A fatal case of multi-organ failure due to acute yellow phosphorus poisoning

Abstract

Yellow phosphorus is a non-metallic irritant used in various industries such as the rodenticide, firecracker, match, and fertiliser industries. Yellow phosphorus poisoning is fatal in both children and adults. Accidental yellow phosphorus poisoning is frequently reported in children, whereas suicidal consumption is not uncommon among adults. Herein, we present the case of a 30-year-old woman who ingested Ratol paste containing yellow phosphorus in an attempt to commit suicide. Her initial chief complaints were nausea, vomiting, and diarrhoea during hospitalisation, followed by a symptomless phase with stable vital parameters on the second day of hospitalisation. She was managed conservatively and discharged against medical advice. She was readmitted to the same hospital on the fourth day after Ratol ingestion with complaints of generalised weakness, body pain, drowsiness, loss of appetite, and breathing difficulties. She developed severe complications towing to the intoxication and died. An autopsy was performed, and histopathological and toxicological examinations revealed characteristic features of yellow phosphorus toxicity in her organs. We concluded that the cause of death was hepatic encephalopathy and multi-organ dysfunction syndrome caused by yellow phosphorus poisoning.

Keywords: Phosphorus, Hepatic encephalopathy, Multi-organ failure

Introduction

In India, approximately 70% of rural households still depend primarily on agriculture for their livelihood [1]. An unchecked growth of rodents such as rats around houses and sometimes in farms and fields can be problematic because rodents can potentially spread diseases that would hamper food supply and consequently lead to economic loss. Hence, rodenticides are widely marketed in India, and various preparations are available, such as yellow phosphorus in the form of Ratol paste and powder. This preparation is cheap and readily available in the open market and on online e-commerce sites in India; this contributes to the frequently reported cases of suicide due to Ratol ingestion. The accidental consumption of Ratol paste at home is not uncommon among children. Rodenticides containing 3-5% yellow phosphorus are currently available; Ratol paste contains 3% yellow phosphorus [2]. It is highly toxic and does not have an antidote. Accidental poisoning with Ratol paste is very common since it is very similar to toothpaste [3–5]. Yellow phosphorus is also used in fireworks and matches, which leads to chronic poisoning in workers [6]. Yellow phosphorus is a kind of non-metallic protoplasmic poison. It is rapidly absorbed from the digestive tract and is primarily metabolised by the liver [7]. The smallest fatal dose is 8 mg; however, the usual fatal dose is 1 mg/kg [8]. The vomitus after phosphorus ingestion is luminescent and has a characteristic garlic odour. If the patient survives the initial gastrointestinal irritation phase, hepatic toxicity ensues secondary to systemic poisoning. Herein, we report a case of suicidal yellow phosphorus poisoning.

CASE REPORT

A 30-year-old woman was admitted to the Department of Trauma and Emergency Medicine in a tertiary care hospital with complaints of a burning sensation in the mouth, nausea, and vomiting. The vomitus had a garlic odour. Her husband stated that she had ingested 10-12 g Ratol paste approximately 2 h before. Gastric lavage with 1:5000 $KMnO_4$ and activated charcoal was performed. The patient was conscious with a blood pressure of 140/80 mmHg, pulse rate of 84 beats per

Commented [A1]: As per journal guidelines, the main article types published are Articles (original research papers) and Reviews. Please confirm with the journal whether it accepts case reports and whether this format is acceptable. I have, nevertheless, applied all general formatting guidelines.

Commented [A2]: Please provide the authors' full first and last names. The initials of any middle names can be added. The PubMed/MEDLINE standard format is used for affiliations: complete address information including city, zip code, state/province, and country. At least one author should be designated as corresponding author, and his or her email address and other details should be included at the end of the affiliation section.

Commented [A3]: **Author Biography**
Authors are encouraged to add a biography (maximum 150 words) to the submission and publish it. This should be a single paragraph and should contain the following points:
1.Authors' full names followed by current positions;
2.Education background including institution information and year of graduation (type and level of degree received);
3.Work experience;
4.Current and previous research interests; ...

