ORIGINAL ARTICLE

Toxic outcomes of fatal Oduvan poisoning in South India: An autopsy-based study.

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ABSTRACT

Background: the Oduvan is Cleistanthus collinus having two major active principles Cleistanthin a and B. There are growing numbers of self-harm by consuming Oduvan in Southern region of India. The mechanism of action of Oduvan and its active principles in humans are not well established. Limited literatures available on the microscopic end-organ damage caused by the Oduvan toxicity in human beings.

Aim: This study was carried out to assess the histopathological and autopsy features of liver, kidney, and lungs in fatal Oduvan poisoning cases.

Methods: The anonymous data regarding the autopsy, clinical records, and histopathology findings of fatal Oduvan poisoning cases reported during the period January 2014 to December 2016 was collected and analysed using Epidata V.2.0 program.

Results: a total six number of cases was reported during the study period. The common findings in lungs were intra-alveolar hemorrhage, pulmonary edema, and septal congestion. The findings in kidney were acute tubular necrosis and medullary congestion. The findings in liver were intra canicular and intra hepatic cholestasis, focal feathery changes, and necrosis. The toxicological analysis of viscera was positive for only one case and rest five cases were negative

Conclusion: The acute tubular necrosis, hepatic necrosis and intra alveolar hemorrhages were the common findings in this study and caused the death in majority of cases. Intra alveolar hemorrhages usually showed a late manifestation beyond 72 hours of hospitalization. Most of the findings are consistent with animal studies except the intra alveolar hemorrhages.

INTRODUCTION

As per World health organization 8,00,000 people die every year due to suicide, of which 79% occurs in developing countries. The rate of suicide has increased to 60% in the past 45 years. [1] A total of 1,34,516 suicides were reported in India during 2018. Tamil Nadu reported around 13,896 (10.3%) suicides, second highest among all states in India. Among Union territories Puducherry ranked first with 33.8%. Poisoning was the second most common method of committing suicide in India. [2] Suicide by poisoning was more common among men than females. Organ phosphorus compounds and rodenticides are commonly preferred agent.[3,4] Plant poisons are the second most common agents used for suicide, with yellow oleander and Oduvan as preferred plants.[5] Oduvan (Cleistanthus collinus) is a poisonous plant, is unique to the south Indian states of Tamil Nadu, Telangana, Andhra Pradesh, Kerala and Pondicherry. C. collinus is commonly known as Oduvanthalai or Oduvan in (Tamilnadu), Vadisaaku in (Andhra Pradesh), Nilapala (Kerala) and Garari in Northern India.[6] The decoction of leaves of Oduvan is the common method of ingestion followed by crushed leaves mixed with jiggery.[7] There are many epidemiological, clinical, laboratory studies and autopsy based case reports on Oduvan in literature. However, autopsy-based studies on histopathological analysis of lungs, kidney and liver in Oduvan toxicity is uncommon in literature. Since the principle organs affected such as liver, kidney, and lungs in C. collinus poisoning histopathological organs will give an important data for medical literature.

Materials and Method

This is a 3-year record based retrospective study on the fatal Oduvan (*Cleistanthus collinus*) poisoning cases reported for autopsy at the Forensic Medicine and Toxicology department during the period January 2014 to December 2016. The anonymous data regarding the autopsy, clinical records, and histopathology findings of fatal Oduvan poisoning cases reported during the study period was collected and analysed using Epidata V.2.0 program. This study was approved by the Institute Ethics Committee who confirmed that as we are reporting on routinely collected non-identifiable record based audit data, no approval from a research ethics committee was additionally required under the institute ethics policy framework for Human Studies.

RESULTS

A total number of six fatal Oduvan poisoning cases was autopsied during the study period. Out of 6 cases four were female (66%) and two were male (33). **Tables 1** summarize the observations. Histopathology report was documented for 5 cases and in 1 case the sample were autolysed. Toxicological analysis of viscera was positive for only one case and rest five cases were negative. The common findings in lungs were Intra-Alveolar Hemorrhage, Pulmonary edema, and septal congestion. The findings in kidney were Acute Tubular Necrosis and Medullary Congestion. Acute Tubular Necrosis was seen in both the proximal and distal convoluted tubules. The findings in liver were intra canicullar and intra hepatic cholestasis, focal feathery changes, and necrosis.

