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A Case Report Of A Successfully Treated Severe Case Of Isoniazid Overdose Induced Seizure And Hepatotoxicity(DILI)Following Alleged Isoniazid Consumption

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ABSTRACT: An anti-tuberculosis medication, isoniazid is extensively used for the prevention and treatment of tuberculosis. Characterized by a clinical triad, acute poisoning from isoniazid includes raised anion gap metabolic acidosis, coma, and recurrent seizures.

The prognosis is generally favorable when treatment, including the administration of pyridoxine, is initiated promptly.Delayed treatment can lead to serious complications, including prolonged seizures, respiratory failure, and potentially fatal outcomes.

A 27 years old female who intentionally ingested 3600mg of isoniazid and presented with generalized tonic-clonic seizures. She was successfully managed with 10 grams of pyridoxine along with other supportive management, including sodium bicarbonate for metabolic acidosis and mechanical ventilation.Patient was diagnosed as a case of Isoniazid induced seizures with drug induced liver injury and treated in MICU with ventilator support,anti epileptics,antibiotics ,gastic lavage and loading dose of Pyridoxine (1g pyridoxine for each gram of isonizid ingested - total 4g) and was continued on Pyridoxine supplementation and in view of increasing liver enzymes , patient was administered N-Acetyl cysteine infusion according to protocol for 21 hours.Liver enzymes were continuously monitored and patient symptomatically improved and has had no further siezures and discharged after 6 days in hemodynamically stable condition with follow up advice.

KEYWORDS:Isoniazid,hepatic injury,seizure,pyridoxine

I. INTRODUCTION

Isoniazid (INH) overdose is a serious condition that can be fatal, especially with the recent rise in tuberculosis cases in the United States, potentially leading to more frequent occurrences of INH overdose. Patients who overdose on INH may exhibit a range of symptoms, including nausea, vomiting, ataxia (loss of coordination), and manifestations similar to atropine intoxication, such as dry mouth and dilated pupils. Severe cases can lead to coma and grand mal seizures.

Laboratory evaluations typically reveal lactic acidosis, which indicates a buildup of lactic acid in the bloodstream due to metabolic disturbances. The management of INH overdose requires intensive care unit (ICU) admission for close monitoring and ventilatory support, especially if respiratory depression occurs. Treatment also involves addressing seizures and correcting acid-base imbalances.

II. CASE REPORT

A 27 years old female patient referred from outside hospital in a private ambulance in intubated state with alleged history of consumption of tablet ISONIAZID 300MG (~ 12 Tablets =3,600MG) ON 20/06/2024 at around 6:30PM TO 8:30PM at her residence after having an arguement with her husband.

patient was cooking at her residence while she had sudden onset of fall and decrease responsiveness following which she had 3 episodes of involuntary movements involving all 4 limbs,each episode was lasting for ~ 2 minutes following which she became drowsy. History of tongue bite and headche present enroute to hospital. No history of involuntry urination and defecation

No history of breathlessness,fever,cough,chest pain,palpitations,pain abdomen,vomiting,loose stools

No history of HTN,DM,Asthma,Thyroid disorder

No history of smoking/alcohol consumption

normal bowel and bladder habits

No family history of stress disorder.

Patient had LMP on 6/06/2024, regular

There are no known allergies.

She was initially taken to a local clinic followed by 2 local hospitals and finally admitted and intubated outside hospital i/v/o compromised airway and severe metabolic acidosis and treated with ventilator support,loaded with anti epileptics , gastic lavage done ,CT brain and thorax done showing changes of aspiration and bronchiectasis of right middle lobe ,scalp haematoma noted over right parietal region , no intracranial bleed or infarcts and referred to our hospital for further management

Patient was diagnosed as a case of Isoniazid induced seizures with drug induced liver injury and treated in MICU with ventilator support,anti epileptics,antibiotics and loading dose of Pyridoxine (1g pyridoxine for each gram of isonizid ingested - total 4g) and was continued on Pyridoxine supplementation.Neurology, Psychiatry and Medical Gastroenterologist opinion were taken and advice followed.I/V/O recurrent hypokalemia corrections were given.in view of increasing liver enzymes , patient was administered N-Acetyl cysteine infusion according to protocol for 21 hours.Patient was extubated on 22/6/24 and shifted to ward on 24/6/24

All hepatoprotrctive measures were taken.Continuous blood glucose monitoring was done Antiepileptics were continued .Antibiotic was given for 5 days and stopped.CBNAAT was sent i/v/o suspicion of tuberculosis -negative

Repiratory Medicine opinion taken in view of outside CT changes and adviced for nil Respiratory Medicine intervention ,USG abomen pelvis was done and reported altered echotexture of liver,bulky and hetergenous cervix,left ovarian simple cyst.Liver enzymes were continuously monitored and

patient symptomatically improved and has had no further siezures and discharged after 6 days in hemodynamically stable condition with Follow up advice.

