Section: Pediatrics

Research

PROSPECTIVE OBSERVATIONAL STUDY ON THE CLINICAL PRESENTATION AND MORTALITY PREDICTORS OF RAT-KILLER PASTE POISONING IN A TERTIARY CARE HOSPITAL

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Abstract

Background: Rat killer paste which contains yellow phosphorus (3%), is the most toxic poison of all those poisons reported next to OPC and hair dye poisoning in Tamil Nadu. Unfortunately, studies on the clinical-epidemiological information of yellow phosphorous poisoning are scarce. This study analyses the clinical presentation and mortality predictors of rat-killer paste poisoning. **Materials and Methods:** This study was a short-term prospective observational study conducted at the Department of Internal Medicine, Thoothukudi Government Medical College. Included participants were inpatients admitted with a history of consuming rat poison paste between December 2021 and May 2022. Morbidity in the form of fulminant hepatic failure and mortality were analysed. **Result:** A total of 17 patients were identified, and 15 patients completed the study protocol. 53.33% were female, 73% of the cases were < 30 years of age, 73.33% were from rural areas, 67% were unmarried, 40% were illiterate, 13.5% were housewives, and 60% were students. All cases consumed the paste containing 3% yellow phosphorus. Age > 30 years of the need for resuscitation, shock, encephalopathy, multi-organ dysfunction syndrome (MODS), and model for end-stage liver disease (MELD) score > 25 were the predictors with significant ($p<0.05$) effects on mortality and morbidity. The mortality was 20% (n = 3), of which 67% (n = 2) died of fulminant hepatic failure. The mean time for death was 6.3 days since exposure (range 4-12 days). **Conclusion:** In this study, we identified Age > 30yrs, need for resuscitation, shock, encephalopathy, MODS, and MELD score > 25, as reliable predictors of a bad outcome in this patient population. In addition, fulminant hepatic failure was the common mode of death.

INTRODUCTION

Pesticide poisoning as a method of suicide is very common in developing nations, of which rat killer poisoning incidence is very high in India. Rat killers can be compounds ranging from yellow phosphorus to superwarfarins.[1] Of which yellow phosphorus can cause hepatocellular necrosis and fulminant hepatic failure leading to high mortality.[2] Yellow phosphorus, the commonest rat killer used for suicide, can cause about 30% of fatalities.[3] In our institute, rat killer poisoning is the third most common cause of suicidal poisoning. Also, studies on the clinical-epidemiological information of yellow phosphorous poisoning are scarce in India. Thus, we have studied the clinical presentation and mortality predictors of rat-killer paste poisoning in a tertiary care hospital in a prospective observational study.

MATERIALS AND METHODS

The present study was a short-term prospective observational study. It was conducted at the Department of Internal Medicine, Thoothukudi Government Medical College. Inpatients admitted with a history of rat killer paste ingestion from December 2021 to May 2022 were the eligible participants. Morbidity in the form of fulminant hepatic failure etc., and mortality were analysed.

Inclusion Criteria

Adult patients admitted with H/O rat killer paste poisoning as inpatients in the Department of Internal

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Medicine, Government Thoothukudi Medical College.

Exclusion Criteria

- Patients who consumed rat killer paste mixed with other poisons.
- Patients with preexisting co-morbidities like chronic liver disease and kidney disease.

A total of 17 patients fulfilled the eligibility standards. Of which 2 were lost for follow-up, and 15 patients were finally analysed. Socio-demographic information such as age, sex, marital status, residential place, education, and occupation was documented. The presenting signs or symptoms were recorded chronologically along with the laboratory parameters. The variables were charted and analysed for significance related to frequency and mortality. Finally, statistical analysis was done. Fisher's exact test of association was used. Significance was defined as a p-value of <0.05.

RESULTS

This study's sample size was 16, based on the population incidence of 2% and a 95% confidence interval with a 7% margin of error. This means 16 or more measurements/surveys are needed to have a confidence level of 95% that the real error value is within ±7.08% of the measured/surveyed value. Seventeen patients were identified, and 15 completed the study protocol. Out of these 15 patients' mortality was reported in 3 patients, 2 had a fulminant hepatic failure, and one had multi-organ dysfunction syndrome (MODS).

