YELLOW PHOSPHOROUS POISONING: AN OBSERVATIONAL STUDY FROM A TERTIARY CARE HOSPITAL

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ABSTRACT

BACKGROUND
Yellow phosphorous, a rodenticide, is a lethal toxin in humans that can cause damages to hepatic, cardiovascular, gastrointestinal and the renal systems and it carries significant morbidity and mortality. The current study evaluated the mortality, outcomes and complications associated with acute yellow Phosphorous poisoning.

MATERIALS AND METHODS
The retrospective study was conducted at a teaching hospital in South India, between January 2015 and March 2017. Subjects >13 years of age with acute poisoning due to 3% yellow phosphorous were included in the study. They were classified into various groups based on age, gender, the amount consumed, and time delays in receiving hospital care. The various outcomes including the incidence in different age groups, amount of poison consumed, proportion of patients died, and proportion of patients cured were analysed. Statistical analyses were performed using GraphPad Prism 5.0.

RESULTS
The study enrolled a total of 334 cases, and the male-to-female ratio noted was 0.94:1. Majority of the subjects belonged to the age group of 20-29 years. A mortality rate of 76.24% was observed among the subjects with known outcomes.

The complications noted in the subjects included toxic hepatitis, clinical jaundice, hepatic encephalopathy, hypoglycaemia, myoccarditis, bleeding, respiratory failure and shock. Highest rate of survival was noted in the group treated with N-acetyl cysteine.

CONCLUSION
The study further corroborates the increased incidence of mortality, due to the unavailability of appropriate antidote to yellow Phosphorous. Additionally, increased incidence of self-poisoning was noted in younger age group.

KEYWORDS
Hepatic toxicity, N-Acetyl Cysteine, Rodenticides, 3% Yellow Phosphorous.


BACKGROUND
Yellow phosphorous, a highly toxic form of elemental phosphorous, is widely used as a rodenticide and a fireworks ingredient. Rodenticides are the most easily available source of yellow phosphorous containing around 2%-5% of the element. Intoxication due to suicidal or accidental ingestion can cause damage to cardiovascular, gastrointestinal, hepatic, and renal systems.

This form of elemental phosphorous is extremely lethal for humans. The study by Fernandez and Canizares has cautioned against the use of yellow Phosphorous for fireworks manufacturing and it has been reported to cause a mortality rate up to 27%. A case series from south India has concluded that yellow Phosphorous consumption is more common among younger age group patients reporting with poisoning and there are very limited literature studies on yellow Phosphorous poisoning from tropical nations.

Yellow phosphorous poisoning can occur from industrial accidents, suicidal attempts and also by accidental oral intake. Acute liver failure and cardiovascular collapse occurs when consumed at a dose of 1 mg/kg. The complications associated with ingestion of yellow phosphorous include...
fulminant hepatic failure with parenchymal haemorrhages, hepatorenal failure, cardiovascular collapse, duodenal perforations, and encephalopathy.5,6 The present study evaluated the mortality, outcomes and complications associated with acute poisoning from yellow Phosphorous in a rural Indian population.

MATERIALS AND METHODS
The observational study was conducted at a referral teaching hospital in south India between January 2015 and March 2017. The study included subjects >13 years of age with acute poisoning due to the ingestion of 3% yellow phosphorous paste. Demographic details such as age, sex, mode of consumption of yellow phosphorous, time delay in reaching hospital and outcomes of poisoning were collected from the patients.

Based on the gender, the subjects were classified as male and female and based on the age group as: children: 0-12 years; adolescent: 13-19 years; early adulthood: 20-29 years; middle adulthood: 30-44 years; late adulthood: 45-60 years; and elderly: >60 years. Based on the amount of 3% yellow phosphorous consumed, they were classified as: <3.75g; 3.75g; >3.75-7.5g; >7.5-15g; >15-<30g; and >30g and based on the time delay in receiving hospital care as within one hour, one to two-hours; 3-6 hours; >6-12 hours; >12-24 hours; >24 hours- 2 days; >2-4 days; and >4 days.

Statistical Analysis
The descriptive data are provided as mean±SD for data with normal distribution, as median (range) for data without normal distribution, and as frequency counts for categorical data. Mann-Whitney test and Fisher’s exact test were used to determine significant variation between variables like age (years), amount of poison consumed (g), proportion of patients cured, and proportion of patients died in both the genders. P value of < 0.05 was considered as statistically significant. All the statistical analysis was performed using the Graphpad Prism version 5.0.