Commented [A4]: Abstract word count: 179/200.
The abstract is unstructured as per the guidelines.

Commented [A5]: Since your study focuses on yellow phosphorus poisoning, I have added this here and in the next sentence for consistency with the main text.

Commented [A6]: This is a direct translation of the source text. Unfortunately, the exact point in time is not clear. D ...

Commented [A7]: I have phrased this portion in this way to ensure consistency with the main text.

Commented [A8]: The number of keywords falls within the 3-10 range prescribed by the journal.

Commented [A9]: Please note that the journal has no restrictions regarding the length of manuscripts.

Commented [A10]: Please note that I have retained the current section headings as the journal guidelines did not mention the section headings to be used for case reports.

Commented [A11]: I have used in-line in-text citations before punctuations in all relevant instances, as per the journal requirements.

Commented [A12]: This is a direct translation of the source text. However, the association between the two parts of this phrase is unclear. Do you mean ...

Commented [A13]: This is a direct translation of the source text. However, please clarify what "it" refers to here. Are you referring to "yellow phosphorus" or "Ratol paste"?

Commented [A14]: This is a direct translation of the source text. However, how exactly the two are similar is ...

Commented [A15]: This is a direct translation of the source text. However, the exact timeline is unclear. Do yo ...

minute, and respiratory rate of 20 breaths per minute. Results of different tests performed at the time of admission are shown in Table 1.

Bedside abdominal ultrasonography was unremarkable. Symptomatic management was achieved with N-acetylcysteine (NAC). On the second day of admission, the patient's clinical status improved, and she was asymptomatic. The patient, supported by her relative, was discharged against medical advice. On the fourth day after Ratol ingestion, the patient returned to the hospital with generalised weakness, body pain, drowsiness, and breathing difficulty. She presented with hypotension (blood pressure of 88/58 mmHg), tachycardia (110 beats per minute), and tachypnoea.

On general examination, icterus was present. Laboratory workup results from the fourth day are shown in Table 1. Bedside abdominal ultrasonography showed hepatomegaly and fatty changes. Hence, a provisional diagnosis of yellow phosphorus poisoning with hepatic encephalopathy and multi-organ failure was made. On the fifth day, the patient developed sudden-onset bradycardia and hypotension, which rapidly progressed to death with no opportunity to perform liver transplantation. An autopsy was performed.

Commented [A16]: This is a direct translation of the source text. However, do you mean "scleral icterus"?

Commented [A17]: This implies that Table 1 contains information of both the first and fourth days. Please check to confirm that there is no error with this sentence.

Commented [A18]: This is a direct translation of the source text. However, do you mean "fatty liver changes"?

AUTOPSY FINDINGS

On post-mortem examination, scleral icterus was present. Both pleural cavities were filled with approximately 350 mL of haemorrhagic fluid. Interlobular fissures of both lungs showed petechial haemorrhages. The right and left lungs weighed 410 g and 455 g, respectively (RV: 450 g and 375 g, respectively). The cut section showed that the lungs were congested. Pinpoint haemorrhages were present over the heart surface. The heart weighed approximately 270 g (RV: 243 g). The peritoneal cavity was filled with 750 mL of haemorrhagic effusion. The stomach mucosa was haemorrhagic. Pinpoint to pinhead-sized petechial haemorrhages were present over the mesenteries, liver, and kidneys (Figure 1A, 1B). A yellowish discoloration was present on the liver, kidney, and brain surfaces. The weight of the liver was about 1100 g (RV: 1100 g); the weights of the right and left kidneys were 114 g and 129 g, respectively (RV: for both 288 g); and the weight of the brain was 1177 g (RV: 1233 g). Cut sections of the liver (Figure 1C) and kidneys (Figure 1D) showed pinpoint haemorrhages.

Commented [A19]: Please expand this abbreviation on first mention in the text.

