

Rodenticide Poisoning: Critical Appraisal of Patients at a Tertiary Care Center

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ABSTRACT

Importance: Rodenticide poisoning is a common occurrence in India. Of the different classes of rodenticides available, yellow phosphorus is considered highly toxic. There are scarce epidemiological data regarding the ingestion of yellow phosphorus in the subcontinent.

Objectives: This study aimed to identify the clinical profile of rodenticide-poisoned patients and delineate mortality predictors.

Design: Prospective observational study.

Setting and participants: Study was conducted at the Department of Internal Medicine, Government Villupuram Medical College and Hospital. All adult inpatients with a history of rodenticide poison exposure were eligible participants. A total of 99 patients completed the study protocol.

Main outcome: Survival with or without morbidity and death.

Results: In all, 90.91% of patients consumed the paste formulation of rodenticide [yellow phosphorus (67.2%) and yellow phosphorus + zinc phosphide (24%)]. The time to resuscitation showed significance to mortality. Survival rate among patients instituted gastric decontamination within 2 hours of exposure (97.87%) was significantly higher than those who were not (84.62%) ($p = 0.033$). The clinical picture revealed conspicuous absence of signs and symptoms during the first 24 hours. In all, 72.73% ($n = 72$) manifested with toxidrome after a lag period of 24–36 hours (range 18–72 hours). The dominant clinical manifestations included abdominal pain (52.53%), jaundice (22.21%), coagulopathy (15.15%), encephalopathy (10.10%), shock (10.10%), acute kidney injury (AKI; 7.08%), and multi-organ failure (17.17%). Laboratory data showed elevated aspartate transaminase (AST; 48.47%), alanine aminotransferase (ALT; 49.50%), bilirubin levels (22.21%), metabolic acidosis (10.12%), serum creatinine (7.08%), prothrombin time prolongation (PT/INR; 15.15%), and activated partial thromboplastin time (aPTT) (3.30%). The mortality was 9.1% ($n = 9$) of which 77.78% ($n = 7$) died of fulminant hepatic failure. The mean time for death was 4.22 days since exposure (range 2–8 days).

Conclusion: Rodenticide poisoning in Southern India is dominated by yellow phosphorus. In this study, we identified delayed resuscitation, jaundice, hepatic encephalopathy, elevation of AST and ALT to >1000 IU/L, metabolic acidosis, and refractory shock as reliable predictors of bad outcome in this patient population. The common mode of death was fulminant hepatic failure.

Relevance: Rodenticide poisoning ranks second in mortality hierarchy at our institute, and systematic analysis of this patient population is an urgent need.

Keywords: Mortality, Rodenticide poisoning, Yellow phosphorus.

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INTRODUCTION

Pesticide abuse for self-harm is a global concern, more so in developing nations. In India, rodenticide poisoning is a common occurrence, though the exact incidence is yet to be ascertained. Rodenticides as a group encompass divergent compounds ranging from yellow phosphorus to superwarfarins.¹ Among the various congeners of this group, yellow phosphorus stands high in mortality hierarchy as it can cause hepatocellular necrosis and fulminant hepatic failure.² Previous research work in the area revealed that yellow phosphorus is the commonest rodenticide used for intentional self-harm, causing 30% fatalities.³ Preliminary observation at our institute revealed a high case burden and compelling mortality indices of rodenticide poisoning. This study was designed to critically appraise the clinical characteristics of these patients and possibly identify prognostic determinants.

MATERIALS AND METHODS

A prospective observational study was designed to recruit a sample size of 100 inpatients with rodenticide poison exposure. The eligibility was decided based on the predefined criteria (Table 1). A total of 115 patients fulfilled the eligibility standards.

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After attrition, there were 99 patients whose data were consolidated (Fig. 1). Preliminary information, such as age, sex, demographics, etc., were documented. The case presentation and the time scale of development of signs/symptoms were recorded chronologically

as also the laboratory parameters. The variables were charted and analyzed for significance related to frequency and mortality. Statistical analysis was carried out using the SPSS version 20.0 software. For frequency distribution and descriptive statistics Fisher's exact test of association was used, whereas binary logistic regression model applied for mortality determinants. Significance was defined as a p value of <0.05 .

