YELLOW PHOSPHOROUS POISONING (RATOL)-ROLE OF N-ACETYL CYSTEINE AND POSTMORTEM TOXICOLOGICAL FINDINGS – A PROSPECTIVE STUDY

DISSERTATION SUBMITTED FOR

M.D GENERAL MEDICINE

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CHENNAI, TAMILNADU

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Dr.D.MARUTHU PANDIAN M.S.,FICS.,FRCS.,
THE DEAN ,
Madurai Medical College,
Government Rajaji Hospital,
Madurai.

CERTIFICATE FROM THE HOD

This is to certify that the dissertation entitled **YELLOW PHOSPHOROUS POISONING (RATOL)-ROLE OF N-ACETYL CYSTEINE AND POSTMORTEM TOXICOLOGICAL FINDINGS – A PROSPECTIVE STUDY** is the bonafide work of **Dr.M.MANIKANDAN** in partial fulfillment of the university regulations of the Tamil Nadu Dr. M.G.R. Medical University, Chennai, for **M.D General Medicine Branch I** examination to be held in **May 2018**.

Dr.V.T. PREMKUMAR M.D.,
Professor and HOD,
Department of General Medicine,
Government Rajaji Hospital,
Madurai Medical College,
Madurai.

CERTIFICATE FROM THE GUIDE

This is to certify that the dissertation entitled **YELLOW PHOSPHOROUS POISONING (RATOL)-ROLE OF N-ACETYL CYSTEINE AND POSTMORTEM TOXICOLOGICAL FINDINGS – A PROSPECTIVE STUDY** is the bonafide work of **Dr.M.MANIKANDAN** in partial fulfillment of the university regulations of the Tamil Nadu Dr. M.G.R. Medical University, Chennai, for **M.D General Medicine Branch I** examination to be held in **May 2018**.

Dr.R.BALAJINATHAN M.D.,
Professor and chief,
Department of General Medicine,
Government Rajaji Hospital,
Madurai Medical College,
Madurai

DECLARATION

I, **Dr.V.MANIKANDAN,** solemnly declare that, this dissertation **"YELLOW PHOSPHOROUS POISONING(RATOL)- ROLE OF N-ACETYL CYSTEINE AND POSTMORTEM TOXICOLOGICAL FINDINGS – A PROSPECTIVE STUDY"** is a bonafide record of work done by me at the Department of General Medicine, Govt. Rajaji Hospital, Madurai, under the guidance of **Dr.R.BALAJINATHAN,M.D**, Professor, Department of General Medicine, Madurai Medical College, Madurai. This dissertation is submitted to The Tamil Nadu Dr. M.G.R Medical University, Chennai in partial fulfilment of the rules and regulations for the award of **M.D Degree General Medicine Branch-I;** examination to be held in **May 2018.**

Place: Madurai

Date: **Dr.V.MANIKANDAN**

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INTRODUCTION

INTRODUCTION

Poisoning is a major problem globally and its incidence is rising due to rapid industrialization and urbanization. The exact incidence of acute poisoning is not known in India because of lack of any central poison registry. The toxins involved in acute poisoning cases vary from place to place. In western countries, the commonest toxins are medicinal agents. In contrast, in India, insecticide, pesticides and rodenticide are the most commonly consumed agents in adults.

Ratol is a rodenticide (rat killer paste) ,it contains yellow phosphorus, a severe local and systemic toxin causing damage to gastrointestinal, hepatic, cardiovascular, and renal systems. Among these liver is the most commonly affected organ and acute liver failure with coagulopathy is the most dreaded complication. Other fatal complications are acute tubular necrosis, hepato-renal syndrome, hypotension and arrhythmias.

Clinical manifestations of yellow phosphorous poisoning has three stages. First stage has gastrointestinal symptoms like nausea and vomiting in the absence of any laboratory abnormalities. Second stage occurs after 24–48 hours characterised by rising transaminases, although the patient may be asymptomatic. In some cases, this progresses to the third stage characterised by acute liver failure with coagulopathy and encephalopathy, which can be fatal.

The Role of N acetyl cysteine (NAC) in acetaminophen induced Acute fulminant hepatic failure (ALF) was well established. Additionally some studies have shown that NAC may be useful in non-acetaminophen induced ALF like yellow phosphorous poisoning also. These toxins damages the liver by depleting glutathione stores. NAC acts by stimulate the glutathione synthesis and enhances glutathione transferase activity . other beneficial effects of NAC are anti-inflammatory, inotropic and vasodilatory effects .Therefore, treatment with NAC, which is inexpensive and relatively safe, would be a viable treatment option for patients admitted with yellow phosphorous consumption with ALF but those who are not eligible for liver transplant.

A post-mortem liver biopsy shows hydropic or fatty infiltration of hepatocytes, collapsed reticulin framework with fibrosis between the hepatocytes and periportal necrosis suggestive of an acute fulminant hepatitis

AIMS AND OBJECTIVES

AIMS AND OBJECTIVES

1. To study the prevalence of yellow phosphorus poisoning in our hospital
2. To evaluate the usefulness of N-Acetyl cysteine in yellow phosphorous poisoning
3. Postmortem findings in liver and kidney

REVIEW OF LITERATURE

REVIEW OF LITERATURE

RODENTICIDE

Rodenticides for many years have been an important cause of significant morbidity and mortality in patients who present to an emergency room with deliberate self harm.

An annual incidence of 500,000 cases has been reported. . One recent study shows Incidence of hospital admission of rodenticide poison in tamilnadu is approximately 9%.

Substance consumed	No. of patients	Percentage
Organophosphates	49	18.77
Oleander seeds	38	14.55
Snake bite	32	12.26
Nail polish	24	9.19
Rodenticide	22	8.42
Alcohol (methanol)	20	7.66
Antifungal drugs	18	6.89
Antipsychotic drugs	12	4.59
Ant killer	9	3.44
Endosulphan	8	3.06
Food	7	2.68
Hair dye	5	1.91
Kerosene	3	1.14
Miscellaneous	14	5.36

The easy availability of these compounds has made this a problem almost impossible to control. Most rodenticides produce their toxic or lethal effects in humans mainly by ingestion of a large enough single dose. Of the different classes of rodenticides available, yellow phosphorus is considered a highly toxic

compound and it can cause hepatocellular necrosis and fulminant hepatic failure in up to 50% of patients.

CLASSIFICATION OF RODENTICIDES

HIGHLY TOXIC COMPOUNDS

(LD50 - less than 50mg/kg body weight) .

Thallium,

Sodium monofluoroacetate,

Strychnine

Zinc phosphide,

Yellow phosphorus

Arsenic

MOERATLY TOXIC COMPOUNDS

(LD50 - more than 500 mg/kg body weight)

Alpha-naphthyl-thiourea (ANTU)

DDT.

LOW TOXIC COMPOUNDS

(LD50 - between 500 and 5,000 mg/kg body weight)

Red squill,

Norbomide

Anticoagulant - warfarin

Commonly available preparations are

Rat killer powder – barium ,arsenic

Rat killer cake - anticoagulants like warfarin and related

compounds ,coumarins

Rat killer paste - yellow phosphorous ,zinc phosphide Rat killer spray

YELLOW PHOSPHOROUS

GENERAL PROPERTIES

Also called as white phosphorous

Translucent appearance

It has garlic like odour and taste

It is highly reactive

It is soft waxy solid

Luminous in the dark

Ignition temperature is low(303k) so burns easily in air

Burns easily in cl2

Highly toxic

YELLOW PHOSPHOROUS (YP)– RAT KILLER PASTE(RATOL) POISONING

Commonly available as 3% yellow phosphorous

MODE OF POISONING

Suicidal

Accidental

LETHAL DOSE

More than 1mg/kg

MECHANISM OF ACTION

YP is a protoplasmic poison ,it causes multi organ damage due to uncoupling of oxidative phosphorylation

After ingestion YP is rapidly absorbed through the intestinal tract and phosphorous remains stable in the gut for longer period because it has more water content and low oxygen tension . After absorbtion 69% to 73% of the total ingested dose concentrates in the liver , some amount of YP reaches the brain, striated muscle, and the kidneys also. peak level is reached 2 to 3 hours after of toxic oral ingestion.so liver is most vulnerable organ to damages occur.

Yellow phosphorous

↓

Phosphoric acid

↓

Exothermic reaction

↓

Direct tissue damage due to production of free radicals

CLINICAL MANIFESTATION

The course of events following yellow phosphorus poisoning has three stages.

FIRST STAGE: (first 24 hours)

May be asymptomatic or

Burning pain in the throat and abdomen

Nausea ,vomiting diarrhoea and severe abdominal pain

Laboratory values are normal .

SECOND STAGE : STAGE OF HEPATITIS (24 TO 48 HOURS)

Patient may be asymptomatic.

AST & ALT are elevated

Haematological abnormalities are present

THIRD STAGE : STAGE OF ACUTE LIVER FAILURE

Only few cases are progresses to the third stage

Systemic toxicities are present

GASTROINTESTINAL SYSTEM

Prolonged vomiting and diarrhoea

Features of acute fulminant hepatic failure

Liver tenderness and enlargement

Hematemesis and melena due to coagulopathy

Jaundice and pruritus

Hepatorenal syndrome

Marked elevation of transamiases, alkaline phosphatases and prothrombin time

RENAL SYSTEM

Acute tubular necrosis

Acute renal failure

CARDIOVASCULAR SYSTEM

Hypotension and tachycardia

Arrhythmias

Acute pulmonary edema

Myocardial injury

Cardiogenic shock

Alteration in ECG such as inverted T waves, changes in QRS complex, tachycardia, arrhythmias and decreased ventricular contractility has been reported

HEAMATOLOGICAL

Direct bone marrow suppression mainly selective myeloid series suppression causes leucopenia with preserved normoblastic erythroid maturation, normal megakaryocytes, lymphocytes, and plasma cells

CENTRAL NERVOUS SYSTEM

Confusion

Psychosis

Hallucinations

Coma

TOXIC HEPATITIS

COMMON CAUSES

1)Alcohol.

Large amount of alcohol drinking over many years can lead to alcoholic hepatitis

2)Over-the-counter pain relievers.

Self medication mainly analgesics such as "acetaminophen , aspirin, ibuprofen and naproxen can damage the liver especially if taken frequently or combined with alcohol".

3)Toxins and chemicals

Like yellow phosphorous

4)Prescriped drugs.

Some commonly used drugs linked to serious liver injury include the statin s, the combination drugs like amoxicillin-clavulanate , phenytoin , azathioprine , ketoconazole, certain antivirals and anabolic steroids.

5)Herbal products.

Some herbs measured dangerous to the liver include aloe vera, black cohosh, cascara, chaparral, comfrey, kava and ephed.

6)Industrial chemicals.

Common chemicals that can cause liver damage include the dry cleaning solvent like carbon tetrachloride, vinyl chloride , paraquat and polychlorinated biphenyls .

RISK FACTORS

1)consumption of over-the-counter pain relievers or certain prescription drugs.

"Taking a medication or over-the-counter pain reliever that carries a risk of liver damage and increases risk of toxic hepatitis".

2)Chronic liver disease.

" Having a serious liver disorder such as cirrhosis or nonalcoholic fatty liver disease makes much more susceptible to the effects of toxins".

3)Viral hepatitis.

Chronic infection with a hepatitis virus like hepatitis B, hepatitis C makes the liver more vulnerable.

4)Aging.

Elder person's liver breaks down harmful substances more slowly. This means that toxins and their byproducts stay in the body longer.so it causes more damage to liver.

5)Drinking alcohol.

Consumption alcohol while taking drugs or certain herbal supplements increases the risk of toxicity.

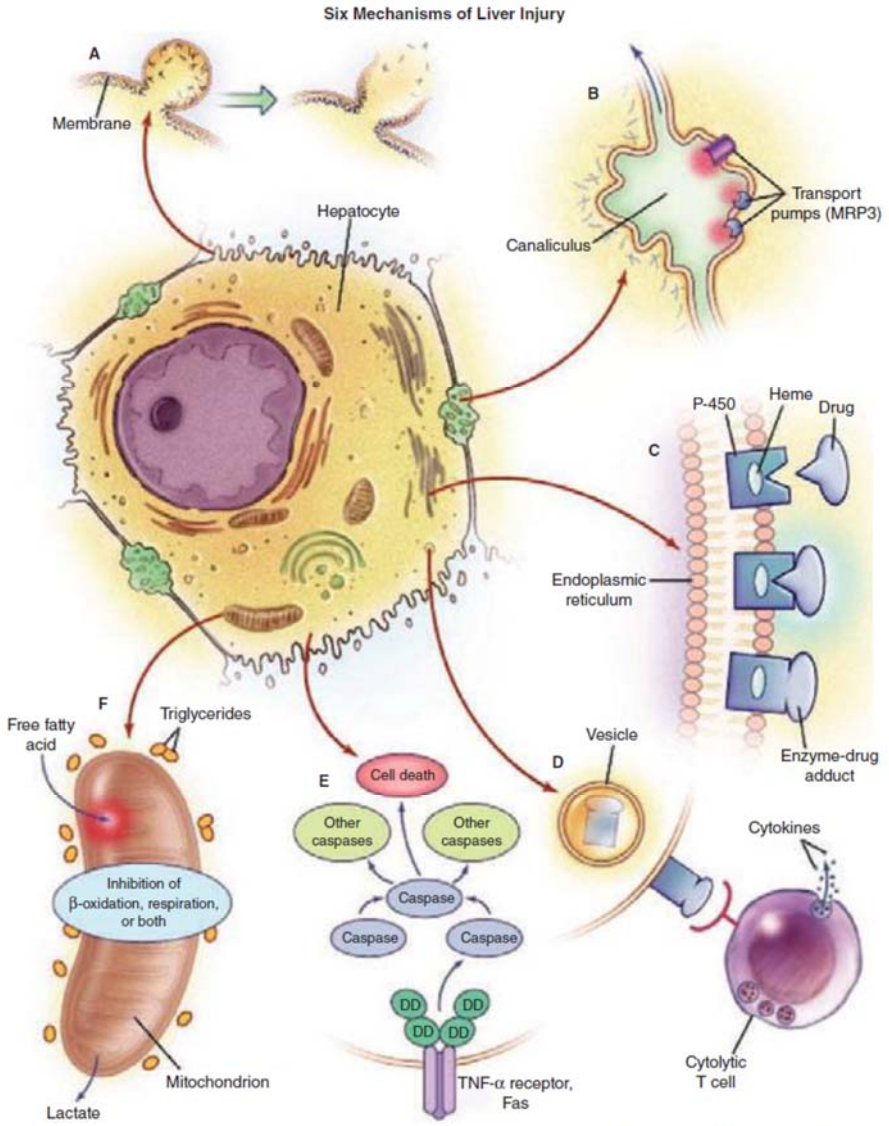
6)Female sex.