Figure 1. Gross examination of the (A) liver showing pinhead-sized haemorrhages over the surface and yellowish discoloration; (B) kidneys showing pinpoint haemorrhages over the surface and yellowish discoloration; (C) cut surface of the liver depicting pinpoint haemorrhages within the hepatic parenchyma; (D) cut section of the kidney depicting pinpoint haemorrhages and yellowish discoloration of the renal parenchyma.

Commented [A20]: This is a direct translation of the source text. However, do you mean "cross-sectional"? If you revise here, consider revising in the figure legends as well.

Commented [A21]: As per journal guidelines:
- File for Figures and Schemes must be provided during submission in a single zip archive and at a sufficiently high resolution (minimum 1000 pixels width/height, or a resolution of 300 dpi or higher). Common formats are accepted; however, TIFF, JPEG, EPS and PDF are preferred.
- All Figures, Schemes and Tables should be inserted into the main text close to their first citation and must be numbered following their number of appearance (Figure 1, Scheme I, Figure 2, Scheme II, Table 1, etc.).
- All Figures, Schemes and Tables should have a short explanatory title and caption.

As per these guidelines, I have inserted the legends into the main text close to their citation. Please confirm with the journal whether you should insert figures here with the legends or submit them separately in a zip, as the guidelines regarding this are a bit unclear

Histopathological examination showed acute interstitial inflammatory cell infiltrates along with multiple focal alveolar haemorrhages in both lungs (Figure 2A, 2B). The heart showed focal necrotic fibres with focal acute myocarditis (Figure 2C).

Figure 2. Photomicrographs of the (A and B) lung and (C) heart. (A and B) Inflammatory cell infiltrates and focal alveolar haemorrhage (H&E, 4X and 10X, respectively); (C) Focal necrotic fibres with neutrophilic infiltrates, suggestive of focal acute myocarditis (H&E, 10X).

Commented [A22]: This is a direct translation of the source text. However, do you mean "cross-sectional image"?

Commented [A23]: Please provide the expansion haematoxylin and eosin instead of the abbreviation or include the expansion below the legend. The journal does not mention a preference. Applicable for the next legend as well.

The liver showed non-zonal necrosis, karyorrhexis, vacuolisation, intracellular bile pigment deposition, mild periportal inflammation, and piecemeal necrosis (Figure 3A, 3B). The kidneys showed vacuolisation of proximal tubular cells and multifocal necrosis of the epithelial cell lining with sparing of the glomeruli (Figure 3C). The pancreas showed focal fat necrosis along with necrosis of large areas of the pancreatic parenchyma (Figure 3D). Histological analysis of the bone marrow was not performed. All features were suggestive of multi-organ failure comprising submassive hepatic necrosis, focal acute myocarditis, acute renal tubular necrosis, and pancreatic necrosis typical of phosphorus poisoning, which was confirmed after a qualitative chemical analysis report showed the presence of phosphorus in tissues sampled during the autopsy.

Figure 3. Photomicrographs of the (A, B) liver, (C) kidney, and (D) pancreas. (A) Non-zonal necrosis, karyorrhexis, vacuolisation, and piecemeal necrosis (H&E, 4X); (B) Vacuolisation in liver tissue (H&E, 10X); (C) Vacuolisation of the proximal tubular cells and multifocal necrosis of the lining epithelial cells with sparing of the glomeruli (H&E, 10X); (D) Parenchymal necrosis of the pancreas (H&E, 10X).

DISCUSSION

Yellow phosphorus is a toxic substance that is used in matches, fireworks, and rodenticides [9]. Several cases of intoxication with yellow phosphorus in developing and underdeveloped countries have been reported; however, this is rarely reported in developed countries. In developing countries, intoxication generally results from accidental oral ingestion, although suicidal ingestion is also not uncommon.