Socio-demographic profile of cases

[Figure 1 and 2] shows the distribution of sex and age among study participants. [Figure 1] indicated that 53.33% were females and 46.67% were males. [Figure 2] indicated that 73% of the cases were < 30 years of age. The socio-demographic data indicated that 73.33% were from rural areas, 67% were unmarried, 40% were illiterate, and 60% were students.

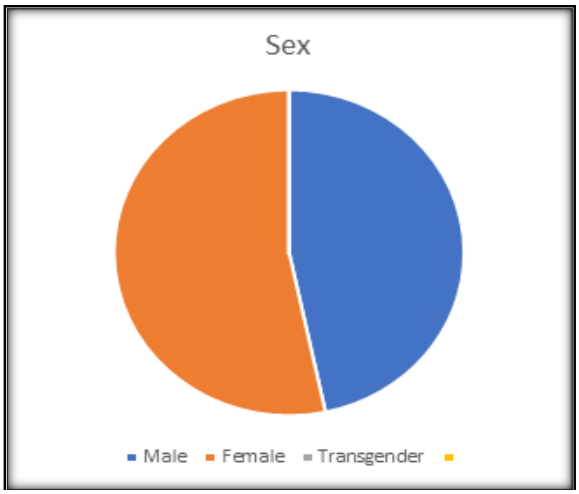

Figure 1: Distribution of the sex among participants

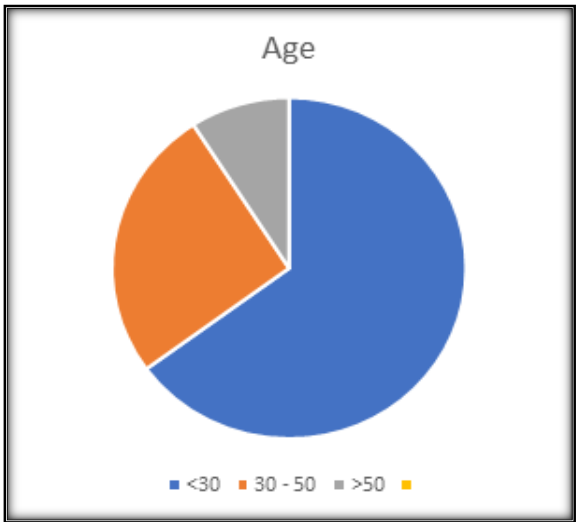

Figure 2: Distribution of the age among participants

Table 1: MELD score and mortality

MELD Score	Mortality
≤9	1.9%
10–19	6.0%
20–29	19.6%
30–39	52.6%
≥40	71.3%

Table 2: Socio-demographic characters, Clinical parameters, lab parameters, and treatment given

Variable	Survived	Died	Fisher's exact p-value
Socio-demographic characters			
Time of presentation Time < 6 hrs Time > 6 hrs	 8 4	 1 2	0.5253
Age Age < 30 yrs Age > 30 yrs	 11 1	 0 3	0.0088
Amount <15gms > 15 gms	 0 12	 1 2	0.2
Clinical parameters			
Resuscitation needed not needed	 0 12	 3 0	0.0022

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Shock Present Absent	 2 10	 0 3	 0.022
Jaundice Present Absent	 8 4	 3 0	 0.5165
Coagulopathy Present Absent	 7 5	 3 0	 0.5055
Encephalopathy Present Absent	 2 10	 3 0	 0.022
MODS Present Absent	 0 12	 3 0	 0.0022
Lab parameters			
MELD score <25 >25	 2 10	 3 0	 0.022
ALT <500 >500	 4 8	 2 1	 0.5253
AST <500 >500	 4 8	 2 1	 0.5253
Treatment			
NAC Given Not given	 12 0	 3 0	 1

Table 3: Stages of Yellow Phosphorus poisoning

Sr. No	Stage	Time since poisoning
1.	Stage of General symptoms	0 – 24 hours
2.	Asymptomatic stage	24 – 72 hours
3.	Advanced stage	>72 hours

