

## Case Reports

### Pyridoxine in Acute Isoniazid Overdose

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Isoniazid is the mainstay of antitubercular therapy and is included in nearly every drug regime. Cases of intentional and accidental overdose have been reported(1,2) though with less than expected frequency considering the drug's extensive use. The principal manifestations of isoniazid overdose include recurrent seizures, metabolic acidosis and coma(3,4). We report two cases of isoniazid overdose and their successful management with high dose oral pyridoxine.

#### Case Reports

*Case I:* An 8-year-old girl was referred to the pediatric Intensive Care Unit with a history of consuming approximately 20 tablets of isoniazid (100 mg) and 4 to 5 capsules of rifampicin (150 mg) about 2 hours prior to admission.

The child was receiving isoniazid and rifampicin four months previously for tubercular lymphadenitis. The reason for the intentional over dosage was to finish her stock of medicines before the next follow up hospital visit and a desire to 'get well' soon. Within a hour of consumption of isoniazid, the

child had vomiting followed by three episodes of generalized tonic-clonic seizures. Postictally, she was drowsy. On examination, the child was drowsy and had slurred speech, but her vital parameters were stable. The fundus examination was normal and there were no cranial nerve deficits. Motor examination and the rest of the systemic examination were within normal limits.

Investigations revealed metabolic acidosis with pH of 7.15 pCO<sub>2</sub> 30.4 mm pO<sub>2</sub> 110 mm, and bicarbonate 11.7 mEq/L, serum sodium 129 mEq/L and potassium 3 .mEq/L. Routine blood counts, sugar, urea and liver function tests were within normal limits.

Gastric lavage was done immediately, and an orange tinted fluid aspirated. The acidosis was corrected. Pyridoxine was administered in the dose of 1 g per g of isoniazid ingested *viz.*, 2 g intravenously as a single dose. The patient thereafter remained seizure free. The repeat arterial blood gases done 12 hr later were normal. Liver function tests done at discharge a week later were normal.

*Case II:* A 3-year-old child, whose mother was on antitubercular therapy for pleural effusion, accidentally consumed 10 tablets of isoniazid (100 mg) and was brought convulsing to the hospital within two hours of ingestion. On examination, the child had acidotic breathing, but the other vital parameters were normal.

Investigations revealed an arterial blood pH of 7.13, bicarbonate 12.5 mEq/L, sodium 126 mEq/L and potassium of 3 mEq/L. Blood counts, sugar, renal and liver function tests were within normal limits.

The child was given a gastric lavage and the acidosis was corrected. This child too was given 1 g of pyridoxine intravenously

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as a single dose. Thereafter he was seizure free and discharged after 1 week. Repeat liver function tests at discharge were normal.

### Discussion

Animal evidence suggests that isoniazid 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 follows(5). An adverse reaction begins between 30 minutes to 2 h after the ingestion of a large amount of isoniazid, 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 g of pyridoxine for each g of isoniazid ingested(6). 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 as has been demonstrated in 3 cases(6). Some patients may require hemodialysis and forced diuresis to facilitate elimination of isoniazid.

Both our patients showed rapid and satisfactory response with single high dose pyridoxine. Although *Case I* had also ingested rifampicin, she did not have any

associated toxic manifestations of rifampicin(7) as the dose was subtoxic. Rifampicin is rarely fatal if the dose is less than 60 g(5).

Our cases illustrate the efficacy of pyridoxine in the management of the manifestations of isoniazid overdose and toxicity. Furthermore, parental education and close supervision is essential to prevent such potentially hazardous overdosing.

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