Ratol paste contains 3% yellow phosphorus, a far more toxic substance than red phosphorus [12,13]. Yellow phosphorus is categorised as a highly lethal rodenticide when ingested in doses exceeding 1 mg/kg. In our case, the deceased ingested approximately 10-12 g of yellow phosphorus rodenticide. Patients with yellow phosphorus poisoning may be initially symptomatic; however, recovery is observed after 2-3 days of ingestion. Nevertheless, symptoms of acute liver failure subsequently develop [12]. In our case, the patient had a similar progression of complications. Hence, we surmise that patients with acute yellow phosphorus poisoning should be monitored closely for 1 week since mortality is not recorded after 8 days [14].

Yellow phosphorus not only affects the liver but also the central nervous system and may cause restlessness, irritability, drowsiness, lethargy, stupor, and coma owing to liver dysfunction [15,16]; cardiovascular toxicity with arrhythmias and hemodynamic instability [12,13], acute tubular necrosis, and bone marrow toxicity such as thrombocytopenia are also observed [17]. Fernandez and Canizares [18] reviewed 15 cases of yellow phosphorus poisoning and found that 87% patients had some hepatic derangement after yellow phosphorus poisoning, and 27% developed fulminant hepatic failure and died. Histological analysis of the liver shows steatohepatitis and necrosis. Santos et al. [19] described three cases of white phosphorus intoxication with acute liver failure secondary to the consumption of firecrackers. In one case, liver injury improved with supportive care; in the second, the patient required liver transplantation; and the third patient died. Similarly, Nalabothu et al. [4] found a 28% mortality rate that was associated with the Model for End-stage Liver Disease (MELD) score. A MELD score greater than 40 was related to death, whereas survivors presented a score lower than 12. Our patient's highest MELD score was 36. McCarron [16] observed a mortality rate of 23-73% associated with yellow phosphorus toxicity depending on clinical manifestations; patients with early central nervous system manifestations had a poorer prognosis. There is no

Commented [A24]: This is a direct translation of the source text. However, your intended meaning is not clear here. Do you mean "…as death after 8 days of ingestion has not been reported"? If so, please rephrase as such.

Commented [A25]: This is a direct translation of the source text. However, the intended meaning is not very clear. Do you mean "some degree of hepatic derangement"?

Commented [A26]: This is a direct translation of the source text. However, kindly elaborate further here. Do you mean

"Histological analysis of the liver of patients with yellow phosphorus poisoning shows…"?

antidote for phosphorus poisoning, [12,15] and the only treatment is early decontamination followed by monitoring of liver function and supportive care [12,13]. Some researchers recommend gastric lavage with 1:5000 $KMnO_4$ followed by activated charcoal and using mineral oil as a cathartic [16,17]. Fernandez et al. [18] found that NAC shows no benefits, whereas Nalabothu et al. [4] suggested that the early administration of NAC improves outcomes for all patients with rodenticide poisoning having liver failure, and survival rates vary with the timing of NAC administration. In their study, the survival rates were 76%, 40%, and 23% if NAC was administered on Day 1, 2, and 3, respectively, following rodenticide ingestion [4]. However, this outcome was confounded by an early gastric lavage in patients who were hospitalised immediately after rodenticide ingestion. In our case, NAC was administered on Day 1 after yellow phosphorus poisoning was confirmed; however, the outcome was unfavourable. Yellow phosphorus is rapidly absorbed through the gastrointestinal mucosa, and approximately 70% accumulates in the liver within 2 to 3 h of ingestion. It also accumulates to a lesser extent in the heart (12%), kidneys (4%), pancreas (0.4%), and brain (0.39%), and leads to damage in those organs [16]. Histopathological changes, in our case, were mainly detected in the lungs, heart, liver, kidneys, and pancreas. No significant pathological change, other than congestion, was observed in the brain. The characteristic histopathological findings are fat infiltration, vacuolisation, and necrosis in different organs, mainly the liver and kidney, along with focal myocarditis. Multi-organ failure, with fulminant hepatic failure, acute tubular necrosis, and toxic myocarditis, is responsible for a fatal outcome. The toxic effect of yellow phosphorus occurs in the endoplasmic reticulum and mitochondrion, leading to (i) decreased synthesis of the apolipoprotein portion of very low-density lipoproteins, (ii) decreased production of adenosine triphosphate, and (iii) inhibition of fatty acid oxidation. This combined effect leads to fat deposition and cellular damage in different organs [20].