Table 1: Showing the histo-pathology and toxico-analysis findings of the studied cases.

S.No	Gender	Histopathological findings			Toxicological analysis
		Kidney	Lungs	Liver	
1	Male	Acute Tubular Necrosis	Intra-Alveolar Hemorrhage	Normal architecture	Negative
2	Female	Acute Tubular Necrosis	Alveolar edema	Intra hepatics & Intra canicullar cholestasis	Negative
3	Female	Acute Tubular Necrosis	Alveolar edema	Steatosis	Negative
4	Female	Interstitial hemorrhage	Intra-Alveolar Hemorrhage	Normal architecture	Negative
5	Male	Acute Tubular Necrosis	Intra-Alveolar Hemorrhage	Focal feathery change, necrosis	Negative
6	Female	autolysis	autolysis	autolysis	Detected the active principles of Oduvan

DISCUSSION

The active principles of oduvan includes diphyllin, cleistanthin A, cleistanthin B, cleistanone, and collinusin.[8] The exact mechanism of action of the toxic constituents of oduvan has been understood clearly. The following are the mechanism of actions of active principle of oduvan. Inhibition of ATPase enzyme in liver, kidney, heart, brain and skeletal muscles.[9] Inhibition of LDH isoenzymes and cholinesterase.[10,11] Cleistanthin A also induces DNA damage and apoptosis by inhibiting DNA synthesis.[12] Cleistanthin A accumulates in the brain, liver and skeletal muscles while cleistanthin B accumulates in the cardiac muscle and skeletal muscles. However all the above mentioned mechanism of action are widely attributed to the animal studies done.[13] Epidemiological studies on oduvan toxicity from the same institute has showed that the mortality rate was around 17.6%.[14] Shankar et al. studied 196 cases and found out that the cause of death was due to respiratory arrest (29%), cardiac arrest (21%), renal failure (18%), acute respiratory distress syndrome(16%), multiple organ failure (5%) and undetermined (34%).[15]

Data on microscopic end organ damage in oduvan toxicity is available based on animal studies. Human studies on microscopic end organ damage is very uncommon in literature. The toxic effects of oduvan is due to cytotoxic effects of lactones on a number of cellular, tissue, and organ systems.[16] Toxins inhibits the vacuolar H+-ATPase activity in the renal brush border membrane and depletion or inhibition of thiol or thiol-dependent enzymes.[9,17] The common renal finding observed in our study was acute tubular necrosis. The acute tubular necrosis may be due the above the direct effect of toxin or due o he inhibion of ATPase and thiol dependent enzymes. The distal tubular cell are susceptible than proximal tubular cells and global tubular dysfunction with diminished GFR occurs in severe cases.[18] The acute tubular necrosis may be one of the cause of oliguric renal failure. Focal hepatic necrosis was seen in in animal studies.[10] The hepatic necrosis was also found in one case in our study consistent to the findings in animal studies. Type 1 respiratory failure and adult respiratory distress syndrome (ARDS) are the pulmonary complications. Pulmonary toxicity is due to the direct effects of the toxin over the neuromuscular junctions of the respiratory muscle paralysis and defect in oxygen transfer at the alveolar-capillary level.[19,20] The intra-alveolar hemorrhages were noted in our study has not been documented in any animal studies. The intra-alveolar hemorrhage could be the important reason for the ARDS during the terminal event. Thus the microscopic findings in this due may be due to the direct effect of Oduvan or its active principles.

CONCLUSION

In the majority of Oduvan toxicity cases direct cytotoxic effects like acute tubular necrosis, hepatic necrosis and intra alveolar hemorrhages were observed and are the important contributors to the cause of death. Intra alveolar hemorrhages, which is not reported in the animal studies is also observed commonly and usually showed a late manifestation. These findings would explain the end organ effects of the toxins and cause of death in Oduvan poisoning. Hence further studies on pulmonary toxicity of Oduvan is recommended.

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