RESULT

The sex distribution was 51 male and 48 female patients. The study population's age ranged between 19 and 46 years. In all, 90.91% consumed paste formulation of rodenticide in which the active constituent was yellow phosphorus (67.68% of patients) and yellow phosphorus + zinc phosphide (23.23%). The remaining 9 patients' choice of rodenticide included brodifacoum cake (2), aluminum phosphide pellets (2), 2% zinc phosphide granules (2), bromadiolone cake (2) and locally manufactured dried strychnine powder (1). The amount consumed could not be ascertained due to obvious reasons and hence was an unreliable predictor of outcome. In general, those who consumed more than 5 g of paste stood more vulnerable to death, though the association was not statistically significant (Table 2). Hitherto, the body mass index, nutritional status, and sex differences did not have any influence on the outcome. The time to resuscitation, however, showed a significant relationship to death. Our institute being a referral center, only 47 patients presented early after rodenticide consumption among whom 46 survived. Survival rate among patients instituted gastric decontamination (activated charcoal) within 2 hours of exposure

(97.87%) was significantly higher than those who were not (84.62%; $p = 0.033$).

The clinical picture revealed conspicuous absence of signs and symptoms on day 1 of exposure. Only 13.13% ($n = 13$) of patients showed symptoms of gastrointestinal (GI) intolerance such as nausea, vomit, and abdominal pain in the initial 24 hours following rodenticide intake. Majority of patients (72.73%) manifested with toxidrome after a lag period of 24–36 hours (range 18–72 hours). A small segment (14.14%) remained asymptomatic through the entire course of inpatient observation. During the hospital stay, 52.53% ($n = 52$) of patients manifested abdominal pain, 22.21% ($n = 22$) developed jaundice, 15.15% ($n = 15$) suffered bleeding manifestations, 10.10% ($n = 10$) had altered mentation, 10.10% ($n = 10$) experienced symptomatic hypotension, 7.08% ($n = 7$) developed oliguric acute kidney injury (AKI), and 17.17% ($n = 17$) had features of multi-organ dysfunction. Baseline laboratory parameters such as liver function test, blood glucose, blood urea level, serum creatinine, arterial blood gas analysis, and coagulation parameters were essentially within the normal limits. Further follow-up investigations showed elevated aspartate transaminase (AST; 48.47%), alanine transaminase (ALT; 49.50%), bilirubin levels (22.21%), metabolic acidosis (10.12%), serum creatinine (7.08%), prothrombin time/international normalised ratio (PT/INR) prolongation (15.15%), and activated partial thromboplastin time (aPTT; 3.30%) (Table 2). The treatment rendered included *N*-acetylcysteine (NAC) in various formulations, vitamin K supplements, and supportive care. The mortality was 9.1% ($n = 9$) of which 77.78% ($n = 7$) died of fulminant hepatic failure. The mean time for death was 4.22 days since exposure (range 2–8 days).

Table 1: Participant selection criteria

Inclusion criteria
<ul style="list-style-type: none"> Adult patients admitted for rodenticide poison exposure. Presentation within 24 hours.
Exclusion criteria
<ul style="list-style-type: none"> Patients who consumed rodenticide mixed with other poisons. Patients who consumed indigenous rodenticides (constituents not known) Patients with preexisting chronic liver disease, chronic kidney disease.

DISCUSSION

Previous research on rodenticide poisoning highlights that yellow phosphorus is the most culprit agent.³ Probable reasons motivating this choice include easy availability, low cost, and high toxicity profile.³ The compound is manufactured predominantly in paste formulation either alone or in combination with zinc phosphide under various commercial nomenclatures (RATOL, RATNIL, RATOUT, etc.). The estimated killing dosage of around 8–12 mg/kg is not very accurate, with deaths reported on either side of the reference value.^{4,5} The toxicity is due to phosphoric acid liberated via an exothermic reaction upon exposure of yellow phosphorus to the gastric milieu. Phosphoric acid acts like a general protoplasmic

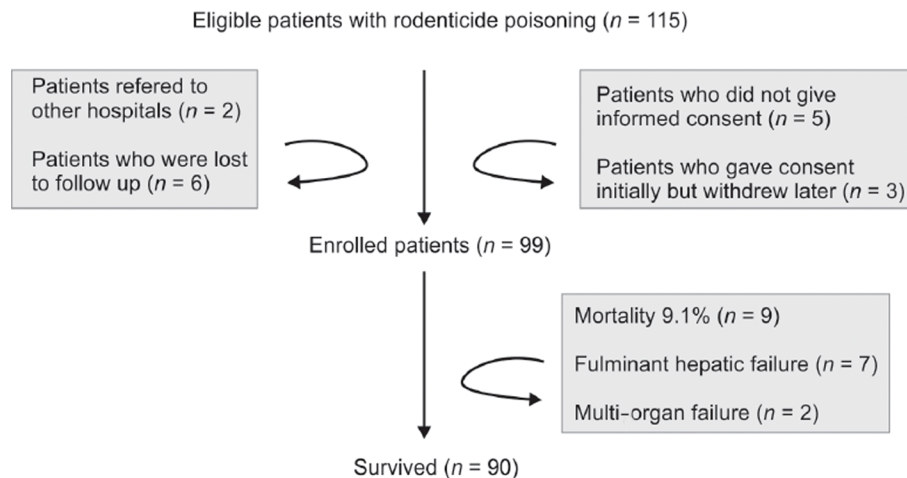


Fig. 1: Patient enrollment for the study

poison, causing direct cellular lysis by inhibition of ribosomal function.⁶

The clinical picture is falsely reassuring in the first few hours wherein minimal, if any, symptoms occur. The term “toxic time bomb” used to denote this phenomenon is well founded. Absence

