(International Print/Online Journal)

SJIF IMPACT FACTOR: 5.565
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume 6, Issue 4 , Page No: 107-115
July-August 2023

IJMSCR

Study On The Outcomes Of Therapeutic Plasma Exchange In Hepatotoxicity Due To Rat Killer Paste (Yellow Phosphorus) Poisoning

[1]Dr. R. Balamurali, [2]Dr. Chitra S , [3]Dr. Manimaran M, [4]Dr. Sathya G, [5]Dr. Raghavendra Ashok Navi

[1]Associate Professor, [2,3,4]Assistant Professor, [5]Senior Resident,
Department Of Medical Gastroenterology, Govt. Stanley Medical College Chennai

***Corresponding Author:**
Dr. R. Balamurali
Associate Professor, Department Of Medical Gastroenterology, Govt. Stanley Medical College Chennai

Type of Publication: Original Research Paper
Conflicts of Interest: Nil

Abstract

Keywords: NIL

Introduction

Rodenticides are available as pastes or powders, which contain around 2% to 5% yellow phosphorus. Elemental phosphorus is a non metallic substance that exists in two common forms, red and white (or "yellow" phosphorus). The red form, commonly used in match-tip production, is not absorbed and has very limited toxicity. The white form, a yellowish, waxy solid, is highly toxic and used worldwide in a large number of rodenticide preparations.

White phosphorus is rapidly absorbed from the intestinal tract. After getting absorbed into the systemic circulation, it is mainly getting concentrated in the liver, renal cortex, bowel mucosa, epidermis, pancreas and adrenal cortex. Within several hours of ingestion 75% of the total ingested dose is concentrated in the liver. The mechanism by which ingested (white) phosphorus causes tissue damage are direct tissue toxicity caused by an exothermic reaction, local production of phosphoric acid leading to tissue corrosion, and formation of phosphorus pentoxide which reacts with organic molecules.

This is a highly toxic compound which can cause hepatocellular necrosis and fulminant hepatic failure. The estimated lethal dose of yellow phosphorus is 1 mg/kg that results in death due to acute liver failure (ALF) and cardiovascular collapse.

Therapeutic plasma exchange (TPE) is defined as the removal of patient's plasma and replacing it with plasma from a donor along with colloid by using an extracorporeal device. It is an effective method for the removal of accumulated toxins from plasma in liver failure patients. Though TPE reduces blood ammonia levels, it has an added advantage of providing deficient clotting factors and albumin. Therapeutic plasma exchange (TPE) can be used in various liver diseases including acute liver failure (ALF). There is limited data on the efficacy of TPE in patients with ALF

Aims and objectives:

Aim:

To study the outcomes of plasma exchange in patients with yellow phosphorous induced acute hepatotoxicity.

Objectives:

1) To study the clinical profile of yellow phosphorous poisoning induced hepatotoxicity in patients and outcomes
2) To study the factors which predict the prognosis

Materials and methods:

Study design: Retrospective observational study.

Study place: Department of Medical gastroenterology, Govt. Stanley Medical College

Study duration: August 1 st 2020 to September 30 th 2021.

Study population: All the rat killer paste (RATOL) poisoning patients admitted during mentioned study period who developed hepatotoxicity and underwent therapeutic plasmapheresis.

Exclusion criteria:

[1] Patients who has taken Yellow phosphorous along with alcohol, paracetamol, or other hepatotoxins were excluded.

[2] Patients who have underlying chronic liver disease

Study protocol and technique:

1. Institution Ethics Committee approval was obtained for the study
2. Epidemiological data, amount of poison consumed, day of admission, LFT values and occurrence of Hepatic encephalopathy were recorded from available data(rat-killer poisoning register) for patients who fulfilled inclusion criteria
3. Number of PLEX sessions patient underwent
4. Improvement in LFT and coagulopathy, encephalopathy after PLEX and outcomes were analysed.

The indications for PLEX in patient with rodenticide hepatotoxicity were presence of deranged LFT AND any of the following three criteria: 1) INR ≥4,

worsening INR on serial tests OR

depressed consciousness/ altered behaviour

The contra-indications for PLEX in patient with rodenticide hepatotoxicity were presence of either 1)Hemodynamic instability 2)active sepsis

Statistical Analysis

The collected data were analysed with IBM SPSS Statistics for Windows, Version 23.0.(Armonk, NY: IBM Corp).

To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables.

To find the significant difference in the multivariate analysis for repeated measures the Repeated measures of ANOVA was used with Bonferroni correction to control the type I error on multiple comparison.

In all the above statistical tools the probability value .05 is considered as significant level.