Table: 4 Clinical features in Advanced stage.[21,22]

System	Clinical features
Cardiovascular	Hypotension, Tachycardia, Arrhythmias, Cardiogenic shock
Gastrointestinal	Acute fulminant hepatitis, Hepatic encephalopathy, Coagulopathy. (Liver histology shows steatohepatitis and necrosis)
Central nervous system	Irritability, Confusion, Hallucinations, Psychosis, Coma
Renal	Acute tubular necrosis, Anuric renal failure

Model for end-stage liver disease (MELD) score:
Candidates who are at least 12 years old receive an initial MELD(i) score equal to:
$MELD(i) = 0.957 \times \ln(Cr) + 0.378 \times \ln(bilirubin) + 1.120 \times \ln(INR) + 0.643$
Then, round to the tenth decimal place and multiply by 10.
If MELD(i) > 11, perform additional MELD calculation as follows:
$MELD = MELD(i) + 1.32 \times (137 - Na) - [\ 0.033 \times MELD(i) \times (137 - Na)]$
The statistical analysis for socio-demographic characters, clinical parameters, lab parameters, and treatment are shown in table 2. There was a significant difference in age, resuscitation need, shock, MODS, Encephalopathy, and MELD score. However, there was no significant difference for time of presentation, amount consumed, Jaundice, Coagulopathy, ALT (alanine transaminase), AST (aspartate aminotransferase), and NAC treatment given [Table 2]. Thus, age > 30 years, need for resuscitation, shock, encephalopathy, MODS, and MELD score > 25 were the predictors with significant ($p<0.05$) effects on mortality.

DISCUSSION

A total of 17 patients fulfilled the eligibility standards. Of which 2 were lost for follow-up. Fifteen patients were finally analysed. Socio-demographic information such as age, sex, marital status, residential place, education, and occupation was documented. The clinical picture was asymptomatic during the first few hours. After 6 hours, abdominal pain with nausea was the major presenting complaint. Following this phase is the onset of features related to acute hepatic failure, encephalopathy, myocardial dysfunction, and or multi-organ failure were set in.[4,7] This phase lasts between 4 to 12 days and is followed by either death or clinical resolution over the next few days. The mean time for recovery was estimated at 8 days in most previous reports, similar to our study.[8]

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In this study, we observed that in 53.33% of patients, symptoms manifested after 24 hours of poison exposure. The major features included abdominal pain (47%), vomiting (53.33%), jaundice (80%), bleeding manifestations (6.67%), encephalopathy (26.67%), shock (53.33%), and multi-organ dysfunction (20%). In addition, age> 30 years of the need for resuscitation, shock, encephalopathy, MODS, and MELD score > 25 were the predictors with significant ($p<0.05$) effects on mortality.

Clinical manifestations and outcomes vary in different reports. In an earlier analysis, 87% of 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 was 20%, of which 67% died of fulminant hepatic failure. The mean time for death was 6.3 days since exposure (range 4-12 days). The amount consumed was more than 10 g in most cases. Therefore, it was an unreliable predictor of outcome. Those who consumed more than 15 g of paste were more vulnerable to death, though the association was not statistically significant. Other parameters like the time of presentation and sex differences did not have any influence on the outcome. The main mode of death was refractory shock and multi-organ failure.

The laboratory parameters like AST, ALT, prothrombin time (PT), and activated partial thromboplastin time (aPTT) were elevated but not statistically significant in our study. The literature search revealed that AST/ALT elevations >10 times the normal value, derangements in PT/INR, metabolic acidosis, and hypoglycemia were important portenders of death.[2] Nalabothu et al., in their cross-sectional case series, identified a model for end-stage liver disease (MELD) score as a predictive tool for yellow phosphorus poisoning.[3] Similar to previous research, our study also observed elevated MELD SCORE > 25 to death. Unfortunately, there is no known antidote for yellow phosphorus poisoning.

