Acute isoniazid intoxication with hypokalemia, acidosis, coma, and status epilepticus in a child treated with pyridoxine

Piridoksinle tedavi edilmiş hipokalemi, metabolikasidoz, koma ve status epileptikusun eşlik ettiği çocukta izoniazid zehirlenmesi

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Abstract

Isoniazid intoxication can cause refractory seizures, metabolic acidosis, rhabdomyolysis, coma, and even death. We report a case of acute isoniazid intoxication presenting with hypokalemia, acidosis, coma, status epilepticus, and pyridoxine treatment. A previously healthy 13-year-old Turkish girl presented to our hospital due to vomiting and generalized tonic -clonic seizures that started two hours after ingesting 15 tablets of 300 mg isoniazid (80 mg/kg) for the purpose of suicide. On laboratory examination, metabolic acidosis, hypokalemia and elevated transaminase, creatine phosphokinase (CPK) were detected. Five gram of pyridoxine was infused in 500 mL of 10% dextrose over 30 minutes. In follow-up, no hepatic and renal failure was found. We describe A child who presented with status epilepticus and coma after taking overdose of isoniazid in this study. When isoniazid is taken in high doses, pyridoxine depletion occurs, which results in siezures. We would like to emphasize that intravenous pyridoxin should be administered as soon as possible in isoniazid intoxications.
Keywords: Child, coma, isoniazid, status epilepticus, pyridoxine

Öz

İzoniazid zehirlenmesi dirençli nöbetler, metabolic asidoz, rabdomiyoliz, koma ve hatta ölüme sebep olabilir. Biz piridoksinle tedavi edilmiş hipokalemi, asidoz, koma, status epileptikusla karşımıza çıkan akut izoniazid zehirlenmesi olan bir olguyu sunduk. Daha öncesinden sağlıklı 13 yaşında Türk kız çocuğu intihar amacıyla 300 mg'lık 15 tablet isoniazid (80 mg/kg) alımından iki saat sonar kusma, generalize tonik klonik nöbetler nedeniyle hastanemize başvurdu. Laboratuvar incelemesinde metabolic asidoz, hipokalemi, artmış transaminaz ve keratin kinaz düzeyleri tespit edildi. 500 mL %10 dekstrozlu sıvı içerisinde 5 g piridoksin 30 dakikada verildi. Kontrol değerlendirmesinde hepatik ve renal yetersizlik görülmedi. Bu sunumda izoniazid fazla alımı sonrası koma ve dirençli nöbetlerle başvuran bir hasta sunuldu. Yüksek doz izoniazid alımı piridoksin seviyesini düşürür ve nöbetlere sebep olur. İzoniazid zehirlenmesinde intravenöz piridoksinin en kısa sürede başlanması gerektiğini vurgulamak istedik.
Anahtar kelimeler: Çocuk, koma, izoniazid, status epileptikus, piridoksin

Introduction

Isoniazid has a pivotal role in the prophylaxis and therapy of tuberculosis. The classical features of isoniazid intoxication can be identified as refractory seizures, metabolic acidosis, rhabdomyolysis, coma, and even death (1). When isoniazid is taken in high doses, pyridoxine depletion occurs, which results in inadequate synthesis of gamma-aminobutyric acid (GABA), an inhibitory neurotransmitter responsible of refractory seizures of isoniazid intoxication (2).

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Case Report

A previously healthy 13-year-old Turkish girl presented to our hospital due to vomiting and generalized tonic clonic seizures that started two hours after ingesting 15 tablets of 300 mg isoniazid (80 mg/kg) for the purpose of suicide. The pupils were isochoric and responded to light, bilaterally. The patient's plantar response and deep tendon reflexes were normal. Two prolonged tonic clonic seizures occurred within an hour after admission which subsided within five minutes after administrating 5 mg of diazepam intravenously. Physical examination revealed a Glaskow Coma Scale score of 9, temperature of 37°C, pulse rate of 92 beats/min, blood pressure of 110/70 mmHg, and a respiration rate of 15/min.