RESULTS
The present study retrospectively reviewed a total of 334 cases with 3% yellow phosphorous poisoning. The male to female ratio was noted as 0.94:1. Majority of the subjects belonged to an age group of 20-29 years; 44% males (n=71) and 46% females (n=79). The corresponding proportions noted in the middle adulthood group were 32% (n= 52) and 25% (n=44). The least number of subjects belonged to the age group more than 60 years (Table 1).

Yellow Phosphorous Poisoning

The mean ages noted for male and the female subjects were 31.04 ± 12.54 years and 27.49 ± 12.54 years respectively. The descriptive details of the parameters evaluated and compared between the male and female subjects are provided in table 2. The route of administration was noted as oral in all the cases. Among the subjects studied, the amount of poison consumed was known only in 145 cases. Among the patients with known outcome (n=181), 76.24% died and 23.75% recovered. Among the subjects who recovered, a higher percentage belonged to the male gender (55.81%), and in the proportion who died, a higher percentage belonged to the female gender (58.61%). The outcome was not derived in majority of the patients, as they were discharged at request and/or went against medical advice or absconded.

Among the parameters compared, only age was noted to be significantly higher in the male population (P 0.0017). Other parameters evaluated like amount of poison consumed (P 0.3009) the proportion of patients cured, and the proportion of patients died (P 0.1146) did not differ significantly between the male and the female subjects (Table 2). The study also noted that the incidence of poisoning decreased with increasing age.

Data Is Expressed as Numbers (Percentage)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Male</th>
<th>Female</th>
<th>p Value</th>
<th>Statistical Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age     (Years)</td>
<td>31.04 ± 12.54∞</td>
<td>27.49 ± 12.54∞</td>
<td>0.0017*</td>
<td>Mann-Whitney test</td>
</tr>
<tr>
<td>Amount of Poison Consumed (g) (n=145)</td>
<td>14.09 ± 11.61∞</td>
<td>11.7 ± 8.22∞</td>
<td>0.3009</td>
<td>Mann-Whitney test</td>
</tr>
<tr>
<td>Proportion of Patients Cured (n=43)</td>
<td>55.81%</td>
<td>44.18%</td>
<td>0.1146</td>
<td>Fisher’s exact test</td>
</tr>
<tr>
<td>Proportion of Patients Died (n=138)</td>
<td>41.3%</td>
<td>58.61%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Distribution and Comparison of Variables Between Male and Female Subjects

∞ Mean ± SD
Data are expressed as mean with SD for age and amount of poison consumed. *indicates p<0.05 and considered statistically significant.

The N for amount of poison consumption is 145 as in remaining 189 cases the amount of poison consumed were unknown. The various mode of consumption of poison noted were- accidental intake, direct consumption, along with alcohol, kerosene, other poisons or with food. There were no records on the mode of consumption of poison in around 76% of the cases (n=255). Alcohol was noted as the most common substance used for the consumption of 3% yellow phosphorous (n=55). Direct consumption of 3% yellow phosphorous and consumption with kerosene was noted in least number of cases (0.59%), followed by accidental intake and with other poisons (1.49% each) (Table 3).

<table>
<thead>
<tr>
<th>Mode of Consumption</th>
<th>Number of Patients n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Records</td>
<td>255 (76.3)</td>
</tr>
<tr>
<td>With Alcohol</td>
<td>55 (16.46)</td>
</tr>
<tr>
<td>With Food</td>
<td>10 (2.99)</td>
</tr>
<tr>
<td>Accidental Intake</td>
<td>5 (1.49)</td>
</tr>
<tr>
<td>With other Poisons</td>
<td>5 (1.49)</td>
</tr>
<tr>
<td>With Kerosene</td>
<td>2 (0.59)</td>
</tr>
<tr>
<td>Direct Consumption</td>
<td>2 (0.59)</td>
</tr>
</tbody>
</table>

Table 3. Mode of Consumption of Poison in The Study Subjects

Data Is Expressed as Absolute Numbers (Percentage). N= 334

The complications noted in the subjects were: toxic hepatitis, clinical jaundice, hepatic encephalopathy, hypoglycaemia, myocarditis, bleeding, respiratory failure and shock (Table 4). The highest reported complication was toxic hepatitis (n=134), followed by hepatic encephalopathy (n=95). Compared to males, complications like toxic hepatitis, clinical jaundice, hepatic encephalopathy, hypoglycaemia, myocarditis and respiratory failure were predominantly reported in the female population. Shock and bleeding were more common in the male subjects than females (Table 4).

