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Original Work

Oleander toxicity – the clinical spectrum and mortality predictors: an observational study

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ABSTRACT: A major cause of mortality in Government Villupuram Medical College & Hospital is due to toxin exposure. Oleander poisoning ranks second in the list being superseded only by organophosphate poisoning. Data on the incidence, clinical features and the determinants of mortality are scanty. Standardized treatment or monitoring protocols are lacking. The study aimed to identify key mortality predictors in oleander poisoning, document the clinical spectrum of patients presenting with oleander poisoningand to devise a standard assessment protocol in oleander-poisoned patients. This is a prospective, observational study conducted at Villupuram Medical College. Consecutive hospitalized patients who had consumed oleander seeds, fruits or leaves were included in the study after obtaining informed, written consent. Upon registration, detailed history, clinical examination, baseline investigations and targeted investigations were performed. The data were documented in the standardized case proforma and subsequently computed. Patients were followed up 12 hourly by clinical examination and ECG recordings for a duration of 3 days. The data were analyzed using standard statistical methods. A total of 101 patients (46 male and 55 female) were enrolled into the study. There were 18 deaths, most of them (82.55%) occurring within 24 hours of intake. Among the parameters assessed, females, low BMI (Body Mass Index), consumption of > 3 seeds, delayed presentation (after 120 minutes), altered mental status, clinical shock, presence of heart block and absent p waves in ECG were significantly associated with mortality. Males, high BMI, low dosage of poison (<=3 seeds) and hemodynamic stability on day 1 were associated with favorable outcomes. ST-T segment changes, sinus tachycardia, ventricular premature contractions and administration of orciprenaline had no significant effect on the outcome. Oleander poisoning claims lives in the rural tropics. Institutional assessment and treatment protocols based on the infrastructure and expertise available are the need of the hour. Prompt first aid, critical assessment and timely referral for cardiac pacing can cut down mortality to a large extent.

KEY WORDS: ***Oleander poisoning; Cardiac glycoside toxicity; Mortality predictors***

INTRODUCTION

Deliberate ingestion of oleander seeds – Common oleander (*Nerium oleander*) and Yellow oleander (*Thevetia peruviana*) – is a popular method of self-harm in South Asia[1]. Previous investigators have shed light on the clinical features of oleander toxicity[2,3]. However the spectrum is large and mortality predictors need to be highlighted. Easy availability, low cost, high toxicity and relative lack of morbidity tilts the balance towards oleander poisoning among suicide intenders (**Figure 1**). In India the condition is grossly under-reported with

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sparse reliable data on mortality (approximately 5-10%)[4].

Government Villupuram Medical College is a tertiary care center which caters to the health needs of a population of approximately three million. The study center is based at a rural district in Southern India, the prime occupation of the feeder population being agriculture. The majority belongs to the lower socioeconomic strata with low literacy rates. Nevertheless, most of them are aware that all parts of the plant are poisonous and tend to select the seeds for their high toxicity. Oleander plants are plentiful in availability round the year. For obvious reasons oleander-poisoning cases are encountered very frequently at our center, however standard management or monitoring protocols are far from satisfactory. Data on the incidence, clinical features and the determinants of mortality are scanty. The study aimed to identify key mortality predictors in oleander poisoning, document the clinical spectrum of patients presenting with oleander poisoning and to devise a standard assessment protocol in oleander poisoned patients.

Figure 1: Yellow Oleander (*Thevetia peruviana*) Seeds

METHODOLOGY

The study team comprised of the treating physicians, resident doctors, nursing staff of Internal Medicine Department, laboratory staff and ECG technicians. The study was conducted from July 2014 to June 2015. Upon admission patients were interviewed by the physician or resident and eligibility ascertained. The standardized inclusion and exclusion criteria are given in **Table 1**. If found eligible the patients were registered after getting written, informed consent. Subsequently the patients were followed up clinically and investigated for a period of 3 days or discharge or death, whichever was later. The Institutional Ethics Committee approved the research project.