Results

Total 116 patients with yellow phosphorous poisoning underwent TPE were included in the study, 57were males, 59were females. Most were in age group of 18-30(80).

Volume 6, Issue 4; July-August 2023; Page No 107-115

Table:1. BASELINE CHARACTERISTICS

	N	Minimum	Maximum	Mean	SD
AGE	116	18	65	27.6	10.2
DOA	116	1	10	3.9	1.8
TB 0	116	0.4	31	7.4	4.5
SGOT 0	116	76	8578	986	1147.4
SGPT 0	116	36	3375	626.5	626.9
PT 0	116	5	111	44.3	20.6
INR 0	116	1.2	12	4.1	2.2
1ST PLEX	116	4	15	6.1	1.6
TB 1	114	1.8	28	8.8	4.7
SGOT 1	114	15	5755	611.4	965.6
SGPT 1	114	10	2836	400.6	378.4
PT 1	114	12	140	31.9	18.7
INR 1	114	0.1	7.4	2.6	1.5
2ND PLEX	94	5	17	7.6	1.9
TB 2	87	1.8	23	9	4.7
SGOT 2	87	24	1028	232.9	179.7
SGPT 2	87	19	980	246.7	177.4
PT 2	87	1.8	82	25.3	14.5
INR 2	87	0.6	9	2.3	1.5
3RD PLEX	72	6	19	9.5	2.2
TB 3	72	0.5	20	6.3	4.4
SGOT 3	72	20	336	92.9	56.6
SGPT 3	72	21	306	108.4	61.6
PT 3	72	11	26	15.7	2.9
INR 3	72	0.8	2.1	1.3	0.3

Table.2

DAY OF ADMISSION		Frequency
	D1-D2	30
	D3-D5	64
	D5D8	19
	D9-D10	3
	Total	116

Table.3

SENSORIUM 0		Frequency	Percent
	HE-1	43	37.1
	HE-2	23	19.8
	HE-3	2	1.7
	NORMAL	48	41.4
	Total	116	100.0

Volume 6, Issue 4; July-August 2023; Page No 107-115

Table.4

DOSE		Frequency	Percent	Expired
	7.5-15gm	60	51.7	15
	15gm	43	37.1	15
	30gm	10	8.6	3
	45gm	3	2.6	2
	Total	116	100	35

Table.5

SGOT

RECOVERED		Mean	SD
SGOT 0	Yes	917.9	935.3
	No	1143.7	1535.6
SGOT 1	Yes	473.2	738.6
	No	950.6	1327.2
SGOT 2	Yes	199.2	133.0
	No	394.3	273.6
SGOT 3	Yes	92.9	56.6
	No		

(I) SGOT		Mean Difference (I-J)	Std. Error	p-value	95% Confidence Interval for Difference[b] Lower Bound	Upper Bound
SGOT 0	SGOT 1	436.508*	130.724	.008	80.581	792.434
	SGOT 2	682.538*	117.780	.0005	361.855	1003.222
	SGOT 3	793.769*	119.330	.0005	468.864	1118.674
SGOT 1	SGOT 2	246.031*	78.780	.016	31.533	460.529
	SGOT 3	357.262*	80.103	.0005	130.995	583.528
SGOT 2	SGOT 3	111.231*	15.764	.0005	68.309	154.152

Based on estimated marginal means

*. The mean difference is significant at the .05 level.

b. Adjustment for multiple comparisons: Bonferroni.

Volume 6, Issue 4; July-August 2023; Page No 107-115

Table.6

SGPT

RECOVERED		Mean	SD
SGPT 0	Yes	644.5	653.5
	No	585.3	568.2
SGPT 1	Yes	335.7	281.7
	No	559.9	520.0
SGPT 2	Yes	211.3	131.8
	No	416.9	260.2
SGPT 3	Yes	108.4	61.6
	No		

(I) SGPT		Mean Difference (I-J)	Std. Error	p-value	95% Confidence Interval for Difference[b] Lower Bound	Upper Bound
SGPT 0	SGOT 1	269.385*	77.685	.006	57.869	480.900
	SGOT 2	385.108*	76.437	.0005	176.991	593.225
	SGOT 3	495.338*	74.977	.0005	291.196	699.481
SGOT 1	SGOT 2	115.723*	26.796	.0005	42.766	188.681
	SGOT 3	225.954*	29.115	.0005	146.681	305.227
SGOT 2	SGOT 3	110.231*	15.030	.0005	69.309	151.153

Based on estimated marginal means

*. The mean difference is significant at the .05 level.

b. Adjustment for multiple comparisons: Bonferroni.

