Case Report

Acute Datura Poisoning: Clinico-Toxicological Analysis & Correlation in Poison Detection Center as an aid in Evidence Based Medicine

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ABSTRACT

This work was aimed at mounting and validating thin layer chromatography, and ultraviolet-visible spectrophotometer analysis for identification of toxic substances ingested and at employing this method for analysis of gastric wash sample, urine samples and blood sample in a patient who had consumed datura, as part of evidence-based medicine where blood sample taken 12 hours after datura ingestion was analyzed with chromatography and mass spectrometry that was found to be positive for atropine. The atropine excreted in urine was serially determined by using thin layer chromatography in three subsequent urine samples at an interval of 3hours. The method showed good intra-day and inter-day precisions for analyte. Minimal matrix effects were observed during the thin layer chromatography. Results for forensic case samples demonstrated that the method successfully detected datura active principles in the lethal concentrations. Biochemical markers are extremely helpful in the diagnosis of a patient's illness when they are properly correlated with the clinical signs and symptoms. It also marks an important fact in the current practice of evidence-based medicine. In this incidence we want to discuss the importance of Poison Detection Center in tertiary health care center and the toxicity due to tropane alkaloids with due stress on its biologic and forensic aspects in relation to the clinico-toxicological analysis.

Keywords: datura; tropane alkaloids; scopolamine; atropine; hallucinogens; poison detection center; evidence-based medicine

INTRODUCTION

In India, Datura (Atropa belladonna, Thorn apple, Jimson weed, Angel's trumpet) grows at high altitudes, waste lands and seen all over the world.[1] The name belladonna in Atropa belladonna means beautiful women and refers to the past use of this plant in European medicine to dilate the pupils in order to make a woman appear more attractive.[2] The incidence of toxicity is sporadic. However, the Worldwide incidence is unknown, but cases have been reported in Germany, Italy, Greece, Saudi Arabia, Tanzania, Australia, Brazil, Hong Kong, Taiwan, Mexico, Chile, and Venezuela, attesting to broad geographic distribution of Datura species.[3] Datura poisoning is the third commonest poisons in India.[4] In United States, sporadic cases occur or sometimes clusters of cases are reported mostly among adolescents using plants for their hallucinogenic effects.[3] Datura species consists of tropane alkaloids, plant metabolites which are nitrogenous ring structure with alkali-like reactivity and pharmacologically active in preventing acetyl-choline binding to its receptor, thus affecting heart rate, respiration and central nervous system functions (anticholinergic effects). Lin et al[2] from Taiwan, in 2002 revealed that one of the tropane alkaloids possesses cholinergic rather than anticho-linergic activities and a study conducted on mice, with a related herb, has demonstrated renal, hepatic, and erythrocyte toxicity.

The active principles are hyosin, hyocymine, scopolamine, atropine and tropane found in all parts of the plants, with highest concentrations in roots and seeds. Scopolamine, acting as an antagonist at both peripheral and central muscarinic receptors, is thought to be the primary compound responsible for the

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toxic effects of these plants. Rapid impairment of the individual is common in these type of toxin facilitated self infliction.

In the present study we had a patient referred from a primary health center where there was an intact intra-venous line with normal saline running without necessary documents, frequently creates essential doubts in the subsequent clinician at the referral center. During such circumstances it is the history given by the attendants and investigations done play an important role in both therapeutic and medico-legal aspect, but how far is it reliable without selective and sensitive toxicological evaluation? Thus we aim to present a case of toxin facilitated self infliction due to the influence of datura consumption, where the active principles were identified in blood, gastric aspirate and urine, which aided in diagnosis and management.

CASE - REPORT

A 17 year old girl brought to the emergency department with a history of consumption of unknown seeds. Initially she had nausea, vomiting later disorientation, agitation, delirium with persecutory ideation and frightening visual and tactile hallucination of insects crawling and being assaulted by animals. On examination, moderately built and nourished, heart rate 130/minute, blood pressure 70mm Hg, diastolic not recordable, respiratory rate 30/minute shallow, SpO2 60% and responding to painful stimuli but not to verbal commands. Pupils were dilated 6mm and sluggishly reactive. An in-situ intra-venous line with normal saline was present. On enquiring there were no other treatment modalities done to the patient. Other basic clinical parameters and routine investigations were within the normal range.