Table 1. Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Patients exposed to oleander toxin (seed, leaves, fruits). Presentation within 24 hours.	Patients presenting after 24 hours. Comorbidities like Heart failure, Ischemic heart disease, Pacemakers.

The findings were recorded in standard case pro forma and computed. The study team met at regular intervals to review the data and monitor the study process. The data were finally analyzed using SPSS software version 20.

RESULT AND DISCUSSION

A total of 101 patients (46 male and 55 female) were enrolled into the study. The mean age of the study population was 28.50 ± 10.89 years. There were 18 deaths (mortality rate 17.65%), most of them (82.55%) occurring within 24 hours of intake. There was a striking female preponderance both in the incidence of symptomatic oleander toxicity as well as mortality. The female mortality rate was 23.41%, whereas males scored only 10.91%. Among the parameters assessed, females, low BMI ($<23.2 kg/m^2$), consumption of > 3 seeds (Chi sq 6.769, p = 0.009), intake of crushed seeds (Chi sq 9.255, p = 0.002), delayed presentation (after 120 minutes) (Chi sq 3.911, p = 0.047), altered mental status (Chi sq 41.5, p < 0.001], clinical shock (Chi sq 51.152, p < 0.001), presence of heart block (Chi sq 13.652, p < 0.001) and absent p waves in ECG were significantly associated with mortality. Males, high BMI, low dosage of poison (< 3 seeds) and hemodynamic stability on Day 1 were associated with favorable outcome. ST-T segment changes, sinus tachycardia, Ventricular premature contractions and administration of orciprenaline had no significant effect on the outcome.

In our study the predominant plant involved was yellow oleander (*Thevetia peruviana*) the toxic components being thevetin, thevetoxin, etc. Previous literature on the subject is controversial regarding the exact fatal dosage of the toxin[2,3]. Consumption of as little as one leaf or half a seed has been associated with mortality. In our study the seed count gave a reliable toxic dosage, since we could not actually measure the dried weight of consumed poison. Intake of > 3 seeds resulted in significant mortality among the patients (Chi sq 6.769, p =0.009). The death rate was worse for women and for those who consumed dried /crushed seeds. The obvious explanation is that women with their low BMI suffered more per kilogram toxin exposure for the same dosage than their male counterparts.

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The clinical spectrum extended from totally asymptomatic patients to a wide array of manifestations like shock, syncope and death. The relative frequency of vomiting (54.5%), giddiness (21.8%) and abdominal pain (10.9%)seen among these patients is of note. GI symptoms,usually evolving within minutes to hours, are nonspecific, and include nausea, vomiting, diarrhea and abdominal pain. Perioral paresthesia and sialorrhea also have been documented[5]. Consumption of the seeds on empty stomach further worsened the pain, whereas alcohol co-ingestion did not significantly alter the same. Confusion, dizziness, drowsiness, weakness, visual disturbances, and mydriasis are central nervous system manifestations of toxicity[2]. Cardiac manifestations included palpitations, sweating, dyspnea and shock. The occurrence of various symptoms and signs are summarized in **Table 2**.

Table 2: Clinical features of oleander poisoning

Clinical features	Occurence (%)
Vomiting	54.5
Giddiness	21.8
Abdominal pain	10.9
Diarrhoea	8.9
Sleepiness/drowsiness	3
Palpitations	3
Altered mentation	3
Chest pain	1
Dyspnoea	1
Bradycardia	33.1
Irregular heart rate	35
Shock	13.8

The study was instrumental in identifying a few mortality predictors, which need emphasis (**Figure 2**). Firstly, the consumption of dried seeds was uniformly associated with signs of toxicity and significantly predicted mortality. The probable reason for this phenomenon is because these seeds need to be crushed before eating thereby enhancing systemic absorption. Furthermore their toxin concentration per gram is also enhanced[6]. The unripe fruit or seeds were usually swallowed like pills hence their digestion and absorption were suboptimal.

