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Original Research Paper

Hepatic Injury in Poisoning Cases: An Autopsy Study

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Abstract

Poisons act on various organs in the body that may result in fatality. In the present study, the liver pathology in various poisoning cases was studied in autopsied bodies that were conducted in a tertiary care hospital in Mangalore. The incidence of poisoning was equal in third, fourth and fifth decades with male to female ratio 7:3. The predominant poison responsible for fatality was Organophosphorus compound followed by Pyrethyroid, zinc sulphide and Carbamates. Majority of the victims survived for less than 6 hours. Serum bilirubin level was raised in organophosphate, Pyrethyroid and zinc phosphide poisoning. Serum liver enzyme levels were raised in zinc phosphide, copper sulphate, Pyrethyroid and organophosphate poisoning. Congestion was the predominant gross finding seen in all the poisoning cases. Yellowish discoloration of liver was mainly seen in paraquat, zinc phosphide and organophosphate poisoning. The predominant microscopic finding was congestion, steatosis, periportal lymphocytic infiltration, intrahepatic haemorrhage, centrilobular necrosis and intrahepatic cholestasis.

Key Words: Poisoning, Hepatotoxicity, Liver Pathology, Liver function test

Introduction:

Poisoning is one of the major social problems worldwide. The morbidity and mortality due to poisoning varies in different parts of the world due to variation in consumption of toxic substances. The commonly used compounds include pesticides, opioids, benzodiazepines, alcohol, antidepressants, etc. [1-6]

Since majority of the drugs and toxic compounds are metabolized in the liver, it is more prone for injury caused by these agents.

The relative importance of hepatic injury due to various types of toxins has changed considerably over the years. Poisoning by phosphorus has almost disappeared from the USA, but remains a problem in other parts of the world due to suicidal or accidental ingestion of rodenticides.

A cause of hepatotoxicity outstripping all others in the UK and of growing importance elsewhere is the suicidal ingestion of Paracetamol. [7] The hepatic toxicity induced by pharmaceuticals, toxins, recreational drugs and pesticides can range from steatosis to massive necrosis.

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The present investigation is undertaken to study the liver cell changes in autopsy samples of various poisoning deaths.

Material and Methods:

Forty cases of deaths due to poisoning were subjected to postmortem examination in the Department of Forensic Medicine, Father Muller Medical College, Mangalore, Karnataka from January 2009 to December 2011.

The gross findings were noted at autopsy and liver tissue was subjected to histopathological examination in the Department of Pathology, Father Muller Medical College, Mangalore, Karnataka.

The routine viscera and blood samples were collected at autopsy and sent to Forensic Science Laboratory for chemical analysis and confirmation of the poison consumed.

Observations and Results:

Majority of the cases were in the age group of 21-50 years. Incidence was more common in males (27 cases) compared to females (13 cases) with male to female ratio was 7:3. (Fig. 1) The predominant poison responsible for fatality was Organophosphorus compound (OPC), followed by Pyrethyroid, zinc sulphide and Carbamates. (Fig. 2)

Majority of the victims survived for less than 6 hours followed by 6-24 hours. (Fig. 3)Clinical investigations were done in only 25 cases. Serum bilirubin level was raised only in organophosphate, Pyrethyroid and zinc phosphide poisoning. Out of 11 organophosphate cases, total bilirubin was

raised in 2 cases, but there was no rise in conjugated or unconjugated bilirubin level. Out of six Pyrethyroid cases, total bilirubin was raised in two cases and conjugated as well as unconjugated bilirubin was raised in only one case. Total bilirubin was raised in all five cases of zinc phosphide, but conjugated as well as unconjugated bilirubin was raised in only one case. Serum protein level was raised only in 20% of zinc phosphide poisoning with raised Albumin-Globulin ratio.

Other poisoning cases did not show any rise in these levels. Serum liver enzyme levels were mainly raised in zinc phosphide and copper sulphate poisoning followed by Pyrethyroid and Organophosphate poisoning. (Table 1) During autopsy, predominant gross finding of the liver was congestion in all the cases of poisoning. However, in paraquat and zinc phosphide cases, congestion was seen only in 50% of cases.

Cut surface of liver showed yellowish discoloration in 50% of paraquat and zinc phosphide cases and 9% of organophosphate poisoning. Blackish discoloration of liver surface adjacent to stomach was observed in both sulphuric and formic acid cases.

Multiple petechial haemorrhages over the surface and in the cut sections were observed in 80% and 9% of zinc phosphide and organophosphate cases respectively. Cirrhotic changes were visible in 18% of organophosphate cases. The viscera and blood were sent for chemical analysis, which showed positive results for poisoning in only 32 cases.

On histopathological examination the predominant microscopic findings were congestion and steatosis in most of the poisoning cases in the present study. (Table 2)

Steatosis was microvesicular and macrovesicular in the organophosphate, Pyrethyroid, Carbamates, zinc phosphide, and sulphuric acid poisoning; while it was mainly microvesicular in alcohol, copper sulphate, benzodiazepine and Organochlorine poisoning.

Congestion was seen in all cases except alcohol, sulphuric acid, formic acid and Organochlorine poisoning.

