

Human Exposure to *Ecballium elaterium* Fruit Juice: Fatal Toxicity and Possible Remedy

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ABSTRACT

The human serious adverse reactions of the folkloric plant, *Ecballium elaterium* (EE), are well documented in the literature. This report is presenting the medical literature of 74 cases, which experienced severe adverse reactions or deaths that resulted from the administration of the plant juice. The survey of these human cases exhibits several adverse effects such as: acute rhinitis, uvular edema, soft palate, upper airway edema. In conclusion, the use of EE juice in folk medicine can cause severe adverse reactions that should not be ignored but it should be medically treated.

Keywords: *Ecballium elaterium*; Cucurbitacine; Uvular Edema; Sinusitis; Rhinitis, Conjunctivitis; Angioedema; Soft Palate; Hypoxemia

1. Introduction

The plant EE, known as squirting cucumber, is a weed belongs to cucurbitacea family. The plant is perennial, fleshy, rough hairy with stems 30 - 100 cm long. The flowers are greenish-yellow and the fruit are large juicy berry, 3 - 4 cm, ovate-oblong, detaching itself explosively at maturity scattering seeds and juice (**Figure 1**). The plant is widely distributed in the Mediterranean countries. In Jordan, it grows wild in many places including the roadsides and cultivated areas [1].

The fresh juice of EE had been used in folk medicine to treat jaundice since antiquities. Avicenna (980 - 1037) described the use of the juice in his famous book, AL-Kannon, almost one thousand years ago [2]. Nowadays, the people in Jordan as well as in other countries, are using the juice in the treatment of acute and chronic jaundice, rhinosinusitis, sinusitis, and other ailments of inflammations [3-8].

The fruit juice of the plant contains several bioactive ingredients such as cucurbitacins. These tetracyclic triterpenoids compounds such as A, E, D, I are of interest medicinally because of their cytotoxic, antitumor and antijaundice properties.

Still these bioactive compounds have been reported to possess other pharmacological activities for example: purgatives, analgesics and hemorrhoids [6,7,9-11].

The purpose of this report is to present a recent review

the medical available literature of seventy three human cases as appeared in the Pub-med and other available literature. Further to discuss the possibility of safely use of the plant juice despite its life-threatening adverse effects.

2. Results

Literature Search

Pub med was used to search for patients whom treated by EE juice for jaundice and other ailments. It was possible to allocate 73 different human cases. All of these cases are presented in (**Table 1**) [Pub-Med: 3,12,14-22]. One



Figure 1. *Ecballium elaterium* plant (Amman, countryside, Summer, 2010).

Table 1. Reported folkloric cases of patients exposed to *Ecballium elaterium* fruit juice.

| Folkloric use/exposure (administration and number of cases) | Adverse effects | Emergency Treatment (route of administration) | References (authors) |
|---|---|---|---|
| Acute rhinosinusitis (intranasal, 5 cases) | Uvular edema, nasal and tongue edema | Hydrocortisone (iv) antihistamines (oral) Prednisone (oral) | Mazokopakis, E.A., <i>et al.</i> [3] |
| Sinusitis, in retrospective study (42 cases) | Upper airway edema, swelling of uvular mucosa | Corticosteroids antihistamines | Kloutsos, G., <i>et al.</i> [12] |
| Eye exposure (1 case) | Late onset diffuse of lamellar keratitis | Topical steroids treatment for 2 weeks | Kocak, I., <i>et al.</i> [13] |
| Sinusitis (intranasal, 2 cases) | Uvular angioedema | | Satar, S., <i>et al.</i> [14] |
| Acute maxillary sinusitis (intranasal, 1 case) | Airway obstruction and edema, severe uvular edema, shortness of breath, sore throat | Oxygen (100% pure with mask). adrenaline (sc) prednisolone (iv) | Eray, O., <i>et al.</i> [18] |
| Sinusitis (1 case) | Soft palate uvular edema | Adrenaline, Methylpradnisone | Koussidis, G.A., <i>et al.</i> [17] |
| Sinusitis and liver cirrhosis (intranasal, 3 cases) | Irritation of mucosal membranes | Oxygen, steroids antihistamines, beta-2-agonist | Raiklin-Eisenkraft, B., Bentur, Y. [15] |
| Unwitting fruit oral ingestion (3 cases) | Edema of pharynx, dyspnea, drooling | | Raiklin-Eisenkraft, B., Bentur, Y. [15] |
| Ocular exposure (6 cases) | Conjunctivitis, cornealedema | Topical steroids, antibiotics. | Raiklin-Eisenkraft, B., Bentur, Y. [15] |
| Dermal exposure (Toddler, 1 case) | asymptomatic | Topical steroids, antibiotics. | Raiklin-Eisenkraft, B., Bentur, Y. [15] |
| Sinusitis (intranasal, 3 cases) | Uvular and soft palate edema | O ₂ , antihistamines. methylprednisolone, epinephrine. | Kokkonouzis, I., <i>et al.</i> [16] |
| Sinusitis (intranasal, 1 case) | Death of cardiac and renal failure. | | Vlachos, P., <i>et al.</i> [20] |
| Sinusitis, nasal drops(1 case) | Severe uvular edema, hypoxemia | Oxygen, hydrocortisone | Apostolos, P., <i>et al.</i> [19] |
| Chronic sinusitis (intranasal, 1 case) | Shortness of breath, severe uvular edema, nasal necrosis | Pheniramine malate, ranitidine prednisolone epinephrine | Eken, C., <i>et al.</i> [22] |
| Chronic rhinosinusitis, (intranasal, 1 case) | Burning sensation, sore throat, difficulty of breathing, uvular and soft palate. | NA | Kenan, A., <i>et al.</i> [21] |
| Jaundice (intranasal, 1 case) | NA | NA | Personal communication [24] |