CONCLUSION

Yellow phosphorus is a cheap and effective rodenticide. However, the number of cases of accidental poisoning and deaths among children and adults cannot be neglected. We agree with several other authors that the use of yellow phosphorus in rodenticides and fireworks in its currently packaged and lethal form should be banned. We have also discussed the diagnosis, management, and prognosis of liver failure due to yellow phosphorus poisoning. Early and effective supportive care is key to reducing the morbidity and mortality associated with yellow phosphorus poisoning.

References

1. Food and Agriculture Organization of the United Nations (FAO) India at a glance. Rome: FAO; 2019. Available online: http://www.fao.org/india/fao-in-india/india-at-a-glance/en/ [accessed on 23 September 2019].

2. Brent, J., Wallace, K.L., Burkhart, K.K. Phosphorus. In: *Critical Care Toxicology – Diagnosis and management of the critically poisoned patient*. Elsevier Mosby, Philadelphia, PA, USA, 2005. pp. 851-861.

3. Karanth, S.; Nayyar, V. Rodenticide-induced hepatotoxicity. *J. Assoc. Physicians India* **2003**, *51*, 816-817.

4. Nalabothu, M.; Monigari, N.; Acharya, R. Clinical profile and outcomes of rodenticide poisoning in tertiary care hospital. *IJSRP* **2015**, *5*, 1-12.

Commented [A27]: This is a direct translation of the source text. However, do you mean "70% of the absorbed substance"? If so, please consider using this phrase for clarity.

Commented [A28]: Given the use of present tense in the original source text, I have assumed that you are referring to the general properties of yellow phosphorus poisoning. In case you are referring specifically to the patient in the reported case, please use past tense.

Commented [A29]: I have deleted the abbreviation VLDL since it occurs only once in the text.

Commented [A30]: Please include the following information before the references:
Acknowledgments: In this section you can acknowledge any support given which is not covered by the author contribution or funding sections. This may include administrative and technical support, or donations in kind (e.g., materials used for experiments).
Author Contributions: Each author is expected to have made substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data; or the creation of new software used in the work; or have drafted the work or substantively revised it; AND has approved the submitted version (and version substantially edited by journal staff that involves the author's contribution to the study); AND agrees to be personally accountable for the author's own contributions and for ensuring that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and documented in the literature.
For research articles with several authors, a short paragraph specifying their individual contributions must be provided. The following statements should be used "Conceptualization, X.X. and Y.Y.; Methodology, X.X.; Software, X.X.; Validation, X.X., Y.Y. and Z.Z.; Formal Analysis, X.X.; Investigation, X.X.; Resources, X.X.; Data Curation, X.X.; Writing – Original Draft Preparation, X.X.; Writing – Review & Editing, X.X.; Visualization, X.X.; Supervision, X.X.; Project Administration, X.X.; Funding Acquisition, Y.Y.", please turn to the CRediT taxonomy for the term explanation. For more background on CRediT, see here. "Authorship must include and be limited to those who have contributed substantially to the work. Please read the section concerning the criteria to qualify for authorship carefully".
Informed Consent Statement: Written informed consent for publication must be obtained from participating patients who can be identified (including by the patients ...

Commented [A31]: This reference needs to be provided in the following format:
Author 1, A.; Author 2, B. Title of the chapter. In *Book Title*, 2nd ed.; Editor 1, A., Editor 2, B., Eds.; Publisher: Publisher Location, Country, Year; Volume 3, pp. 154–196.

I have underlined the information you need to add. Please note that I did not make these changes since they are beyond the scope of this service.

Commented [A32]: Please include dois in all relevant instances as per the guidelines.