Table 2: Bivariate analysis of clinical features and laboratory values in rodenticide-poisoned patients

Variable	Survived	Died	Fisher's exact p value
Consumed <5 g (42)	39	3	0.729
Consumed >5 g (57)	51	6	
Resuscitated <2 hours (47)	46	1	0.033
Resuscitated >2 hours (52)	44	8	
Shock			
Present	3	7	0.0001**
Absent	87	2	
Abdominal pain			
Present	47	5	1.00
Absent	43	4	
Jaundice			
Present	17	5	0.0024*
Absent	73	4	
Encephalopathy			
Present	3	7	0.0001**
Absent	87	2	
Acute kidney injury			
Present	5	2	0.122
Absent	85	7	
Multi-organ dysfunction			
Present	15	2	0.650
Absent	75	7	
Prothrombin time/INR			
Prolonged	46	7	0.169
Normal	44	2	
Metabolic acidosis			
Present	0	7	0.0001*
Absent	90	2	
Aspartate aminotransferase			
>1000	2	7	0.0001*
<1000	88	2	
Alanine aminotransferase			
>1000	3	7	0.0001*
<1000	87	2	
N-Acetylcysteine injection			
Given	38	4	0.729
Not given	56	5	
N-Acetylcysteine tablets			
Given	56	5	1.0
Not given	38	4	

of reliable clinical or biochemical markers to identify the ongoing systemic toxicity in this early phase is the stumbling stone for intensive care physicians working in this field. The initial phase lasting for 18–36 hours is punctuated by GI symptoms such as nausea, vomit, and abdominal pain in a few patients.⁷ Following this phase is the stormy onset of features related to acute hepatic failure, encephalopathy, myocardial dysfunction, AKI, and/or multi-organ failure.^{4,7} This phase lasts between 36 hours and 96 hours and is followed by either death or clinical resolution over the next few days. The mean time for recovery was estimated at 8.8 days in previous reports.⁸ In our study, we observed that 72.73% of patients manifested after 24 hours of poison exposure. The predominant features included abdominal pain (52.53%), jaundice (22.21%), bleeding manifestations (15.15%), encephalopathy (10.10%), shock (10.10%), AKI (7.08%) and multi-organ dysfunction (17.17%). In our case series, we identified hepatic encephalopathy, jaundice, and shock as reliable forerunners of death (Table 2). Clinical manifestations and outcome vary in different reports. In an earlier analysis, 87% patients had some hepatic derangement and 27% died of fulminant hepatic failure.² Similarly, mortality in a second case series was 28%.³ The mortality in our series was 9.1% ($n = 9$) which is far less than the regional estimates (30%). This was probably attributed to the intake of sublethal amounts of xenobiotic. Since there is no foolproof quantitative assessment method to ascertain the amount of poison consumed, its effect on mortality could not be deciphered in our study. The main mode of death was fulminant hepatic failure in 77.78% ($n = 7$) with the remaining two dying of refractory shock and multi-organ failure (Figs 2 and 3).

The laboratory picture was dominated by liver function abnormalities such as AST (48.47%/ $n = 48$) and ALT 49.50%/ $n = 49$) elevation. We could not plot the mean area under AST/ALT curve because of the huge variation between survivors and nonsurvivors. The mean value of liver enzymes for survivors vs nonsurvivors was AST (123.50 ± 57.24 vs 1035 ± 314 IU/L) and ALT (147.61 ± 65.12 vs 1153 ± 245 IU/L), respectively. The difference was statistically significant ($p < 0.01$). The PT/INR was prolonged in 53 patients (53.54%), but no statistically significant difference was found between survivors and the dead (mean 28 ± 15 seconds). Metabolic acidosis was documented in seven patients all of whom died, thereby showing statistical importance ($p < 0.01$). Literature search revealed that AST/ALT elevations >10 times the normal value, derangements in PT/INR, metabolic acidosis, and hypoglycemia were important

