Introduction

Intoxications are among the most common reasons of emergency department visits among children. Especially adolescence is a risky period characterized by a high incidence of intoxications secondary to suicidal intake of medications.

Isoniazide (INH) is one of the most commonly utilized medications for childhood tuberculosis. In parallel to its widespread use, intoxication cases due to its intentional or unintentional intake occur.

Intoxication due to INH results in reduced gamma amino butyric acid (GABA) levels in the central nervous system, which lowers convulsion threshold with resultant treatment-resistant convulsions.[1]

The preferred treatment of convolution episodes due to INH intoxication is pyridoxine administration. Pyridoxine is a cofactor for the synthesis of GABA, a major inhibitor in the central nervous system. Therefore, pyridoxine administration specifically prevents isoniazide-induced neurotoxicity.[2] This paper reports a patient who was admitted to emergency department for acute INH intoxication characterized by recurrent seizures, rhabdomyolysis, and metabolic acidosis, and was successfully treated.

Case report

A 16-year-old female patient was admitted to our hospital’s pediatric emergency department in a...
confused mental state. Upon the interrogation of her family it was learned that her older brother residing at the same house was receiving anti-tuberculosis treatment, and our patient was administered INH prophylaxis on an irregular basis for 2 months. One hour before having been brought to the emergency department, she had taken a total of 2 gr (20 pieces of 100 mg tablets) of isoniazide for suicidal purpose. On admission examination she had a Glaskow coma score of 9; her pupils were isocoric and bilateral light reflexes were positive. Her body temperature was 37 °C, pulse rate 120/min, blood pressure 123/78 mmHg, respiratory rate 27/min. Gastric lavage was performed and activated charcoal was administered via nasogastric catheter. She developed generalized tonic clonic convulsions 30 minutes after emergency department admission, and midazolam 0.1 mg/kg was administered intravenously.

However, she suffered a repeat convulsive attack 10 minutes later, for which the bolus midazolam was repeated and infusion was started at a rate of 0.1 mg/kg/hour. Upon the occurrence of a third seizure episode, midazolam dose was increased to 0.2 mg/kg/hour. 1500 cc/m 2 1/3 saline solution was also given. An arterial blood gas analysis showed the following: pH:6.9, partial pressure of oxygen (pO₂): 65 mmHg, partial pressure of carbon dioxide (pCO₂): 5.2 mmol/L, (base excess) BE:-24, lactate:20 mmol/L. Upon the observation that her peripheral oxygen saturation dropped to 80% and her respiratory protective reflexes were lost, she was intubated and admitted to the intensive care unit. Mechanical ventilatory support was provided. A judicial report was compiled and formal notification was sent.

The results of laboratory tests were as follows: hemoglobin:13.2 gr/dL, white blood cell count:18.900 /mm³, thrombocyte count: 289.000/mm³; blood glucose: 200 mg/dL, K: 3,3 mEq/dL, creatine kinase: 446 U/L, LDH: 337 U/L; other biochemistry parameters were normal.

She was administered a total of 2 gr pyridoxine given intravenously in two divided doses. Additionally, NaHCO₃ was administered against metabolic acidosis. Due to increasing CK level at follow-up, hydration therapy was intensified to 3000 cc/m²; urinary alkalisation treatment was also continued so as to attain a urinary pH ≥7. As her convulsions gradually abated, midazolam was tapered and stopped. The patient regained her consciousness, became fully cooperated, and had respi-

ratory parameters completely corrected. She was extubated 38 hours after her admission and consulted with the child psychiatry department. Temporal changes in her biochemical parameters were shown on Table 1.