Womens have slowely metabolising capacity than men , so their livers are more exposed to higher blood concentrations of harmful substances for a longer time. This also increases the risk of toxic hepatitis.

7) Genetic mutations

Inheriting certain genetic mutations that affect the production and action of the liver enzymes that break down toxins may makes more vulnerable to toxic hepatitis.

MECHANISMS OF TOXIC HEPATITIS



A. Rupture of cell membrane.
B. Injury of bile canaliculus (disruption of transport pumps).
C. P-450-drug covalent binding (drug adducts).
D. Drug adducts targeted by CTLs/cytokines.
E. Activation of apoptotic pathway by TNFα/Fas.
F. Inhibition of mitochondrial function.

The pathophysiologic mechanisms of hepatotoxicity are characterized by organic and functional damage of the liver.

The principal alterations are:

(1) Disruption of the hepatocyte;

Absorbed toxins are covalently binding to intracellular proteins ,cause a decrease in ATP levels. It lead to disassembly of actin fibrils on the surface of the hepatocyte with blistering and rupture of the membrane;

(2) Disruption of the transport proteins;

Toxins may affect transport proteins at the canalicular membrane and can interrupt bile flow. It also cause interruption of transport pumps;

(3) Cytolytic T-cell activation:

The covalent binding of a toxin to the P-450 enzyme acts as an immunogen, activating T cells and cytokines and stimulating a multifaceted immune response

(4)toxin adducts targeted by CTLs/cytokines

migration of these enzyme-drug adducts to the cell surface in vesicles to serve as target immunogens for cytolytic attack by T cells, stimulating an immune response involving cytolytic T cells and cytokines.

(5)Apoptosis of hepatocytes;

The apoptotic pathways are activated by the tumor necrosis factor-alpha receptor of Fas may trigger the cascade of intercellular caspases, which results in programmed cell death;

Apoptosis occurs by one of two pathways:

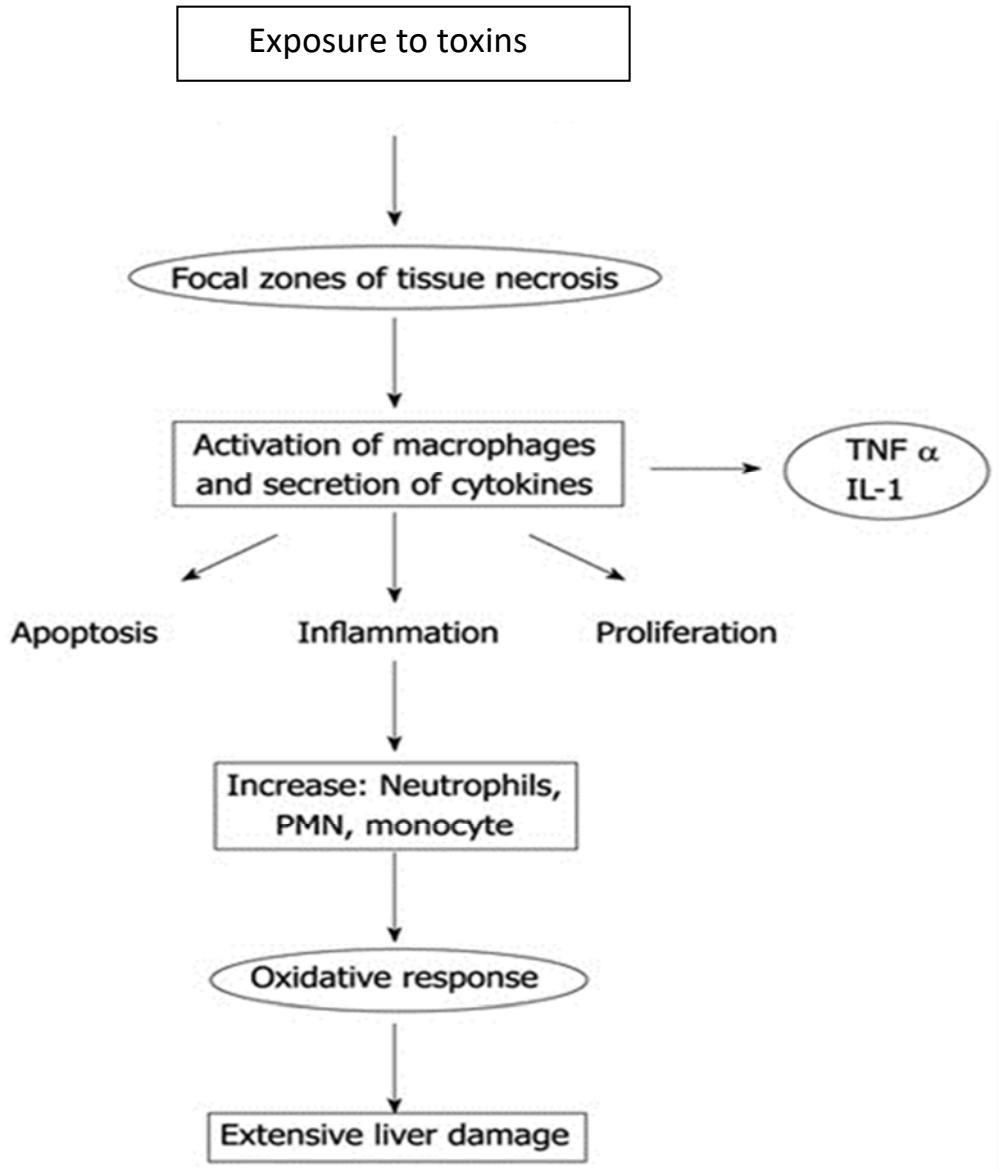
(1)a deathreceptor pathway;

(2) the mitochondrial pathway.

(6) Mitochondrial disruption

Some toxins inhibit the mitochondrial function by by a dual effect on both beta-oxidation and respiratory chain enzymes by inhibiting the synthesis of nicotinamide adenine dinucleotide and flavin adenine dinucleotide, resulting in decreased ATP production causes lack of aerobic respiration,and accumulation of lactate and reactive oxygen species (which may disrupt mitochondrial DNA).

Bile duct injury - toxic metabolites excreted in bile may cause injury to the bile duct epithelium


Exposure to toxins
Focal zones of tissue necrosis
Activation of macrophages and secretion of cytokines
TNF α
IL-1
Apoptosis
Inflammation
Proliferation
Increase: Neutrophils, PMN, monocyte
Oxidative response
Extensive liver damage

MITOCHONDRIAL DYSFUNCTION

Various endogenous and exogenous substances impairs the mitochondrial β-oxidation to cause micro-vesicular steatosis through oxidative stress and damage to mitochondrial proteins, lipids, and DNA. In humans, these oxidative lesions cause mitochondrial DNA (mtDNA) deletions.

mtDNA is a circular, double-stranded molecule. Each cell contains many copies of this DNA. MtDNA is extremely sensitive to oxidative damage .because it is proximity to the inner membrane (the main cellular source of ROS), the absence of protective histones, and incomplete repair mechanisms in mitochondria

OXIDATIVE STRESS

The oxidative damage caused by free radicals is thought to be a basic mechanism underlying the hepatotoxicity produced by toxins.

Oxidative stress develops when there was an imbalance between the pro-oxidant and antioxidant ratio, leading to the generation of ROS. Toxins are known to modulate antioxidant defensive systems and cause oxidative damage in organisms by ROS production.

Oxidative damage accumulates more in mitochondria than in the rest of the cells because electrons continually leak from the respiratory chain to form damaging ROS .

ROS, such as hydrogen peroxide (H2O2), superoxide anion O2-, and hydroxyl radical (OH•) at supranormal levels, can react with biological macromolecules potentially leading to enzyme inactivation, LPO, DNA damage and cell death, but at low concentrations their effects are less pronounced.

These free radicals are capable of damaging many cellular components such as DNA, proteins and lipids.

GLUTATHIONE

Glutathione (GSH) is an important antioxidant . It is capable of preventing damage to important cellular components caused by reactive oxygen species such as free radicals, peroxides, lipid peroxides, and heavy metals. "It is a tripeptide with a gamma peptide linkage between the carboxyl group of the glutamate side chain and the amine group of cysteine, and the carboxyl group of cysteine is attached by normal peptide linkage to a glycine".

Thiol groups are reducing agents. "Glutathione reduces disulfide bonds formed within cytoplasmic proteins to cysteines by serving as an electron donor. In the process, glutathione is converted to its oxidized form, glutathione disulfide (GSSG), also called L-(–)-glutathione".

Once oxidized, glutathione can be reduced back by glutathione reductase, using NADPH as an electron donor. The ratio of reduced glutathione to oxidized glutathione within cells is often used as a measure of cellular oxidative stress."Glutathione exists in both reduced (GSH) and oxidized (GSSG) states". In the reduced state, the thiol group of cysteine is able to donate a reducing

equivalent (H++ e−) to other molecules, such as reactive oxygen species to neutralize them, or to protein cysteines to maintain their reduced forms. With donating an electron, glutathione itself becomes reactive and readily reacts with another reactive glutathione to form glutathione disulfide (GSSG). Such a reaction is probable due to the relatively high concentration of glutathione in cells (up to 7 mM in the liver).

In healthy cells and tissue," more than 90% of the total glutathione pool is in the reduced form (GSH) and less than 10% exists in the disulfide form (GSSG)". An increased GSSG-to-GSH ratio is considered indicative of oxidative stress

Glutathione has multiple functions:

1. It maintains levels of reduced glutaredoxin and glutathione peroxidase
2. It is one of the major endogenous antioxidants produced by the cells, participating directly in the neutralization of free radicals and reactive oxygen compounds, as well as maintaining exogenous antioxidants such as vitamins C and E in their reduced (active) forms.
3. 3)Regulation of the nitric oxide cycle is critical for life, but can be problematic if unregulated.
4. 4)It is used in "metabolic and biochemical reactions such as DNA synthesis and repair, protein synthesis, prostaglandin synthesis, amino acid transport, and enzyme activation". Thus, every system in the body can be affected by the state of the glutathione system, especially the

immune system, the nervous system, the gastrointestinal system, and the lungs.

5. It has a vital function in iron metabolism.
6. It has roles in progression of the cell cycle, including cell death.GSH levels regulate redox changes to nuclear proteins necessary for the initiation of cell differentiation. "Differences in GSH levels also determine the expressed mode of cell death, being either apoptosis or cell necrosis". Manageably low levels result in the systematic breakage of the cell whereas excessively low levels result in rapid cell death

Systemic bioavailability of orally consumed glutathione is poor because the molecule, a tripeptide, is the substrate of proteases (peptidases) of the alimentary canal, and due to the absence of a specific carrier of glutathione at the level of cell membrane.

"Because direct supplementation of glutathione is not always successful, supply of the raw nutritional materials used to generate GSH, such as cysteine and glycine, may be more effective at increasing glutathione levels". Additionally, compounds such as N-acetylcysteine (NAC) capable of helping to regenerate glutathione levels.

DRUG TOXICITY MECHANISM:

Two major types of chemical hepatotoxicity have beenrecognized:

(1) direct toxic

Direct toxic hepatitis occurs with predictable regularity in individuals exposed to the offending agent .It is dose-dependent. The latent period between exposure and liver injury is usually short (often several hours), although clinical manifestations may be delayed for 24–48 h.

Agents producing toxic hepatitis are generally systemic poisons or are converted in the liver to toxic metabolites.The direct hepatotoxins result in morphologic abnormalities that are reasonably characteristic and reproducible for each toxin.

(2) idiosyncratic

Idiosyncratic drug reactions can be subdivided into those that are classified as hypersensitivity or immunoallergic and those that are metabolic-idiosyncratic

SIGNS AND SYMPTOMS OF TOXIC HEPATITIS :

Jaundice,

Pruritus ,

Abdominal pain in the right side of the abdomen,

Easy fatiguablity,

Loss of appetite,

Nausea and vomiting,

Rash,

Weight loss,

Dark coloured urine.

In acute toxic hepatitis the patient's condition is similar to viral hepatitis and rapidly deteriorates, resulting in marked liver dysfunction, encephalopathy and coagulopathy.

The features of toxic hepatitis are:

Apoptosis of hepatocytes,

Ischemic liver injury,

Sepsis,

Cholestasis.

Hepatocyte apoptosis and necrosis, when massive, result in fulminant hepatic failure.

ACUTE LIVER FAILURE

DEFINITION

The original definition of fulminant hepatic failure by "Trey and Davidson in 1959 stipulated an onset of hepatic encephalopathy within 8 weeks of the first symptoms of illness, in patients without pre - existing liver disease" .

A broader definition includes patients with onset of disease to encephalopathy of as long as 26 weeks, although the majority of cases are of much shorter duration.

CLASSIFICATION OF ACUTE LIVER FAILURE

Liver failure subcategory	Jaundice to encephalopathy	Clinical presentation	Common aetiologies	Prognosis
Hyperacute	0–7 days	Cerebral oedema common	Paracetamol, hepatitis A, ischaemia	Fair
Acute	8–28 days	Cerebral oedema less common	Hepatitis B, drugs	Poor
Subacute	29 days to 12 weeks	Cerebral oedema rare; ascites, peripheral oedema and renal failure more common	Drugs, indeterminate	Very poor

CAUSES OF ACUTE LIVER FAILURE

Infections
Hepatitis A, B, C, D, E
Herpes simplex
Epstein–Barr virus
Cytomegalovirus
Transfusion-transmitted virus (TTV)
Dengue fever

Drugs and toxins
Paracetamol
Carbon tetrachloride
Idiosyncratic drug reactions*
Mushroom poisoning
Sea anemone sting

Ischaemic
Cardiogenic shock
Hypotension
Heat stroke
Cocaine, methamphetamines, ephedrine

Vascular
Acute Budd–Chiari syndrome
Sinusoidal obstruction syndrome

Miscellaneous
Wilson's disease
Acute fatty liver of pregnancy
Eclampsia/ HELLP syndrome
Malignancy
Primary graft non-function after liver transplantation

CLINICAL FEATURES

The patient with "acute liver failure typically develops non - specifi c symptoms such as nausea, vomiting, malaise, jaundice and signs of hepatic encephalopathy, evolving relatively quickly".

