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Original Research Article

Study on clinical profile, electrolyte and electrocardiographic abnormalities in patients with yellow oleander poisoning

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ABSTRACT

Background: Poisoning occurs following the ingestion of crushed seeds or fruits of yellow oleander. Objectives of the study were to investigate various arrhythmias and electrolyte abnormalities seen in patients with yellow oleander poisoning and to find out the correlation between various arrhythmias, duration and form of exposure of oleander.
Methods: Fifty patients from the toxicology ward in the Institute of Internal Medicine, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai, who fulfilled the eligibility criteria, were enrolled for this prospective and observational study among the patients admitted for the ingestion of yellow oleander.
Results: Oleander seed poison was most prevalent in the 21-40 years of age. Incidence was more among the young males. Mortality was independent of the number of seeds consumed. More the crushed seeds consumed and delay to admission to the hospital, poorer was the outcome. ECG abnormalities were found in majority of the individuals. Electrolyte disturbances (hyperkalemia and hypermagnesemia) were found in significant proportion of the patients.
Conclusions: Prognosis was poor among those who presented with bradycardia, electrolyte disturbances and complex arrhythmias. The arrhythmias produced by this poisoning might range from sinus bradycardia to complete heart block and ventricular tachycardia. Sinus bradycardia was the most common arrhythmia seen in this study. As there are no standard guidelines at present to recommend the indications for temporary pacemaker in the management of oleander induced arrhythmias, uniform guidelines have to be formulated.

Keywords: Electrolyte and electrocardiographic abnormalities, Poisoning, Yellow oleander

INTRODUCTION

Cerbera thevetia also known as yellow oleander is a shrub with long green lanceolate leaves with bell shaped yellow flowers and a green fruit with two pale yellow seeds.[1] It is prevalent in South Asian countries like India and Srilanka. Poisoning occurs following the ingestion of crushed seeds or fruit. The active principles are thevetin, thevetoxin, cerberin and nerifolin. These are all digitalis like glycosides.[2] These substances acts by inhibition of Sodium Potassium ATPase pump on cell membranes which in turn increases intracellular calcium and inotropic effect. These increase vagal tone and decrease resting membrane potential thereby increasing the automaticity and triggered activity.[3]

Accidental cases of poisoning have been reported in children.[4] Adults have died by consuming the leaves in herbal tea. But many cases were reported about the yellow oleander seeds as an agent of self-harm in Sri Lanka.[5] Patients may be asymptomatic or may present with cardiac arrhythmias including sinus bradycardia, sinus node and AV node dysfunction.

Tachyarrhythmias are uncommon. Other symptoms include nausea, vomiting, diarrhoea, abdominal pain,

paraesthesias, hypotension and altered sensorium. Patients usually presents with hyperkalemia.[6]

In this study authors tried to find the presence of various arrhythmias and its association with duration and form of exposure of yellow oleander. Since hyperkalemia is a usual manifestation in yellow oleander poisoning, authors attempted to find association between serum potassium, calcium and magnesium levels and the arrhythmias in yellow oleander poisoning in this study.

Objectives of the study were to investigate the presence of various arrhythmias and electrolyte abnormalities seen in patients with yellow oleander poisoning and to find out the correlation between various arrhythmias, duration and form of exposure of oleander.

METHODS

Source of data

Patients who were admitted in the Toxicology ward in the Institute of Internal Medicine, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai-3, for the ingestion of yellow oleander, with fulfillment of inclusion and exclusion criteria were included in this study.

***Sample size*:** 50

***Study design*:** Prospective and observational study

***Study duration*:** 6 months (February 2017 to July 2017)

Inclusion criteria

- Healthy patients
- Age 15 – 70 years
- Smoker, alcoholics
- Patients with hypertension

Exclusion criteria

- Patients with diabetes mellitus
- Patients with chronic renal failure
- Patients with heart failure
- Patients with pre existing arrhythmias
- Patients taking digoxin
- Patient with thyroid disease

Data collection and methods

Among patients who consumed yellow oleander, subjects were selected for this observational study according to inclusion and exclusion criteria. Then they were subjected to history taking regarding the form of oleander, quantity and time of consumption to admission in hospital and clinical examination was done.

