Liver Transplantation Society of India Guidelines for the Management of Acute Liver Injury Secondary to Yellow Phosphorus–Containing Rodenticide Poisoning Using the Modified Delphi Technique of Consensus Development

Mettu S. Reddy [*], Akila Rajakumar [†], Johns S. Mathew [‡], L. Venkatakrishnan [§], Dinesh Jothimani [¦], S. Sudhindran [‡], Mathew Jacob [¶], Krishnasamy Narayanasamy [#], Radhika Venugopal [¦], Ravi Mohanka [**], Ilankumaran Kaliamoorthy [†], Joy Varghese [††], Charles Panackel [‡‡], Zubair Mohamed [§§], Mukul Vij [¦¦], Deepti Sachan [¶¶], V. V. Pillay [##], Sanjiv Saigal [***], Radhakrishna Dhiman [†††], Arvinder S. Soin [‡‡‡], Subhash Gupta [§§§], Julia Wendon [¦¦¦], Mohamed Rela [*], Shiv K. Sarin [¶¶¶]

[*] *Institute of Liver Disease & Transplantation, Dr Rela Institute & Medical Center, Chennai, India,* [†] *Department of Liver Anesthesia & Intensive Care, Dr Rela Institute & Medical Center, Chennai, India,* [‡] *Department of Liver Transplantation & Gastrointestinal Surgery, Amrita Hospitals, Kochi, India,* [§] *Department of Gastroenterology, PSG Hospitals, Coimbatore, India,* [¦] *Department of Hepatology, Dr Rela Institute & Medical Center, Chennai, India,* [¶] *Multiorgan Transplantation & Hepatobiliary Surgery, Aster Medicity, Kochi, India,* [#] *Department of Hepatology, Madras Medical College, Chennai, India,* [**] *Department of Liver Transplantation & HPB Surgery, Global Hospital, Mumbai, India,* [††] *Department of Hepatology & Liver Transplantation, Gleneagles Global Hospital & Health City, Chennai, India,* [‡‡] *Department of Hepatology & Liver Transplantation, Aster Medicity, Kochi, India,* [§§] *Department of Anesthesiology & Critical Care Medicine, Amrita Hospitals, Kochi, India,* [¦¦] *Department of Pathology & Laboratory Medicine, Dr Rela Institute & Medical Center, Chennai, India,* [¶¶] *Department of Transfusion Medicine, Dr Rela Institute & Medical Center, Chennai, India,* [##] *Department of Forensic Medicine & Toxicology, Amrita Hospitals, Kochi, India,* [***] *Department of Hepatology & Liver Transplantation, Medanta Medicity, Gurgaon, India,* [†††] *Department of Hepatology & Liver Transplantation, Post-graduate Institute of Medical Education & Research, Chandigarh, India,* [‡‡‡] *Department of Liver Transplantation & Regenerative Medicine, Medanta Medicity, Gurgaon, India,* [§§§] *Centre for Liver & Biliary Sciences, Max Super Specialty Hospital, Saket, Delhi, India,* [¦¦¦] *Institute of Liver Studies, Kings College Hospital, London, UK and* [¶¶¶] *Department of Hepatology, Institute of Liver & Biliary Sciences, New Delhi, India*

Background: **Acute liver failure caused by the ingestion of yellow phosphorus–containing rodenticide has been increasing in incidence over the last decade and is a common indication for emergency liver transplantation in Southern and Western India and other countries. Clear guidelines for its management are necessary, given its unpredictable course, potential for rapid deterioration and variation in clinical practice.** ***Methods:*** **A modified Delphi approach was used for developing consensus guidelines under the aegis of the Liver Transplantation Society of India. A detailed review of the published literature was performed. Recommendations for three areas of clinical practice, assessment and initial management, intensive care unit (ICU) management and liver transplantation, were developed.** ***Results:*** **The expert panel consisted of 16 clinicians, 3 nonclinical specialists and 5 senior advisory members from 11 centres. Thirty-one recommendations with regard to criteria for hospital admission and discharge, role of medical therapies, ICU management, evidence for extracorporeal therapies such as renal replacement therapy and therapeutic plasma exchange, early predictors of need for liver transplantation and perioperative care were developed based on published evidence and combined clinical experience.** ***Conclusion:*** **Development of these guidelines should help standardise care for patients with yellow phosphorus poisoning and identify areas for collaborative research.** **(J Clin Exp Hepatol 2021;11:475–483)**

Yellow phosphorus (YP) is the main constituent of commonly available rodenticides in India. The natural history of acute liver failure (ALF) after YP poisoning and the pathology of liver injury have been well known for nearly a hundred years.[1,2] In India, YP poisoning due to rodenticide ingestion is increasingly