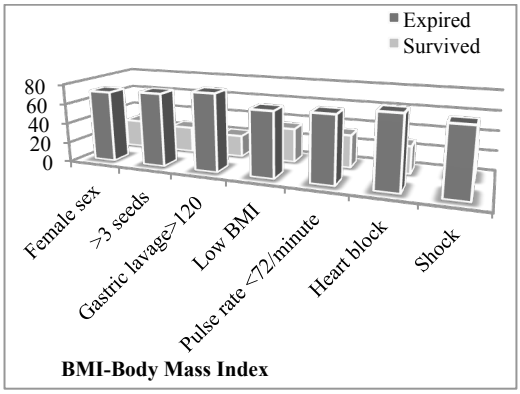

Figure 2. Factors involved in oleander toxicity

Secondly, the time interval between consumption and institution of gastric lavage largely determined the outcome. All patients who underwent gastric lavage within one hour of consumption suffered minimal symptoms. There was no mortality in this group. However those who underwent gastric lavage after a delay of 120 minutes suffered symptoms proportionate to their toxin dosage with a mortality of 25.21%.

Cardiac glycosides primarily affect the cardiovascular, neurologic, and gastrointestinal systems. Of these, effects on the cardiac system are most significant[2]. On a clinical perspective, the occurrence of altered mental status, clinical shock and symptomatic bradycardia in our study population were associated with significant mortality. The cardiac glycosides in *Nerium oleander* have vagotonic effects, resulting in bradycardia and heart block. Inhibition of Na^+-K^+-ATPase in skeletal muscle results in increased extracellular potassium and contributes to hyperkalemia[7,8]. The shock is attributable to both dysrhythmia as well as dyselectrolytemia[9]. Decreased cerebral perfusion explains the giddiness and altered mentation in our patients[10]. Though gastrointestinal symptoms were more common and dominated the clinical picture, they had little effect on mortality.

Finally, the sequential ECG recordings revealed a few important markers like Heart Block (Chi sq 13.652, $p < 0.001$) and absent P waves (Chi sq 24.26, $p < 0.001$) predicting death. On the contrary, sinus tachycardia and premature ventricular complexes were not associated with mortality. Use of atropine or orciprenaline had no bearing on the mortality. Previous studies have highlighted the conduction abnormalities associated with oleander poisoning[8]. Dysrhythmias characterized by increased automaticity and conduction blockade, when combined, are highly suggestive of glycoside etiology[11]. These include dysrhythmia, sinus bradycardia with all types of AV nodal block, junctional rhythms and sinus arrest[9,12].