ECG was taken to find arrhythmias. Blood samples were collected for the electrolytes.

1. Potassium
2. Magnesium
3. Calcium

In this study, the distribution of age, sex, form of oleander, quantity, duration since consumption to admission, bradycardia, serum potassium, serum corrected calcium, serum magnesium, electrocardiographic changes and outcome in the patients with yellow oleander poisoning were studied.

Correlation between the arrhythmias and following variables:

- Form of oleander
- Quantity
- Duration since consumption to admission
- Serum potassium
- Serum calcium
- Serum magnesium

Correlation between the serum potassium and following variables:

- Form of oleander
- Quantity
- Duration since consumption to admission
- Finally, I compared the duration since consumption to admission with the arrhythmias and outcome of the patient.

Statistical methods

The data was analysed using SPSS software. P values were calculated to find the statistical significance. Variables were considered to be significant if p value <0.05.

RESULTS

Table 1: Patients distribution according to their age and sex (n=50).

Characteristics	Number of patients	%
Age group (years)		
1 – 20	13	26
21 – 40	26	52
41 – 60	9	18
>60	2	4
Sex		
Male	30	60
Female	20	40

In this study, 26% patients were less than 20 years, 52% patients were 21-40 years, 18% patients were 41-60 years, 2% patients were more than 60 years. So, consumption of oleander poison was more among 21-40 year age group in my study. In this study, 60% patients were males, 40% patients were females (Table 1).

Table 2: Distribution of patients according to their exposures (n=50).

Characteristics	Number of patients	%
Exposure		
Crushed seeds	38	76
Whole seeds	11	22
Leaf	1	2
Fruit	0	0
Quantity of exposure		
1 - 5	38	76
6 - 10	12	24
Duration since consumption to admission (hours)		
0 – 1	7	14
1 – 2	12	24
2 – 3	8	16
3 – 5	17	34
5 - 8	6	12

Table 3: Distribution of patients according to clinical characteristics (n=50).

Characteristics	Number of patients	%
Pulse rate (per min)		
<40	5	10
41 - 50	10	20
51- 60	27	54
>60	8	16
Serum potassium (mEq/l)		
3.5 - 5.0	10	20
5.1 - 6.0	26	52
6.1 - 7.0	10	20
7.1 - 8.0	3	6
>8.0	1	2
Serum magnesium (mg/dl)		
1.7 - 2.3	42	84
>2.3	8	16
Corrected calcium (mg/dl)		
<8.7	5	10
8.7 - 10.2	45	90
ECG (arrhythmias)		
Sinus rhythm	8	16
Sinus bradycardia	11	22
Sinoatrial exit block	5	10
Junctional rhythm	4	8
First degree av block	10	20
Second degree av block	7	14
Complete heart block	3	6
Ventricular ectopics	1	2
Ventricular tachycardia	1	2

Table 2 shows the distribution of patients according to their exposures76% patients consumed crushed seeds, 22% patients consumed whole seeds, 2% patients consumed leaves, none consumed fruit. So crushed seeds consumption was more common in this study. 76% patients consumed less than 5 seeds, 24% patients consumed 6 to 10 seeds. In this study, 14% patients came to the hospital within 1 hour, 24% patients came to the hospital within 1-2 hours, 16% patients came to the hospital within 2-3 hours, 34% patients came to the hospital within 3-5 hours and 12% patients came to the hospital within 5-8 hours.