Periportal lymphocytic infiltration was observed in organophosphate, Pyrethyroid, zinc phosphide, benzodiazepine and turpentine poisonings. Intrahepatic haemorrhage was seen in 2 cases of zinc phosphide and one case of organophosphate poisoning.

In two cases each of Pyrethyroid and zinc phosphide poisoning centrilobular necrosis was seen, while periportal fibrosis was seen in one case, each of combined organophosphate with Pyrethyroid consumption and Organochlorine poisoning. Intrahepatic cholestasis was seen in three cases of zinc phosphide poisoning.

Discussion:

Poisoning is one of the global health problems. Earlier studies have shown that the incidence of poisoning was more common in the age group of 21-30 years. [1, 8, 9] However, in the present study, the incidence of poisoning fatalities were equal in third, fourth and fifth decades. This could be due to the fact that the causes for poisoning fatalities (i.e., social, economic and psychological reasons) vary in different places as well as individuals.

The incidence of poisoning fatalities was more common in males (67.5%) in the present study and is consistent with those of earlier reports [1, 9, 10] Men are the predominant gender in developing countries involved in jobs to take care of the family and they are more prone for psychological stress.

Hence, suicidal tendencies are more in men. In the present study, the commonest agent responsible for the fatality was Organophosphate, and is consistent with earlier studies. [1, 8-10] Common use of the Organophosphates as pesticides**/** insecticides in agricultural fields and domestic areas is prone for accidental poisoning while easy accessibility accounts for its use for suicidal purpose.

In the present study, the second commonest compound responsible for fatality was Pyrethyroid followed by aluminum and zinc phosphides. However, aluminum and zinc phosphides stand second in other studies. [1, 8, 9] The pyrethroids are commonly used in agriculture, and aluminum and zinc phosphides are used as rodenticides in houses and agriculture fields crops, which are easily available for suicidal purpose.

In the present study, majority of the victims survived for less than 6 hours followed by 6-24 hours. This is consistent with other studies. [11, 12] In most of the poisoning cases, the initial few hours is very critical. Most of the fatalities result in this period because the victims are not able to reach the hospital in time for treatment. Hepatotoxicity is indicated by decreased level of serum albumin and increased levels of AST, ALT, INR, serum bilirubin and blood ammonia levels.

In the present study, serum bilirubin and liver enzyme levels were raised mainly in organophosphate, Pyrethyroid, zinc phosphide and copper sulphate poisoning.

Co-poisoning with Organophosphorus and Pyrethyroid pesticides causes inhibition of glutathione S-transferase, superoxide dismutase, catalase, transaminases and phosphatases leading to reduced glutathione content, increased activity of lactate dehydrogenase and thiobarbituric acid levels. [13] Elevated transaminase and alkaline phosphatase can persist for 3 to 6 days in survivors of organophosphate intoxication. [14]

In our study, congestion was the predominant gross finding followed by yellowish discoloration and multiple petechial haemorrhages especially in zinc phosphide, organophosphate and Pyrethyroid poisoning. This is consistent with earlier studies. [15, 16]

Sulphuric acid caused blackish discoloration over the surface where the stomach was in contact with liver.

In this study, microvesicular and macrovesicular steatosis was the predominant histopathological finding in most of the cases.

Pesticides and ethanol causes oxidative stress in the liver mainly by an induction of microsomal cytochrome P-450 that may lead to modification of lipids, proteins and nucleic acids in the liver. [17, 18] Also, ethanol-modified epigenetic parameters such as DNA methylation, different site-specific modifications in histone proteins and microRNAs lead to fatty liver. [19] In this study, centrilobular hepatic necrosis was mainly observed in Pyrethyroid and zinc phosphide poisoning, which is consistent with earlier studies. [20, 21]

Pyrethroids metabolize in the liver by the action of cytochrome P450 microsomal enzyme system via esoteric and oxidative pathways which results in oxidative stress causing hepatic necrosis. [22]

Phosphide ingestion leads to a high superoxide dismutase activity and low catalase levels that causes increased free radicals and accelerates lipid peroxidation, which results in cellular death. [23]

Centrilobular necrosis followed by rapid disappearance of necrotic cells was observed in Paracetamol overdose. [24]

In the present study, serum alkaline phosphatase was raised in 4 cases of zinc phosphide, 2 cases of organophosphate and one case of Pyrethyroid poisoning, which indicates bile duct pathology.

However, histological evidence of intrahepatic cholestasis was demonstrated in only 3 cases of zinc phosphide poisoning. It has been reported that surrogate alcohol mixtures containing guanidine derivatives cause irreversible disturbance of bile transport in hepatocytes and biliary capillaries. [25]

Summary and Conclusion:

In the present study, liver injury was due to direct cytotoxicity of the consumed poisons. Liver cell injury was invariably present in all the cases and the severity of injury ranged from congestion, haemorrhage, periportal inflammation, steatosis, cholesterol granuloma to zonal necrosis and massive necrosis.

The predominant poison consumed in majority of the deaths was Organophosphorus compounds and phosphides. Middle aged men formed the largest group of poisoning deaths.