<table>
<thead>
<tr>
<th>Complications</th>
<th>Percentage of Patients Who Developed Complications n (%)</th>
<th>Frequency of Complications Developed at &lt; 7.5g of Yellow Phosphorous Poison n (%)</th>
<th>Frequency of Complications Developed at &gt; 7.5g of Yellow Phosphorous Poison n (%)</th>
<th>Frequency of Complications Developed at an Unknown Amount of Yellow Phosphorous Poison n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total (n=334)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toxic Hepatitis</td>
<td>134 (40.11)</td>
<td>18 (5.38)</td>
<td>38 (11.37)</td>
<td>78 (23.35)</td>
</tr>
<tr>
<td>Clinical Jaundice</td>
<td>70 (20.95)</td>
<td>10 (2.99)</td>
<td>20 (5.98)</td>
<td>40 (11.97)</td>
</tr>
<tr>
<td>Total Bilirubin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 2 mg/dl</td>
<td>146 (43.71)</td>
<td>28 (8.4)</td>
<td>31 (9.29)</td>
<td>87 (2.04)</td>
</tr>
<tr>
<td>2-3 mg/dl</td>
<td>3 (0.9)</td>
<td>0 (0)</td>
<td>2 (0.59)</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>&gt;3 mg/dl</td>
<td>12 (3.59)</td>
<td>3 (0.89)</td>
<td>3 (0.89)</td>
<td>6 (1.79)</td>
</tr>
<tr>
<td>Hepatic Encephalopathy</td>
<td>95 (28.44)</td>
<td>12 (3.59)</td>
<td>28 (8.38)</td>
<td>55 (16.46)</td>
</tr>
</tbody>
</table>

Table 4. Frequency of Complications Noted in The Study Subjects
Data are expressed as absolute numbers with percentage. The number of subjects consumed ≤ 7.5g and > 7.5 g of yellow phosphorous poison in the study were 74 and 71 respectively.

The frequency of complication was noted to be proportional to quantity of the poison. Toxic hepatitis, clinical jaundice, hepatic encephalopathy, hypoglycaemia, myocarditis and shock were mostly observed in subjects consuming >7.5 g of yellow phosphorous poison, compared to those consuming <7.5 g of the poison. However, respiratory failure and gum bleeding were reported only in those who consumed the poison at a dose of <7.5 g.

The frequency of death increased with the amount of yellow phosphorous consumed, and with the time delay in receiving primary care (Fig. 1(A) and 1(B)). No deaths were reported in patients who consumed <3.75 g of yellow phosphorous, and none of the patients who consumed >15-<30 g of the yellow phosphorous survived. More than 25 cases of deaths were reported among those who received the hospital care after 12-24 hrs. The various treatment modalities employed were N-acetyl cysteine (NAC), fresh frozen plasma (FFP), L-Ornithine L-Aspartate (LOLA), NAC & FFP, NAC & LOLA, FFP & LOLA, and combination of FFP, NAC and LOLA. The highest rate of survival was noted in the group treated with NAC, followed by NAC & FFP (Fig. 1(C)).
Figure 1c

Figure 1. Outcome Measures of Different Variables.
(A) With Respect to the Amount of Yellow Phosphorous Consumed Excluding the Absconded and the Unknown Cases.
(B) With Respect to the Time Delay in Receiving Hospital Care, Excluding the Absconded and Unknown Cases.
(C) With Respect to Various Treatment Modalities Employed.

DISCUSSION
The current study, conducted for a period of ~2 years, has reported rodenticide (3% yellow phosphorous) poisoning in around 334 cases. A similar study by Chikkaveeraiah et al. (2016) has reported a total of 64 cases admitted with rodenticide poisoning, during a period of one year, among which the yellow phosphorous poisoning was noticed in 18 cases.7 Nalabothu et al. (2015), also reported suicidal cases of rodenticide poisoning (44% by yellow phosphorous) in around 95% of the cases. Among the reported cases the incidence was found to be higher in the age group of 18-40 years.8 The current study indicates an alarming increase in the proportion of individuals depending on rodenticides (3% yellow phosphorous) for self-poisoning. Accidental consumption was recorded only in 2% of the study subjects.