The results showed that 10% patients had bradycardia of less than 40 per minute. 20% patients had bradycardia of 41-50 per minute, 54% patients had bradycardia of 51-60 per minute, 16% patients had pulse rate of more than 60 per minute. So most of our patients had pulse rate of 51-60 per minute (Table 3). 20% patients had serum potassium in the normal range, 52% patients had hyperkalemia in the range of 5.1-6 mEq/l, 20% patients in the range of 6.1-7 mEq/l, 6% patients in the range of 7.1-8 mEq/l, 2% patients in the range of more than 8 mEq/l. So most of the patients had mild hyperkalemia. 84% patients had normal serum magnesium and 16% patients had hypermagnesemia. 90% patients had normal serum calcium and 10% patients had hypocalcemia. 16% patients had normal sinus rhythm, 22% patients had sinus bradycardia, 10% patients had Sinoatrial exit Block, 8% patients had junctional rhythm, 20% patients had first degree AV block, 14% patients had second degree AV block, 6% patients had complete heart block, 2% patients had ventricular ectopic beats and 2% patients had ventricular tachycardia. So, sinus bradycardia was the most common arrhythmia in this study.

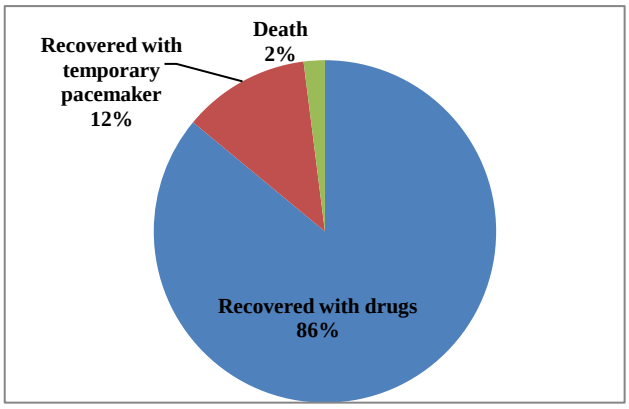

Figure 1: Distribution of patients according to outcome (n=50).

Figure 1 shows 86% patients recovered with drugs, 12% patients recovered with temporary pacemaker and 2% patients died.

Figure 2 shows comparison of form of exposure with arrhythmias. First degree AV block was the most common among the patients who consumed crushed

seeds and sinus bradycardia was commonly observed among the patients who consumed whole seeds and leaves. Sinus rhythm was commonly seen with whole seeds. Sinus bradycardia was commonly seen with leaves. Sinoatrial exit block was commonly seen with crushed seeds. Junctional rhythm and ventricular ectopic beats were commonly seen with whole seeds. First and second degree, complete AV blocks and ventricular tachycardia were common with the crushed seeds.

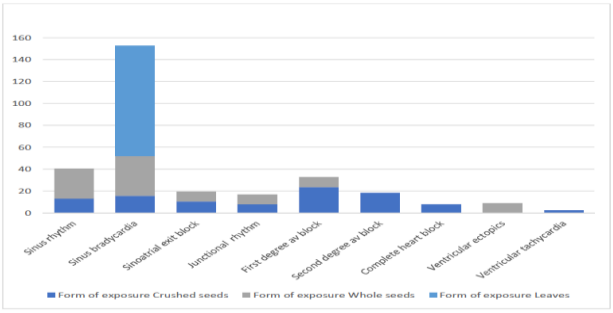

Figure 2: Comparison of form of exposure with arrhythmias (n=50).

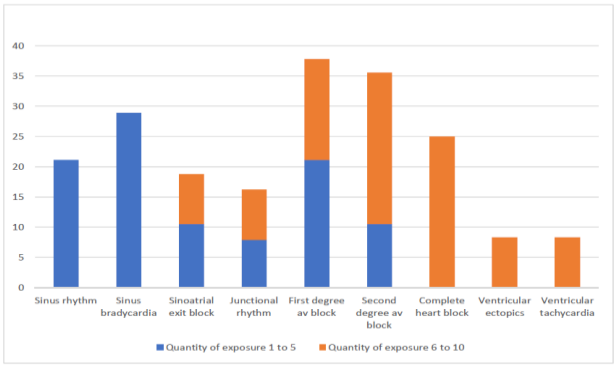

Figure 3: Comparison of quantity of exposure with arrhythmias (n=50). Fisher's Exact Test value = 20.330; p=0.001.

Figure 3 displays comparison of quantity of exposure with arrhythmias. Among the patients who consumed 1 to 5 seeds, sinus bradycardia was commonly seen.

