ORIGINAL RESEARCH PAPER

General Medicine

RATIFICATION TO SURVIVAL BY PLASMA PHERESIS – YELLOW PHOSPHORUS POISONING

KEY WORDS: Rodenticide, Fatal dose, Therapeutic Plasma Exchange, Yellow Phosphorous, Recovery, INR, Acute Liver Injury.

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ABSTRACT

Introduction: Rodenticides poisoning accounts for 0.5% of cas es that present to emergency facilities. Rodenticides(RATOL paste) provide the commonly available source of Yellow Phosphorus(YP). Toxic manifestations can be both local and systemic with multi -organ failure with a very high mortality rate.No specific ant idote is available . Only liver transplants had been advocated as the final treatment of fulminant liver failure . In this report, an innovative Treatment approach employed to liver cell failure case who had consumed yellow phosphorus paste.

Case Report: We report a case of 19 yr old girl who ingested Ratol paste dissolved in water around 5 gm(3% yellow phosphorus) that led to acute liver failure, successfully treated with therapeutic plasma exchange.

Conclusion: The patient ingested yell ow phosphorus had liver damage.Early Therapeutic plasma exchange(TPE) has shown significant improvement in the correction of coagulopathy, the reversal of encephalopathy, and liver recovery.TPE is extremely useful in preventing life -threatening bleeding while maintaining appropriate volume status. Yellow Phosphorous is very lethal, rigorous, and early supportive care should be given to have a good outcome

INTRODUCTION

Yellow phosphorous is widely used worldwide to prepare rodenticides, pesticides, fertilizers, and fireworks. As per national crime records bureau statistics, about 1,31,666 people lost their lives by committing suicide.[1]

In India, suicidal or accidental poisoning with rodenticides containing yellow phosphorous (RATOL – zinc-phosphorous in paste form containing 2 to 5% of yellow phosphorus)[2] is the most frequent cause of drug-induced Acute Liver Failure. It is the second most commonly used poison in India.It is a protoplasmic toxin [3], which causes multiple organ failure. LD50 of the compound after acute exposure is approx. 1mg/kg body weight Ratol paste contains more than 15 gm (450 mg of yellow phosphorus).[4]

In the past three years of our hospital admissions, the survival rate of yellow phosphorus poisonings was meager. Methods of treatment commonly adopted are Gastric lavage with Potassium permanganate solution to prevent absorption of poison, FFP transfusion, N -acetyl cysteine infusion, and vitamin -K. Most of the patients die due to severe coagulopathy, metabolic dysfunction & hepatic encephalopathy. The only definitive treatment for acute liver failure due to the ingestion of YP is liver transplantation because no antidote or medical treatment is available to reverse the liver's toxic effects.[5]

For the first time in our institution, we adopted Therapeutic Plasma Exchange for Yellow Phosphorous Poisoning along with standard medical management to treat 19 yr old young female who is in ACUTE LIVER FAILURE.

CASE REPORT

A 17-year-old female brought to casualty with a history of consumption of ratol paste. Gastric lavage was done in a local hospital and brought to casualty. The patient had three episodes of vomiting, which was non-bilious and non-blood tinged. On arrival, PR:106/min; BP 90/60mmhg; RR: 22 cpm; SpO2-98% with room air; GRBS-127 mg/dl; Systemic examination: Normal; Blood Gas Analysis: Normal. On initial examination, she was conscious, oriented. There were no bleeding manifestations, jaundice, or other signs of liver failure. Laboratory investigations showed normal biochemical parameters. Electrocardiogram was within normal limits. Ultrasonography of the abdomen showed a fatty liver. She was treated with supportive measures such as intravenous pantoprazole 40 mg and intravenous ondansetron 4 mg, N-acetylcysteine (NAC) infusion as per the protocol, IV Thiamine. From day two onwards, INR started to derange, so Inj. vitami n-K administered along with FFP transfusion. Patient's coagulation profile and LFT worsened further, followed by the development of Hepatic encephalopathy.

On day 5 of admission, the patient initiated on the first cycle of **Therapeutic Plasma Exchange(TPE)**. Standard Protocol for TPE given with informed consent by experts for 2 hours along with certified and checked 4 -6 packs of fresh frozen Human Plasma at room temperature, Albumin 20%, Calcium gluconate 10ML. The patient had hypotension, fever with chills f ollowing plasmapheresis. Blood c/s showed **Methicillin-Resistant Staphylococcus Aureus (MRSA)** and antibiotics administered accordingly. **CECT abdomen** done, and the result was suggestive of **ACUTE PARENCHYMAL LIVER DISEASE.**

Further three cycles of Therapeutic Plasma Exchange done on alternate days with regular monitoring of biochemical markers such as AST, ALT, INR, Total Bilirubin, Conjugated, and Unconjugated Bilirubin, serum creatinine.

OUTCOME:

Table No 1 . Biochemical Parameters

DAY	PLATELETS 10^3/UL	INR	TB	UCB	CB	AST	ALT
1	184	2.38	1.5	1.3	0.02	27	11
5	100	5.1	32.1	3.7	14.96	4716	1494
7	65	3.47	30.3	4.3	13.48	1640	421

8	48	2.03	28.7	4.1	11.19	323	155
9	108	1.42	22.4	3.6	10.36	203	115
10	136	1.33	16.3	2.2	4.97	174	82
12	152	1.33	11.6	1.7	3.56	152	71
20	178	1	10.5	1.1	4.03	115	78
22	214	1	5.4	0.02	2.1	102	76
MELD Score: 38 points on day 5 of admission							

In between the cycles of plasmapheresis, Hepatic Encephalopathy improved. ECG was normal throughout the hospital stay. There was no evidence of Toxic myocarditis, which is a rare manifestation of yellow phosphorous poisoning. There w as no evidence of pancreatitis, pancreatic abscess, or pancreatic duct stenosis in the CT abdomen. The patient's highest MELD score was 38 on day 5, with 19 score at the time of discharge. After four cycles of TPE along with FFP and albumin transfusion pat ient INR improved from 5.1 to 1, AST from 4716 to 102, Total bilirubin from 32.1 to 5.4, ALT 1476 to 76. On followup after one -week MELD score was 19.