The liver is often shrunken due to loss of hepatic mass and may be as small as 600 g in size (normal approximately 1600g)."Declining hepatocellular function impairs synthesis of clotting factors and glucos leading to coagulopathy and hypoglycaemia".

Metabolic acidosis results from reduced clearance and increased production of lactate. Tachycardia, hypotension, hyperventilation and fever may occur and signs of the systemic infl ammatory response may be present.

Patients with a more gradual onset of hepatic insufficiency (over weeks rather than days, and variously called" subfulminant, subacute or late onset") infrequently develop cerebral oedema. Ascites, oedema and renal failure are more likely in this slowly evolving setting outcome depends on the underlying aetiology . Those patients that survive without transplant usually have a complete recovery .

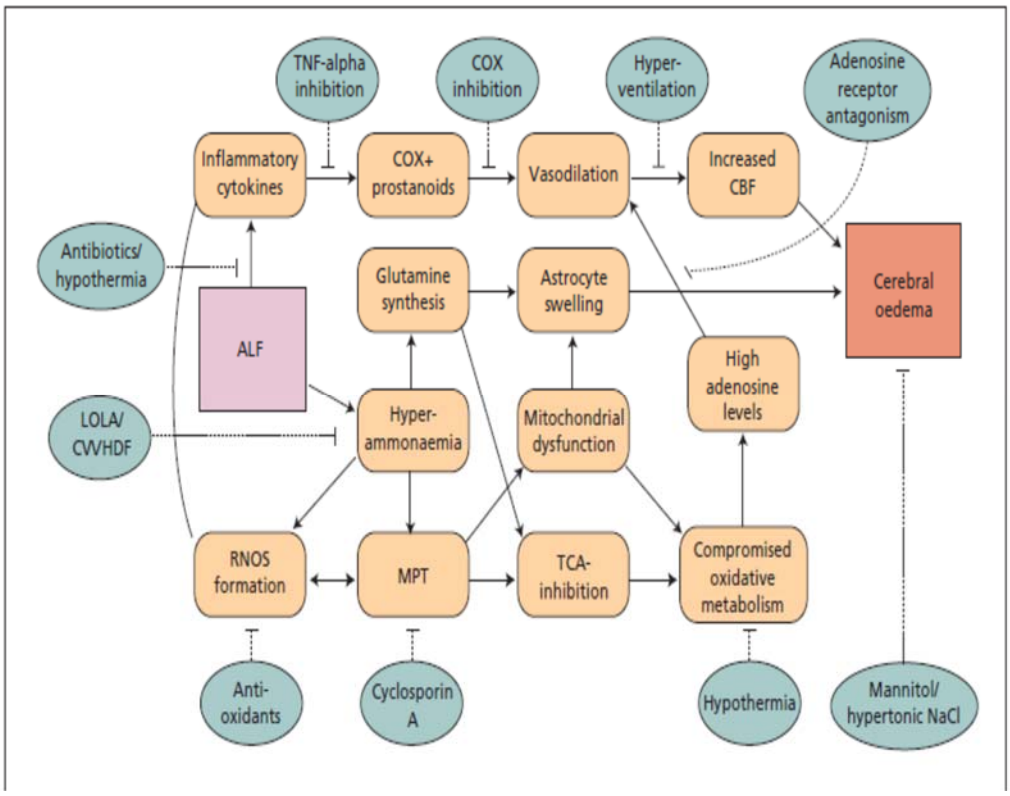
Hepatic e ncephalopathy

Hepatic encephalopathy and cerebral oedema with raised intracranial pressure (ICP) are hallmarks of acute liver failure. The pathogenesis of hepatic encephalopathy is multifactorial and centres on failure of the liver to remove toxic, mainly gut - derived, substances from the circulation. Arterial ammonia

levels rise and appear to contribute to astrocyte swelling. Levels greater than 150 to 200 mmol/L have been shown to correlate with cerebral oedema and herniation .

The onset of encephalopathy is often sudden, may precede jaundice, and, unlike chronic liver disease, may be associated with agitation, changes in personality,delusions and restlessness. Asterixis may be transient.Fetor hepaticus is usually present.

Pathogenesis of cerebral oedema and potential targets for therapy:



TREATMENT:

In order to optimize survival, one must establish the diagnosis of acute liver failure quickly, evaluate the potential aetiologies and therapies, and estimate the severity to appropriately identify those that will need transplantation.

King ' s College Hospital criteria for liver transplantation in acute liver failure

Paracetamol

pH <7.30 (irrespective of grade of encephalopathy)

or

Prothrombin time >100 s (INR >7) and serum creatinine >300 mmol/L (>3.4 mg/dL) in patients with grade 3 or 4 encephalopathy

Non-paracetamol patients

Prothrombin time >100 s (INR >7) (irrespective of grade of encephalopathy)

or

Any three of the following variables (irrespective of grade of encephalopathy)

age <10 or >40 years

aetiology: non-A–E hepatitis, 'viral' hepatitis no agent identified, halothane hepatitis, idiosyncratic drug reaction

duration of jaundice before onset of encephalopathy >7 days

prothrombin time >50 s (INR >3.5)

serum bilirubin >300 mmol/L (17.4 mg/dL)

DIAGNOSIS OF YELLOW PHOSPHOROUS POISONING LAOBORATORY LIVER FUNCTION TEST

1)ENZYMES

Liver damage can be of two types:

(A) Hepatocellular damage (death of liver cells), in which alanine aminotransferase and aspartate aminotransferase are altered;

(B) Cholestatic damage (bile stasis) with an increase of parameters such as alkaline phosphatase and γ-GT.

Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities are routinely used as clinical endpoints indicative of hepatotoxicity.

ASTand ALT concentrations begin to rise within 24 hours after an acute ingestion and peak at about 72 hours. In severe overdose, transaminase elevation can be detected as early as 12-16 hours post-ingestion of yellow phosphorous.

ALT is considered to be liver-specific ,elevated serum AST is indicative of tissue and cellular damage, but is not specific for hepatotoxicity. As a general rule, clinically significant liver injury is often defined as ALT > 3 times the upper limit of normal .

2)SERUM BILIRUBIN

Serum bilirubin level will be elevated depending upon the amount of poison consumed ,serial monitoring should be needed.

3)PROTHROMBIN TIME/INR

Prothrombin time (PT) and international normalized ratio (INR) should be measured and followed closely. PT is a indicator of impaired hepatic synthetic function in the setting of hepatic dysfunction and developing liver failure. Abnormal values are also predictors of mortality.

RENAL FUNCTION TEST

Renal function tests (blood urea,serum creatinine and serum electrolytes concentrations) can reveal evidence of co-existing renal failure and hepatorenal syndrome.

An elevated serum creatinine concentration is also a predictor of mortality.

Urinalysis showing proteinuria and hematuria may indicate acute tubular necrosis.

SERUM GLUCOSE

Obtain serum glucose concentration to assess hypoglycemia as the result of impaired hepatic gluconeogenesis

ECG

Alteration in ECG such as inverted T waves, changes in QRS complex, tachycardia, arrhythmias and decreased ventricular contractility has been reported

ACID BLOOD GAS ANALYSIS

Arterial blood gas and serum lactate concentrations should be monitored. A pH of less than 7.3 or a lactate concentration greater than 3.5 after fluid resuscitation are laboratory indicators predictive of mortality.

SERUM AMMONIA

Serum ammonia level should be monitored if patient presented with altered mental status or clinical signs of encephalopathy .Some research shows that arterial ammonia concentrations are higher than venous ammonia concentrations in a patient with acute liver failure and may be predictive of neurologic death. However, in a clinical picture that is consistent with acute hepatic dysfunction and encephalopathy, a venous sample may be considered sufficient in the context of other indicators of acute liver failure

Key laboratory findings during the first 3 phases of hepatotoxicity are :

Phase 1: Approximately 12 hours after an acute ingestion, liver function studies show a subclinical rise in serum transaminase levels (ALT, AST)

Phase 2: Serum studies reveal elevated ALT and AST concentrations, PT, and bilirubin concentration; renal function abnormalities may also be present and indicate nephrotoxicity

Phase 3: Severe toxicity is evident on serum studies, and include: lactic acidosis, prolonged PT or INR, markedly elevated ALT and AST , elevated total

bilirubin level of more than 4 mg/dL (primarily indirect), hypoglycemia, and hyperammonemia are reported.

RADIOLOGICAL INVESTIGATIONS

USG ABDOMEN

Abdominal ultrasonography is a noninvasive diagnostic tool that may reveal hepatic enlargement or renal abnormalities, as well as inflammatory changes of other abdominal organs .

Toxic hepatitis is characterized by different degrees of steatosis and fibrosis, which can lead to cirrhosis.

In USG abdomen , steatosis can be classified as:

(1) light steatosis - presence of slight “bright liver” and no deep attenuation;

(2) moderate steatosis - presence of mild “bright liver” and with deep attenuation; and

(3) severe steatosis - presence of diffusely severe “bright liver” and deep attenuation without visibility of the diaphragm

CT BRAIN

Computed tomography (CT) scanning of the brain should also be considered in patients with altered mental status. CT may reveal cerebral edema in patients with late presentation and encephalopathy (grade III or IV).

Additional neuroimaging with magnetic resonance imaging (MRI) may be indicated to further define cerebral changes.

LIVER BIOPSY

Post-mortem liver biopsy showscollapsed reticulin framework with fibrosis between the hepatocytes showing a bubbly and vacuolated cytoplasm suggestive of an acute fulminant hepatitis

TREATMENT

As no specific antidote has been identified so far, Supportive management is the mainstay of therapy. The possible benefits of N-acetylcysteine (NAC) in improving the prognosis of patients with yellow phosphorus poisoning have been noticed in recent case series, with the best results seen among patients in whom NAC was started early in the course of illness

1)GASTRIC LAVAGE

Using 1:5000 solution of pottasium permanganate –it oxidises phosphorous in to phosphoric acid and phosphates ,which are harmless.

Activated charcoal absorbs the poison

Stomach wash with 0.2%copper sulphate solution or 0.2 g of copper sulphate may be given every 5minutes until vomiting occurs.it cots theparticles of phosphorous with a film ofcopper sulphide which is relatively harmless.

2) **INTRAVENOUS FLUIDS**

3)**PROTON PUMP INHIBITORS**

4)ANTIEMETICS

5)VITAMIN K

6) N ACETYL CYSTEINE

7)FRESH FROZEN PLASMA

If coagulopathy is present

8)SYRUP LACTULOSE &BOWEL WASH

If pt have features of encephalopathy

9)MECHANICAL VENTILATION

If pt have respiratoy failure or poor GCS

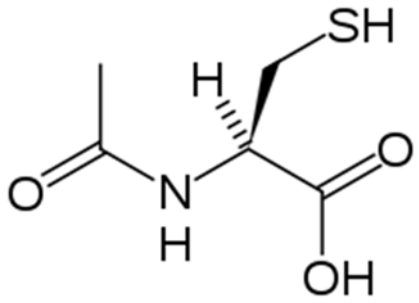
10) LIVER TRANSPLANTATION

Ultimate treatment of acute fulminant hepatic failure not amenable to medical treatment is liver transplantation.

N ACETYL CYSTEINE

N acetyl cysteine is a prodrug for L-CYSTEINE , is a precursor to the biologic antioxidant glutathione. Hence administration of acetylcysteine replenishes glutathione stores.

N-acetyl-L-cysteine is soluble in water and alcohol



MECHANISM OF ACTION OF NAC

It reduce extra-cellular cystine to cysteine

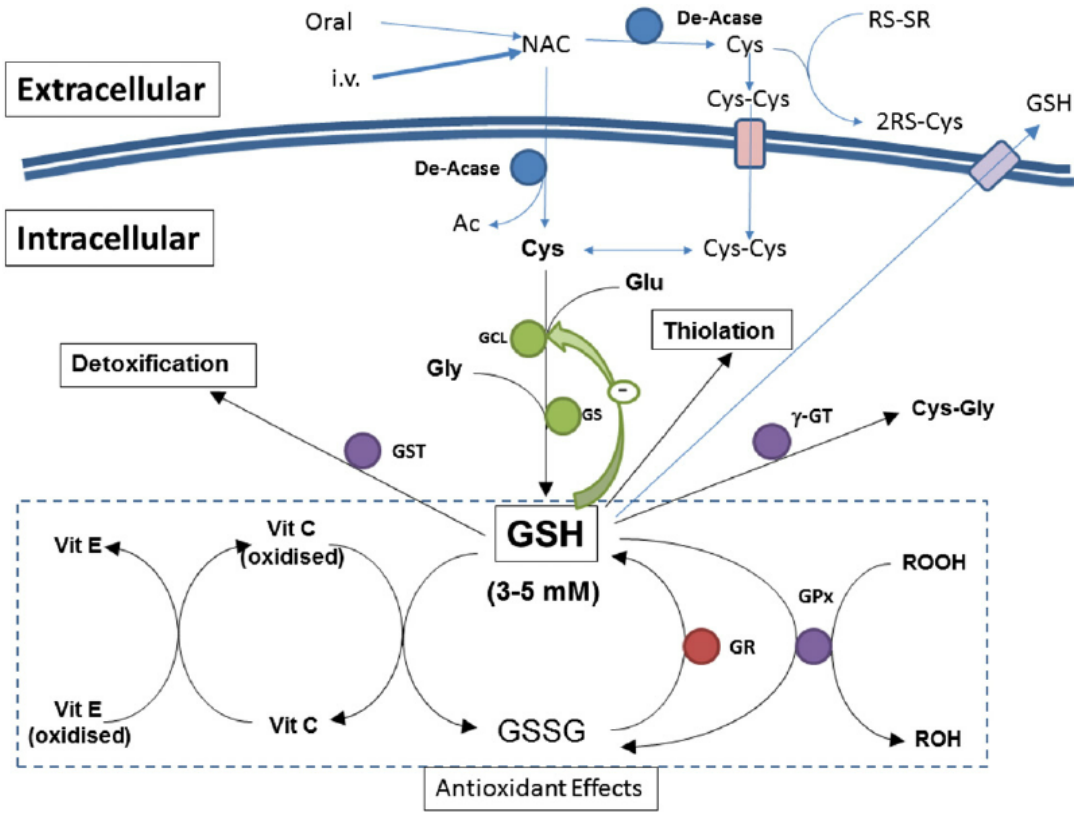
Be a source of SH groups: so

It stimulate glutathione synthesis,

Enhance glutathione-s-transferase activity,

Promote detoxification

Act directly on reactive oxidant radicals



Mechanisms of Protection I: Preventing Covalent Binding

Mechanisms of Protection II: Scavenging of Reactive Oxygen and Peroxynitrite

Mechanisms of Protection III: Mitochondrial Energy Substrates

NAC has anti inflammatory and inotropic activity

It has vasodilatory effects - it improves microvascular circulation and oxygenation.