Among the patients who consumed 6 – 10 seeds, second degree AV block and complete heart block were commonly seen. The most dangerous complete heart block and ventricular tachycardia were seen with the consumption of 6 – 10 seeds. Sinus rhythm and sinus bradycardia were common with the consumption of 1-5 seeds.

Figure 4 illustrates comparison of duration since consumption to admission with arrhythmias. Sinus rhythm was the most common among the patients who came to the hospital within 1 hour. Complete heart block and ventricular tachycardia were more commonly seen with patients who came to the hospital later.

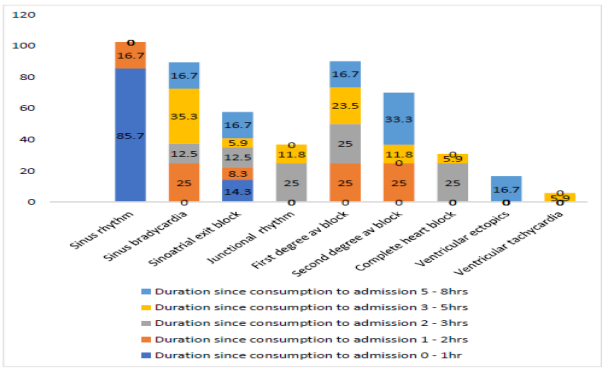

Figure 4: Comparison of duration since consumption to admission with arrhythmias. Fisher's Exact Test value = 41.647; p=0.006.

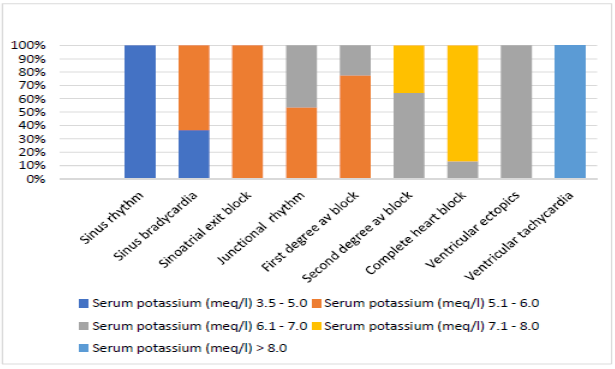

Figure 5: Comparison of serum potassium with arrhythmias. Fisher's Exact Test value = 79.291; p<0.001.

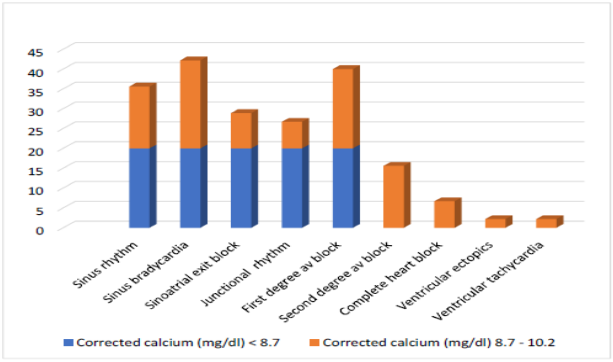

Figure 6: Comparison of serum corrected calcium with arrhythmias.

Figure 5 reports comparison of serum potassium with arrhythmias. Sinus rhythm (80%) was observed only in the patients with the serum potassium of normal range. Arrhythmias commonly seen with the serum potassium of 5.1-6 mEq/l were sinus bradycardia (34.6%), Sinoatrial exit block (19.2%), junctional rhythm (11.5%), first degree AV block (34.6%). Arrhythmias commonly seen with the serum potassium of 6.1-7 mEq/l were second degree AV Block and ventricular ectopic beats. Arrhythmias commonly seen with the serum potassium of

7.1-8 mEq/l were complete AV block (66.7%) and second degree AV block (33.7%). Only arrhythmia seen with the serum potassium of more than 8 mEq/l was ventricular tachycardia (100%).