Keywords: rat killer poison, yellow phosphorus, acute liver failure, consensus guidelines, liver transplantation
Received: 10.6.2020; *Accepted:* 28.9.2020; *Available online 6 October 2020*
Address for correspondence. Mettu S. Reddy FRCS, PhD, Institute of Liver Disease & Transplantation, Dr Rela Institute & Medical Center Chromepet, Chennai, India.
E-mail: smettu.reddy@gmail.com
Abbreviations: ALF: acute liver failure; ALI: acute liver injury; DDLT: deceased donor liver transplantation; ICU: intensive care unit; INR: international normalised ratio; KCC: Kings College Criteria; LDLT: living donor liver transplantation; LT: liver transplantation; LTSI: Liver Transplantation Society of India; MELD: model for end-stage liver disease; RRT: renal replacement therapy; TPE: therapeutic plasma exchange, YP: yellow phosphorus
https://doi.org/10.1016/j.jceh.2020.09.011

being reported as a cause of ALF.[3] The ingestion is commonly suicidal and predominantly reported in individuals between the 2nd and 4th decades of life, although accidental ingestion by children has also been reported. Over the last 5 years, it has become a common indication for emergency liver transplantation (LT) in South India. Reports of YP poisoning through its use in fireworks have also been reported from several other countries[4–6] (Figure 1).

YP affects multiple intracellular components. It damages the rough and smooth endoplasmic reticulum, disrupting protein synthesis and lipid transport, and its action as a mitochondrial toxin leads to inhibition of oxidative phosphorylation and ATP depletion.[7] In addition to liver injury, it also causes gastrointestinal disturbances, bone marrow suppression, cardiotoxicity, pancreatitis and rhabdomyolysis.[1,9] Commercially available rodenticides may also contain other phosphorus compounds such as zinc and aluminium phosphides along with warfarin-like derivatives that compound the multisystem injury after poisoning. Mortality has ranged from 20% to 30% in various reports, with ALF being the most common cause of death.[3,5]

This epidemic of YP poisoning due to rodenticide ingestion is a relatively new phenomenon, and there are no clear guidelines with regard to its management. Most patients are initially treated in smaller peripheral hospitals, not all of which will have the facilities for monitoring or organ support to manage such sick patients. Patients with YP poisoning also have an unpredictable clinical course, can deteriorate rapidly and need urgent LT.[10] Clear guidelines with regard to risk stratification, criteria for escalation of care or transfer to higher centres and indications for liver transplant are essential to achieve consistency in managing these patients.

METHODS

There is limited high-quality data with regard to the natural course, management and outcomes of YP poisoning. The published literature of reports of YP poisoning is summarised in Table 1. Most published reports are single-centre series and have looked at the clinical-epidemiological profile and the indications and outcomes of liver transplant, respectively.[3,10,11] There has however been a gradual accumulation of expertise in many centres in South India and Western India to deal with this emerging problem, and local protocols have been developed to manage these patients. The aim of this collaborative exercise was to bring together a multidisciplinary and multicentre expert panel under the auspices of the Liver Transplantation Society of India (LTSI) to develop guidelines to manage patients with YP poisoning, specifically patients who develop acute liver injury (ALI).

A modified Delphi approach was used for this purpose (Figure 2). The Delphi method of enquiry has been frequently used to develop guidelines and protocols in healthcare when high-quality evidence is lacking, especially in the case of rare or emerging clinical conditions.[12–14] The process involves a series of iterative questionnaires administered to a selected group of experts who may be geographically separated. The feedback from each round helps in modifying the statements and provides opportunities for experts to reassess and if necessary modify their own responses. The iterative process helps in serially reducing the range of expert responses as the

Figure 1 World map showing regions from where yellow phosphorus poisoning has been reported.

Table 1 Review of the Published Literature of Yellow Phosphorus Poisoning Over the last 25 Years.

Author, year, journal	Number of cases	Mode of management	Mortality	Conclusions
Fernandez, 1995, *Journal of Clinical Gastroenterology*[5]	15 (9 developed ALI/ALF)	Medical mgmt	27%	ALF, metabolic acidosis and hypoglycaemia associated with mortality. No benefit of NAC.
Santos et al, 2009, *Annals of Hepatology*[6]	3	1 medical mgmt, 1 transplant, 1 died	33%	
Ates et al, 2011, *Liver Transplantation*[34]	10	1 spontaneous recovery, 3 died without LT, 6 underwent LT	Overall, 60% Post-LT, 50%	Emergency LDLT is life-saving. Poor prognosis if the brain or heart is affected.
Gonsalez-Andrade et al, 2011, *Clinical Toxicology*[35]	85 (firecracker ingestion)	30 had liver injury: medical mgmt, with NAC and gastric decontamination	Mortality: 5–9%	
Bhat et al, 2015, *Journal of Clinical and Diagnostic Research*[36]	100	Medical mgmt, NAC used in 26 patients	Without NAC: 24.3%; with NAC: 26.9%	Similar survival despite more patients with severe liver injury in the NAC group
Suneetha et al, 2016, *International Journal of Scientific Study*[37]	56 (YPP = 8, o thers = phosphide poisoning)	Medical mgmt	21%	Greater liver involvement in YPP
Saraf et al, 2015, *Indian Journal of Gastroenterology*[10]	41 (ALF)	Medical mgmt, LT for worsening ALF	19.5%	Emg LT for MELD >36, INR >6 and encephalopathy
Nalabothu et al, 2015, *International Journal of Scientific and Research Publications*[23]	97 (43 YPP)	Medical mgmt and NAC	51% in YPP	Better outcome with early NAC. A high MELD score associated with mortality.
Trakulsrichai et al, 2017, *Therapeutics and Clinical Risk Management*[38]	455 (primarily zinc phosphide)	Medical mgmt	7%	
Mishra et al, 2017, *Tropical Doctor*[39]	9	Medical mgmt + NAC	55%	Liver failure and cytopenias common; higher mortality with delayed presentation.