Table.7

INR

RECOVERED		Mean	SD
INR 0	Yes	4.1	2.3
	No	4.3	2.1
INR 1	Yes	2.2	1.1
	No	3.5	1.8
INR 2	Yes	1.8	1.2
	No	4.2	1.5
INR 3	Yes	1.3	0.3
	No		

(I) INR		Mean Difference (I-J)	Std. Error	p-value	95% Confidence Interval for Difference[b] Lower Bound	Upper Bound
INR 0	INR 1	1.898*	.304	.0005	1.070	2.725
	INR 2	2.312*	.328	.0005	1.419	3.205
	INR 3	2.951*	.293	.0005	2.154	3.748
INR 1	INR 2	.414	.184	.164	-.085	.914
	INR 3	1.054*	.141	.0005	.671	1.436
INR 2	INR 3	.639*	.145	.0005	.245	1.034

Based on estimated marginal means

*. The mean difference is significant at the .05 level.

b. Adjustment for multiple comparisons: Bonferroni.

Volume 6, Issue 4; July-August 2023; Page No 107-115

Fig.1

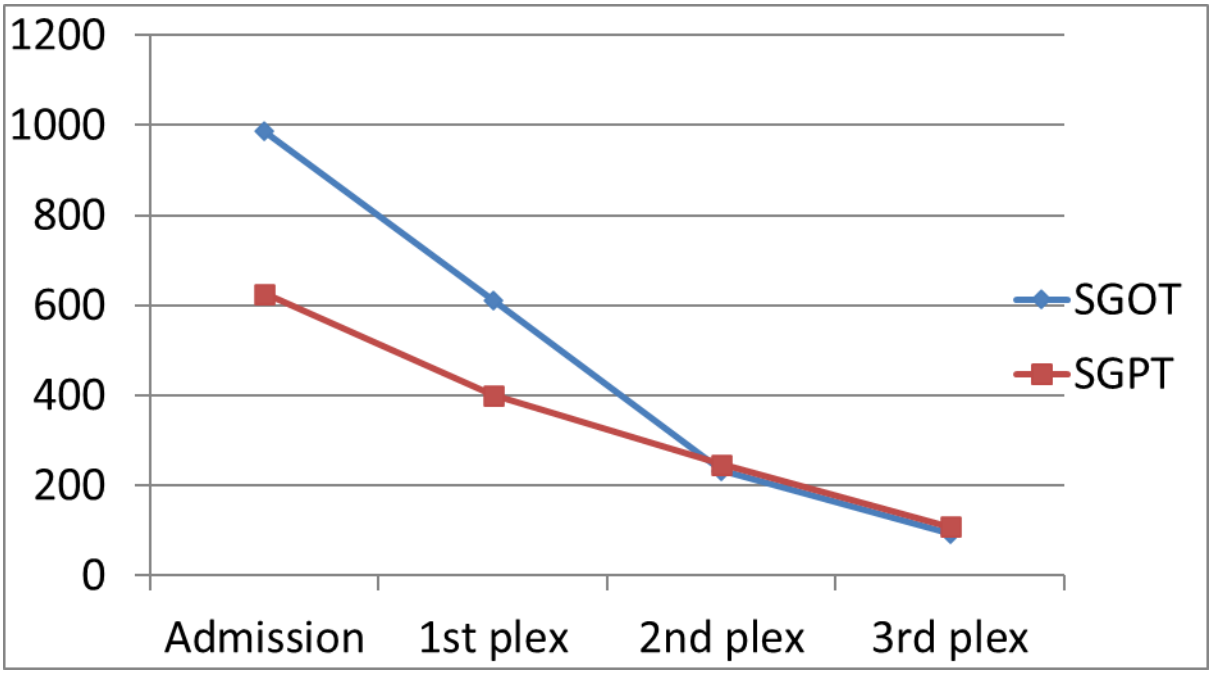
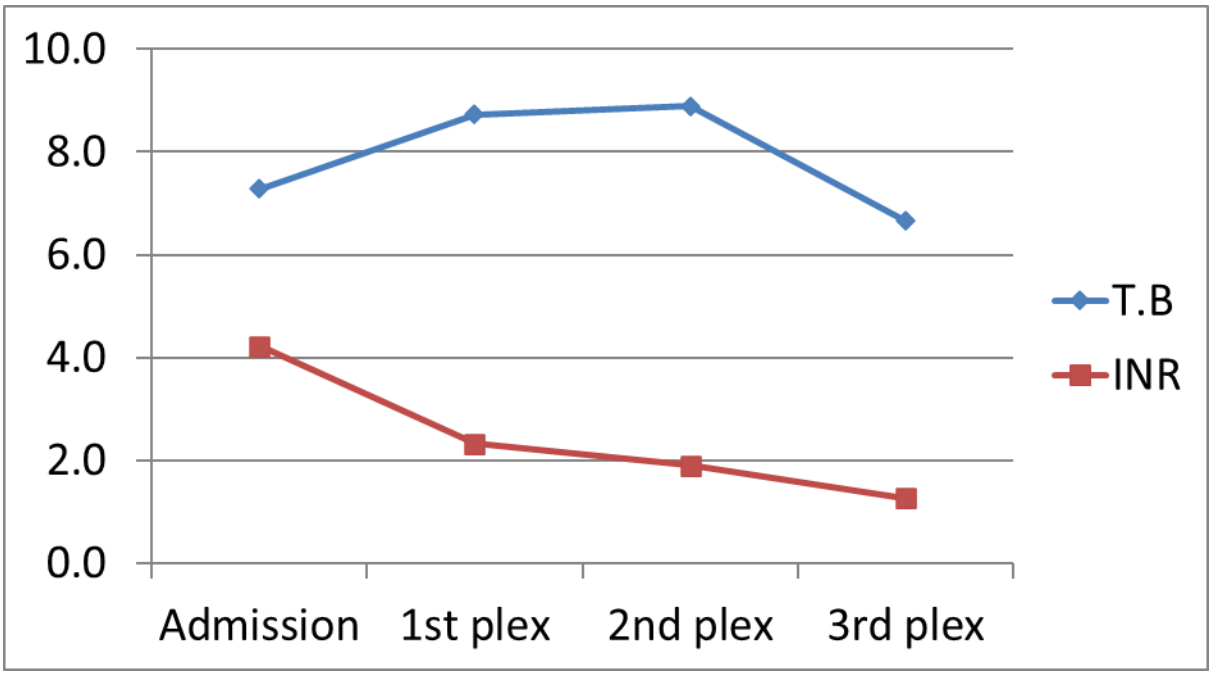