<table>
<thead>
<tr>
<th></th>
<th>1.day</th>
<th>2.day</th>
<th>3.day</th>
<th>4.day</th>
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<th>6.day</th>
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<tr>
<td>CK(U/L)</td>
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<td>6262</td>
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<td>88</td>
<td>87</td>
<td>76</td>
<td>50</td>
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<tr>
<td>LDH(U/L)</td>
<td>337</td>
<td>458</td>
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<td>823</td>
<td>305</td>
<td>246</td>
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<tr>
<td>Lactate(mmol/L)</td>
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<td>3.9</td>
<td>2.2</td>
<td>0.9</td>
<td>0.6</td>
<td>0.2</td>
<td>0.2</td>
</tr>
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**Table 1**: Temporal changes in biochemical panel of the patient during follow-up.

On 7th day of her intensive care unit admission her overall status was well and her vital signs were all stable; she was therefore transferred to the department of pediatrics for further follow-up.

**Discussion**

Intake of high dose INH causes recurrent convulsions resistant to anticonvulsant medications, high anion gap metabolic acidosis, lactic acidosis, coma, and rhabdomyolysis in a dose-dependent manner; this condition may lead to death unless treated effectively. INH intoxication should be definitely considered in patients presenting to emergency department with the triad of metabolic acidosis, convulsions, and coma.

The initial symptoms of intoxication starts within 30-120 minutes of medication's intake and may include nausea-vomiting, speech disturbance, and impaired orientation. In severe cases of intoxication convulsions may suddenly arise[3,4]. The clinical picture may also include metabolic acidosis, hyperglycemia, hypokalemia, glucosuria, and ketonuria. Hepatitis, renal failure, respiratory arrest, and rhabdomyolysis occurring in a dose-dependent fashion are other possible manifestations. Serum isoniazide level has no value in assessing its toxicity and guiding treatment[5]. Our case also had severe intoxication and developed seizure 1.5 hour after drug intake. Convulsions were also accompanied by metabolic acidosis, hypokalemia, and hyperglycemia, and rhabdomyolysis developed at follow-up.

Rhabdomyolysis is a rare but potentially fatal complication of INH intoxication. Its mechanism of occurrence is not clear, and has been related to a direct toxic effect of the drug or one of its metabo-

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lites, or alternatively, severe muscle breakdown.\(^\text{8}\)

Pyridoxine (Vitamin B6) is the specific antidote of INH and is the most effective treatment for INH intoxication. It should be parenterally administered as soon as possible after admission. It is administered intravenously at a dose equal to the total INH intake. When the ingested INH amount is unknown, it is recommended that pyridoxine 5 gr be administered parenterally in adults and 70 mg/kg in children; the dose may be repeated as necessary.\(^\text{7}\) Hemodialysis is an effective treatment option for those who failed other therapies or developed renal failure.\(^\text{8}\) Our patient’s renal function remained normal and she maintained a normal stable urine output. Rhabdomyolysis regressed with hydration and urinary alkalinization, and hemodialysis was not required.

Drug absorption should be minimized by gastric lavage and activated charcoal. Hence, we administered both treatments at the emergency department.

Benzodiazepines should be preferred when convulsion develops. Midazolam at a starting dose of 0.1 mg/kg is administered intravenously; the dose may be repeated as needed and infusion may be started. Administering pyridoxine with anticonvulsants augments their efficacy. Also in our patient midazolam boluses were followed by infusion, and pyridoxine effectively controlled seizure activity.

In conclusion, INH intoxication should be considered in the differential diagnosis of cases admitted to emergency department with high anion gap metabolic acidosis, convulsions resistant to classical anticonvulsants, and coma. INH-mediated intoxications has recently been on the rise especially in the young. Therefore, the intravenous form of pyridoxine should be found in every emergency department.

References

1) Gokhale YA, Vaidya MS, Mehta AD, Rathod NN. Isoniazid toxicity presenting as status epilepticus and severe metabolic acidosis. J Assoc Physicians India. 2009; 57: 70-7
4) Gokhale YA, Vaidya MS, Mehta AD, Rathod NN. Isoniazid toxicity presenting as status epilepticus and severe metabolic acidosis. J Assoc Physicians India. 2009 Jan; 57: 70-1.