Similar to the present study findings, Chikkaveeraiah et al. have reported that majority of the admitted subjects (53.1%) belonged to the age group of 21-30 years.7 Ramesha et al. (2009) have also noted increased incidence of poisoning in subjects belonging to 20-29 years age, followed by 12-19 years.9 Banerjee et al. (2014), reported poisoning majorly in younger age group individuals.10 Suneetha et al. have suggested that the increased rate of poisoning noted in this age group can be attributed to the elevated psychological stress to which the youth are subjected to.11

The Indian studies by Chikkaveeraiah et al., Ramesha et al. and Nalabothu et al. have noted an increased preponderance of poisoning in male subjects than females.7-9 Whereas, the present study has noted a significant predominance in females, belonging to the younger age group compared to male cases. In concurrence with these findings, Banerjee et al. and Suneetha et al. have observed that the incidence of poisoning was higher in female subjects than in males.10-11 The corresponding proportions of males and females admitted due to poisoning noted in the study by Suneetha et al. were (41% and 59%), which is comparable to that of the present study (48.5% and 51.4%).

Yellow phosphorous consumption was reported to impair the gastrointestinal tract, liver, cardiovascular, nervous and the respiratory systems.7 Several studies have investigated the adverse effects of yellow phosphorous poisoning on the hepatic system. Mauskar et al. have reported the development of symptoms of hepatic failure in a 3-year old child, after 48-hours of consumption of 3% yellow phosphorous.1 Karanth et al. reported acute hepatitis along with the symptoms of hepatocellular failure in a 25-year old female who consumed 3% yellow phosphorous containing rodenticide.12 Ravikanth et al. have reported fulminant hepatic failure with parenchymal haemorrhages and duodenal perforation in a case with yellow phosphorous poisoning.6 The most common outcomes of yellow phosphorous poisoning noted in the present study were toxic hepatitis and hepatic encephalopathy, followed by myocarditis and clinical jaundice. Alcohol was the most commonly used substance along with 3% yellow Phosphorous during consumption. However, it did not significantly interfere with the mortality of the patients.
Several studies have concluded that amount of poison consumed is directly proportional to rate of death. The current study has noted an increase in the rate of mortality with the increase in the dose of 3% yellow phosphorous consumption and also with the time delay in receiving hospital care. In the study by Chikkaveeraiah et al. the corresponding amount of yellow phosphorous consumption noted in subjects who had survived and those who expired were 3.52 g and 5.75 g respectively. The present study has noted a significant increase in the mortality rate with increase in the dose of 3% yellow phosphorous from >7.5 g to 15 g. None of the subjects with known outcome who had consumed a dose more than 15 g survived. The outcomes like toxic hepatitis, clinical jaundice, hepatic encephalopathy, hypoglycaemia, myocarditis and shock were the most commonly noted complications in subjects who consumed >7.5 g of yellow phosphorous poison compared to those who had <7.5 g.

Studies have reported mortality in about 27% of the cases who consumed yellow phosphorous, claiming it as an extremely lethal toxin. McCarron et al. have reported mortality rate ranging from 23% to 72% in cases of yellow phosphorous poisoning. Maharani and Vijayakumari (2013) reported that rat killer poison (aluminium phosphide and zinc phosphate) had a higher mortality rate compared to organo Phosphorous compounds, due to the unavailability of the appropriate antidote. The present study also noted a mortality rate >76% in subjects with known outcomes of 3% yellow phosphorous. The absence of specific antidote against the poison remains the major challenge in tackling the issue. In acute phosphorous poisoning, the affected subject may show gastrointestinal symptoms and shock during the first 24 hours, followed by a quiescent period for 1-3 days. Hepatic damage, hepatic failure, renal failure, arrhythmia, seizures and coma occur in the final stage. The present study has noted that the time delay in hospitalization or commencing treatment was proportional to the rate of mortality. A significant increase in mortality was noted with the time delay of more than 12 hours.

Fernandez et al. have suggested that N acetyl cysteine treatment did not have a significant effect on the outcome in patients with yellow phosphorous poisoning. Whereas, Bhat et al. have reported considerably lower mortality in people receiving NAC treatment. Early treatment with NAC has been reported to render favourable prognosis in people with rodenticide poisoning. Complying with these findings, the present study has noted highest rate of survival in patients treated with NAC alone, and with both NAC and FFP.

CONCLUSION
Yellow phosphorous poisoning is associated with significant mortality due to the unavailability of appropriate antidote and delay in receiving hospital care. The present study highlights the need of restricting the access to inorganic Phosphorous and increasing the awareness regarding the lethality of such poisons. The increased incidence of self-poisoning with yellow phosphorous was noted in younger age group. This finding warrants further studies to explore the association between suicidal poisoning and psychological stress levels in this age group.

REFERENCES