PHARMACOKINETICS

Oral bioavailability is 10%

Protein binding -50 to 83%

Extensively metabolized in liver;

Metabolism by CYP450 minimal.

Urine excretion 22-30%

Half-life is 5.6 hours in adults

USEFULLNESS IN YELLOW PHOSPHOROUS POISONING

The Role of N acetyl cysteine (NAC) in acetaminophen induced Acute fulminant hepatic failure (ALF) was well established. Additionally some studies have shown that NAC may be useful in non-acetaminophen induced ALF like yellow phosphorous poisoning also.

If the patient presents less than eight hours after poisoning, then NAC significantly reduces the risk of serious hepatotoxicity .

If NAC is started more than 8 hours after ingestion, there is a sharp decline in its effectiveness because the cascade of toxic events in the liver has already begun, and the risk of acute liver necrosis and death increases dramatically.

Although acetylcysteine is most effective if given early,some studies showed that it still has beneficial effects if given as late as 48 hours after ingestion.

DOSSAGE

For YP poisoning we use the same dossage protocol of NAC used for acetaminophen poisoning.

The FDA-approved dosage regimen for oral NAC :

Loading dose of 140 mg/kg, followed by 17 doses, each at 70 mg/kg, given every 4 hours.

The total duration of the treatment course is 72 hours

Available strength of tablet is 600mg

***-INTRAVENOUS NAC**

IV NAC administration depend on the patient's body weight and/or on whether the ingestion is acute or chronic.

Continuous IV infusion is recommended for acute ingestion, as follows:

Loading dose: 150 mg/kg IV; mix in 200 mL of 5% dextrose in water (D5W) and infuse over 1 h

Dose 2: 50 mg/kg IV in 500 mL D5W over 4 h

Dose 3: 100 mg/kg IV in 1000 mL D5W over 16 h

ADVERSE EFFECTS

For IV formulations

The most commonly reported adverse effects of acetylcysteine are

Rash

Urticaria,

Itchiness.

Up to 18% of patients have been reported to experience anaphylaxis reaction, which are defined as rash, hypotension, wheezing, and/or shortness of breath.

Lower rates of anaphylactoid reactions have been reported with slower rates of infusion.

For oral formulations

Nausea,

Vomiting,

Rash,

Fever.

POSTMORTEM FINDINGS IN YELLOW PHOSPHOROUS POISONING

APPEARANCE OF THE BODY

Shows signs of jaundice

SKIN &MUCOUS MEMBRANE

Multiple hemorrhages are seen

STOMACH&INTESTINES

Contents have a smell of garlic and may be luminous

Mucous membrane of stomach and intestines are yellowish or greyish-white in colour and are softened,thickened,inflammed and corroded or destroyed in patches.

LIVER

It becomes swollen ,yellow ,soft,fatty and easily ruptured and shows marbled appearance

Small hemorrages may be seen on the surface

POSTMORTEM LIVER BIOPSY

Hydropic or fatty degeneration of hepatocytes,progress to acute parenchymal inflammation with cellular necrosis.

Necrosis mostly involves central ,periportal areas of liver but centrilobular or panlobular involvement occurs in some patients.

KIDNEY

Kidneys are large,greasy,yellow and shows hemorrhages on the surface

BIOPSY

Congested vessels and focal areas of calcifications are seen.

HEART

Heartis flabby,pale and shows fatty degeneration

PULMONARY

Fat emboli may be found in the pulmonaryarterioles and cappilaries

BLOOD

It may appear tarry and its coagulability is diminished.

MATERIALS AND METHODS

MATERIALS AND METHODS

STUDY POPULATION:

- The study was conducted on 25 patients with history yellow phosphorous poison (ratol) consumption who fulfill the inclusion and exclusion criteria getting admitted at Government Rajaji Hospital & Madurai Medical College during the period of june to september 2017.

- The control group patients are taken from retrospective data obtained in year 2016 at GRH , who had similar management protocol except for NAC use.

INCLUSION CRITERIA:

All patients admitted with history yellow phosphorous poison(ratol) consumption at Government Rajaji Hospital & Madurai Medical College during the period of june to september 2017.

EXCLUSION CRITERIA:

1. Patient who have ingested other substance in addition to yellow phosphorous will be excluded
2. Patients who are known to have preexisting liver disease
3. Patients with chronic kidney disease
4. Patients with heart disease
5. Absconded within 24hrs of admission

DATA COLLECTION:

Informed consent obtained from all patients to be enrolled for the study. In all the patients relevant details will be collected in a predesigned proforma.

The patients are selected based on history of yellow phosphorous poisoning, clinical examinations, biochemical tests and ultrasound abdomen ,toxicological autopsy findings of expired patients

STUDY PROTOCOL:

DESIGN OF STUDY:

Prospective cross sectional hospital based observational study

PERIOD OF STUDY:

4 MONTHS (June 2017 to september 2017)

METHODOLOGY:

History wsa taken from patients who consumed yellow phosphorous poisoning, about time of consumption, amount of consumption,any prior hospital admission and treatment before arrived to our hospital. History regarding details and duration of alcohol intake was taken,and history of vomiting,abdominal pain ,loose stools, altered sensorium also noted.

Clinical examination about presence of icterus,anemia, edema legs , features of encephalopathy, abdominal tenderness was noted during admission.

After stomach wash and initial resuscitation, Loading dose of 140 mg/kg of N Acetyl cysteine was started and then followed by 17 doses, each at 70 mg/kg, given 4th hourly.The total duration of the treatment course is 72 hours. Time of stomach wash and intiation of N Acetyl cysteine was noted.

serial monitoring of vitals and complete blood count ,blood sugar ,urea ,creatinine, serum bilirubin, AST, ALT, prothrombin time, INR ,urine analysis, ECG, USG abdomen was estimated. Post-mortem toxicological findings of liver and kidney was noted in all expired patients.

LABORATORY INVESTIGATIONS:

Complete blood cuunt, liver function tests including serum bilirubin, transaminases, prothrombin time and INR, blood sugar, urea creatinine, serum electrolytes.

COLLABORATING DEPARTMENTS:

DEPARTMENT OF MEDICAL GASTROENTEROLOGY DEPARTMENT OF BIOCHEMISTRY

DEPARTMENT OF RADIOLOGY

DEPARTMENT OF FORENSIC MEDICINE

DEPARTMENT OF PATHOLOGY

ETHICAL CLEARANCE:

Clearance obtained

CONSENT:

Individual written and informed consent obtained.

STATISTICAL ANALYSIS:

All data were entered in Excel 2007 and statistical analysis was "performed using the statistical software SPSS 16.0.Data were expressed as mean values with standard deviation".

For continuous variables "Mann Whitney U-test was performed to find the differences between two groups and for categorical variables Pearson's chi-square test was performed". Results were defined as statistically significant when the *P* value was less than 0.05.

CONFLICT OF INTEREST: NIL

FINANCIAL SUPPORT: SELF

RESULTS AND OBSERVATIONS

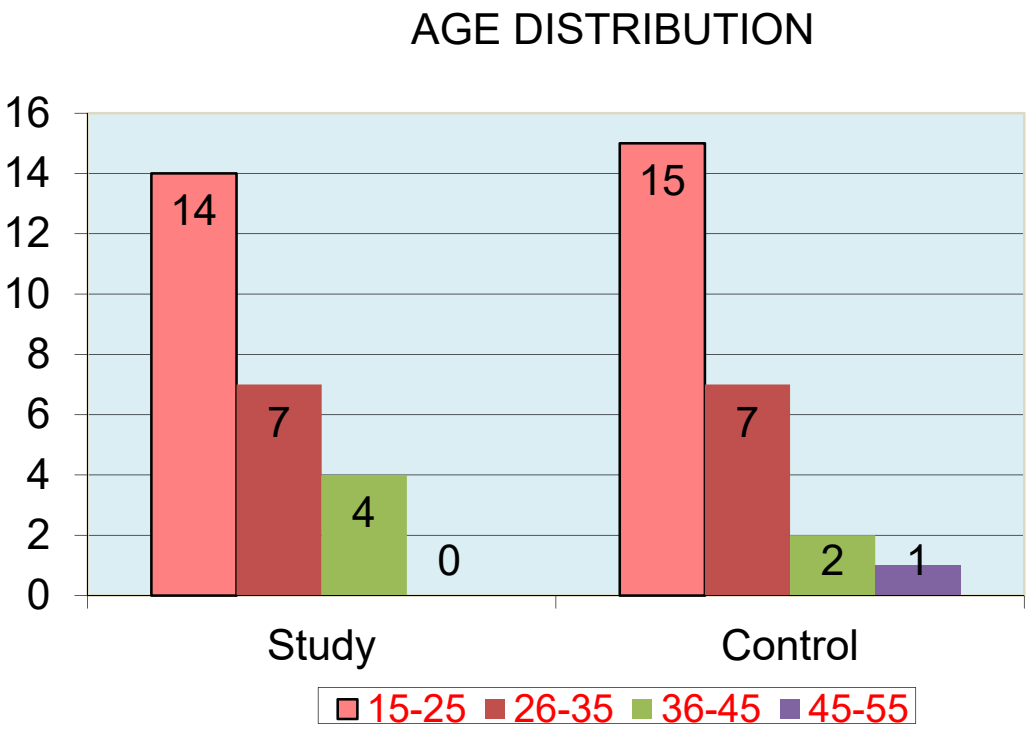
RESULTS AND OBSERVATIONS

TABLE:1 AGE DISTRIBUTION

Age in years	Study	Control
15-25	14	15
26-35	7	7
36-45	4	2
45-55	0	1
total	25	25
mean	26.52	25.72

COMMENTS:

Among 50 patients of both group, majority are in the age group of 15 to 25years.so these young adults are more vulnerable to poisoning with yellow phosphorous (ratol).


AGE DISTRIBUTION
16
14
12
10
8
6
4
2
0
14
7
4
0
15
7
2
1
Study
Control
15-25
26-35
36-45
45-55

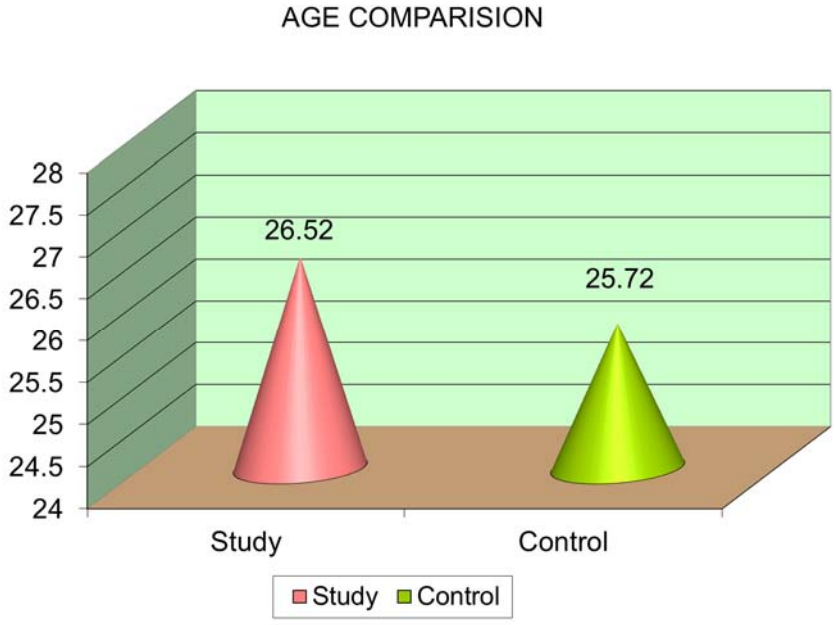

AGE COMPARISION
28
27.5
27
26.5
26
25.5
25
24.5
24
26.52
25.72
Study
Control
Study
Control

TABLE 2 :GENDER DISTRIBUTION

Sex	Study	Control
Male	**10**	**8**
Female	**15**	**17**
Total	**25**	**25**

COMMENTS:

Our studies shows 60%of patients in the study group and 68% of patients in the control groups are female sex.so females are more prone for poisoning.

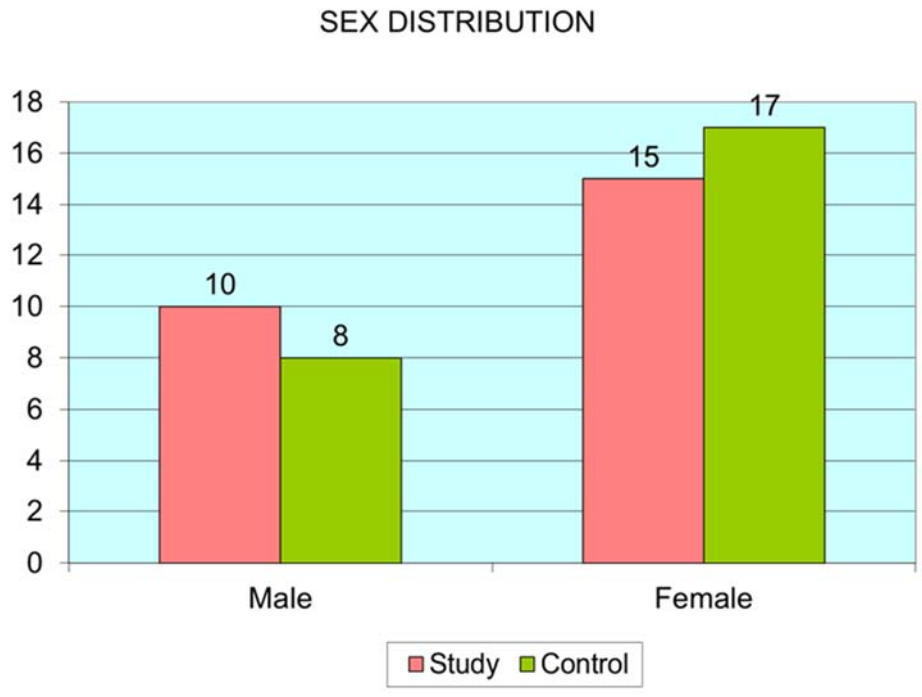


TABLE 3:RELATION TO ALCOHOL CONSUMPTION

Alcoholic	Study	Control
Yes	3	3
No	22	22
Total	25	25

COMMENTS:

Among 50 patients only 6 persons are chronic alcoholic because majority of poison consumed persons are in the age group of 15 to25years.