(*Continued on next page*)

Table 1 (*Continued*)

Author, year, journal	Number of cases	Mode of management	Mortality	Conclusions
Bhat, 2018, *Indian Journal of Basic and Applied Medical Research*[11]	35 (60% with ALI/ALF)	Medical mgmt with NAC	Recovered 54%	No benefit with NAC
Venugopal et al, 2018, *Journal of Gastroenterology and Digestive System*[3]	101	Medical mgmt + NAC + vitamin K	19% mortality	Mortality associated with liver and renal injury
Banjan, 2019, *International Journal of Scientific Research*[29]	11	Medical mgmt with TPE	45%	TPE is beneficial
Saravanan et al, 2019, *International Journal of Scientific Study*[19]	30	Medical mgmt and NAC	16.6%	Better survival with early NAC (within 6 h of ingestion)
Sardar et al, 2019, *Indian Journal of Gastroenterology*[30]	24	Medical mgmt + NAC + TPE	12%	Three of 4 patients satisfying LT criteria survived without LT. Possible role of the vWF level in prognostication
Yuksekkaya et al, 2019, *Pediatric Emergency Care*[40]	11 (children)	Medical mgmt and LT (1)	9%	
Mark et al, 2020, *Current Clinical Pharmacology*[20]	229 (all types of rodenticides)	Medical mgmt		Survival better with early admission and receiving NAC; worse with YP
Gopalakrishnan et al, 2020, *Indian Journal of Critical Care Medicine*[18]	99	Early resuscitation, medical mgmt.	9.1% mortality	Better survival with early decontamination with activated charcoal

Publications reporting at least 3 cases are included.
ALI: acute liver injury, ALF: acute liver failure, YP: yellow phosphorus, YPP: yellow phosphorus poisoning, LT: liver transplantation, LDLT: living donor liver transplantation, mgmt: management, NAC: N-acetyl cysteine, vWF: von Willebrand factor, TPE: therapeutic plasma exchange, MELD: model for end-stage liver disease; INR: international normalised ratio, Emg: Emergency.

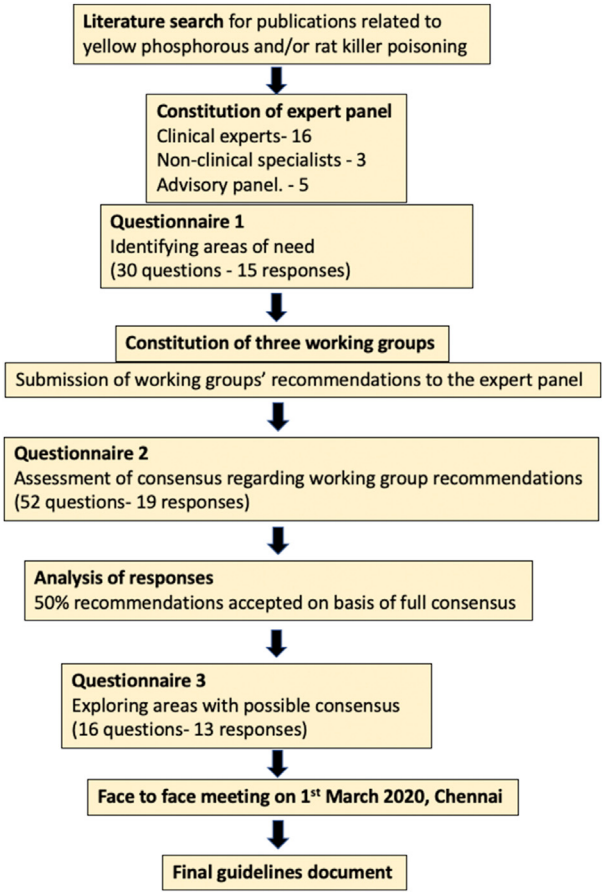

Figure 2 Flowchart depicting the modified Delphi consultative process used in the development of the consensus document.

group converges towards the 'correct' response. The relatively anonymous mode of data collection also minimises the 'bandwagon effect' or 'halo' effect.[15] Once agreement is reached on these key practices, future research can build upon that framework to evaluate the effectiveness of the approach. Although the original Delphi method was restricted to using questionnaires, several modifications have included a combination of questionnaires and face-to-face meetings to finalise recommendations.[16] The Delphi process used in development of these guidelines is summarised in Figure 2 (also see supplementary methods). A modification of the Grading of Recommendations Assessment, Development and Evaluation system was used to grade the level of evidence (high, moderate, low) and strength of recommendations (strong, weak).[17]

RESULTS

The literature review showed that a majority of recent publications were from India and were retrospective case series. The level of evidence was low to moderate. There were no clinical trials—randomised or otherwise, systematic reviews or well-designed case-control studies—identified in the literature search. All studies published before January 2020 were reviewed as part of the Delphi consultation process.