5. Chikkaveeraiah, S.K.; Marijayanth, M.; Reddy, P.K.; Kaluvakuri, S. Clinical profile and outcome of rodenticide poisoning in patients admitted to a tertiary care teaching hospital in Mysore, Karnataka. India. *Int. J. Res. Med. Sci.* **2016**, *4*, 5023-5027.

6. González-Andrade, F.; López-Pulles, R. White phosphorous poisoning by oral ingestion of firecrackers or little devils: Current experience in Ecuador. *Clin. Toxicol. (Phila)* **2011**, *49*, 29-33.

7. Ghoshal, A.K.; Porta, E.A.; Hartroft, W.S. The role of lipo-peroxidation in the pathogenesis of fatty livers induced by phosphorus poisoning in rats. *Am. J. Pathol.* **1969**, *54*, 275-291.

8. Kannan K. Modi. *A textbook of medical jurisprudence and toxicology*, 25th ed.; Lexis Nexis Butterworths Wadhwa: New Delhi, India, 2016; pp. 57.

9. Eldad, A.; Simon, G.A. The phosphorous burn - a preliminary comparative experimental study of various forms of treatment. *Burns* **1991**, *17*, 198-200.

10. Konjoyan, T.R. White phosphorus burns: Case report and literature review. *Mil. Med.* **1983**, *148*, 881-884.

11. Mozingo, D.W.; Smith, A.A.; McManus, W.F.; Pruitt, B.A. Jr; Mason, A.D. Jr. Chemical burns. *J. Trauma Inj. Crit. Care* **1988**, *28*, 642-647.

12. Mohideen, S.K.; Kumar, K.S. Should ratol paste be banned? *Indian J. Crit. Care Med.* **2015**, 19, 128-129.

13. Lakshmi, C.P.; Goel, A.; Basu, D. Cholestatic presentation of yellow phosphorus poisoning. *J. Pharmacol. Pharmacother.* **2014**, *5*, 67-69.

14. Lee, W.M.; Larson, A.M.; Stravitz, R.T. AASLD position paper: the management of acute liver failure: *Update Hepatology* **2011**, *55*, 965-967.

15. Saoji, A.A.; Lavekar, A.S.; Salkar, H.R.; Pawde, G.B.; Tripathi, S.S. A case on suicidal poisoning associated with Ratol and a perspective on yellow phosphorus poisoning. *Int. J. Recent Trends Sci Technol.* **2014**, *10*, 223-225.

16. McCarron, M.M.; Gaddis, G.P.; Trotter, A.T. Acute yellow phosphorus poisoning from pesticide pastes. *Clin. Toxicol.* **1981**, *18*, 693-711.

17. Tafur, A.J.; Zapatier, J.A.; Idrovo, L.A.; Oliveros, J.W.; Garces, J.C. Bone marrow toxicity after yellow phosphorus ingestion. *Emerg. Med. J.* **2004**, *21*, 259-260.

18. Fernandez, O.U.; Canizares, L.L. Acute hepatotoxicity from ingestion of yellow phosphorus-containing fireworks. *J. Clin. Gastroenterol.* **1995**, *21*, 139-142.

19. Santos, O.; Restrepo, J.C.; Velásquez, L, et al. Acute liver failure due to white phosphorus ingestion. *Ann. Hepatol.* **2009**, *8*, 162-165.

20. Agency for Toxic Substances and Disease Registry Toxicological Profile for White Phosphorus. Atlanta: ATSDR; 1997. Available from: http://www.atsdr.cdc.gov/toxprofiles/tp103.html [accessed on 29 November 2005].

Commented [A33]: Please clarify if this is a single name. Author names are to be presented in the format: Author 1, A.; Author 2, B.
If this is a single name, it needs to be written as Modi, K.K.

Commented [A34]: This journal was not found on an online search. Please confirm the journal name and I can then abbreviate this for you.

Commented [A35]: Please either cite all authors or cite the first 10 authors before mentioning “et al.”, as per the guidelines.