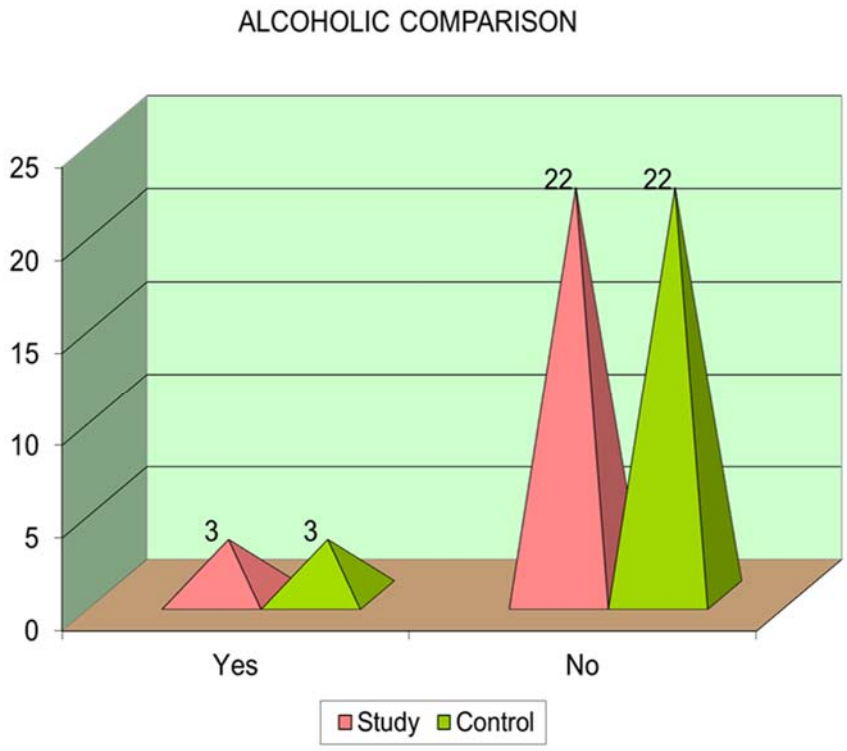


TABLE 4:AMOUNT OF POISON CONSUMPTION

Amount of poison consumed	Study	Control
<1gms	5	6
>1gms	20	19
Total	25	25
Mean	3.74	2.56

COMMENTS:

Calculated Leathal dose of YP is >1mg/kg.our study also shows that,80% of the admitted patients are consumed more than 1gm of poison and has more mortality.

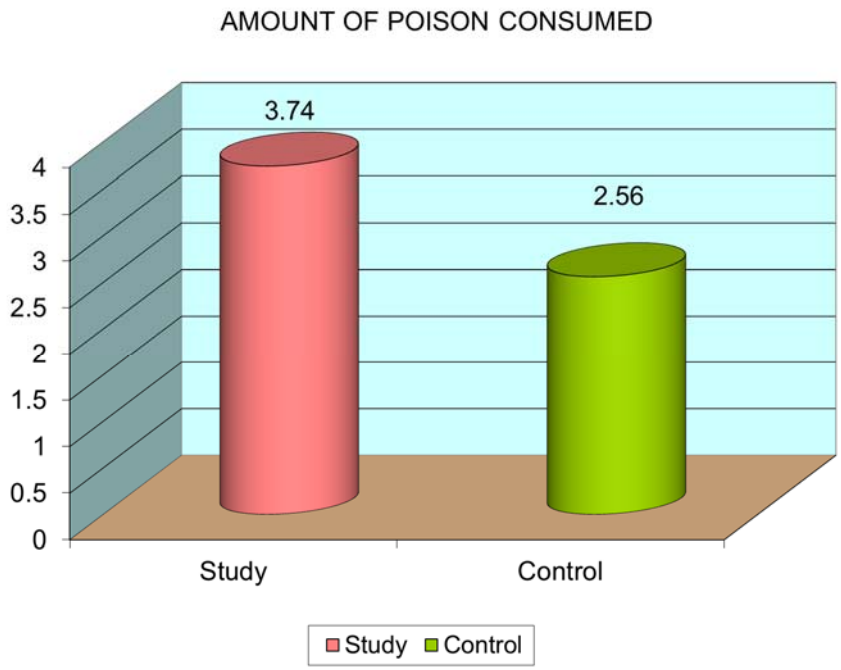


TABLE 5:COMPARISON OF PRESENCE OF ICTERUS

Presence Of Icterus	Study	Control
Yes	18	18
No	7	7
Total	25	25

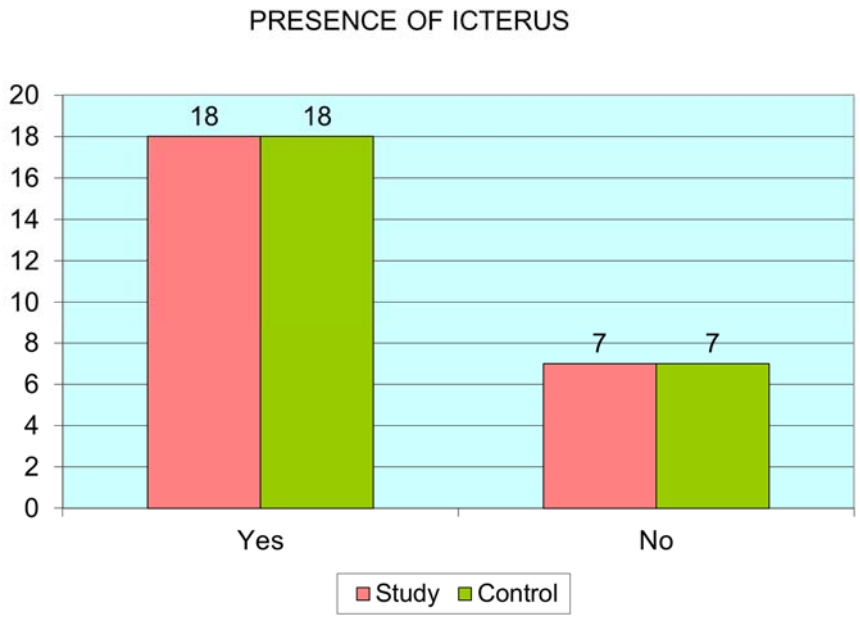


TABLE 6;COMPARISON OF PRESENCE OF HEPATIC ENCEPHALOPATHY

ENCEPHALOPATHY	Study	Control
Yes	5	13
No	20	12
Total	25	25
p value	0.039 Significant	

COMMENTS:

20% of the patients in the study group has hepatic encephalopathy compared to 52% in the control group .so early NAC initiation prevents from occurrence of encephalopathy. It is statistically significant (p value is 0.039).

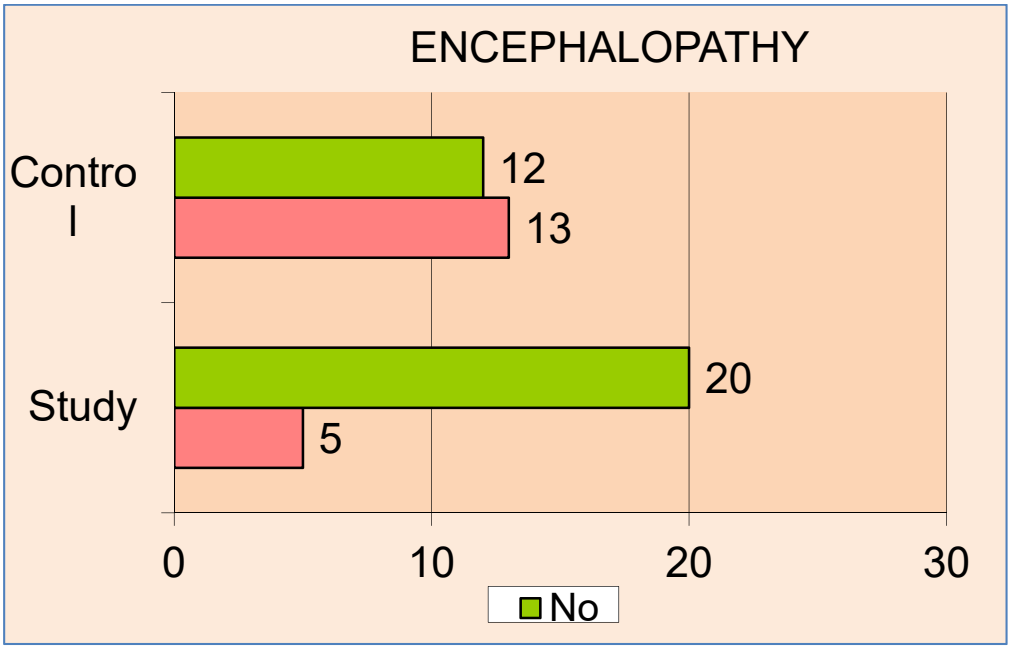


TABLE 7:COMPARISON OF HYPOTENSION

HYPOTENSION	Study	Control
Yes	6	14
No	19	11
Total	25	25
p value	0.043 significant	

COMMENTS:

24% of patients in the study group and 56%in the control group have hypotension ,it shows that early treatment with NAC has beneficial in reducing hypotensive complication. It is statistically significant (p value is 0.043).

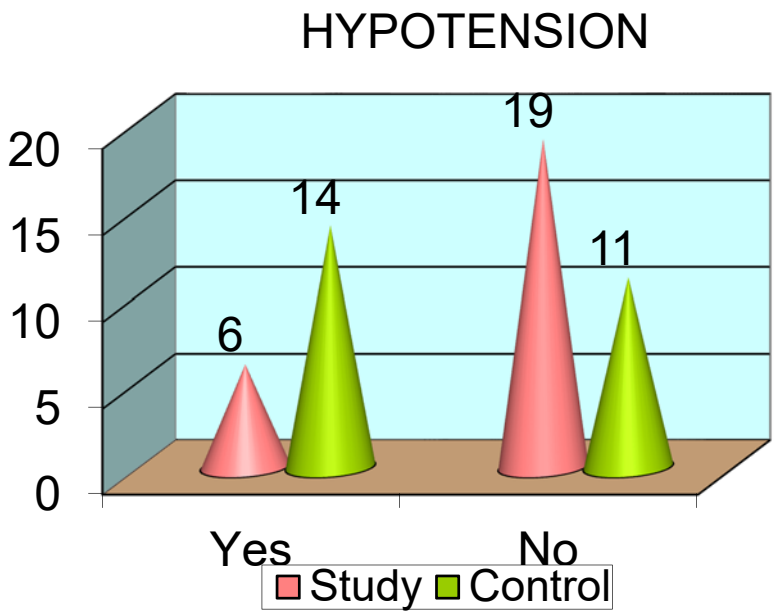


TABLE 8:COMPARISON OF OLIGURIA

OLIGURIA	Study	Control
Yes	5	13
No	20	12
Total	25	25
p value	0.039 Significant	

COMMENTS:

20% of patients in the study group and 52%in the control group have oliguria.It is statistically significant (p value is 0.039).

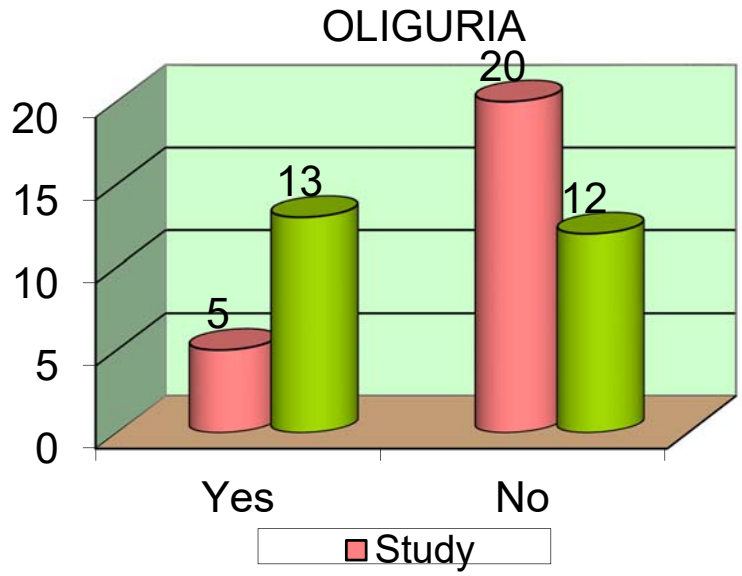


TABLE 9:COMPARISON OF LEUCOPENIA

LEUCOPENIA	Study	Control
Yes	3	9
No	22	16
Total	25	25
p value	0.098 Not significant	

COMMENTS

Both group have leukopenia ,but control group(36%) is affected more than study group(12%). It is not statistically significant (p value is 0.098).