An initial questionnaire sent to the expert panel included 30 questions to identify the 'areas of need'. Fifteen separate responses were recorded and tabulated. Based on these responses, the list of 19 questions covering the three clinical areas was used to guide consensus development (Figure 2). The management algorithm for a patient presenting with rodenticide ingestion is depicted in Figure 3. The full set of guidelines is available as a supplementary file (Supplementary file 2).

Initial assessment and management

YP poisoning is recognised to have three clinical stages. The first stage lasting 24–48 h is associated primarily with gastrointestinal symptoms. Patients may present with excessive vomiting, abdominal pain, fluid-electrolyte imbalance and rarely cardiac arrhythmias. The second phase lasting up to 2–3 days may be clinically quiescent, although there may be ongoing biochemical injury to the liver and other organs. The third stage of toxic hepatitis and clinical organ failure usually starts after the fourth day of ingestion. However, significant overlap of these three phases has been reported in clinical practice. Several studies have reported the survival benefit of early start of medical management.[18–20] However, these being retrospective studies, the risk of bias cannot be completely excluded. The panel however agreed that early assessment, hospital admission and monitoring of patients presenting with YP consumption are necessary to ensure that early biochemical changes of organ injury are not missed. Apart from correction of fluid and electrolyte disturbances, vitamin K is recommended owing to the common addition of warfarin-like agents in rodenticides. N-Acetyl cysteine[21–23] has been reported in several uncontrolled studies to improve recovery. The role of gastric lavage in reducing the toxic load was discussed; however, given the risk of aspiration and some reports of chemical burns, it is not included in the recommendations[18,24] (Figure 3).

Patients who do not develop ALI after 5 days of observation or those who recover from ALI can be discharged into the community after their clinical and laboratory parameters have started recovering. These patients should be reviewed twice weekly on an outpatient basis until complete resolution of their laboratory parameters.

Intensive care unit management and transfer to a liver unit (Figure 3)

Patients who develop any signs of organ injury are best managed in an intensive care unit with close