Liver, being the main organ of metabolism, is the target of injury in poisoning. The nature of the poison and the type of cell injury caused in other organs including liver determine the course of poisoning.

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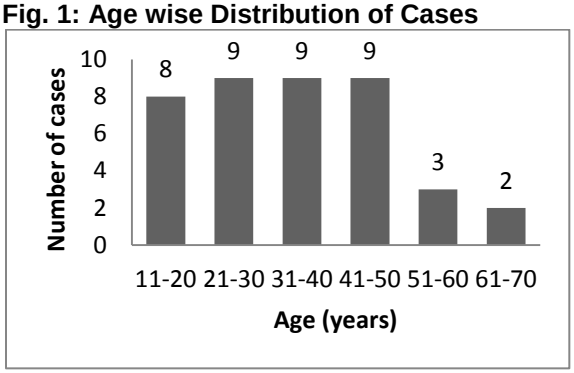
Fig. 1: Age wise Distribution of Cases



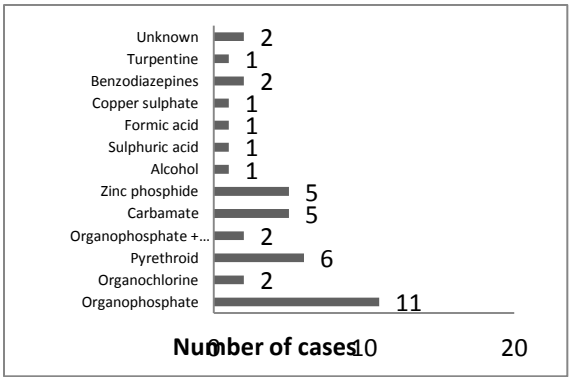


Fig. 3: Duration of Survivability of Cases

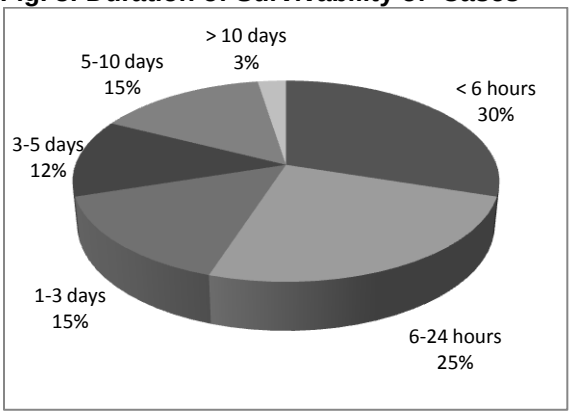


Fig. 2: Distribution of Poisoning Cases

Table 1: Liver Enzyme Levels in Different Cases of Poisoning

Poisonous compounds	AST (SGOT) No. (%)	ALT(SGPT) No. (%)	ALP No. (%)
Organophosphate (n=11)	3 (27)	3 (27)	2 (18)
Pyrethroids (n=6)	5 (83)	3 (50)	1 (17)
Organophosphates + Pyrethroids (n=2)	1 (50)	1 (50)	-
Zinc phosphide (n=5)	5 (100)	5 (100)	4 (80)
Copper sulphate (n=1)	1 (100)	1 (100)	-

AST – Aspartate aminotransferase, SGOT – Serum glutamic oxaloacetic transaminase, ALT – Aalanine transaminase, SGPT – Serum glutamic pyruvic transaminase, ALP – Alkaline phosphatase. # The above investigations were not done in remaining cases.

Table 2: Liver Histopathology Findings in Different Cases of Poisoning

Poisonous compounds	Congestion	Steatosis	PLI	Haemorrhage	Necrosis	Fibrosis	
		Microvesicular	Macrovesicular				
Organophosphate (n=11)	5 (45%)	7 (64%)	3 (27%)	4 36%)	1 (9%)	-	-
Pyrethroids (n=6)	2 (33%)	3 (50%)	2 (33%)	2 (33%)	-	2 (33%)	-
Organophosphate + Pyrethroids (n=2)	2 (100%)	2 (100%)	1 (50%)	1 (50%)	-	-	1 (50%)
Carbamates (n=5)	2 (40%)	2 (40%)	1 (20%)	-	-	-	-
Zinc phosphide (n=5)	2 (40%)	4 (80%)	2 (40%)	2 (40%)	2 (40%)	2 (40%)	-
Alcohol (n=1)	-	1 (100%)	-	-	-	-	-
Sulphuric acid (n=1)	-	1 (100%)	1 (100%)	-	-	-	-
Formic acid (n=1)	-	1 (100%)	-	-	-	-	-
Copper sulphate (n=1)	1 (100%)	1 (100%)	-	-	-	-	-
Benzodiazepine (n=2)	1 (50%)	1 (50%)	-	2 (100%)	-	-	-
Organochlorine (n=2)	-	1 (50%)	-	-	-	-	-
Turpentine (n=1)	1 (100%)	-	-	1 (100%)	-	-	-
Unknown (n=2)	2 (100%)	-	-	-	-	-	-

PLI – Periportal lymphocytic infiltration