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Research Paper

Paracetamol Poisoning-A Case Report

Medical Science

KEYWORDS : Paracetamol Poisoning , Hepatotoxicity , N Acetyl Cysteine

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ABSTRACT

Paracetamol is probably the most widely used drug in the world. This report aims to review a case of Paracetamol poisoning and management. 18-year-old male presented to the emergency department with acute intoxication. He ingested a total amount of 12.5 gram (g) of Paracetamol for suicidal attempt. and N-acetylcysteine (NAC) regime was given intravenously following a treatment protocol due to acute liver injury. During observation there was acute pain in abdomen, vomiting and his Liver Function Tests were markedly deranged. He was treated successfully and discharged 7 days after admission by confirming normal liver functions.

Introduction:

Paracetamol (Acetaminophen, N-acetyl-p-aminophenol) is an effective, mild analgesic, antipyretic agent and probably the most widely used drug in the world because is inexpensive . Doses of paracetamol exceeding 150mg/kg in a patient can be life threatening. The most important complication of a major overdose of paracetamol is acute centrilobular hepatic necrosis, but only a small minority of patients are at risk. Some 25 years ago before effective antidotal therapy became generally available, less than 10% of patients referred to the hospital with paracetamol poisoning developed severe liver damage (defined as maximum plasma alanine or aspartate aminotransferase exceeding 1,000 IU/L), and 1% to 3% developed fulminant hepatic failure (1). Analgesics were found most commonly the first or second cause of intoxication in various reports (2,3,4,5,6,7,8,9). In this presentation we aimed to review a case of paracetamol intoxication due to suicide with late presentation after 36hours of ingestion, which leads to profoundly elevated liver enzymes, who was successfully rescued with intravenous (I.V.) N-acetylcysteine (NAC) regime over three days.

Case Report :-

18-year-old male patient with body weight 50kg was admitted to Hospital on 09/08/14 at about 11am as case of excessive consumption of 25 tablets of paracetamol (500mg, appx. 12.5 gram) to commit suicide. He swallowed tablet at around 10pm. on date 07/08/14 and not taken treatment for 36 hours since ingestion. He was not previously known to have any psychiatric problem and there was his first suicidal attempt. He was chronic alcoholic. After 24hours of ingestion of paracetamol tablets he started acute pain in abdomen, in right Hypochondriac region, Nausea, Vomiting, Chest pain, Breathlessness. He was immediately brought to emergency department and Gastric lavage was given. He was started on N-acetylcysteine Regime (NAC) I.V. in Emergency department about 36 hours after ingestion. Serum paracetamol level couldn't be done due to economic constraint. Blood was drawn for laboratory accessement.

During physical examination he was irritable. There was evidence of icterus but no asterixis. His Blood Pressure was 130/80 mm of hg, pulse rate was 110/min, Respiratory Rate was 24/min. Clinically his look was toxic, tachypnic but no Kussmaul's Respiration. Tenderness present in right Hypochondriac region. Rest examination was normal. The patient was started on I.V. N-acetylcysteine Regime (NAC), have been initiated on 150mg/kg over 50 minutes followed by 50mg/kg in 500ml of D5% over next 4 hours and then 100mg/kg in 1000ml of D5% over the next 16 hours. After that he was continued on oral N-Acetylcysteine (NAC) for next 3 days. On review the next day he was icteric, no kussmaul's respiration, tenderness decreases in right Hypochondriac region. Liver function test at the time of admission was markedly raised, SGOT-5120U/L, SGPT-1115U/L, Alkaline phosphatase-739 U/L, suggestive of acute liver injury. His Prothombin time was 22 second, INR value was 1.56. Daily Liver Function Test monitoring was done. After seven days LFT and PT-INR came to normal. Patient was discharged well on 7th day of hospitalization.

His serial investigations are shown in Table 1.

