CASE REPORT

Status Epilepticus and Metabolic Acidosis in Isoniazid toxicity

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Abstract: A four year child with history of accidental ingestion of 13 tablets isoniazid-rifampicin i.e. 1.3 gm of isoniazid presented with status of generalized tonic-clonic seizure and fast breathing. The child did not respond to lorazepam, phenytoin and phenobarbitone but responded only after giving intravenous pyridoxine therapy and correction of acidosis.

Key words: Isoniazid, seizure, Pyridoxine

Introduction: Tuberculosis (TB) is common in tropical countries including India and isoniazid is the cornerstone of anti-tuberculous therapy in nearly every drug regime. Cases of intentional and accidental overdose of antituberculous drugs have been reported though with less than expected frequency considering the extensive use (1). The common manifestations of isoniazid (INH) overdose include recurrent seizure, metabolic acidosis and coma (2). We report a case of INH toxicity with status epilepticus and metabolic acidosis, which was treated successfully with intravenous pyridoxine therapy.

Case Report: A four year old girl was referred to the pediatric emergency unit with generalised tonic clonic seizure after accidental ingestion of 13 tablets of isoniazid-rifampicin combination (100mg+150mg) of her mother. Her mother was suffering from HIV and receiving anti tubercular therapy for pulmonary TB along with antiretroviral therapy. Child was brought to the hospital within one hour of ingestion and there was no history of vomiting after consumption of the tablets. On examination child was convulsing and had acidotic breathing. Arterial blood gas analysis revealed severe uncompensated metabolic acidosis (pH: 7.11, bicarbonate: 10.2 mEq/L), serum sodium 133.8 mEq/L and potassium of 4.1 mEq/L. Routine blood counts, ionised calcium, blood sugar, renal and liver function tests were within normal limits. Repeat liver function tests after 24 hours showed elevation of transaminases levels with ALT of 240 IU/L and AST of 146 IU/L which normalized at 72 hours. Toxicological estimation of INH and rifampicin were not done due to unavailability of this facility. Initially, after care of airways and breathing, intravenous line was established and usual anticonvulsant agents, lorazepam (two doses), phenytoin (20 mg/kg intravenously over 20 minutes) and then Phenobarbitone (20 mg/kg) were given. However, her seizures did not subside, and midazolam infusion was initiated. After initiation of midazolam infusion, the seizures intensity was decreased but not completely controlled. Then pyridoxine was administered in the dose of 1 gram per gram of INH ingested intravenously as bolus dose which controlled the seizure, thereafter patient was maintained on pyridoxine treatment (40 mg per day) for another 72 hours. The child was also given a gastric lavage and the acidosis was corrected by infusing bicarbonate. The patient remained seizure free during hospital stay. Other anticonvulsants were tapered off gradually and child became well. EEG and CT-cranium done on next day were also normal. Patient was asymptomatic on follow up on day 7 and one month later even without pyridoxine treatment.

Discussion: The manifestations of INH toxicity include nausea, vomiting, blurred vision, and slurred speech and usually occur between 30 minutes to 2 hour after the ingestion of a large amount of isoniazid and if not treated early then refractory seizure, unconsciousness and coma may follow (3). INH inhibits 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 (4). Besides its role in the synthesis of GABA, pyridoxine is also an essential cofactor in the metabolic pathways of other major neurotransmitters, dopamine, serotonin and tryptamine (5). Thus, decreased pyridoxine could theoretically result in an alteration of mental status by a variety of mechanisms. Pyridoxine is a specific antidote for isoniazid toxicity and its dose is 1 gram of pyridoxine for each gram of INH ingested (5,6). 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 (3). Some patients may require haemodialysis and forced diuresis to facilitate elimination of INH. Although the child had also ingested rifampicin, she did not have any associated toxic manifestations of Rifampicin (7).

Clinicians should consider this potential etiology of cerebral dysfunction including seizure because pyridoxine deficiency is easily treated. If unrecognized, serious consequences may result.

Learning points:

- Isoniazid toxicity in children is usually accidental
- Status of generalized tonic clonic seizure may occur with metabolic acidosis and coma
- Pyridoxine is the effective antidote for toxicity

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