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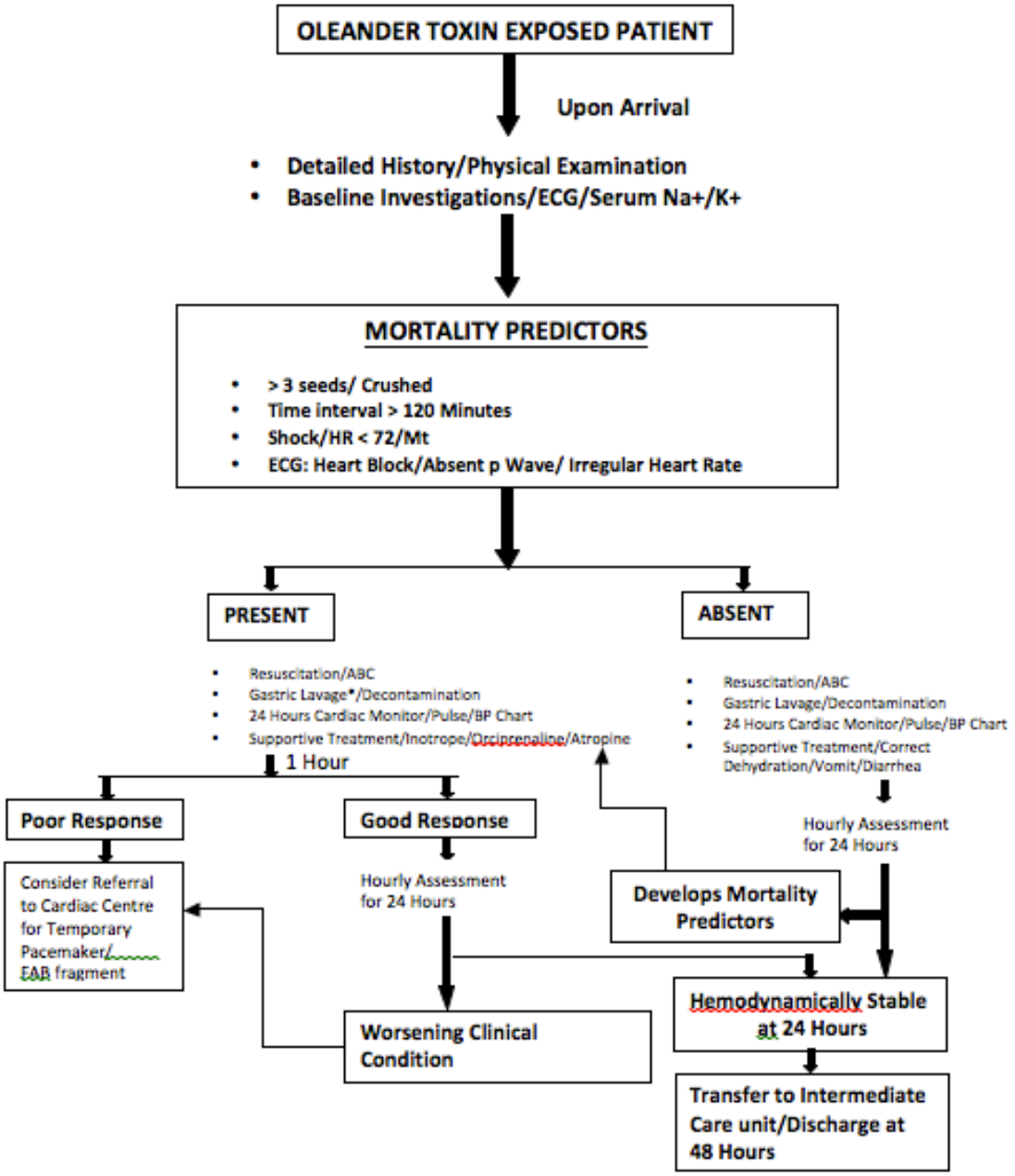
The revelations from our research enabled the formulation of an institutional protocol for management of oleander-poisoned patients (**Figure 3**). This protocol would befit most of the tertiary care level institutes across the state who face similar case burden and lack super-specialty intervention like cardiac pacing.

Limitations of the study

The major limitation of the study is that our center is not an expert toxicology management center. The definitive treatment of oleander poisoning is digoxin specific FAB (fragmented antibodies) to digitalis alkaloids, which is not available here, as also cardiac pacing. However, the situation is quite similar in most other centers in the country, given the high cost of antibody treatment. In view of this we performed an observational study only and those patients who were referred for expert intervention were excluded from the study.

Figure 3. Assessment protocol for oleander poisoned patient



*Gastric Lavage is not of much value if instituted after 120 minutes[12].

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CONCLUSION

Oleander poisoning claims lives in the rural tropics. Critical assessment and meticulous clinical examination have revealed important mortality predictors for these patients. Institutional assessment and treatment protocols based on the infrastructure and expertise available are the need of the hour. Prompt first aid, intensive monitoring and timely referral for cardiac pacing can cut down mortality to a large extent.

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