Table 1:- Serial laboratory investigations in our patient

Investigations	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
Hb (g/dl)	13.2	_	_	_	_	_
Total white count(/L)	$7x10^9$	_	_	_	_	_
Platelets (/L)	$220x10^9$	–	–	–	–	–
Bilirubin(mg/L)	1.4	1.1	_	0.9	0.9	0.9
ALT(U/L)	5120	1458	180	55	36	20
AST(U/L)	1115	828	152	78	56	18
ALP(U/L)	739	422	72	58	24	24
Albumin(G/L)	41	_	44	_	_	43
Creatinine (mg/L)	0.8	_	0.8	_	_	0.9
Urea	26	_	24	_	_	22
Prothombin time (sec)	22	_	_	16	_	_
INR	1.56	_	_	1.1	_	_

Discussion:

Paracetamol (Acetaminophen, N-acetyl-p-aminophenol) is probably the most widely used of all drugs in the world. Paracetamol poisoning is frequently seen due to accident or suicide. A toxic exposure to paracetamol is suggested when greater than 150 mg/kg is ingested in a single dose or when greater than 7.5 g is ingested within a 24-h period (10).

The clinical presentation of human paracetamol toxicity can be approximately divided into four stages. During the first 24 hour after exposure (stage 1), patients often have minimal signs and

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symptoms of toxicity. Some may have minor, nonspecific signs and symptoms such as anorexia, nausea, vomiting, pallor, and malaise. By days 2 to 3 (stage 2), clinical signs of hepatotoxicity that may be discerned in hepatotoxic patients include right upper quadrant abdominal pain and tenderness, and abnormal laboratory tests, such as elevated serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), and bilirubin. Even without treatment, most of these patients will recover without sequelae. By days 3 to 4 (stage 3), however, the conditions of some patients will progress to fulminant hepatic failure. Characteristic findings include metabolic acidosis, coagulopathy, renal failure, encephalopathy, and recurrent gastrointestinal (GI) symptoms. Those patients who survive the complications of fulminant hepatic failure will begin to recover over the next week (stage 4), with complete resolution of hepatic dysfunction in survivors (10).The plasma paracetamol concentration provides a good diagnostic indicator, and treatment is successful in patients presenting early with an accurate history, particularly with regard to time of ingestion which is essential for interpreting paracetamol concentration (3).

Table 2: Clinical presentation of acute paracetamol poisoning.

Stage	Approxi-mateTime Postingestion	Symptoms
I	0 to 24 hours	Anorexia, Nausea and Vomiting
II	24 to 72 hours	Right upper quadrant abdominal pain(common);AST ,ALT ,and , if poisoning is severe, bilirubin and PT(usually reported as the INR) sometimes elevated.
III	72 to 96 hours	Vomiting and symptoms of liver failure; peaking of AST,ALT, bilirubin and INR; sometimes renal failure and pancreatitis.
IV	>5 days	Resolution of hepatotoxicity or progression to multisystem organ failure(sometimes fatal)

ALT= Alanine aminotransferase; PT=prothrombin time; INR= international normalized ratio.

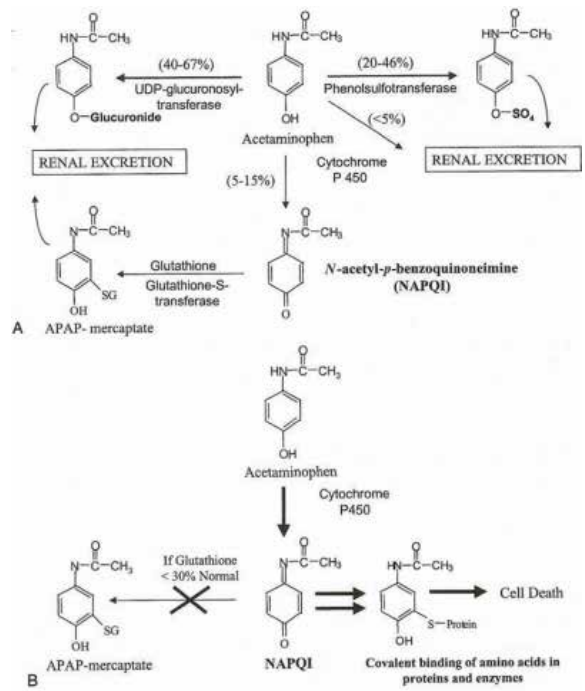
Table 3: Risk factors for paracetamol toxicity