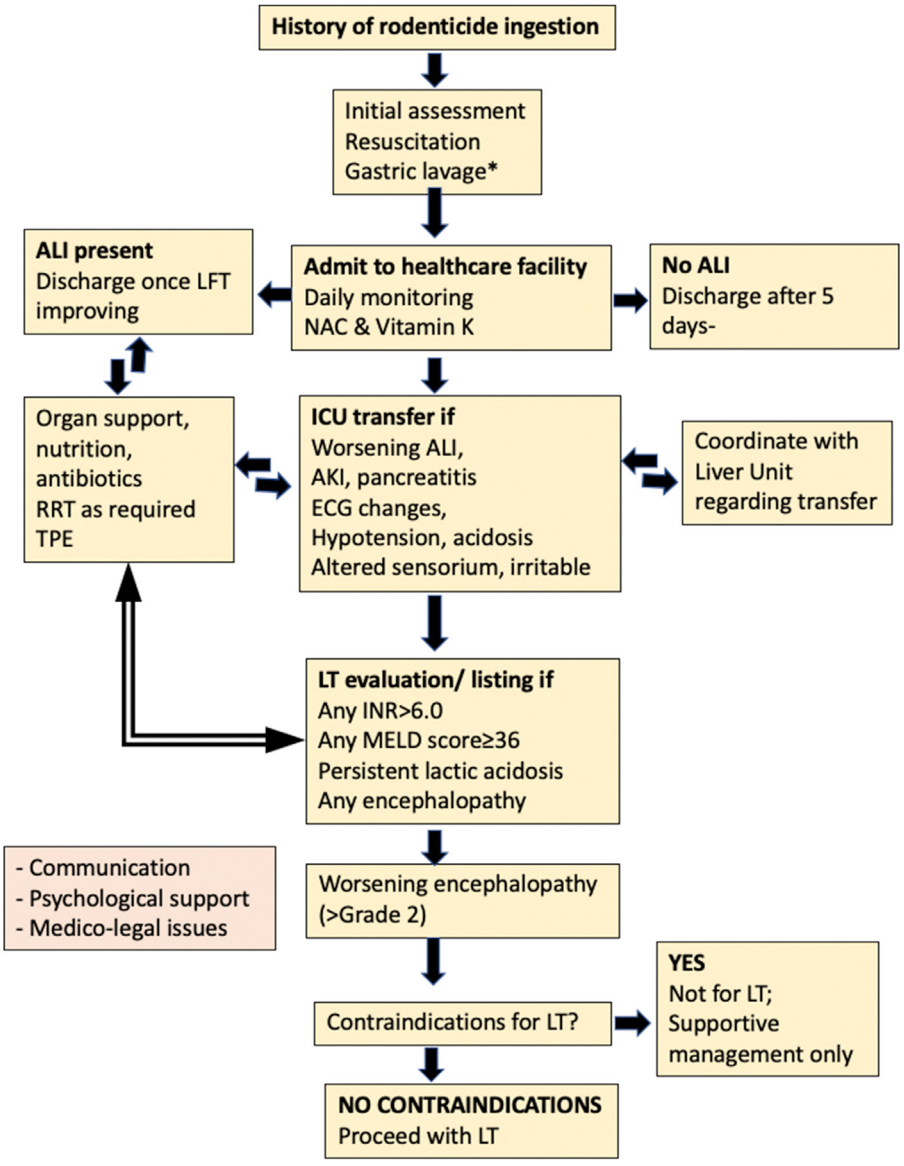

Figure 3 Flowchart depicting the management algorithm for patients presenting with history of rodenticide ingestion based on the current guidelines. ALI: acute liver injury, LFT: liver function test, RRT: renal replacement therapy, TPE: therapeutic plasma exchange, NAC: N-acetyl cysteine, AKI: acute kidney injury, LT: liver transplantation, INR: international normalised ratio, MELD: model for end-stage liver disease, LDLT: living donor liver transplantation, ECG: electrocardiogram.

monitoring for signs of deterioration. Early contact with the closest liver transplant unit is recommended so that further guidance can be obtained and plans for transfer can be discussed. The timing of transfer can vary depending on the patient's condition, level of care feasible in the patient's primary unit and the logistics of transfer. This should be decided after discussion between the primary clinician and the patient or patient's family in consultation with the liver transplant unit. The mode of transfer and need for accompanying clinical staff should take into account the clinical condition of the patient and travel time.

Role of extracorporeal therapies

Renal replacement therapy has a well-established role in the management of ALF both for neuroprotection and for managing incidental acute kidney injury.[25] Kidney injury is common in YP poisoning both owing to direct toxicity and less frequently owing to rhabdomyolysis. Exchange transfusion as a means to manage YP poisoning was initially reported by Marin *et al.*[26] Recent evidence from randomised clinical trials has shown that therapeutic plasma exchange (TPE) improves transplant-free survival in ALF.[27,28] Many centres are currently using TPE as a means to reduce the toxin load in patients with YP poisoning. Two retrospective

studies of 11 and 24 patients each have reported the beneficial effect of TPE in managing patients with YP poisoning and improving transplant-free survival.[29,30] TPE or any invasive extracorporeal therapy has its adverse effects and complications, and the risks and benefits should be considered. Significant heterogeneity in the usage, indications and dose of TPE was identified between centres during the consensus development process. The group recognised that this is an important area for further studies with potential for interinstitutional research.

Indications and timing of LT

LT has a key role in the management of ALF unresponsive to medical management. In the Indian setting, the majority of transplants performed are living donor liver transplantations (LDLTs).[31] The Kings College Criteria (KCC), developed three decades ago, are still the most commonly used system to identify patients who need an urgent LT.[32] The KCC may not be applicable in YP poisoning as most of the patients are between 20 and 40 years of age, and criteria of peak international normalised ratio (INR) and bilirubin may not be reached in patients being treated with TPE. Finally, the time interval between the onset of encephalopathy and rapid deterioration beyond which LT has no survival benefit appears to be much narrower in YP poisoning–induced ALF. Sardar *et al*[30] reported improved prediction of transplant-free survival using serum von Willebrand factor levels. However, neither these levels nor standard transplant criteria were used to identify transplant need.[30] In the largest series published by Saraf *et al*,[10] the authors proposed an INR higher than 6 and encephalopathy and a model for end-stage liver disease (MELD) score higher than or equal to 36 and encephalopathy as predictors of mortality or need for LT. Other studies have corroborated the link between high MELD scores and mortality.[3] As part of the consensus development process, these criteria were revalidated using data from a second centre, and an additional criterion to identify patients being managed with TPE (INR >2.5 after 2 cycles of TPE) was added. Any of the criteria can be used as a basis for starting LT evaluation. However, the panel was in agreement that the single most factor that predicts the need for liver transplant was encephalopathy (West Haven grading ≥2), and this should be the sole criteria for listing and to proceed with LT. The committee agreed that this will need discussion with regulatory authorities to modify current organ allocation guidelines for ALF after YP poisoning.

Contraindications for LT

The prognosis of nonhepatic organ failure in YP poisoning is variable, and recovery depends on patients' comorbidities, continued insult from the remaining toxin and the level of organ support. Although several forms of organ failure can be considered as relative contraindications for LT, the panel felt that irreversible neurological damage alone can be considered as an absolute contraindication. In view of the younger demographics, recovery of nonhepatic organ failure is possible, and the treating clinician will be in the best position to assess the risk and benefit of transplantation after discussion with the patient and family.