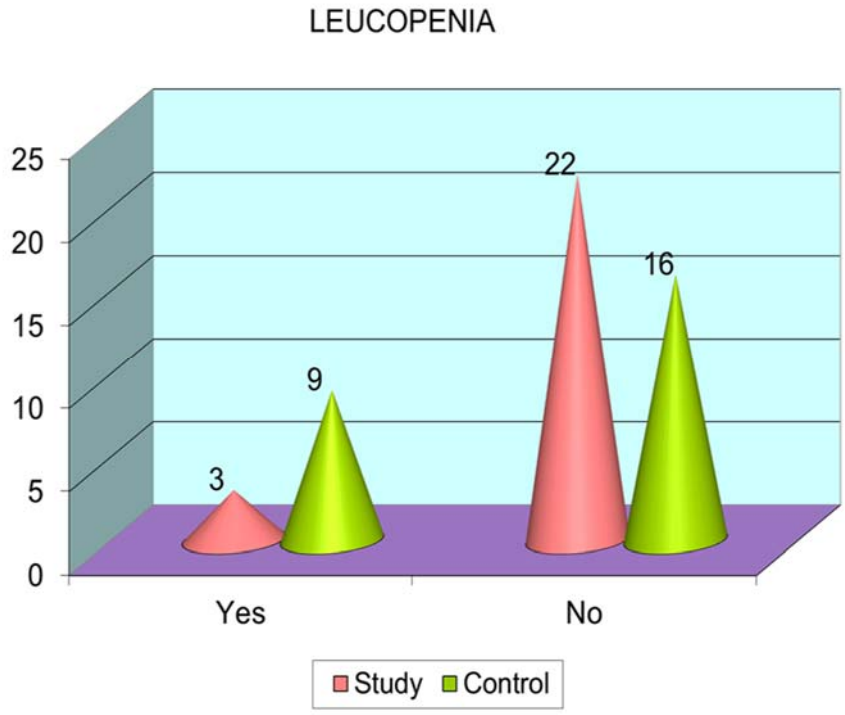


TABLE 10 A:LIVER FUNCTION TEST

LIVER FUNCTION TEST	Study	Control
Elevated	19	18
Normal	6	7
Total	25	25

COMMENTS:

3/4 of patients in the both group have elevated LFT value,remaining 1/4 of patients are probably not consumed poison or very minimal consumption.

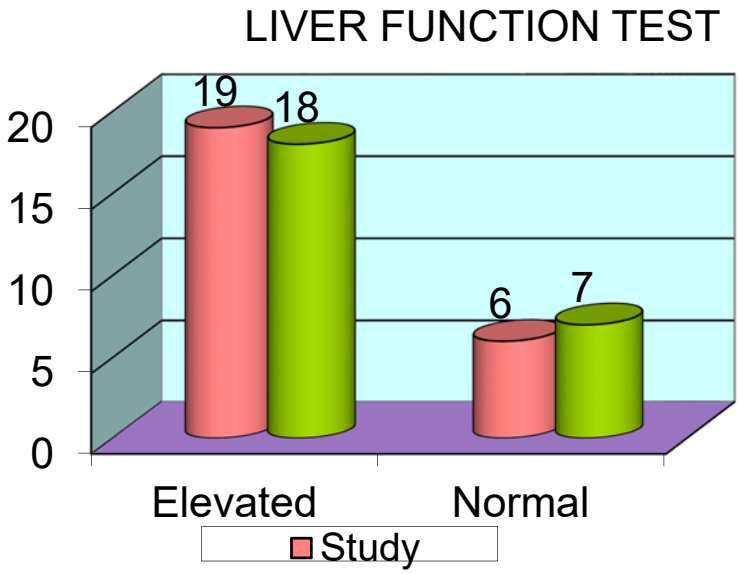


TABLE 10B:TIME TO NAC INITIATION:

TIME TO NAC INITIATION	Study
< 1 day	14
> 1 day	11
Total	25

COMMENTS:

Among 25 patients ,14 reaches our hospital within 24hrs of poison consumption ,so NAC initiated early .Remaining patients are admitted in peripheral hospital and refered later after pt had features of toxic hepatitis.

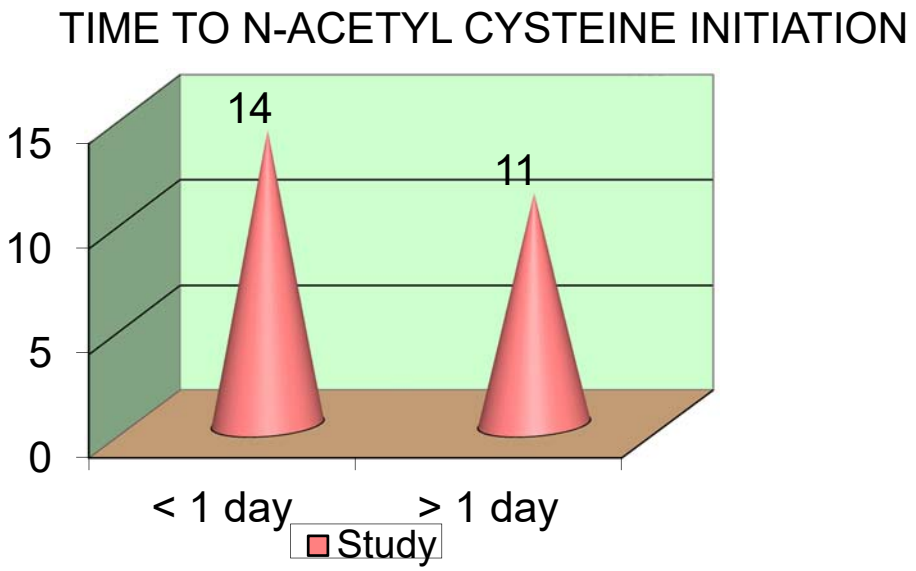


TABLE 10 C:RESPONSE TO NAC(RECOVERY)

RESPONSE TO NAC(RECOVERY)	Study	Control
Yes	17	0
No	8	25
Total	25	25
p value	< 0.001 Significant	

COMMENTS:

Among 25 patients17 have good recovery ,because of earlier treatment with NAC,Among their some has features of toxic hepatitis and recovered also. It is statistically more significant pvalue is <0.05 (0.001).

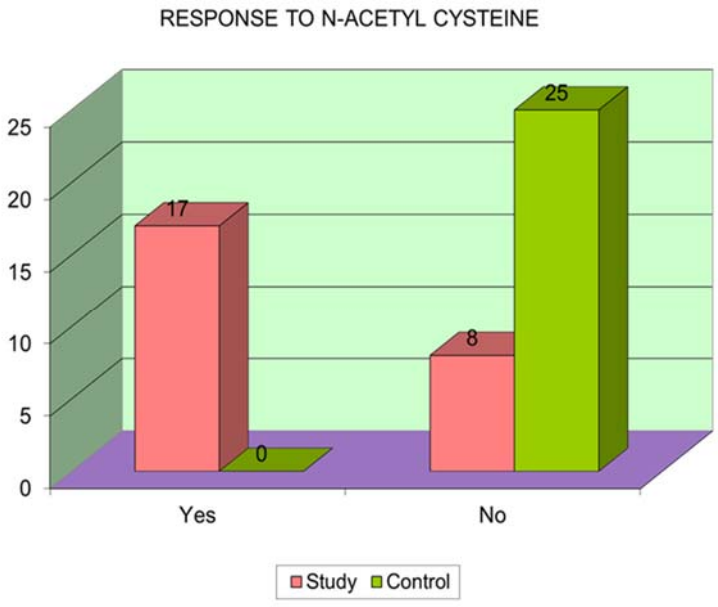


TABLE 10 D:SERUM BILIRUBIN RESPONSE TO NAC

CASE NO	1ST DAY	3RD DAY	6TH DAY
C1	1.1	1.5	0.9
C2	0.9	2.9	1.3
3	1.2	7.9	1.9
4	1.1	2.5	1.3
5	1	2.7	1.2
6	2.1	5.6	3.1
C7	5.4	23.9	8.1
C8	0.8	4.1	1.4

Bilirubin values in mgs

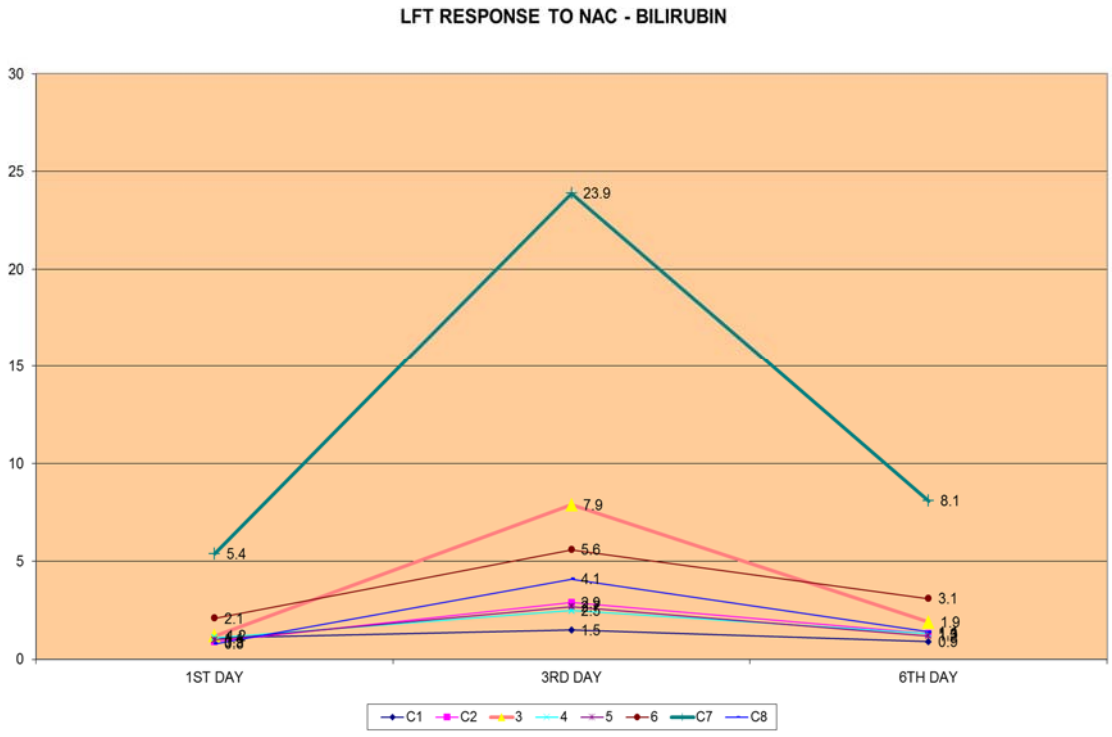


TABLE 10 E:LIVER ENZYME (ALT) RESPONSE TO NAC

CASE NO	1ST DAY	3RD DAY	6TH DAY
C1	40	39	31
2	21	118	53
3	51	213	70
4	39	139	56
5	29	105	41
6	33	71	34
7	198	720	232
C8	21	255	63

ALT values in IU/L

COMMENTS:

In the study group 17 patients have good response to NAC, among their 8patiens have elevation of LFT (bilirubin,AST,ALT,prothrombin time) mostly in the 3rd and 4th day of admission. That LFT values become near normal on 6th or 7th day .

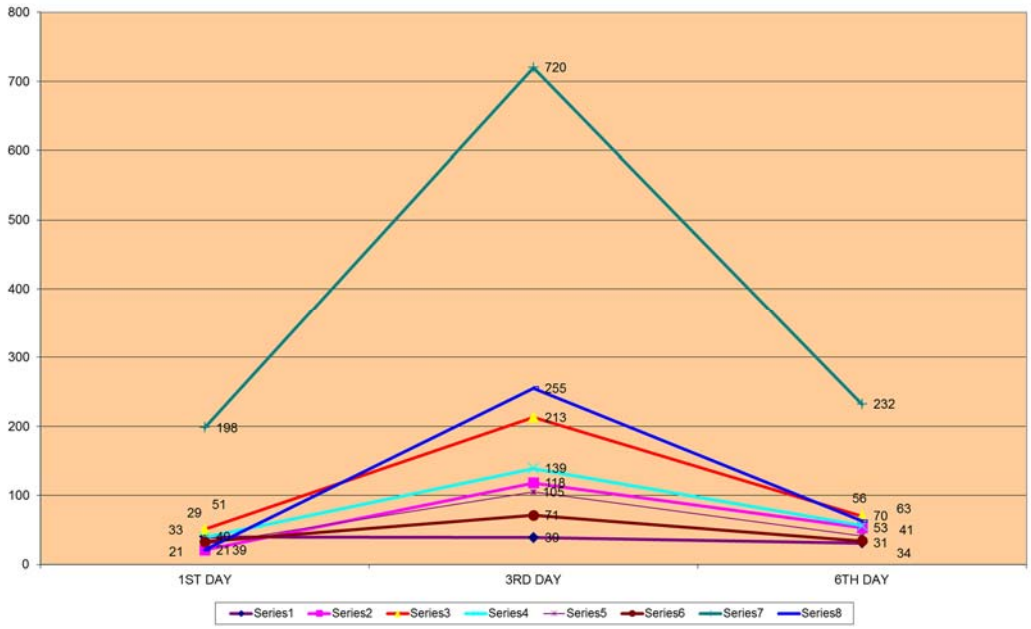


TABLE 11:COMPARISON OF RENAL FUNCTION TEST

RENAL FUNCTION TEST	Study	Control
Elevated	7	12
Normal	18	13
Total	25	25
p value	0.244 Not significant	

COMMENTS:

RFT value is elevated in both group, but more in control group(48%) than study group(28%). It is statistically not significant (p value is 0.244).