No	High- risk group
1	Pre-existing Liver disease
2	Alcohol intake
3	Poor nutrition
4	Enzyme inducing drugs
5	Anorexia nervosa
6	Human immunodeficiency virus infection

With therapeutic dosing, 90% of N-acetyl-p-aminophenol (NAPAP) is conjugated with glucuronide or sulphate to form nontoxic metabolites (10). Approximately 5% of APAP is metabolized by the hepatic cytochrome p450 mixed-function oxidase enzyme to a toxic metabolite, N-acetyl-p-benzoquinoneimine (NAPQI). In normal dosing, NAPQI is rapidly detoxified by glutathione (GSH) to nontoxic metabolites (figure-1).

Treatment for paracetamol toxicity consists of GI decontamination, timely use of the antidote, iv-acetylcysteine (NAC), and supportive care. In most of the cases of paracetamol poisoning, adequate GI decontamination consists of the early administration of activated charcoal orally or through a nasogastric tube (10) Activated charcoal can be given within one hour of ingestion (3). Despite NAC is adsorbed by activated charcoal, there is no evidence that activated charcoal inhibits the clinical effectiveness of NAC (10). The mainstay for the prevention or treatment of paracetamol induced liver toxicity is the administration of NAC. Although its mechanisms of action are not fully understood (3,10). NAC is thought to have two important beneficial effects. In early paracetamol toxicity (less than 8 h after ingestion), NAC prevents toxicity by inhibiting the binding of the toxic metabolite NAPQI to hepatic proteins. NAC may do this by acting as a glutathione precursor or substitute, a sulphate precursor, or it may directly reduce NAPQI back to paracetamol. In established paracetamol toxicity, or greater than 24 h after paracetamol ingestion, NAC diminishes hepatic necrosis by acting as an antioxidant, decreasing neutrophil infiltration, improving microcirculatory blood flow, or increasing tissue oxygen delivery and extraction

Figure-1: Paracetamol metabolism (10)



Paracetamol overdoses overwhelm conjugation pathways, resulting in increased use of the cytochrome p450 pathway and increased formation of NAPQI, increased depletion of GSH, and, ultimately, hepatic injury (11,12,13,14). Acetylcysteine acts as a precursor for the synthesis of glutathione and by enhancing the reduction of NAPQI to APAP. NAC used can be orally or intravenously.

The standard 72-hour oral NAC regime is a loading dose of 140 mg/kg followed by maintenance doses 70 mg/kg every 4 hours for 17 doses. The 20-hour IV NAC protocol is 150 mg/kg loading dose over 15 minutes, followed by an additional dose of 50 mg/kg over 4 hours and then 100 mg/kg over 16 hours for a total dose of 300 mg/kg (10,15,16). If treatment is initiated within 8 h of paracetamol ingestion, NAC is nearly 100% effective in preventing the development of hepatotoxicity, as defined by an AST level of greater than 1000 U/L (10). The most commonly reported adverse effects of intravenous acetylcysteine are anaphylactoid reactions, including rash, pruritus, angioedema, bronchospasm, tachycardia, and hypotension (16). He was administered NAC according to intravenous treatment protocol and he tolerated NAC well without any side effects. He was discharged after

7th day of hospitalization with normal liver enzymes.

Conclusion:

Acute paracetamol poisoning is a straight forward problem. Paracetamol is one of the agents frequently used for suicide. Activated charcoal seems the best choice to reduce absorption. NAC should be given to patients with paracetamol poisoning. Our patient was treated with I.V. NAC for 3 days without any side effects. From this experience in severe paracetamol poisoning with late presentation (36 hours after ingestion) with profoundly elevated liver enzymes, we feel that NAC for 3 days is safe and efficacious.

Conflicts Of Interest : None

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