Type of LT and perioperative management

Both LDLT and deceased donor liver transplantation have been successfully performed for YP poisoning. The choice will depend on the availability of a suitable living donor vis-a-vis access to deceased donor organs. There have been anecdotal reports of poor outcomes with auxiliary LT for this condition from two of the participating centres. It was agreed that until more data are available, a standard orthotopic liver transplant with complete native liver replacement should be performed. There is no evidence in the literature to support modification of immunosuppression after LT for YP poisoning, unless required for sepsis or renal injury. One unit reported cases of early graft dysfunction with biopsies showing severe steatosis similar to the original toxin injury, which improved with TPE. This has however not been the experience in other units.

Counselling and legal procedures

Most patients with YP poisoning are one-off suicidal attempts by young individuals during a period of stress. Counselling for the patient and his/her family is important from the time of initial admission to recovery. Ideally, arrangements for postdischarge psychological support should be arranged for the patient and family. All poisonings, whether accidental, suicidal or homicidal, are medicolegal cases and should be reported. Clinicians should ensure complete documentation throughout the period of illness, including discussions with the patient and family. All medicolegal requirements should also be fulfilled as per the law.

DISCUSSION

YP-containing rodenticide poisoning has emerged as one of the most common causes of ALF needing LT in Southern India. While YP poisoning has been recognised for nearly 100 years, public health initiatives, including modifying manufacturing practices in the matchbox and firework industries, had significantly reduced the incidence of accidental poisoning in many countries.[1] The clinical progression of this poisoning includes a quiescent second phase, which may provide false reassurance for both the patient and the treating doctor.[8] By the time the patient presents with obvious signs of liver failure such as jaundice and encephalopathy, significant lead time is lost. Given the extent of the problem, there is an urgent need to develop a comprehensive set of guidelines to help the clinician manage these patients right from the time of initial presentation. As several

of the liver units in South and Western India have gained experience in managing these patients, it was felt that the LTSI should be the platform to develop these guidelines.

These guidelines will hopefully provide a basis for research in this area and prepare the ground for more evidence-based recommendations in the future. This exercise has shown that there is significant concurrence in practice with regard to the management of YP poisoning among various centres. There is good awareness with regard to the natural history of the poisoning, and the need for extended observation in patients with gastrointestinal symptoms is well recognised. Most of the expert panelists were convinced with regard to the role of LT in these patients and the development of encephalopathy as a sine qua non for irreversible liver injury and the need for LT.

There are however some differences in clinical practice that have been brought to light during this consensus process. The key area of difference between centres was the role of TPE, indications for initiating and stopping TPE, whether it can avoid progression to ALF or avoid LT and its role in extrahepatic organ injury. Although there is no clear evidence for its use in the YP poisoning setting, the beneficial role of TPE in the general ALF setting has informed the application of standard-volume TPE in YP poisoning in many centres.[27,28] There is however controversy related to its use as several panelists highlighted the adverse effects of such invasive therapies and the risk of overuse.

The long-term solution for dealing with this epidemic is a stricter control over the sales of rodenticides. Its sudden spurt in incidence is primarily linked to the easy availability of rodenticidal agents in rural and suburban India. Some of our patients had actually managed to acquire them through e-shopping websites. Although an outright ban will be the best option to reduce YP poisoning, it is unlikely to be feasible, given their utility as a cheap and effective rodenticide. Legislative controls through measures such as identity proof during purchase, reduction in the package size and a limit on the quantity that can be purchased at a time can reduce their access and hence their use as an impulsive suicidal agent. Similar measures used in the United Kingdom have helped in reducing the incidence of paracetamol-induced ALF.[33]

To summarise, we report the outcome of the LTSI consultative process for developing management guidelines of patients with YP poisoning. This consultative process can be a template for developing India-specific guidelines for other conditions using the vast knowledge and clinical expertise available.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Mettu S. Reddy: Conceptualization, Data curation, Formal analysis, Methodology, Writing - original draft, review of final manuscript. **Akila Rajakumar:** Conceptualization, Data curation, Formal analysis, Methodology, Writing - original draft. **Johns S. Mathew:** Conceptualization, Data curation, Formal analysis, Methodology, Writing - original draft. **L. Venkatakrishnan:** Conceptualization, Data curation, Formal analysis, Methodology. **Dinesh Jothimani:** Conceptualization, Data curation, Formal analysis, Methodology, Writing - original draft. **S. Sudhindran:** Conceptualization, Data curation, Formal analysis, Methodology, Writing - original draft. **Mathew Jacob:** Methodology, review of final manuscript. **Krishnasamy Narayanasamy:** Methodology, review of final manuscript. **Radhika Venugopal:** Conceptualization, Data curation, Formal analysis, Methodology, Writing - original draft. **Ravi Mohanka:** Conceptualization, Data curation, Formal analysis, Methodology, Writing - original draft. **Ilankumaran Kaliamoorthy:** Conceptualization, Data curation, Formal analysis, Methodology, Writing - original draft. **Joy Varghese:** Conceptualization, Data curation, Formal analysis, Methodology, Writing - original draft. **Charles Panackel:** Conceptualization, Data curation, Formal analysis, Methodology, Writing - original draft. **Zubair Mohamed:** Conceptualization, Data curation, Formal analysis, Methodology, Writing - original draft. **Mukul Vij:** Methodology, review of final manuscript. **Deepti Sachan:** Methodology, review of final manuscript. **V.V. Pillay:** Methodology, Supervision, review of final manuscript. **Sanjiv Saigal:** Supervision, review of final manuscript. **Radhakrishna Dhiman:** Supervision, review of final manuscript. **Arvinder S. Soin:** Supervision, review of final manuscript. **Subhash Gupta:** Supervision, review of final manuscript. **Julia Wendon:** Supervision, review of final manuscript. **Mohamed Rela:** Supervision, review of final manuscript. **Shiv K. Sarin:** Supervision, review of final manuscript.