DISCUSSION

Phosphorus is a non-metallic chemical element.On oral ingestion approxima tely 70% accumulates in Liver ,Heart (12%),kidney (4%),pan creas (0.4%), brain 0.3%. [1]It causes death by irreversible anoxia of tissues, changes in carbohydrate, and fat metabolism.

The clinical profile of acute poisoning with YP divided into three stages. The initial gastrointestinal (GI) stage is characterized by vomiting, nausea, diarrhea, and abdominal pain, which occur in the first 24 hrs of ingestion. Laboratory tests are almost normal during this period. Sudden death may occur because of the ingestion of a substantial amount of YP due to cardiovascular arrhythmia within the first 24 h secondary to electrolyte abnormalities such as hypocalcemia and hyperkalemia. [6]The second stage (1–4 days) is a symptom-free period, but liverenzyme levels start to derange, and toxic hepatitis begins. It is a quiescent stage where the patient seems improving and discharged prematurely. The third stage (4 - 7 days) can end in acute liver failure and acute renal failure with me tabolic derangements, encephalopathy, coagulopathy, arrhythmias, cardiogenic shock, and multi - organ failure. [11]Reported mortality is 23 - 73% and is related to ingestion dosage.[7] liver transplantation is the only treatment during the last stage; if not performed, mortality is inevitable.

Garlic odor, mucosal burns, and phosphorescent vomitus or feces are seen in only a small proportion of cases. [7] The systems affected were gastrointestinal tract (100%), liver (66.70%), CVS, Nervous and respiratory systems along with associated metabolic abnormalities (66.7%). [8]Liver toxicity occurs in the form of acute hepatitis with or without fulminant hepatic failure.[9]N - Acetylcysteine, which is an antidote for paracetamol poisoning, adopted for the treatment of yellow phosphorus poisoning, which is followed in advanced medical institutions all over the country. Yellow Phosphorous has a fatal effect, and no proper guidelines were formulated in the annals of toxicology

TPE is used for various acute or chronic life -threatening medical conditions. TPE in hepatic failure removes albumin - bound as well as HMW toxins, including ammonia, endotoxin, indols, mercaptans responsible for hepatic coma. Several studies show improved c erebral blood flow, mean arterial pressure, cerebral perfusion pressure, cerebral metabolic rate, increased hepatic blood flow, and improvements in other laboratory parameters such as cholinesterase activity or galactose elimination capacity.TPE may also r estore hemostasis by providing coagulation factors and removing activated clotting factors, TPA, fibrin and FDPs .[10]

Aggressive TPE has been used as a bridge to liver transplantation. In a recent large case series, TPE was shown to decrease cytokine levels (IFN -g, IL-10, IL-4, IL-2, and TNF-a), generally seen as necessary for the systemic inflammatory state in these patients .[10]Prothrombin Time between 17-24 seconds with control of Standard 14, INR between 1.24 -2.93, Liver cellu lar enzymes in the range of 23-381 units SGPT and SGOT 10-376, responded best to TPE. Age>60 years associated with poor outcome. The liver function tests restored to normal within 7 -21 days after therapy. TPE is given for only the cases in whom phosphorus-containing rodenticide was confirmed, not as a blanket therapy for general rodenticide poisoning .[10] In some patients, the liver may recover during TPE, and in other patients, failure may persist necessitating liver transplantation.

Treatment Strategies We Adopted In Our Institute For This Case.

Along with conservative management (N -acetyl cysteine, Vitamin K, Vitamin B1, Steroids, Urso - Deoxycholic Acid), four cycles o f Therapeutic plasmapheresis were done, which showed improvement in this case.

Table No .2 Biochemical Parameters At The Time Of Discharge

TOTAL BILIRUBIN	AST	ALT	INR
5.4	102	76	1

At the time of discharge appetite improved with normal bowel and bladder functions. RFT is monitored during the hospital stay, and it is in a normal range of 0.6 to 0.7. The patient was advised for review after seven days and to continue high carbohydrate, low protein, and a low-fat diet. On review date, MELD Score is 15. The patient was counseled for MRI in the next visit to exclude Fatty Infiltration o f Liver.

CONCLUSION

Almost all patients with yellow phosphorus poisoning, have acute live Injury. Most of them are directed towards hepatic transplantation after failure of conservative treatment. However, satisfying the pre-requisites(Finding the donor, HLA typing, and approval from the Selection Committee) for hepatic transplantation is a time -consuming process. By that time, the patient usually succumbs to acute liver failure, followed by hepatic encephalopathy an d death.

Plasma exchange therapy has shown significant improvement in the correction of coagulopathy, the reversal of encephalopathy, and the prevention of end -organ damage. The success rate of TPE is 60% - 70% in the treatment of acute yellow phosphorus poisoning. It can be pursued to reduce the morbidity and mortality of patients.

During the waiting period of Hepatic transplantation, patients can be subjected to EXTRA-CORPOREAL LIVER SUPPORT SYSTEMS like TPE(Therapeutic Plasma Exchange), MARS (molecular adsorbent recirculating system) and Albumin Dialysis as a bridging therapy, keeping in view that patient's economic status.

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DECLARATIONS

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Informed Consent
Approval for the study was obtained from the Institutional Ethics Committee.

Abbreviations: Therapeutic plasma exchange(TPE)

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