

An Interesting Case of Isoniazid and Rifampicin Suicidal Poisoning

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Abstract

Isoniazid (INH) is an important drug whose toxicity profile is well studied. Acute toxicity of INH manifests as a clinical triad of seizures, coma, and metabolic acidosis^{1,2}. We present here an interesting case of a 25-year-old female who attempted suicide by consuming 12 tablets of (isoniazid 300/rifampicin 600) from blister packs of DOTS ATT regimen and presented to the emergency department with generalised tonic clonic seizures (GTCS). Thus, clinicians should be aware of this potentially fatal but treatable cause of seizures.

Key words: *Isoniazid, Rifampicin, seizures.*

Introduction

Isoniazid (INH) and Rifampicin are considered first-line agents for the treatment of TB. These drugs are well absorbed after oral administration, with peak serum levels at 2 - 4 hours and nearly complete elimination within 24 hours.

The common side-effects of INH are peripheral neuropathy and hepatotoxicity. However, lesser known, severe INH toxicity is characterised by recurrent seizures, lactic acidosis, coma, and death¹.

The common side-effects associated with rifampicin are abdominal discomfort, rash, fever, nausea, diarrhoea, vomiting; and the uncommon side-effects are bleeding manifestations, haemolysis, anaemia, thrombocytopenia leucopenia elevated serum transaminase levels, acute renal failure, nephrotic syndrome, and flu-like syndrome².

During treatment, patients should be monitored for drug toxicity. The most common adverse reaction of significance is hepatitis, while acute poisoning may present with seizures, metabolic acidosis, and eventually coma with fulminant hepatic failure.

Case history

A 25-year-old female presented to the emergency department in an unconscious state. On detailed history, the patient had some familial problems and, as a result of misunderstanding with her husband, she had abstained from food for the last one day. Then subsequently, on the next day in a fit of anger, she consumed 12 tablets of isoniazid (300 mg) and rifampicin (600 mg) which her husband was taking, in an attempted bid of suicide. The

ingestion of the drugs was followed by 2 episodes of vomiting, following which she developed 3 episodes of GTCS (Generalised Tonic Clonic Seizure) and loss of consciousness. She was brought to the emergency department within one-and-half hour of ingestion of the drug, where she again developed an episode of GTCS. There was no history of fever, headache, trauma, or seizures in the past. On examination: BP 110/80 mmHg, PR -100/min, RR -22/min, acidotic breathing, afebrile, hydration adequate. On neurological examination, patient was unconscious, responding to painful stimuli (GCS E3V2M4), pupils were bilaterally semi-dilated and reacting to light. Bilateral plantars were extensor. No focal neurological deficit was found. No signs of meningeal irritation were found. On respiratory system examination, bilateral coarse crepitations were heard in the infra-axillary regions. Per abdominal and cardiovascular examinations were normal.

Investigations sent were complete blood count, liver function test, arterial blood gas and coagulation profile. Hb = 11.3 gm/dl, TLC = 13,400/cumm, DLC: neutrophils 88%, lymphocytes = 8%, platelet count = 1,20,000/cumm, S. bilirubin = 7.4 mg/dl, SGOT = 188 IU, SGPT = 259 IU. Blood sugar = 104 mg/dl pH = 7.23, HCO₃⁻ = 14 mmol/l, PaCO₂ = 35 mmHg, Na⁺ = 119 mmol/l, K⁺ = 2.9 mmol/l, Cl = 93 mmol/l, anion gap = 14.9 control PT = 14, patient PT = 24, patient's INR = 1.83. APTT was normal. CSF analysis was within normal limits. Renal functions and USG abdomen were normal. The patient was admitted and intravenous access was secured. Inj phenobarbitone was given to cease the seizure activity in a dose of 15 mg/kg IV loading dose, infused at 30 mg/min. Gastric lavage was done and orange red coloured fluid was aspirated.

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Injection pyridoxine 3.6 gm in one pint of 5% DNS was infused in 30 minutes. Intravenous antibiotics were given as the patient had developed aspiration pneumonitis, which was evident by coarse crepitation in infra-axillary areas. Metabolic acidosis and serum electrolytes were corrected. Symptomatic treatment for drug-induced hepatitis was given. Though the patient did not have a second episode of seizure in the hospital, she had not regained consciousness. Concomitant fulminant hepatic failure was managed by giving inj vitamin K for correction of deranged coagulation profile, lactulose via Ryles tube, tablet rifaximin 550 mg as a gut sterilizer. Injectable methylcobalamin was continued. Patient regained consciousness after 2 days of admission.

On repeating investigations: Hb = 11.2, TLC = 10,400/cumm, DLC = N68 L28 E4, SGOT = 44 IU, SGPT = 42 IU, Na = 136 mmol/l, K = 3.7 mmol/l, HCO_3^- = 24 mmol/l, Cl = 106 mmol/l. All the other lab parameters were also within normal limits and vitals were stable. The patient was discharged after a psychiatry opinion on oral pyridoxine (tab pyridoxine 40 mg OD).

Follow-up in the outpatient department showed that she had no repeat episodes of seizure/loss of consciousness.

Discussion

Animal evidence suggests that INH inhibits the activity of brain pyridoxal-5-phosphate, the active form of pyridoxine, resulting in decrease in the brain levels of gamma aminobutyric acid (GABA) and that this decrease is responsible for the seizure activity that follows⁵. An adverse reaction begins between 30 minutes to 2 hours after the ingestion of a large amount of INH, as was seen in our patients. The earliest manifestations include nausea, vomiting, blurred vision, increased visual sensitivity, and slurred speech. In the absence of adequate treatment stupor, respiratory distress, coma and seizures quickly ensue. Laboratory data reveals severe metabolic acidosis and electrolyte imbalance. Pyridoxine is a specific antidote for isoniazid toxicity and its dose is 1 gm of pyridoxine for each gm of isoniazid ingested⁶. If the dose of isoniazid ingested is not known, 10 g of pyridoxine may be given intravenously.

High dose pyridoxine is beneficial in such patients as it leads to rapid seizure control and correction of metabolic acidosis. Bicarbonate alone may be inadequate to control the acidosis in these patients. Rifampicin toxicity at times causes anaemia, leucopenia, thrombocytopenia, haemolysis, bleeding manifestations, and elevated serum transaminase levels²; however, it is rarely fatal if the dose is less than 60 gm⁶. When rifampicin-containing anti-TB treatment is instituted, jaundice occurring within 1 week should suggest rifampicin toxicity. However, if only indirect hyperbilirubinaemia is found and if haemolysis is excluded the patient may be restarted on rifampicin with close monitoring of bilirubin. Rifampicin at times leads to severe hepatitis with hyperbilirubinaemia and marked elevations of SGOT and SGPT. The exact mechanism of rifampicin induced hepatotoxicity is not known, however, it has been postulated that it is due to idiosyncratic reaction to rifampicin metabolites which may be directly toxic or induce an immunologically mediated liver injury. The drug induced hepatitis caused by rifampicin occurs earlier than that caused by INH and is characterised by patchy cellular involvement with marked periportal inflammation⁷. In our case, it was postulated that the elevated liver enzymes, deranged coagulation profile and fulminant hepatitis were all a result of acute rifampicin intoxication and the seizures were a result of INH intoxication.

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