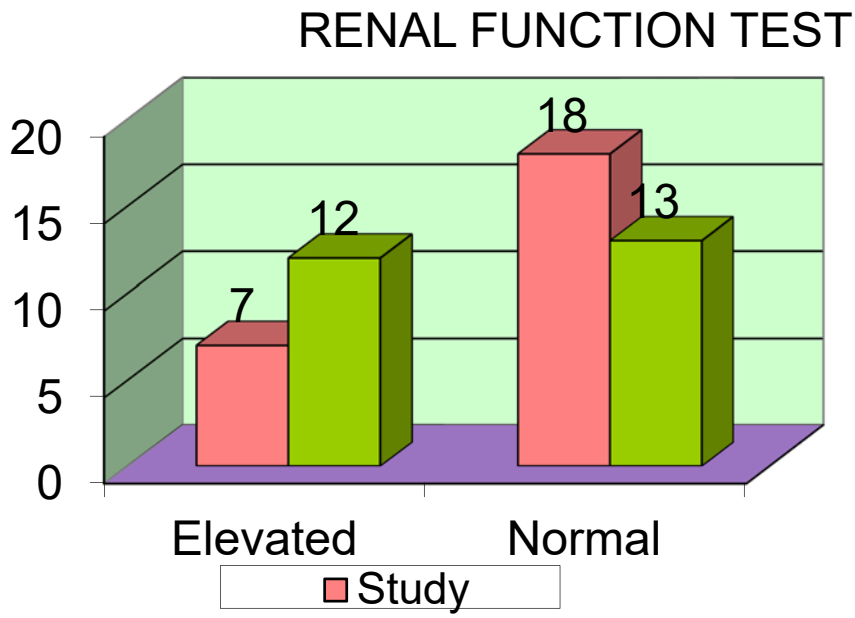
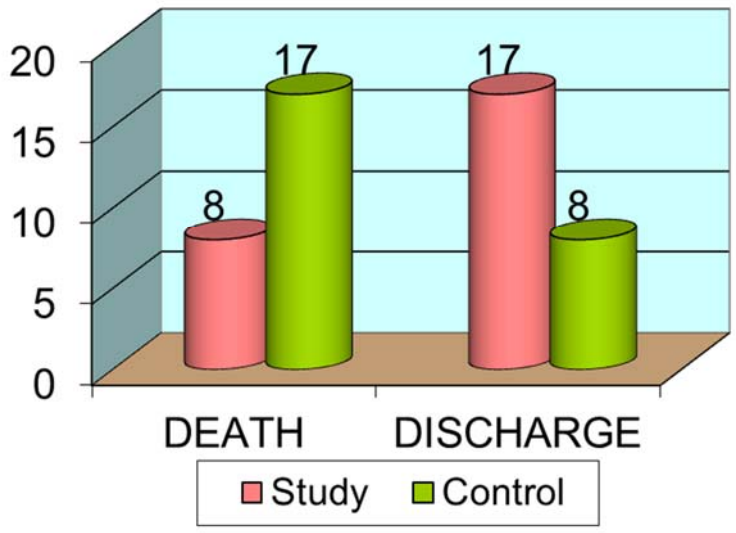


TABLE 12 :OUTCOME OF THE STUDY

OUTCOME	Study	Control
DEATH	8	17
DISCHARGE	17	8
Total	25	25
p value	0.024 Significant	

COMMENTS

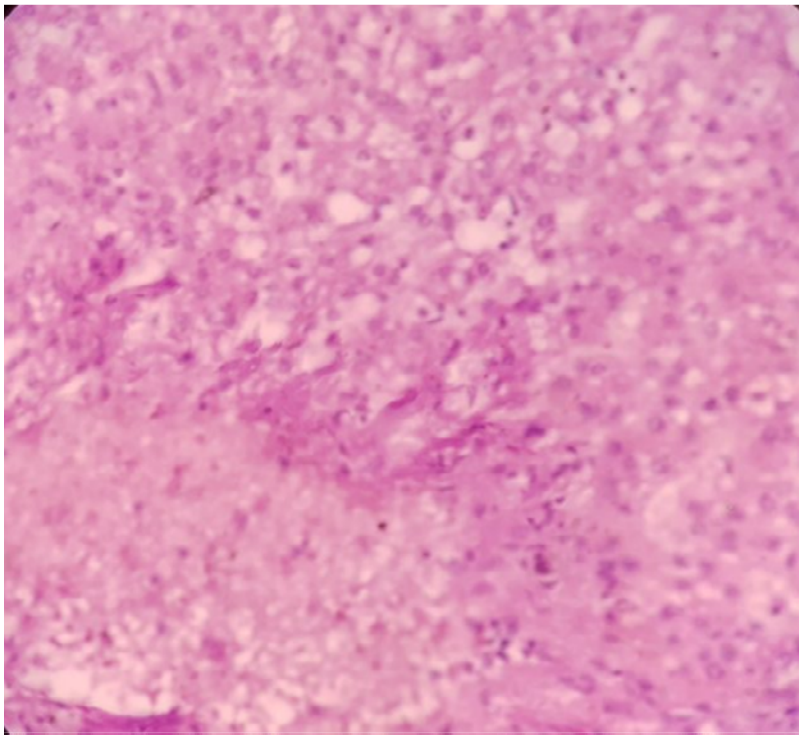
In the study group among 25 yellow phosphorous consumed patients 8patients (32%) died inspite of NAC treatment mostly due to delayed admission with features of acute liver failure. In the control group 17 patients (68%) died . So treatment with NAC REDUCES 50% OF MORTALITY.It is statistically more significant (p value is 0.024 , <0.05).

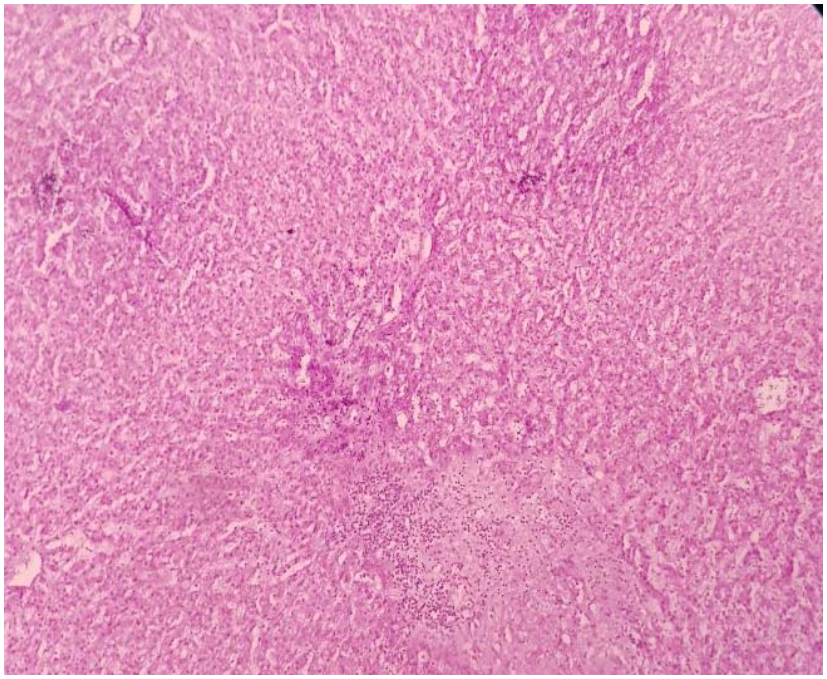


POSTMORTEM TOXICOLOGICAL FINDINGS:

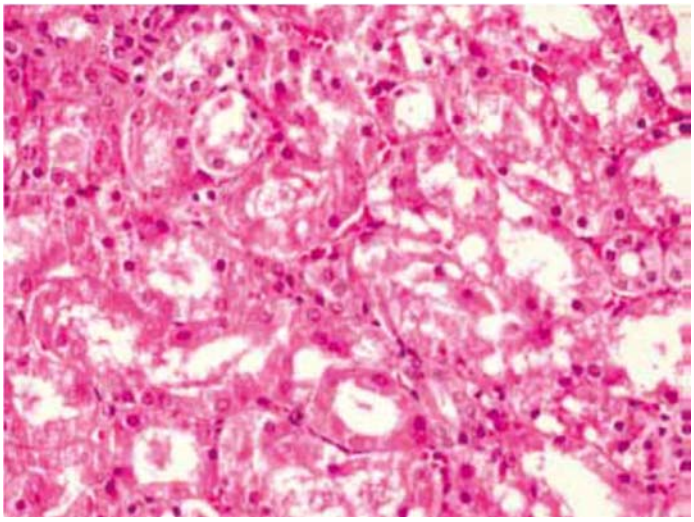
LIVER:

Sections from liver shows hepatic parenchyma with hepatocytes arranged in trabecular pattern ,hepatocytes shows ballooning degeneration with ground glass cytoplasm and fatty degeneration in many areas. Also shows many congested blood vessels and hemosiderin laden macrophages.





KIDNEY: Section studied from kidney shows renal parenchyma with few congested blood vessels,vacuolar degeneration of proximal tubular epithelium and focal areas of Calcifications are seen.



DISCUSSION

DISCUSSION

Our study was done to identify the prevalence of yellow phosphorus poisoning in our hospital and to evaluate the usefulness of N-Acetyl cysteine in yellow phosphorous poisoning and also study the postmortem findings in liver and kidney.

Out of 50 patients 25 were study group those who were treated with N Acetyl cysteine (NAC) and another 25 patients were taken from retrospective data collected from those who not treated with NAC.

Our study showed that most vulnerable age group of yellow phosphorous (ratol) poisoning was 15 to 25 years. More than 60% of the victims were females. So influence of alcohol is not much significant. Calculated Leathal dose of YP in previous study was >1mg/kg.This study also told that,80% of the admitted patients are consumed more than 1gm of poison and has more mortality.Most of the patients were admitted with vomiting, abdominal pain, on 3rd day pt developed icterus, feaure of hepaic encephlopathy, bleeding manifestation, hypotension , tachycardia and oliguria ,some patients had respiratory failure also.

In our study approximately 20% of the patients in the study group and 50% in the control group had features of hepatic encephalopathy,hypotension and oliguria .These data pointed that earlier admission and treatment with NAC prevents from occurrence of above said complications. Both group have leukopenia ,but control group(36%) is affected more than study group(12%).

3/4 of patients in the both group had elevated LFT value,remaining 1/4 of patients are near normal LFT, probably they not consumed poison or very minimal consumption. Among 25 patients ,14 reaches our hospital within 24hrs of poison consumption ,so NAC initiated early .Remaining patients are admitted in peripheral hospital and refered later after pt had features of toxic hepatitis.

In the study group 17 patients have good response to NAC, among their 8patiens have elevation of LFT (bilirubin, AST, ALT,prothrombin time) mostly in the 3rd and 4th day of admission. That LFT values become near normal on 6th or 7th day due to timely treatment with NAC . It is statistically more significant(pvalue is 0.001) .

In the study group among 25 yellow phosphorous consumed patients, 8patients (32%) died inspite of NAC treatment mostly due to delayed admission with features of acute liver failure. In the control group 17 patients (68%)died . So treatment with NAC REDUCES 50% OF MORTALITY. It is statistically more significant (p value is 0.024 , <0.05).

A recent study conducted in South India showed that "yellow phosphorus was the most common rodenticide used in suicide attempts in the region and carried a 30% mortality despite maximal supportive therapy"."The LD50 dose in yellow phosphorus poisoning is 10 mg/kg body weight; however, ingestion of a dose as low as 100 mg has been seen to result in death". Indicators for poor outcome included early elevation of liver transaminases and alkaline

phosphatase, more than 10-fold increase in alanine aminotransferase, derangement in prothrombin time, metabolic acidosis, and hypoglycemia. These individuals usually demonstrate only minimal gastrointestinal symptoms during the first 48–72 h but subsequently develop acute liver failure, progressing to multi-organ failure and death in severe cases.

Another study showed that "who consumed lethal dose of poison, presenting early and received NAC, 43% had moderate and 43% had severe hepatic injury. Among severe injury, 14% developed fulminant hepatic failure [FHF] and died". Among patients "who consumed lethal dose, presenting early but not receiving NAC, 33.3% had moderate and 66.7% had severe hepatic injury. All severe cases in this group developed FHF with mortality of 100%. Patients presenting late after consumption of lethal dose, who receive did not NAC developed FHF with mortality of 100%". Patients consuming sub lethal dose had 100% survival without hepatic damage.

Our study also revealed that 32% of mortality occur in NAC group compared to 68% in control group (those who not received NAC). Eventhough guidelines do not exist regarding routine use of NAC in non acetaminophen induced ALF, and in hepatic failure due to yellow phosphorous consumption, Patients admitted with ALF after phosphorus ingestion have better survival with NAC treatment. So early admission and initiation of NAC reduces mortality up to 50% and better survival.

" Prevention strategies by restricting access to this poison can be the one of the best method to avoid complications. Public as well clinicians should be made aware of lethality of inorganic phosphorus in miniscule quantities, and regulating the market sale of this compound should be helpful". However, this lethal ratol paste is easily available at cheaper costs and accidental poisoning is also more common, especially among children. Hence, we call for a ban on market sales of ratol paste.

CONCLUSION

CONCLUSION

Most patients admitted with history of suicidal consumption of ratol (yellow phosphorous) were young and belonged to poorer socio-economic sections. Mortality was reduced to 50% in the study group who was admitted early and treated with NAC, eventhough they consumed lethal dose of ratol. Therefore treatment with NAC, which is inexpensive and relatively safe, would be a viable treatment option for patients admitted with ratol consumption.

SUMMARY

SUMMARY

A prospective cross sectional observational study was done at Government Rajaji Hospital, Madurai among 50 yellowphosphorous poison (ratol) consumed patients. Study group(25 patients) contains those who were treated with NAC ,The control group(25 patients) are taken from retrospective data obtained in year 2016 at GRH , who had similar management protocol except for NAC use. Data was collected about timing and amount of poisoning,timing of initiation of stomach wash and NAC, clinical and laboratory parameters. Most of the patients were young females who consumed more than 1gm of poison(more than lethal dose) presented with icterus ,features of hepatic encephalopathy ,hypotension ,oliguria , and elevated serum bilirubin ,transaminases and prothrombin time. Those who were treated with NAC had improvement in both clinically and biochemically . Morbidity and Mortality was reduced to 50% in the study group who was admitted early and treated with NAC, eventhough they consumed lethal dose of ratol.

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PROFORMA

PROFORMA

Name :

Age / Sex :

Occupation :

Presenting complaints

- Time of Consumption
- Time of Arriving at Hospital
- Any prior treatment before admission
- Delay of stomach wash.
- Amount of poison consumed
- Time of initiation of NAC.