Gastric aspirate showed the presence of intact seeds of datura, identified by the specialists in Department of Forensic Medicine & Toxicology. A solid phase extract of the seeds was subjected to thin layer chromatography, and ultraviolet-visible spectrophotometer analysis was done for the detection and confirmation of atropine and scopolamine, the principal toxic alkaloids responsible for dilated pupil in the present case. After prompt intervention, with the general care and antipsychotics, the patient returned to normal 36 hours after ingestion. The agitation, delirium, anxiety, and frightening visual, auditory and tactile hallucination came down after 12-18hours of intervention.

A. Toxicological Analysis

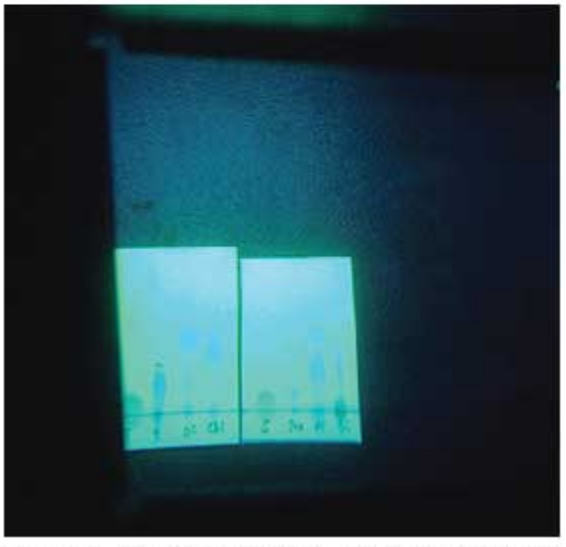
Sample Treatment: The study was conducted at the Poison Detection Center, Department of Forensic Medicine & Toxicology, Jawaharlal Nehru Medical College, Belgaum, Karnataka. Gastric wash was subjected to centrifugation and the concentrate was tested for the strongly suspected datura toxic principles. The internal standard was prepared by using homogenised datura seed extract with methanol. After extraction (30 min) by means of centrifugation, the supernatant (2 ml) is filtered through a 30kD ultra filter and qualification done by thin layer chromatography (TLC). After dissolving in ethanol, the selected samples were spotted on silica gel 60 F254 TLC plates of dimensions 20X20cm (Merck, Germany) with the help of fine-bore glass capillaries. Three TLC chambers were saturated with the three mobile phases, i.e., Solvent system 1-ethanol: diethyl ether:acetone (60:20:20); Solvent system 2-ethanol:diethyl ether:acetone (75:15:10), and Solvent system 3-ethanol:diethyl ether (60:40). The plates were made to run for a standard distance of 10cm and later dried at room temperature. They were examined in daylight, ultraviolet light. Photographs of these plates were taken with the help of a digital camera, and hRf values were recorded using templates. Samples were also screened for all other possible poisonous substances (organophosphorous compounds, organo-chlorines, pyrethroids) and drug overdoses (barbiturates, paracetamol, phenobarbitone) of local incidence and in particular to the clinical picture.

The blood sample taken 12 hours after datura ingestion was analyzed with chromatography and mass spectrometry that was found to be positive for atropine. The atropine excreted in urine was serially determined by using thin layer chromatography in three subsequent urine samples at an interval of 3hours. The method showed good intra-day and inter-day precisions for analyte. Minimal matrix effects were observed during the thin layer chromatography. Results for forensic case samples demonstrated that the method successfully detected datura active principles in the lethal concentrations.

B. Results

The active principles of datura were identified in gastric wash sample, blood and urine. Simultaneous management of the patient in the line of acute datura poisoning yielded favorable results.

Fig1: TLC of Sample screened for possible poisonous substances and drug overdoses



S: Gastric sample, Di: Diazepam, Chl: Chlorine tablets, Dra: Datura, OC: Organochlorine, OP: Organo-phosphorous compound