Fig.2



Volume 6, Issue 4; July-August 2023; Page No 107-115

Table: 8. OUTCOME

RECOVERED	Frequency	Percent
No	35	30.2
Yes	81	69.8
Total	116	100.0

Table 9

EXPIRED		Frequency	Percent
	After 1st Plex	15	42.8
	After 2nd Plex	11	35.1
	After 3rd Plex	9	25.7
	Total	35	100.0

Mean Total Bilirubin at admission, after 1st,2nd3rdplex were 7.4,8.8,9,6.1 respectively.

Mean SGOT/SGPT at admission, after 1st,2nd3rdplex were 986/626,611/400,232/246,92/101.

Mean PT/INR at admission, after 1st,2nd3rdplex were 44/4.1,34/2.6,25/2.3,15/1.3 respectively**.** There is significant improvement(P<0.05) in liver function test and PT/INR after each session plex.

Of 116 80(70%) patients recovered, while 35(30%) patients expired. High dose, late presentation were associated with poor outcome.

Discussion

Rodenticides are commonly used poison in India, containing 5% yellow phosphorus paste. It causes direct tissue toxicity, and forms phosphorus pentoxide which reacts with organic molecules causing acute liver failure. Therapeutic plasma exchange(TPE) is an effective method for the removal of accumulated toxins from plasma in liver failure patients.

Our study showed that most vulnerable age group of yellow phosphorous (ratol) poisoning was 15 to 30 years(80%). More than 55% of the victims were females.

Calculated Leathal dose of YP from previous study was >1mg/kg(4). In current study all patients were consumed more than 1gm of poison.

Most of the patients developed, Jaundice, hepatic encephlopathy, bleeding manifestation after day 3 of ingestion

Most patients were admitted after Day 3 of ingestion 86 out of 116,

Volume 6, Issue 4; July-August 2023; Page No 107-115

Majority of patients had HE on day of admission (58%), HE1- 43Patients, HE2- 23, HE-3- 2, normal sensorium -48 patients

The treatment of YP is aimed at the removal of the poison, prevent absorption

The fatality rate is >50% depending on the amount of phosphorus absorbed.