Yellow phosphorus is a highly toxic inorganic element commonly used in crackers, ammunition, fertilizers, and rodenticides. It has a garlic-like odour and is also called "White Phosphorus". As there is an emerging resistance to conventional rodenticides, yellow phosphorus is now being used as a rodenticide in the form of a paste. Since it comes in a paste formulation, there is an increased chance of accidental poisoning. Yellow phosphorus was the most common agent among rat killer poisonings in past studies.[3] Its easy availability, low cost, tastes of sweet and sour, and high toxicity profile could have been the reason.[3] The compound is manufactured predominantly in paste formulation. The estimated killing dosage of around 15gms.[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 poison, causing direct cellular lysis by inhibiting ribosomal function and periportal injury.13 Its toxic effect is mainly due to the alterations that occur in the ribosomal function leading to altered protein synthesis. It also causes dysregulation of blood sugar and glycogen deposits. It also affects the lipoprotein synthesis and secretion of triglycerides, causing fatty degeneration in multiple organs.

Intoxication occurs with suicidal or accidental ingestion. It is easily absorbed from the gastrointestinal tract and other mucosal surfaces and even through the skin.[14] It is evenly distributed and concentrated in many tissues in our body, particularly the liver,[15,16] and the peak level is reached after 2 to 3 hours of ingestion. The toxic dose is 15mg, and more than 50 mg is considered fatal (1 mg/kg on average).[17] Patients with yellow phosphorus intoxication pass through 3 stages.

Stage of general symptoms

This stage is predominantly characterised by gastrointestinal symptoms.[21,22]

1. Abdominal pain
2. Nausea and vomiting
3. loose stools and
4. Fever.

Apart from these clinical symptoms, the patients do not have any abnormalities that can be detected using lab investigations.

Asymptomatic stage

The patient seems to be well-preserved and has no symptoms during this stage. But there will be a mild elevation of bilirubin and hepatic transaminase (SGOT, SGPT) with demonstrable histological changes suggestive of toxic hepatitis. This is a stage where the patient may be discharged from the hospital as the patient is symptom-free.

Advanced stage

This stage occurs after 3 days of poisoning and lasts until recovery or death of the patient.

Depending on the amount of yellow phosphorus ingested, some patients spontaneously recover from the initial phase of insult. The reason for spontaneous recovery is unknown.

Management.[21,22]

1. **Skin Decontamination:** As yellow phosphorus can be absorbed across the skin, all the particles must be washed cleanly with water.

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2. **Supportive Management:** Airway securing and seizure control must be done before gastric lavage and catharsis.
3. **Gastric Lavage and Catharsis:** Gastric lavage with 0.01-0.1% KMO4 (potassium permanganate) or 0.2-0.4% CuSO4(copper sulphate) solution is done to convert the phosphorus to relatively harmless oxides which should then be followed by administration of activated charcoal adsorbent after 30 minutes.

Fat favours additional phosphorus absorption; hence patients must avoid fat in their diet for 3-4 days or longer. Mineral oil dissolves phosphorus and prevents its absorption; therefore, it can be taken orally. It is usually given at a dose of 1.5 ml per Kg body weight. Unfortunately, there is no specific antidote for yellow phosphorus. Therefore, close monitoring of hepatic and renal function must be done and managed accordingly.

Limitation

The present study had a small sample size. We are planning to continue this study as a long-term one with more recruits. In our research study, management was at the treating physician's discretion, which could have caused discrepancies. This being an observational study, the institutional policy of administering NAC to all cases of rat killer poisoning was followed; hence, its benefits or shortfall could not be assessed.

CONCLUSION

Rat killer paste poisoning is the third most common form of suicidal poisoning in Tamil Nadu. In this study, we identified age > 30 years, need for resuscitation, shock, encephalopathy, MODS, and MELD score > 25, as reliable predictors of a bad outcome in this patient population. Phosphorus-based rat killer poisoning claims many human lives. Given that there is no specific antidote, good monitoring and timely resuscitation could be the only factors to save those patients. Law enforcement to restrict the unregulated sales of yellow phosphorus should be done.

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