Fig2: TLC to demonstrate the presence of similar toxic principle in the sample

S: gastric Sample, B: Blood and U: Urine

DISCUSSION

Tropane alkaloids naturally occur in plants of the families Erythroxylaceae (including coca) and Solanaceae (including mandrake, henbane, deadly nightshade, datura, potato, and tomato). Important tropane alkaloids are atropine, hyoscyamine and scopolamine.[2] Datura plants are known for their hallucinogenic use from ages immemorial and have been connected with sorcery, witchcraft, native medicine and magic-religious rites dating back to 1500 BC.[3] Datura has been used as a recreational hallucinogen.[3] Poisoning cases with intention of suicide is rare with datura, but it is not uncommon among adolescents using plants for their hallucin-ogenic effects. Moreover, due to its hallucinogenic properties, the victims are less liable to recall accurately the circumstances and it makes the diagnosis and management difficult. Incidences of anticholinergic effects are found in people ingesting contaminants in foods, including commercially purchased Paraguay tea (an herbal tea derived from Ilex paraguariensis), hamburger, honey[3] stiff porridge made from contaminated millet and homemade "moon flower" wine. Other accidental ingestions include misuse as an edible wild vegetable3 and inclusion in homemade tooth-paste.[4] A large epidemic in New York and the eastern United States was reported as a result of heroin contaminated with scopolamine. The usual route of ingestion is as a tea, however ingesting seeds or other plant parts and smoking dried leaves also are common.[6]

The tropane class of alkaloids consists of more than 200 compounds.[7] The toxicity due to ingestion of plants containing tropane alkaloids manifests as classic anticholinergic poisoning and selectively interacts at the neuro- muscular junction to manifest as several side effects including visual and tactile hallucination. Symptoms usually occur 30-60 minutes after ingestion and may continue for 24-48 hours. The longevity of persistent toxicity is explained on the fact that the tropane alkaloids delay gastric emptying and absorption. As the toxin is short acting, it can impair an individual rapidly. Thus the longevity and short acting nature of the toxin contributes to the severity of toxicity. Scopolamine, the primary compound responsible for the toxic effects of these plants acts as an antagonist at both peripheral and central muscarinic

receptors. Tropane alkaloids are found in all parts of the plants, with highest concentrations in roots and seeds. Fatality from cardiopulmonary arrest has been reported from consumption of one-half teaspoon of datura seed, equivalent to 0.1 mg of atropine per seed.[3]

Results by toxicological analysis in late sampling allow to document the presence of hallucinogenic toxins in toxin facilitated self infliction. Thus in case of late report or in case of post- mortem toxicological analysis, the positive findings are of paramount importance for a victim and/or their family, in order to start therapy, psychological or medico-legal follow ups. These cases are often sensitive with little other forensic evidence.

Lethality of the toxin : In 1gm of datura seed, an average concentration of 2.3 and 0.5 mg/g atropine and scopolamine was detected respectively.[8] The estimated lethal dose of atropine in humans is 10 mg and 2–4 mg for scopolamine. Without treatment the intake of 2 to 5 berries of deadly nightshade in children and 10 to 20 berries in adults is considered lethal.[9] Jimson weed toxicity usually occurs within 60 minutes after ingestion and clinical symptoms may persist for 24 to 48 hours.[10] One jimsonweed seed weighs approximately 8 mg[11], which means that approximately 100 seeds are equivalent with 10 mg atropine. EMEA, Atropa Belladonna summary report9 states that 100 mg atropine, 100 mg scopolamine or 10 mg hyoscyamine in adults (10 to 20 berries), few milligrams in children (2 to 5 berries) is considered a lethal dose. In 1995 Baselt RC and Cravey[12] cited by Namera[13] in 2005 reported a male ingested about 1 g of atropine together with alcohol, survived with blood atropine concentration was 130ng/mL. Same authors report an 18-year-old male ingested atropine tablets (30 mg per tablet, but the number of the tablets is not known), and died with atropine concentration of 200ng/mL in his whole blood. Boumba[14] et al reported Hyoscyamine and scopolamine were detected in postmortem blood and urine in a 19 year old male who intentionally ingested an unknown quantity of Datura stramonium seeds to experience its hallucinogenic effects.

CONCLUSION

Biochemical markers are extremely helpful in the diagnosis of a patient's illness when they are properly correlated with the clinical signs and symptoms. This case of intoxication with Datura is, to our knowledge, the first clinical report correlated with toxicological analysis for the presence of atropine in gastric contents, blood and urine in Poison Detection Center setting. As a part of evidence-based medicine it is mandatory to establish Poison detection center in hospitals. TLC has remained one the most desirable methods of investigation in Forensic Science Laboratories because of inexpensive equipment and ease. This study has concentrated on developing a preliminary screening of some toxins by using only a single TLC solvent system to facilitate easy and rapid identification.

LIMITATIONS

The sensitivity and selectivity of analytical toxicology appear as a pre-requisite to document any case involving toxin facilitated self infliction which could not be done.

CONFLICTS OF INTEREST

Declared none

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