LABS	21/06/2024	22/06/2024	23/06/2024	24/06/2024	25/06/2024	26/06/2024
TB	1.40				0.9	0.72
DB	0.50				0.3	0.20
AST	129		182	576	669	431
ALT	29		51	129	193	205
ALP	124				82	82
LDH	1181				3890	992
K	3.6	3.40	3.1	3.50	3.40	3.90
PT	14.3	14.00			13.3	12.1
INR	1.29	1.27		1.20	1.20	1.09

Tab. LEVETIRACETAM 500 mg 1-0-1 to continue

Tab. PYRIDOXINE 20 mg 1-0-0 X 30 days

Tab. URSODEOXYCHOLIC ACID 300 mg 1-0-1 X 7 days

Tab. S ADENOSYL METHIONINE 400 mg 1-0-1 X 7 days

Tab. RIFAXIMIN 550 mg 1-0-1 X 7 days

Syrup LACTULOSE 10 ml 0-0-1 to maintain stool frequency 3-4 times x 7 days

Tab. PANTOPRAZOLE 40 mg 1-0-0 30mins before food x 3 days

GRBS monitoring at home. Patient advised to review in General Medicine OPD with repeat LFT reports ,PT/INR/S.E, stool occult blood and Iron profile

On 8/07/2024 Patient visited to General Medicine OPD with blood reports

LABS	8/07/2024
TB	0.50
DB	0.30
AST	34
ALT	38
ALP	89
NA+	140
K+	4.20
CL-	107
CA++	0.90

Tab LEVETIRACETAM 500mg 1-0-1 for 2 months continued
Continue Tab PYRIDOXINE 20mg for 15 days continued
Advised Neurology and Psychiatry consultation.

III. CASE DISCUSSION

The American College of Gastroenterology (ACG) offers guidelines for classifying drug-induced liver injury (DILI) using the formula

(R=ALT/ULN ÷ ALP/ULN) This formula helps identify three types of DILI:

Acute Hepatocellular Injury ($R \geq 5$): This type is characterized by significantly elevated liver function tests (LFTs) and only mild increases in alkaline phosphatase (ALP). It can be life-threatening, potentially leading to serious complications such as coagulopathy and encephalopathy.

Cholestatic Injury ($R \leq 2$): In this case, ALP levels are notably high while LFTs show minimal elevation, often accompanied by symptoms like jaundice and pruritus.

Mixed Injury (R 2–5): This type presents with intermediate elevations in both LFTs and ALP, resembling atypical hepatitis or granulomatous hepatitis.

In the context of isoniazid (INH), the injury typically aligns with acute hepatocellular damage, similar to acute viral hepatitis, with a latency period that may range from approximately one week to over 90 days, and in some rare cases, extending up to a year. The reported patient had an R score of 11.10, confirming the diagnosis of acute hepatocellular injury.

It is important to note that chronic DILI can occur in 15-20% of cases, particularly when symptoms or laboratory abnormalities persist for more than six months after the initial onset. Patients experiencing cholestatic liver injury generally face a higher risk of complications compared to those with acute liver injury.

I. CONCLUSION

The only effective antidote for INH toxicity is pyridoxine (vitamin B6), which should be administered in a dose that corresponds to the amount of INH ingested. Early recognition and prompt treatment are crucial for improving patient outcomes in cases of INH overdose/Toxicity
In patients experiencing non-acetaminophen acute liver failure, IV NAC may facilitate faster hepatic recovery and decrease in transplantation rates or mortality, as well as in transplantation alone.

REFERENCES:

1. Isoniazid. September 2015, http://livertox.nlm.nih.gov/Isoniazid.htm.

2.D Y Tai 1, J K Yeo, P C Eng, Y T Wang Intentional overdosage with isoniazid: case report and review of literature **1996 Apr;37(2):222-5.** PMID: 8942271

3.Chalasani N. P., Hayashi P. H., Bonkovsky H. L., Navarro V. J., Lee W. M., Fontana R. J. ACG clinical guideline: the diagnosis and management of idiosyncratic drug-induced liver injury. The American Journal of Gastroenterology. 2014;109(7):950–966. doi: 10.1038/ajg.2014.131. [DOI] [PubMed] [Google Scholar]

4.Kaplowitz N. Drug-induced liver injury. Clinical Infectious Diseases. 2004;38(supplement 2):S44–S48. doi: 10.1086/381446. [DOI] [PubMed] [Google Scholar]

5.Kaplowitz N. Drug-induced liver disorders: implications for drug development and regulation. Drug Safety. 2001;24(7):483–490. doi: 10.2165/00002018-200124070-00001. [DOI] [PubMed] [Google Scholar]

6.Kaplowitz N. Drug-induced liver disorders: introduction and overview. In: Kaplowitz N., DeLeve L. D., editors. Drug-Induced Liver Disease. New York, NY, USA: Marcel Dekker; 2002. pp. 1–13. [Google Scholar]

7.Singh S., Hynan L. S., Lee W. M. Improvements in hepatic serological biomarkers are associated with clinical benefit of intravenous N-acetylcysteine in early stage non-acetaminophen acute liver failure. Digestive Diseases and Sciences. 2013;58(5):1397–1402. doi: 10.1007/s10620-012-2512-x. [DOI] [PMC free article] [PubMed] [Google Scholar]