Past History

H/o DM, HT, CKD, CVD, DRUG INTAKE, CAD, Thyroid disorders, Alcohol intake

Clinical Examination:

General Examination:

□ Consciousness,

□ Pallor, □ Jaundice,

□ Clubbing,

- Lymphadenopathy,
- Hydration status

Vitals:

- PR
- BP
- RR
- SpO2
- Urine output

Systemic examination:

CVS :

RS :

ABDOMEN :

CNS :

Laboratory investigations:

a) Complete blood count,

b) Liver function test,

c) Renal function test,

d) Urine routine,

e) Serum electrolyte,

f) prothrombin time and INR,

g) Bleeding time ,clotting time,

h) Arterial blood gas analysis,

i) Electrocardiogram,

j) USG abdomen,

AUTOPSY FINDINGS

LIST OF ABBREVIATION

LIST OF ABBREVIATION

LFT-liver function test

AST- Aspartate aminotransferase

ALT- Alanine aminotransferase

NAC –N Acetyl cysteine

YP –Yellow phosphorous

MASTER CHART

LIVER FUNCTION TEST – STUDY GROUP

S.NO.	**STUDY GROUP**-SERUM BILLIRUBIN					LIVER ENZYMES AST/ALT										PROTHROMBIN TIME/INR									
	DAY 1	DAY 3	DAY 5	DAY 6	DAY 7	DAY 1		DAY 3		DAY 5		DAY 6		DAY 7		DAY 1		DAY 3		DAY 5		DAY 6		DAY 7	
1	0.9	1.5	1	0.9		46	27	49	32	38	24	35	25			12.1	0.56	39	3.04	11.9	0.52	13	1		
2	7.1	11.2	13.8			353	22	480	156	650	315					24	1.8	37	2.9	41	3.2				
3	1.1	1.5	0.9			48	40	50	39	38	31					20	1.5	14	1.1	13.6	1.1				
4	0.8	1.3	1			28	21	52	30	48	35					13	1	16.5	1.3	15	1.2				
5	0.9	1.7	2.9	2	1.3	36	21	96	58	169	118	105	51	93	53	11	0.8	19	1.5	23	1.8	15	1.2	13	1
6	8.9	21				540	495	1380	1236							47.1	3.7	>3MIN							
7	1.2	2.9	7.9	4.2	1.9	60	51	196	88	370	213	290	171	160	70	14.5	1.1	21	1.6	33	2.6	21	1.6		
8	1.1	1.8	2.5	1.9	1.3	43	39	131	78	206	139	112	70	93	56	13	1	17	1.3	25	1.9	17	1.3	15	1.2
9	1	1.2	0.9			31	15	40	27	38	22					15	1.2	14.1	1.1	16.3	1.3				
10	2.9	6.4	10.5			296	108	501	302	753	415					17.7	2.1	75.7	5.9	>3MIN					
11	2.2	2.5	1.2			147	767	130	250	130	134					15	1.2	13	1	16.4	1.3				
12	0.9	1.1	1			35	32	46	34	39	30					13	1	12.1	0.9	14	1.1				
13	0.5	1.8	4.7	8.5		38	15	190	102	440	290	752	495			11	0.8	19	1.5	27	2.1	40	3.1		
14	1	2.7	2.3	1.2		4	29	130	105	112	79	78	41			14	1.1	23	1.8	17	1.3	15	1.2		
15	0.9	1.5	2.1	1.7	1.4	30	12	90	73	196	105	126	70	101	47	13	1.01	18	1.4	23	1.8				
16	1.1	2.5	6.9			45	39	215	173	458	360					14	1.1	22	1.7	37	2.9	41	3.2	49.4	3.9
17	2.1	3	4.5	5.6	3.1	49	33	137	91	102	64	86	36	90	43	16.5	1.1	18.5	1.4	21	1.6	17	1.3	15	1.2
18	0.6	2.1	4.5	7.8		49	40	88	28	193	117	370	251			17	1.3	25	1.9	31	2.4	40.5	3.17		
19	1.1	2.2	6.4	7.3		39	98	204	180	615	410	930	1205			16	1.2	32.3	2.5	42.8	3.2	47.5	3.7		
20	13.5	24	26			96	30	209	747	490	936					25.2	1.9	29	2.3	>2MIN					
21	1	2.5	0.9			30	15	22	12	27	20					13	1	15	1.2	13.6	1.1				
22	0.7	1.1				41	18	39	24							14.1	1.1	12	0.9						
23	5.4	11.6	23.9	13	8.1	256	198	34	33	271	499	1255	720	282	232	29.8	2.3	52.5	4.1	21.5	1.7	19.5	1.5	16	1.2
24	1.3	1.6	1.1			37	27	43	31	34	29					12.9	1	16	1.2	14.3	1.1				
25	0.8	2.9	4.1	1.9	1.4	29	21	265	180	310	205	170	90	112	63	15	1.2	21	1.6	24	1.8	19	1.5	16.2	1.3

LIVER FUNCTION TEST – CONTROL GROUP

	CONTROL GROUP -SERUM BILLIRUBIN					LIVER ENZYMES AST/ALT										PROTHROMBIN TIME/INR									
	DAY 1	DAY 3	DAY 5	DAY 6	DAY 7	DAY 1		DAY 3		DAY 5		DAY 6		DAY 7		DAY 1		DAY 3		DAY 5		DAY 6		DAY 7	
						AST	ALT	AST	ALT	AST	ALT	AST	ALT	AST	ALT										
1	1.2	1	0.8			19	11	34	20	39	24					13.2	1	12	0.9	14	1.1				
2	4.9	11.2	22.9			150	114	458	390	680	513					19	1.5	34.2	2.7	51	4				
3	0.9	1.3	1.1			35	29	43	30	38	28					11	0.9	14.8	1.2	13	1				
4	1.5	8.3	17.1	21		106	81	290	105	513	226	740	515			15.6	1.2	18	1.4	28	2.2				
5	9	15.3				315	191	942	905							25	1.92	41	3.2						
6	0.7	1.1	0.9			30	19	37	29	43	24					14.1	1.1	16	1.2	12	0.9				
7	1.3	2.9	6.1	9.3		58	40	190	114	302	173	349	270			11	0.9	19	1.5	27	2.1	39	3		
8	1.1	3.4	5.7			41	26	208	170	760	492					14	1.1	34	2.6	>2MIN					
9	0.7	1.4	1.1			39	24	46	30	41	37					13.6	1.1	12.4	1	11	0.9				
10	3.2	7.9	13.2			190	103	546	280	1102	780					25.3	2	39	3	>3MIN					
11	0.8	1.7	3.4	7		36	22	93	71	370	246	549	403			11.5	0.9	21	1.6	35	2.7	41	3		
12	1.5	4.1	9.8			63	49	156	94	640	491					16	1.2	34.5	2.7	51	4				
13	0.8	1.1				27	24	38	30							11.5	0.9	12.6	1						
14	1.1	7.8	12.9			41	29	280	215	786	543					13.8	1.1	38	3	49	3.9				
15	4.9	10.6				380	443	785	530							24.4	1.9	>2MIN							
16	1	1.4	2.1	1.7	1	40	39	86	39	64	40	53	31	47	29	12.2	1	16	1.2	14.4	1.1	14	1	14	1
17	0.7	1.9	5.3	9.1		34	29	108	94	310	290	741	960			13.2	1	17	1.3	38.6	3	57	5		
18	1	0.8				39	32	30	37							12.2	0.9	11	0.8						
19	0.9	7.4	13.8			38	31	406	290	741	590					11	0.9	34	2.6	55	4.3				
20	2.8	6.9	10.5			240	194	506	470	1178	1040					26	2	49.4	3.9	>2MIN					
21	1.3	4.8	9.3			78	65	209	190	650	497					17	1.3	47	3.7	>3MIN					
22	0.6	1.1	1.5	0.9		30	17	49	56	34	37	41	29			13	1	15	1.2	14.6	1.1	14	1		
23	1	3.6	9.4	16		26	21	99	84	340	490	780	746			10	0.8	25	1.9	34	2.6	52	4		
24	8.6	15.8				476	341	965	650							21	1.6	58	4.5						
25	1.3	4.9	7.6	12		41	40	371	315	690	536	1476	1140			15.2	1.2	29	2.3	47	3.7	>2MIN			

MASTER CHART -STUDY GROUP

S.NO.	AGE	SEX	ALCOHOLIC	AMOUNT OF POISON CONSUMED IN GRAMS	NAC GIVEN	TIME TO NAC	PRESENCE OF ICTERUS	ENCEPHALOPATHY	HYPOTENSION	OLIGURIA	LEUCOPENIA	LFT	RFT	RESPONSE TO NAC	DEATH	DISCHARGE
1	25	F	N	0.5	Y	A	N	N	N	N	N	N	N	Y	N	Y
2	26	F	N	5	Y	B	Y	Y	N	Y	N	E	E	N	Y	N
3	17	F	N	1	Y	A	N	N	N	N	N	N	N	Y	N	Y
4	35	M	Y	0.5	Y	A	N	N	N	N	N	N	N	Y	N	Y
5	24	F	N	2	Y	A	Y	N	N	N	N	E	N	Y	N	Y
6	29	F	N	15	Y	B	Y	Y	Y	Y	Y	E	E	N	Y	N
7	40	M	N	3	Y	A	Y	N	N	N	N	E	N	Y	N	Y
8	22	F	N	2	Y	A	Y	N	N	N	N	E	N	Y	N	Y
9	31	F	N	0.5	Y	B	N	N	N	N	N	N	N	Y	Y	N
10	19	F	N	10	Y	B	Y	Y	Y	Y	Y	E	E	N	N	Y
11	17	F	N	2	Y	B	Y	N	N	N	N	E	N	Y	N	Y
12	35	M	N	0.5	Y	A	N	N	N	N	N	N	N	Y	Y	N
13	20	F	N	5	Y	B	Y	Y	Y	Y	N	E	E	N	N	Y
14	26	M	N	3	Y	A	Y	N	N	N	N	E	N	Y	N	Y
15	18	F	N	2	Y	A	Y	N	N	N	N	E	N	Y	Y	N
16	36	F	N	5	Y	B	Y	N	Y	Y	N	E	E	N	N	Y
17	25	M	N	5	Y	B	Y	N	N	N	N	E	N	Y	Y	N
18	19	M	N	5	Y	A	Y	Y	N	N	N	E	N	N	Y	N
19	41	M	Y	5	Y	B	Y	N	Y	Y	N	E	E	N	Y	N
20	22	M	Y	10	Y	B	Y	Y	Y	Y	Y	E	E	N	N	Y
21	17	F	N	2	Y	A	Y	N	N	N	N	E	N	Y	N	Y
22	23	F	N	0.5	Y	A	N	N	N	N	N	N	N	Y	N	Y
23	21	M	N	5	Y	B	Y	N	N	N	N	E	N	Y	N	Y
24	42	F	N	1	Y	A	N	N	N	N	N	E	N	Y	N	Y
25	33	M	N	3	Y	A	Y	N	N	N	N	E	N	Y	N	Y

MASTER CHART -CONTROL GROUP

S. NO.	AGE	SEX	ALCOHOLIC	AMOUNT OF POISON CONSUMED IN GRAMS	NAC GIVEN	TIME TO NAC INITIATION	PRESENCE OF ICTERUS	ENCEPHALOPATHY	HYPOTENSION	OLIGURIA	LEUCOPENIA	LFT	RFT	RESPONSE TO NAC	DEATH	DISCHARGE
1	19	F	N	0.5	N	A	N	N	N	N	N	N	N	NA	N	Y
2	36	M	Y	5	N	B	Y	Y	Y	Y	Y	E	E	NA	Y	N
3	28	F	N	0.5	N	A	N	N	N	N	N	N	N	NA	N	Y
4	21	F	N	3	N	B	Y	Y	Y	Y	N	E	E	NA	Y	N
5	35	F	N	10	N	B	Y	Y	N	N	N	E	N	NA	Y	N
6	23	M	N	0.5	N	A	N	N	N	N	N	N	N	NA	N	Y
7	20	M	N	2	N	B	Y	Y	N	N	N	E	N	NA	Y	N
8	17	F	N	2	N	B	Y	Y	Y	Y	Y	E	E	NA	Y	N
9	19	M	N	0.5	N	A	N	N	N	N	N	N	N	NA	N	Y
10	20	F	N	1	N	B	Y	Y	Y	Y	Y	E	E	NA	Y	N
11	40	F	N	2	N	A	Y	N	Y	Y	N	E	E	NA	Y	N
12	34	M	Y	2	N	B	Y	N	Y	Y	Y	E	E	NA	Y	N
13	16	F	N	0.5	N	A	N	N	N	N	N	N	N	NA	N	Y
14	23	F	N	2	N	A	Y	Y	N	N	N	E	N	NA	Y	N
15	27	F	N	5	N	B	Y	Y	Y	Y	Y	E	E	NA	Y	N
16	24	M	N	1	N	A	Y	N	N	N	N	E	N	NA	N	Y
17	19	F	N	2	N	A	Y	Y	N	N	N	E	N	NA	Y	N
18	17	F	N	0.5	N	B	N	N	N	N	N	N	N	NA	N	Y
19	52	M	Y	1	N	B	Y	Y	Y	Y	N	E	E	NA	Y	N
20	24	F	N	5	N	B	Y	Y	Y	Y	Y	E	E	NA	Y	N
21	31	F	N	3	N	B	Y	Y	Y	Y	Y	E	E	NA	Y	N
22	18	M	N	1	N	A	N	N	N	N	N	N	N	NA	N	Y
23	26	F	N	2	N	A	Y	N	N	N	Y	E	N	NA	Y	N
24	35	F	N	10	N	B	Y	Y	Y	Y	N	E	E	NA	Y	N
25	19	F	N	2	N	B	Y	N	Y	Y	Y	E	E	NA	Y	N

Y -YES

N-NO

A –TIME TO NAC INITIATION <1 DAY

B – TIME TO NAC INITIATION >1 DAY

E – ELEVATED

NA –NOT APPLICAPLE

ETHICAL COMMITTEE CERTIFICATE

MADURAI MEDICAL COLLEGE
MADURAI, TAMILNADU, INDIA -625 020
(Affiliated to The Tamilnadu Dr.MGR Medical University, Chennai, Tamil Nadu)

ETHICS COMMITTEE CERTIFICATE

Name of the Candidate	:	Dr.V.Manikandan
Course	:	PG in MD., General Medicine
Period of Study	:	2015-2018
College	:	MADURAI MEDICAL COLLEGE
Research Topic	:	Yellow phosphorous poisoning (Ratol) – Role of N- acetyl cysteine and Postmortem toxicological findings – A prospective study
Ethical Committee as on	:	02.06.2017

The Ethics Committee, Madurai Medical College has decided to inform that your Research proposal is accepted.

Member Secretary Chairman Dean / Convenor

DEAN
Madurai Medical College
Madurai-20

Prof Dr V Nagaraajan
M.D., MNAMS, D.M., Dsc.,(Neuro), Dsc (Hon)
CHAIRMAN
IEC - Madurai Medical College
Madurai

ANTI PLAGIARISM CERTIFICATE

URKUND

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