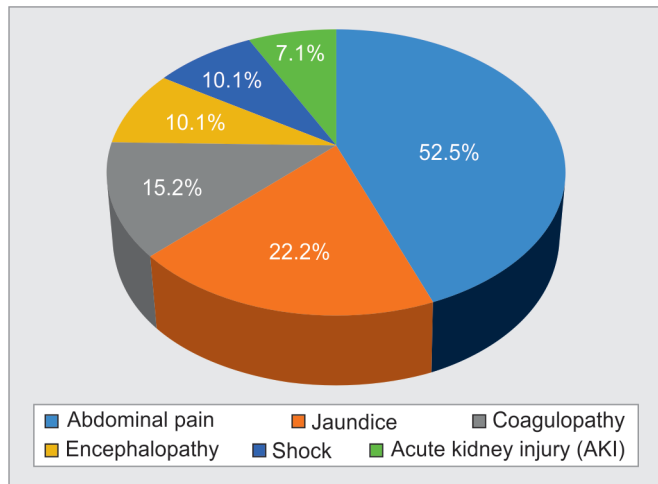


Fig. 2: Clinical profile of rodenticide-poisoned patients

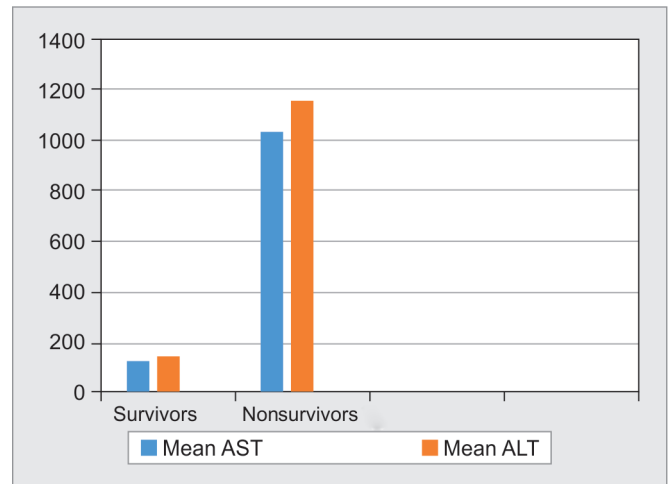


Fig. 3: Comparison of AST/ALT levels between survivors and nonsurvivors

portenders of death.² Nalabothu et al., in his cross-sectional case series, identified model for end stage liver disease (MELD) score as a prognostic tool for yellow phosphorus poisoning.³ Akin to previous research work, our study also observed significant relationship of elevated liver enzymes and metabolic acidosis to death (Table 2).

There is no known antidote for yellow phosphorus poisoning. That said, management of this condition hovers around meticulous monitoring and intensive supportive care. The NAC has received quite some attention in the recent past for its beneficial effects in such cases. The logical theory backing its utility is that it replenishes glutathione stores that neutralize the free radical-induced cytotoxicity of yellow phosphorus.⁹ Administering NAC early in the course of the disease could possibly have a lifesaving effect as proven by previous reports.¹⁰ Ironically many of the yellow phosphorus-poisoned patients remain asymptomatic during the initial few hours. Whether every patient with a history of yellow phosphorus poisoning should be instituted NAC irrespective of his or her clinical status is a matter of speculation. Multiple other efforts that evaluated the validity of NAC in the treatment of yellow phosphorus overdosage have yielded conflicting results.^{6,11,12} Given the excellent therapeutic window of NAC, early administration of this agent for all yellow phosphorus-poisoned patients would definitely outweigh the risk. NAC at our institute was administered without scientific rationale at widely variable dosages and formulations. Furthermore, our study was not designed to evaluate the efficacy of NAC in rodenticide poisoning and hence its impact on the outcome could not be assessed.

CONCLUSION

Phosphorus-based rodenticides claim many human lives. Given the fact that there is no specific antidote, constant vigil and timely resuscitation could be the only factors to tilt the balance favorably. Stringent legislative measures to restrict the indiscriminate and over-the-counter sales of yellow phosphorus are much needed in our country. In this study, we identified delayed resuscitation, jaundice, hepatic encephalopathy, elevation of AST and ALT to >1000 IU/L, metabolic acidosis, and refractory shock as the significant predictors of bad outcome in this patient population. The common mode of death was fulminant hepatic failure.

LIMITATION

Our research study was not designed to be conducted in a controlled environment and hence the management was at the discretion of the treating physician. Although the study team could gain access into time-bound investigation of the patients, they were not part of the decision-making committee. This being an observational study, no particular institutional or evidence-based

protocol was followed in administering NAC and hence its benefits/shortfall could not be assessed.

ETHICS APPROVAL

The study was approved by the institutional ethics committee.

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