ALF due to YP being treated with NAC is still to be validated.5

A recent retrospective study has shown the benefit of NAC if given early. However, a time lag of >24 hours was a significant risk factor for mortality.6

Many studies were reported for the beneficial effect of extracorporeal techniques in ALF caused by acetaminophen, alcohol, viruses, etc.,7 Recent studies suggest PE (high volume) as therapeutic option in ALF.8

Subgroup analysis of baseline characteristics at admission showed higher grades of HE, high dose of YP, late presentation resulted in poor recovery

Seventy percent recovery rate from ALF was seen in our study with a mean PE session of 3. The mean time to get admitted to the hospital was 3.9 days (p= 0.017) and mean time to start of PE was 6 days (p= 0.033) after YP consumption.

A significant difference in various parameters of liver functions and coagulation parameters was observed in pre- and post-PE values (p>0.05) and INR had significant improvement post-PE.9

Laboratory data for univariate analysis for recovery had significant difference (pre bilirubin [before (B/F) and after (A/F) PE], SGOT (B/F and A/F PE), INR (A/F PE), and APTT (A/F PE) among recovered and not recovered

Exchange transfusions in acute YP intoxication were described as early as 1971.9 In that study, 5 among 15 patients of HE were given exchange transfusions (one to three), resulting in 3 survivals and 2 deaths.

Of those 10 patients, who were not given exchange transfusion, 7 died and 3 survived. The study did not show statistically significant conclusions

A prospective study of high volume PE in Caucasian patients by Larsen et al.,6 among 92 patients of ALF with a wide etiology showed a survival benefit of 58.7% with a mean session of PE of 2.4 when compared to standard medical therapy.

There was a statistically significant improvement in INR and ALT post-PE. Extrapolating the results of these studies to ALF caused by only YP needs to be validated by large randomized controlled trials

Limitations:

Retrospective Observational study

Single centre study

Conclusion:

The study revealed that patients with yellow phosphorus poising and ALF therapeutic plasma exchange is a viable treatment option with better outcome, in poor resource settings where liver transplantation is not available.

References

1. Eapen CE, Balasubramanian V, Ramamoorthy G, Jayanthi V, Sathiyasekaran M, Murugan N, et al. Management of rodenticide poisoning: Tamil Nadu chapter of Indian Society of Gastroenterology guidelines. Gastroenterol Hepatol Endosc Pract 2022;2:1-6
2. Govindarajan R, Ramamoorthy G, Shanmugam RM, et al. Rodenticide ingestion is an important cause of acute hepatotoxicity in Tamil Nadu, southern India. Indian J Gastroenterol. 2021 Aug;40(4):373-379.
3. Varghese J, Joshi V, Bollipalli MK, et al. Role of therapeutic plasma exchange in acute liver failure due to yellow phosphorus poisoning. Indian J Gastrol. 2020; 39: 544–9.
4. Mishra AK, Devakiruba NS, Jasmine S, Sathyendra S, Zachariah A, Iyadurai R. Clinical spectrum of yellow phosphorous poisoning in a tertiary care centre in South India: a case series. Trop Doct 2017;47(3):245–249. DOI: 10.1177/0049475516668986
5. Mark K, Hyder S, Rashid M, Chandran VP, Seshadri S, Seshadri S, et al. Survival benefits of N-Acetylcysteine in rodenticide poisoning: Retrospective Evidence from an Indian tertiary care setting. Curr Clin Pharmacol 2020. DOI: 10.2174/1574884715666200513090634. PMID: 32400335.
6. Larsen FS, Schmidt LE, Bernsmeier C, Rasmussen A, Isoniemi H, Patel VC, et al. High-

Volume 6, Issue 4; July-August 2023; Page No 107-115

volume plasma exchange in patients with acute liver failure: An open randomised controlled trial. J Hepatol 2016;64(1):69–78. DOI: 10.1016/j.jhep.2015.08.018.

7. Padmanabhan A, Connelly-Smith L, Aqui N, Balogun RA, Klingel R, Meyer E, et al. Guidelines on the use of therapeutic apheresis in clinical practice – evidence-based approach from the writing committee of the American Society for Apheresis: the eighth special issue. J Clin Apher 2019;34(3):171–354. DOI: 10.1002/jca.21705.
8. Cheng YL, Chang CH, Chen WT, Tsai MH, Lee WC, Tu KH, et al. Prognostic factors and treatment effect of standard-volume plasma exchange for acute and acute-on-chronic liver failure: a single-center retrospective study. Transfus Apher Sci 2018;57(4):537–543. DOI: 10.1016/j.transci.2018.05.030
9. Marin GA, Montoya CA, Sierra JL, Senior JR. Evaluation of corticosteroid and exchange-transfusion treatment of acute yellowphosphorus intoxication. N Engl J Med 1971;284(3):125–128. DOI: 10.1056/NEJM197101212840303.

Volume 6, Issue 4; July-August 2023; Page No 107-115