CONFLICTS OF INTEREST

The authors have none to declare.

FUNDING

None.

REFERENCES

1. Rubitsky HJ, Myerson RM. Acute phosphorus poisoning. *Arch Intern Med Chic Ill 1908*. 1949;83:164–178.
2. Fletcher Gerald F, Galambos John T. Phosphorus poisoning in humans. *Arch Intern Med Chic Ill 1908*. 1963;112:846–852.
3. Venugopal R, Narayanasamy K, Chezhian A, Kumar RS, Jasmine JJ. Rat killer poisoning vs liver damage: a view in South Indian patients of tertiary care center. *J Gastrointest Dig Syst*. 2018;8.
4. Yilmaz R, Yilmaz E, Ozdemir V, et al. An evaluation of childhood deaths in Turkey due to yellow phosphorus in firecrackers. *J Forensic Sci*. 2015;60:648–652.

5. Fernandez OU, Canizares LL. Acute hepatotoxicity from ingestion of yellow phosphorus-containing fireworks. *J Clin Gastroenterol*. 1995;21:139–142.
6. Santos O, Restrepo J-C, Velásquez L, et al. Acute liver failure due to white phosphorus ingestion. *Ann Hepatol*. 2009;8:162–165.
7. Duerksen-Hughes: Toxicological profile for white phosphorus – [cited 2020 May 1]. Available from: https://stacks.cdc.gov/view/cdc/6306.
8. Austin EB, Sivilotti MLA. Phosphorus. In: Brent J, Burkhart K, Dargan P, et al., eds. *Critical Care Toxicology: Diagnosis and Management of the Critically Poisoned Patient*. Springer International Publishing; 2017:1719–1731 [cited 2020 Apr 29].
9. Tafur AJ. Bone marrow toxicity after yellow phosphorus ingestion. *Emerg Med J*. 2004;21:259–260.
10. Saraf V, Pande S, Gopalakrishnan U, et al. Acute liver failure due to zinc phosphide containing rodenticide poisoning: clinical features and prognostic indicators of need for liver transplantation. *Indian J Gastroenterol*. 2015;34:325–329.
11. Bhat DM. Acute yellow phosphorus poisoning – retrospective analysis in a tertiary care centre. *Ind J Basic Appl Medical Res*. 2018;7:163–171.
12. Leenhardt R, Buisson A, Bourreille A, et al. Nomenclature and semantic descriptions of ulcerative and inflammatory lesions seen in Crohn's disease in small bowel capsule endoscopy: an international Delphi consensus statement. *United Eur Gastroenterol J*. 2020;8:99–107.
13. PelvEx Collaborative. Management strategies for patients with advanced rectal cancer and liver metastases using modified Delphi methodology: results from the PelvEx Collaborative. *Colorectal Dis*. 2020;24:1184–1188. https://doi.org/10.1111/codi.15007.
14. Bhatia SJ, Makharia GK, Abraham P, et al. Indian consensus on gastroesophageal reflux disease in adults: a position statement of the Indian Society of Gastroenterology. *Indian J Gastroenterol Off J Indian Soc Gastroenterol*. 2019;38:411–440.
15. Hasson F, Keeney S, McKenna H. Research guidelines for the Delphi survey technique. *J Adv Nurs*. 2000;32:1008–1015.
16. Eubank BH, Mohtadi NG, Lafave MR, et al. Using the modified Delphi method to establish clinical consensus for the diagnosis and treatment of patients with rotator cuff pathology. *BMC Med Res Methodol*. 2016;16:56.
17. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*. 2008;336:924–926.
18. Gopalakrishnan S, Kandasamy S, Iyyadurai R. Rodenticide poisoning: critical appraisal of patients at a tertiary care center. *Indian J Crit Care Med*. 2020;24:295–298.
19. Saravanan S, Karthik B. Efficacy of early N-acetylcysteine in rat killer paste poisoning. *Int J Sci Stud*. 2019;6:73–79.
20. Mark K, Hyder S, Rashid M, et al. Survival benefits of N- Acetylcysteine in rodenticide poisoning: retrospective Evidence from an Indian tertiary care setting. *Curr Clin Pharmacol*. 2020 https://doi.org/10.2174/1574884715666200513090634.
21. Shukkoor Aashiq Ahamed, George Nimmy Elizabeth, Thangavelu Saravanan. N-acetyl cysteine, a boon for yellow phosphorus-induced acute liver failure? A case report. *Asian J Pharmaceut Clin Res*. 2019:1–3.
