endoplasmic

* Corresponding author. Maryland Poison Center, University of Maryland School of Pharmacy, 220 Arch Street, Room 01-108, Baltimore, MD 21201, USA.
E-mail address: wkleinsc@rx.umaryland.edu (W. Klein-Schwartz).

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reticulum degradation pathway of misfolded proteins before being transported back into the cytosol where it halts protein synthesis by removing an adenine from the sarcin-loop of the 28S rRNA of ribosomes (Audi et al., 2005; Worbs et al., 2011). A homologous protein has been identified as the ricin communis agglutinin, a toxic constituent of *R. communis*. The agglutinin is considered to be less cytotoxic than ricin and may target red blood cells, causing agglutination and hemolysis. Because the agglutinin is poorly absorbed in the gastrointestinal system, toxicity would only be expected from parenteral exposure (Audi et al., 2005; Worbs et al., 2011).

Data on toxicity associated with toxalbumin containing plants other than castor bean are very limited. The objective of this study was to evaluate toxalbumin exposures reported to U.S. poison centers in order to determine which toxalbumin-containing plants were involved and to compare their toxicities and outcomes.

2. Methods

2.1. Study design

A retrospective review was performed for single substance toxalbumin exposures reported to the American Association of Poison Control Centers (AAPCC) National Poison Data System (NPDS) between January 2000 and June 2011. NPDS was searched for the following Poisindex (Truven Health Analytics, Inc.) product codes: Plants-Toxalbumins, castor beans, *R. communis*, *R. pseudoacacia*, *A. precatorius*, Jatropha spp (including J. curcas, J. glandulifera, J. intergerrima, J. macrohiza, J. multifida, J. pandurifolia), and *H. crepitans*. Acute exposures that were followed to known medical outcomes were included. Only coded data were available for analysis; narrative fields were not reviewed as they are not part of coded data. Therefore, it is not possible to ascertain whether other methods (e.g., pictures, consultation with botanist) besides history provided by the caller were used to confirm plant identification. Information calls, confirmed non-exposure, and cases with co-ingestants were excluded.

Coded data entered by poison specialists are uploaded to NPDS. Coded data include age, gender, reason, substance, route, related clinical effects, treatments, management site and medical outcomes. For ingestions, poison center specialists may question if the seeds were swallowed whole or chewed but this information is not in the coded data. The dermal route includes thorn or other puncture wounds. Management sites include non-health care facility, emergency department, critical care unit, non-critical care unit, psychiatric admission and other. The management sites reported reflect the highest level of care the patient received. There are no national triage guidelines or hospital admission criteria for toxalbumin plant exposures. Poison center coding of known medical outcomes include no effect, minor, moderate, major, and death. Minor outcomes include some minimally bothersome signs or symptoms as a result of the exposure. Moderate outcomes include signs or symptoms that were more pronounced, more prolonged, or more systemic than minor symptoms, symptoms were not life-threatening and the patient had no residual disability; usually some form of treatment was indicated. Major outcomes exhibit signs or symptoms that were life-threatening or resulted in significant residual disability or disfigurement.

2.2. Data analysis

Cases that fit the inclusion criteria were evaluated for demographics, reason for exposure, routes of exposure, type of toxalbumin-containing plant involved, clinical effects, management site, and coded medical outcomes. Categorical variables are summarized as frequencies and percentages. Association analyses were done with Fisher exact test. After aggregating no effect/minor effect as 'less serious outcome' and moderate/major effect as 'more serious outcome', the procedure PROC FREQ was used to compute the odds ratio of 'not serious outcome' in the charcoal treated patients versus those who did not receive charcoal. Statistical analyses were performed using SAS System for Windows (version 9.2, SAS Institute, Cary, NC). The study was granted exempt status by the University Institutional Review Board.

3. Results

There were 1164 exposures involving a toxalbumin-containing plant that met inclusion criteria. The study cases included 493 (42.4%) females and 671 (57.6%) males. The age distribution was 559 (48%) children less than 6 years, 146 (12.5%) children between the ages of 6 and 12 years, 63 (5.4%) 13–19 years of age, 388 (33.3%) greater than 19 years of age and 8 (0.7%) unknown ages. The reason was unintentional in the majority of cases (Table 1). The frequency of patients experiencing symptoms was high when the reason was coded as adverse reaction, environmental, occupational, suicide attempt and unintentional misuse.

Exposures to *R. communis* (393, 33.8%) and *R. pseudoacacia* (383, 32.9%) were most commonly reported, followed by non-specified toxalbumin containing plants (239, 20.5%). Exposures to other toxalbumin plants were less commonly reported, which include *A. precatorius* (94, 8.1%), *Jatropha curcas* (27, 2.3%), *Jatropha multifida* (14, 1.2%), *H. crepitans* (9, 0.8%), and *Jatropha integerrima* (5, 0.4%).

For the majority of the cases (1,135, 97.5%), there was only one route of exposure: ingestion (904; 79.7%), dermal (166, 14.6%), parenteral (28; 2.5%), other/unknown (18, 1.5%), inhalation (15; 1.3%), and ocular (4, 0.4%). Only 29 (2.5%) exposures involved more than one route, including one ingestion and inhalation; the remainder involved dermal plus another route: 8 ingestion, 8 inhalation, 5 ocular and 7 parenteral. Related clinical effects were reported in 88.6% of dermal and 89.3% of parenteral (89.3%) exposures but in only 28.8% of ingestions and 43.7% of inhalations. The route in abuse cases was ingestion in 10 cases and inhalation/nasal in one case. Table 2 displays route stratified by plant.

Most patients were managed at home or a non-health care facility (non-HCF) (517; 44.4%) or treated and discharged from an emergency department (404; 34.7%). Admission to a non-critical care unit (104; 8.9%), a critical care unit (60; 5.2%), psychiatry (11; 0.9%) or management at an unspecified location (11, 0.9%) occurred less frequently. Additionally, 32 (2.7%) patients refused referral and

Table 1
Reasons and symptom frequency.

Coded reasons	Number of cases	Symptomatic cases
Intentional		
Abuse	11 (0.9%)	5 (45.4%)
Intentional misuse	43 (3.7%)	20 (46.5%)
Suicide	47 (4.0%)	32 (68.1%)
Unknown (intentional)	12 (1.0%)	7 (58.3%)
Unintentional		
Unintentional general	878 (75.4%)	298 (33.9%)
Unintentional misuse	82 (7.0%)	48 (58.5%)
Environmental	37 (3.2%)	30 (81.1%)
Occupational	9 (0.8%)	7 (77.8%)
Unintentional unknown	4 (0.03%)	3 (75.0%)
Miscellaneous		
Adverse Reaction	9 (0.8%)	8 (88.9%)
Contamination/tampering	10 (0.9%)	2 (20.0%)
Malicious	13 (1.1%)	3 (23.1%)
Unknown	9 (0.8%)	7 (77.8%)
Total	1164	470 (40.4%)