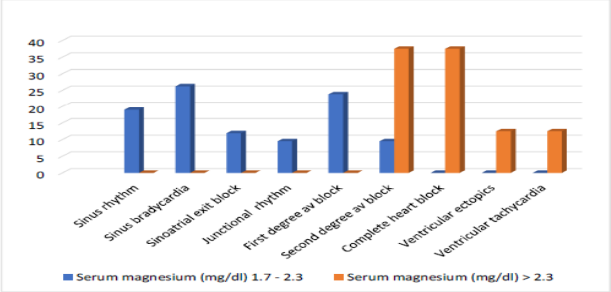

Figure 7: Comparison of serum magnesium with arrhythmias. Fisher's Exact Test value = 25.536; p<0.001.

Figure 6 shows comparison of serum corrected calcium with arrhythmias. Most of the patients had normal serum calcium level, only 5% patients had hypocalcemia.

So corrected serum calcium level seems not to be significant.

Figure 7 indicates comparison of serum magnesium with arrhythmias. Normal magnesium level was seen in the patients with sinus rhythm (19%), sinus bradycardia (26.2%), Sinoatrial exit block (11.9%), first degree AV block (23.8%) and junctional rhythm (9.5%). Hypermagnesemia was seen in the patients with complete heart block (37.5%), ventricular ectopics (12.5%) and ventricular tachycardia (12.5%).

The patients with second degree AV block had both normal serum magnesium level and hypermagnesemia.

Table 4: Comparison of exposures and duration since consumption with serum potassium (n=50).

	Serum potassium (mEq/l)											
	3.5-5.0		5.1-6.0		6.1-7.0		7.1-8.0		>8.0		Total	
	N	%	N	%	N	%	N	%	N	%	N	%
Exposure												
Crushed seeds	6	60	19	73.1	9	90	3	100	1	100	38	76
Whole seeds	4	40	6	23.1	1	10	0	0	0	0	11	22
Leaf	0	0	1	3.8	0	0	0	0	0	0	1	2
Fruit	0	0	0	.0	0	0	0	0	0	0	0	0
Quantity of exposure												
1 - 5	10	100	22	84.6	6	60	0	0	0	0	38	76
6 - 10	0	0	4	15.4	4	40	3	100.0	1	100	12	24
Duration since consumption (in hours)												
0 – 1	6	60	1	3.8	0	0	0	0	0	0	7	14
1 – 2	4	40	4	15.4	4	40	0	0	0	0	12	24
2 – 3	0	0	6	23.1	1	10	1	33.3	0	0	8	16
3 – 5	0	0	12	46.2	2	20	2	66.7	1	100	17	34
5 – 8	0	0	3	11.5	3	30	0	.0	0	.0	6	12

Comparison of exposures and duration since consumption with serum potassium is represented in Table 4. The patients who had consumed crushed seeds had serum potassium level of more than 8 mEq/l, the patients who had consumed whole seeds had serum potassium of 6.1-7 mEq/l, the patients who had consumed leaves had serum potassium of 5.1-6 mEq/l.

Patients with the normal serum potassium were those who had consumed less than 5 seeds, hyperkalemia of more than 7 mEq/l was commonly seen with the patients who had consumed more than 5 seeds.

The patients with normal serum potassium were those who came earlier to the hospital within 1 hour. The patients who came late to the hospital had hyperkalemia upto 8 mEq/l.

In this study, most of the patients who came to the hospital within 1 hour had sinus rhythm and recovered with drugs. Most of the patients who came to the hospital within 1-3 hours had sinus bradycardia, sinoatrial exit block, junctional rhythm and first degree AV block and they recovered with drugs.

Most of the patients who came to the hospital within 3-8 hours had second degree AV block, complete heart block and they recovered with temporary pacemaker. One patient who came to the hospital after 3 hours died due to ventricular tachycardia (Figure 8).

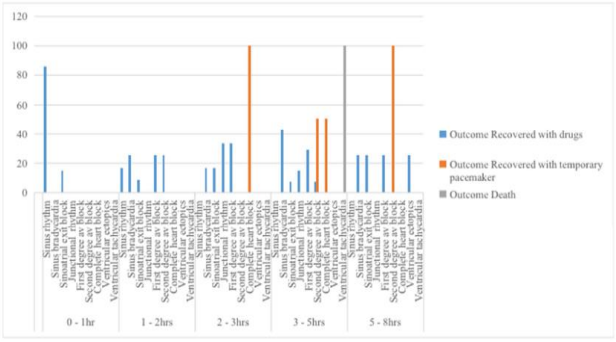

Figure 8: Comparison of duration since consumption to admission and arrhythmias with outcome.