22. Kharkongor M, Mishra A, Ninan Kf, Iyadurai R. Early use of intravenous N-acetylcysteine in treatment of acute yellow phosphorus poisoning. *Curr Med Issues*. 2017;15:136.
23. Nalabothu M, Monigari N, Acharya R. Clinical Profile and outcomes of rodenticide poisoning in tertiary care hospital. *Int J Sci Res Pub*. 2015;5:1–2.
24. Pande TK, Pandey S. White phosphorus poisoning–explosive encounter. *J Assoc Phys India*. 2004;52:249–250.
25. Cardoso FS, Gottfried M, Tujios S, Olson JC, Karvellas CJ. US Acute Liver Failure Study Group. Continuous renal replacement therapy is associated with reduced serum ammonia levels and mortality in acute liver failure. *Hepatol Baltim Md*. 2018;67:711–720.
26. Marin GA, Montoya CA, Sierra JL, Senior JR. Evaluation of corticosteroid and exchange-transfusion treatment of acute yellow-phosphorus intoxication. *N Engl J Med*. 1971;284:125–128.
27. Larsen FS, Schmidt LE, Bernsmeier C, et al. High-volume plasma exchange in patients with acute liver failure: an open randomised controlled trial. *J Hepatol*. 2016;64:69–78.
28. Stahl K, Hadem J, Schneider A, et al. Therapeutic plasma exchange in acute liver failure. *J Clin Apher*. 2019;34:589–597.
29. Banjan DD, Zope DJ, Khadse DS, et al. Successful outcomes in rodenticide poisoning containing yellow phosphorus paste and zinc phosphide by vitamin K, early plasmapheresis & L-Ornithine-L-Aspartate. *Int J Sci Res*. 2019;8.
30. Sardar D, Mathews N, Mammen J, et al. Rodenticidal hepatotoxicity: raised plasma Von Willebrand factor levels predict in-hospital survival and preliminary report of the outcome of Von Willebrand factor reducing management protocol. *Indian J Gastroenterol*. 2019;38:527–533.
31. Narasimhan G, Kota V, Rela M. Liver transplantation in India. *Liver Transplant*. 2016;22:1019–1024.
32. O'Grady JG, Alexander GJ, Hayllar KM, Williams R. Early indicators of prognosis in fulminant hepatic failure. *Gastroenterology*. 1989;97:439–445.
33. Hawton K, Bergen H, Simkin S, et al. Long term effect of reduced pack sizes of paracetamol on poisoning deaths and liver transplant activity in England and Wales: interrupted time series analyses. *BMJ*. 2013;346:f403.
34. Ates M, Abuzer D, Dincer O, et al. Living donor liver transplantation for acute liver failure in pediatric patients caused by the ingestion of fireworks containing yellow phosphorus. *Liver Transplant*. 2011;17:1286–1291. https://doi.org/10.1002/lt.22384.
35. González-Andrade F, López-Pulles R. White phosphorus poisoning by oral ingestion of firecrackers or little devils: current experience in Ecuador. *Clin Toxicol*. 2011;49:29–33. https://doi.org/10.3109/15563650.2010.547860.
36. Bhat S, Kenchetty KP. N-acetyl cysteine in the management of rodenticide consumption — life saving? *J Clin Diagn Res*. 2015;9:10–13. https://doi.org/10.7860/JCDR/2015/11484.5455.
37. Suneetha DK, Inbanathan J, Kannoth S, Reshma PK. Profile of rat killer poisoning cases in a tertiary care hospital at Mysore. *Int J Sci Study*. 2016;3:264–267. https://doi.org/10.17354/ijss/2016/162.
38. Trakulsrichai S, Kosanyawat N, Atiksawedparit P, Sriapha C, et al. Clinical characteristics of zinc phosphide poisoning in Thailand. *Ther Clin Risk Manag*. 2017;13:335–340. https://doi.org/10.2147/TCRM.S129610.
39. Mishra AK, Devakiruba NS, Jasmine S, et al. Clinical spectrum of yellow phosphorous poisoning in a tertiary care centre in South India: a case series. *Trop Doct*. 2016;47:245–249. https://doi.org/10.1177/0049475516668986.
40. Yüksekkaya H, Gumus M, Yucel A, et al. Ingestion of fireworks: rare cause of poisoning in children. *Pediatr Emerg Care*. 2019;35:216–219. https://doi.org/10.1097/PEC.0000000000001450.

SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jceh.2020.09.011.