Case Report

Acute isoniazid poisoning in a child treated with hemodialysis

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ABSTRACT

Isoniazid is widely used as prophylactic and therapeutic anti-tuberculous drug because of its effectiveness and low cost. Acute intoxication with isoniazid is known to cause symptoms of seizures, metabolic acidosis, coma, and even death. We present a case of acute isoniazid poisoning in a seven year old patient who ingested 2100 mg (105 mg/kg) of isoniazid. She was admitted unconscious, with ventilatory insufficiency and convulsions.

Both renal and liver function tests were normal. She was intubated and mechanically ventilated. Despite parenteral midazolam and pyridoxine (vitamin B6) treatments convulsions persisted. Then hemodialysis was performed and after hemodialysis convulsions and ventilatory insufficiency disappeared and the patient was conscious and she was extubated. Hemodialysis may be an effective treatment alternative for the isoniazid poisoning cases resistant to pyridoxine infusion.

KEY WORDS: Isoniazid intoxication, Hemodialysis.

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INTRODUCTION

Isoniazid (INH) is widely used as prophylaxis and anti-tuberculous drug because of its effectiveness and low cost. The most important side effect of isoniazid is moderate reversible hepatic toxicity. In high doses, acute isoniazid intoxication causes seizures, metabolic acidosis, coma, and even death. Hemodialysis might be effective in the treatment of fatal complications due to isoniazid intoxication. There is limited data about the efficacy of hemodialysis for hemodialysis in children. Here we present a case of acute isoniazid poisoning in a seven year old patient who was successfully treated with hemodialysis.

CASE REPORT

Seven years old girl, who had ingested 2100 mg (105 mg/kg) isoniazid four hours ago, was admitted to the emergency service because of convulsions persisting for more than one hour. She was unconscious, with respiratory failure. Physical examination revealed a body temperature of 36'C, a respiratory rate of 48 breaths/min, a pulse rate of 196 beats/min and blood pressure of 80/50 mm Hg. The

patient's general appearance was bad and she was unconscious. Heart sounds were rhythmic and tachycardic. Her respiratory sounds were normal and she was tachypneic and dyspneic. Abdominal examination was normal. Pupils were isocoric and bilateral pupil reflexes were present. There was lateral deviation in right eye. Deep tendon reflexes were brisk. Glasgow coma score of her was six.

A blood count revealed a hemoglobin concentration of 13.9 gr/dL, a total leukocyte count of 21800/mm^3 (82% neutrophils, 18% lymphocytes), and a platelet count of 351000/mm^3. Arterial blood gas determinations showed a pH of 7.40, a PCO_2 of 29.3 mmHg, a PO_2 of 145 mmHg and a HCO_3 of 17.9 mEq/L. Other laboratory values included a blood glucose 184 mg/dL, alanine aminotransferase 16 IU/L, aspartate aminotransferase 26 IU/L, alkaline phosphatase 195 IU/L, total bilirubine 0.3 mg/dl, total protein/albumin 8.1/4.6 gr/dl, blood urea nitrogen 6 mg/dl, creatinine 0,3 mg/dL, sodium 136 mEq/L, potassium 4.1 mEq/L, chloride 97 mE/L, calcium 8.2 mg/dL and, phosphorus 5.1 mg/dL. Phrothrombine time and International Normalized Ratio (INR) were in normal ranges. Brain edema was detected on cranial computed tomography.

After admission of the patient to the pediatric intensive care unit midazolam infusion (0.01 mg/kg/hour) and phenytoin (20 mg/kg) treatments were initiated to stop the convulsions. Then intravenous pyridoxine (100 mg/kg) was given. Because of the brain edema fluid restriction (1200 cc/m^2/24h) and mannitol treatments were applied. Since the respiration of the patient was too superficial, respiratory failure appeared. So that she was intubated and ventilated with mechanically. Despite all these treatments convulsions went on. Then it was decided to perform hemodialysis. After hemodialysis convulsions of the patient stopped. In the sixth hour of the admission to the intensive care unit, respiratory failure disappeared and the patient was conscious. Then she was extubated and mechanical ventilation was ended. All the clinical and laboratory signs and symptoms of the patient improved and she was discharged from the hospital without complications.

DISCUSSION

Isoniazid has been in use as tuberculosis treatment and prophylaxis drug since 1952. Almost all of the ingested amount is absorbed in the gastrointestinal tract. Approximately 10% of it binds to protein. The half life of the drug is 2-4 hours (metabolized with slow acetylation) and 75-90% of the metabolites are excreted in the urine within 24 hours.[1]

Acute toxicity occurs 30-45 minutes after ingestion. Ingestion of 20 mg/kg causes moderate toxicity, while ingestion of more than 30 mg/kg causes generalize tonic clonic convulsions.[2] On the other hand, ingestion of 80 mg/kg or more, associated with recurrent convulsions, lactic acidosis and coma, which is known as isoniazid intoxication triad. Unless it is treated properly, death is inevitable.[3,4]

Although central nervous system symptoms are evident in isoniazid intoxication, patients may be asymptomatic during the first two hours after ingestion. Dizziness, nausea, vomiting, meaningless speech, metabolic acidosis, coma, focal and generalize convulsions may be observed. The treatment of isoniazid intoxication is mainly symptomatic. Agrawal et al, reported eight patients with isoniazid intoxication who were managed with only symptomatic treatment and all of them has recovered without any residual effect.[5] But the patients who don't response to symptomatic treatment may need further treatment options. Pyridoxine is an essential cofactor in the production of gama aminobutyric acid-an important inhibitory neurotransmitter. In case of intoxication isoniazid combines with pyridoxine, and composes inactive complexes. This results in a depletion of gama aminobutyrate levels in the brain, causing central nervous system stimulation and seizures.[6] Pyridoxin gets into competition with INH and prevents neurotoxicity. In clinical studies it was shown that combination of pyridoxin with anticonvulsant drugs supplies rapid control of convulsions.[7,8] In most of the patients pyridoxin with symptomatic treatment was reported to be enough to stop convulsions.[9,10] But in case of insufficient convulsion control with pyridoxin treatment, diazepam infusion may be started after maintaining airway. Diazepam was shown to be more effective than phenytoin and barbiturates.[11]

Hemodialysis is a new and effective treatment option for isoniazid intoxication.[12] It was shown to be effective in the treatment of adults with isoniazid intoxication in adults.[12,13] But there is not enough data about the isoniazid intoxication treatment with hemodialysis in children. There are only two reports of isoniazid intoxication treated with hemodialysis in children.[6,12] From this case report it may be suggested that if medical treatment is ineffective to stop convulsions hemodialysis may be essayed. Hemodialysis removes isoniazid from serum rapidly. As it was in our case if the patient ingests high doses of isoniazid and the patient is comatose or the convulsions are going on, emergency hemodialysis is indicated. Peritoneal dialysis was also shown to be effective in

isoniazid intoxication but it is less effective than hemodialysis.[6]

As a result hemodialysis may be an effective treatment alternative for the patients for whom pyridoxine is ineffective.

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