DISCUSSION

A prospective and observational study was designed among the patients admitted in the toxicology ward in the Institute of Internal Medicine, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai, for the ingestion of yellow oleander. Fifty patients, who fulfilled the eligibility criteria, were enrolled for the study. In this study, 26% patients belong to less than 20 years, 52% patients belong to 21-40 years, 18% patients belong to 41-60 years, 2% patients belong to more than 60 years. So consumption of oleander poison was more among 21-40 year age group in our study. This age group needs to be counseled with rehabilitation to prevent the suicidal tendency. Other age groups are also there. The exact reason could not be identified for a particular age group. So the patients should be counseled properly.

In our study, 60% patients were males, 40% patients were females. Eddleston et al in their observation reported that out of 1939 cases admitted males were 1021 (52.7%).[6]

In this study, 76% patients consumed crushed seeds, 22% patients consumed whole seeds, 2% patients consumed leaves and none consumed fruit. So crushed seeds consumption were more common in our study. Sinus rhythm was commonly seen with whole seeds. Sinus bradycardia was commonly seen with leaves. Sinoatrial exit block was commonly seen with crushed seeds. Junctional rhythm and ventricular ectopic beats were commonly seen with whole seeds. First and second degree, complete AV blocks and ventricular tachycardia were common with crushed seeds.

In our study, the patients who consumed crushed seeds had serum potassium level of more than 8 mEq/l, the patients who consumed whole seeds had serum potassium of 6.1-7 mEq/l, the patients who consumed leaves had serum potassium of 5.1-6 mEq/l. So crushed seeds consumption was more prone to severe arrhythmias and hyperkalemia than whole seeds and leaves. Eddleston et al reported yellow oleander induced cardiotoxicity was associated with hyperkalaemia that exacerbates cardiac glycoside induced cardiac arrhythmias.[7] Bandara et al reported that ingestion of either oleander resulted in nausea, vomiting, abdominal pain, diarrhoea, dysrhythmias, and hyperkalemia.[8]

In this study, 76% patients consumed less than 5 seeds, 24% patients consumed 6 to 10 seeds. In our study, among the patients who consumed 1 to 5 seeds, sinus bradycardia was commonly seen. Among the patients who consumed 6 – 10 seeds, second degree AV block and complete heart block were commonly seen. The most dangerous complete heart block and ventricular tachycardia were seen with the consumption of 6 -10 seeds. Sinus rhythm and sinus bradycardia were common with the consumption of 1-5 seeds. In our study, patients with the normal serum potassium were those who consumed less than 5 seeds, hyperkalemia of more than 7 meq/l were commonly seen with the patients who consumed more than 5 seeds. More dangerous arrhythmias and hyperkalemia were associated with consumption of 6-10 seeds. Zamani et al also reported that seeds are the dangerous among all the parts of oleander.[9]

In our study, 14% patients came to the hospital within 1 hour, 24% patients came to the hospital within 1-2 hours, 16% patients came to the hospital within 2-3 hours, 34% patients came to the hospital within 3-5 hours, 12% patients came to the hospital within 5-8 hours. In our study, sinus rhythm was most common among the patients who came to hospital earlier within 1 hour, complete heart block and ventricular tachycardia were more commonly seen with patients who came to the hospital later. In our study, the patients with the normal serum potassium were those who came earlier to the hospital within 1 hour. The patients who came late to the hospital had hyperkalemia upto 8 mEq/l. So earlier the admission to hospital was associated with less dyselectrolytemias and arrhythmias. So earlier the stomach wash with the activated charcoal will prevent the dyselectrolytemias and arrhythmias.