more new case was the Jordanian female of two months old neonate (Personal communication with Professor Najwa Khori of Pediatrics Department, Faculty of Medicine, University of Jordan, Amman, Jordan).

2.1.1. The Folkloric Use

As presented in (Table 1), the plant juice was used to treat: jaundice; chronic sinusitis; acute rhinosinusitis; sinusitis; acute maxillary sinuate; sinusitis and liver cirrhosis.

2.1.2. Administration

The patients were to receive intranasal administration of few undiluted drops of fresh juice.

2.1.3. Age and Sex

The patients were to include males or females of different ages (Table 1).

2.1.4. Adverse Effects of EE Juice

Patients were admitted to the emergency services with various complaints and different signs and symptoms such like: burning sensation, sore throat, difficulty of breathing, soft palate, uvular angioedema, difficulty of swallow, conjunctivitis (eye exposure), allergic reactions, renal and heart failure and even death (Table 1).

2.1.5. Treatment in the Emergency Room

All patients were treated asymptotically, depends on the signs and symptoms and the condition of the patient. Since, the respiratory system was the major system which was affected by EE Juice, therefore, treatment were to involve the administration of: oxygen, antihistamines, prednisolone, or epinephrine. The eye and skin exposures were treated topically by corticosteroids and antibiotics. Ninety Seven percent of patients were dismissed shortly after recovery (Table 1).

3. Discussion

Jaundice usually comprises a yellow discoloration of the skin and the sclera that produced by accumulations of bilirubin in the tissues and interstitial fluids. It is resulted from increased of bilirubin load and decrease of bilirubin elimination [22,23]. Furthermore, Jaundice is still a common physiological problem affecting over half of all full-term and most preterm infants [23-25]. Although, jaundice is mainly harmless, still the jaundiced of the newborn infant must be monitored for its subsequent consequences such as: hyperbilirubinemia, acute encephalopathy, and kernicterus. At daylight, usually bilirubin becomes visible when the concentration of plasma bilirubin exceeds 2% - 3% mg. The most common causes of jaundice are usually resulted from: increasing of the destruction of red blood cells, the obstruction of the bile ducts and the damage liver hepatocytes [22,23].

The mainstay treatment and intervention of Jaundice is by phototherapy, exchanging transfusion, using of medication such as phenobarbital, baby body massage, and the use of herbal medicine.

The combination of four herbs that sound promising: *Artemisia capillaries*, *Gardenia jasminoides* Ellis, *Rheum officinale* Baill, and *Scutellaria baicalensis*. This combination is called Yin Zhi Huang combination [25,26]. The use of combination and phenobarbital was found to be useful since phenobarbital induced the activity of the enzyme bilirubin glucuronyltransferase, while, the combination has a potent stimulatory effect on bilirubin clearance through the induction of the activity of the nuclear receptor (CAR) [25]. At the meantime, Huang, *et al.*, 2004 reported that the combination enhances bilirubin clearance by activating the nuclear receptor (androstane receptor, CAR) [25].

However, in our previous investigation using four different animal species models [27], we reported, that EE juice resulted a significant marked decrease in bilirubin presented in the serum in a dose related manor. Therefore, the exact mechanism(s) of the juice has to be clarified in future researches.

4. Conclusion

In conclusion, the nostril administration of EE juice, although resulted of serious adverse reactions and even deaths, of patients, still comprehensive research protocols have to be developed to test the safety and the efficacy of the juice.

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