In our study, 10% patients had bradycardia of less than 40 per minute. 20% patients had bradycardia of 41-50 per minute, 54% patients had bradycardia of 51-60 per minute, 16% patients had pulse rate of more than 60 per minute. So most of our patients had pulse rate of 51-60 per minute. So bradycardia correlates with hyperkalemia and arrhythmias.

In our study, 20% patients had serum potassium in the normal range, 52% patients had hyperkalemia in the range of 5.1-6 mEq/l, 20% patients in the range of 6.1-7 mEq/l, 6% patients in the range of 7.1-8 mEq/l, 2% patients in the range of more than 8 mEq/l. So most of the patients had mild hyperkalemia. In our study, 84% patients had normal serum magnesium, 16% patients had hypermagnesemia. Kelly et al reported in their study

that hypermagnesemia influences to digoxin toxicity.[10] But Eddleston et al reported that they found no relation between serum magnesium with arrhythmia.[7]

In our study, 90% patients had normal serum calcium and 5% patients had hypocalcemia. Most of the patients who consumed yellow oleander had normal serum calcium level. Only few people had hypocalcemia. Also there was no correlation between the corrected serum calcium level with the arrhythmias. So corrected serum calcium has no correlation with yellow oleander poisoning.

In our study, 16% patients had normal sinus rhythm, 22% patients had sinus bradycardia, 10% patients had Sinoatrial exit Block, 8% patients had junctional rhythm, 20% patients had first degree AV block, 14% patients had second degree AV block, 6% patients had complete heart block, 2% patients had ventricular ectopic beats, 2% patients had ventricular tachycardia. So sinus bradycardia was the most common arrhythmia in our study. Crushed seeds were associated with life threatening arrhythmias.

In our study, 86% patients recovered with drugs, 12% patients recovered with temporary pacemaker, 2% patients died. Crushed seeds, more the number of seeds, late admission to the hospital, hyperkalemia and hypermagnesemia resulted in poor outcome. So, outcome can be improved by preventing all the factors described above.

One patient died among the study participants. That patient who had consumed 9 crushed seeds and came to the hospital 5 hours after consumption, had hyperkalemia, hypermagnesemia and ventricular tachycardia. So early treating of dyselectrolytemias and arrhythmias with atropine and other drugs and pacemaker will reduce the mortality.

Fifty patients from the toxicology ward, who fulfilled the eligibility criteria, were enrolled for a prospective and observational study for the ingestion of yellow oleander. Oleander in the form of seeds (crushed or whole) and leaves are still used as a suicidal agent. From the study we concluded that oleander seed poison was most prevalent in the 21-40 years of age. Incidence was more among the young males. Mortality was independent of the number of seeds consumed. More the crushed seeds consumed and delay to admission to the hospital, poorer was the outcome. ECG abnormalities were found in majority of the individuals. Electrolyte disturbances (hyperkalemia and hypermagnesemia) were found in significant proportion of the patients. No significant changes were found in the corrected serum calcium level. Prognosis was poor among those who presented with bradycardia, electrolyte disturbances (especially those with hyperkalemia and hypermagnesemia) and complex arrhythmias. The arrhythmias produced by this poisoning might range from Sinus bradycardia to complete heart block and ventricular tachycardia. Sinus bradycardia was the most common arrhythmia seen in this study. The most dreadful arrhythmias associated with poor outcome were complete heart block and ventricular tachycardia. Second degree AV block might revert to sinus rhythm or switch to complete heart block. So careful monitoring is needed for patients with the arrhythmias.

Limitations

The limitations were being a single centre study and exclusion of children. Serum cardiac glycoside (Digoxin) levels were not tested for the patients. Anti Digoxin-antibody (DIGIBIND) treatment was not given.

Recommendations

- Considering mortality and morbidity associated with Oleander poisoning, it may be recommended that the use of oleander as an ornamental plant should be avoided.
- As there are no standard guidelines at present to recommend the indications for temporary pacemaker in the management of Oleander induced arrhythmias, uniform guidelines have to be formulated.

Educating the target age groups and others about the ill effects of oleander poisoning will reduce the incidence of yellow oleander poisoning.

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Ethical approval: The study was approved by the institutional ethics committee

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