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Arterial blood gas analysis was performed and revealed a pH of 7.1, a partial pressure of oxygen of 109 mmHg, a partial pressure of carbon dioxide of 29 mmHg with a bicarbonate concentration of 10 mmol/L and base excess of-17, the potassium concentration level was 2.4 mmol/L, aspartate aminotransferase (AST) 20 units per liter, alanine aminotransferase (ALT) 13 units per liter. Sodium bicarbonate was administered intravenously for the correction of metabolic acidosis. Potassium chloride was administered for the correction of hypokalemia. The patient was treated empirically with 50 g of charcoal administered via nasogastric tube. 5 g of pyridoxine were infused in 500 mL of 10% dextrose over 30 minutes. AST, ALT, lactate dehydrogenase (LDH), and creatine phosphokinase (CPK) that increased on the 5th to 7th days were gradually decreased to their normal values on the 16th day (Table 1). Then, the patient was discharged without any complications; the outpatient follow-upafter the 15th day of discharge was found to be normal without any hepatic nor renal insufficiencies.

Discussion

Tuberculosis is still a serious public health problem in Turkey and all around the world (3,4). Isoniazid has a very important role in prophylaxis and therapy. Together with this wide usage in anti-tuberculosis therapy, adverse and toxic effects can be mostly seen (5). Doses above 30 mg per kg or an average of 1.5 g of isoniazid can cause acute toxicity symptoms after approximately 30 minutes of ingestion, and ingestions more than 50 mg/kg can result in death rapidly. Initial symptoms of toxicity are usually observed as dizziness, vomiting, nausea, slurred speech, tachycardia, and fever (6,7). The triad of isoniazid intoxication can be identified as refractory seizures, metabolic acidosis, and coma (1). When isoniazid is taken in high doses, pyridoxine depletion occurs, which results in inadequate synthesis of GABA, an inhibitory neurotransmitter responsible for refractory seizures of isoniazid intoxication. Coma and other neurological symptoms are also a result of this interaction (2).

The patient ingested 80 mg/kg of isoniazid two hours before admission to the emergency policlinic. Her neurological findings got better rapidly with the administration of pyridoxine. Isoniazid prevents lactate-piruvate conversion, and hence, metabolic acidosis is one of the important clinical signs of intoxication (8). At the same time, refractory seizures can accelerate acidosis, but correction of acidosis does not stop the seizures (2,9). Other clinical symptoms are hypokalemia, hyperglycemia, and elevation of muscle enzymes, ketonuria, and glucosuria. On the fourth or fifth day of ingestion, elevation of AST and ALT was recorded.

Our case had metabolic acidosis with elevated anion gap. She had high CK and CK-MB levels on admission, but symptoms of rhabdomyolysis did not occur. On the fifth day of admission, she had hepatic dysfunction; but it regressed on about the 16th day. In the rapeutic approach, if there is suspicion of isoniazid intoxication, first, airway and an intravenous access should be obtained; gastric lavage and activated charcoal should be administered in the absence of contraindication, and then, the patient should be observed for the presence of seizures, altered sensorium, coma, metabolic acidosis, rhabdomyolysis, renal failure, and hepatotoxicity (6,2).

For the treatment of refractory seizures, diazepam infusion can be administered, deep metabolic acidosis can be treated with bicarbonate infusion, and supportive treatment should be obtained against hypokalemia and other metabolic conditions. Hemodialysis can be considered, if necessary. However, the only chance of this intoxication may be the presence of isoniazid specific antidote. Pyridoxine reverses the adverse reactions of isoniazid. Pyridoxine should be administered at an equal dose of isoniazid by slow intravenous push as soon as possible, and if the dose is not known, 5 mg pyridoxine should be administered (6,10).

Isoniazid intoxication can result in death in a very short time in certain doses. Therefore, intravenous pyridoxine should be obtained in emergency and intensive care units and should be administered as soon as possible in isoniazid intoxications.

Conclusion

A child who presented with status epilepticus and coma after taking overdose isoniazid was presented in this study. When isoniazid is taken in high doses, pyridoxine

Table 1. Biochemical parameters of the patient

Normal values	1st day	2nd day	5th day	7th day	16th day
AST(0-41U/L)	20	93	261	280	45
ALT(0-45 U/L)	13	23	61	84	24
CK(0-25U/L)	252	646	2207	2347	150
K(3.5 - 5.1 mmol/L)	2.8	2.9	3.4	4	4.3

Distribution of smoking frequencies by genders.

depletion occurs, which results inseizures. We would like to emphasize that intravenous pyridoxine should be administered as soon as possible in isoniazide intoxications.

Conflict of Interest

The Authors declare noconflict of interest related to this work and do not have any financial relationship with the organization that sponsored the research. This case was presented in the 10th Congress of the Turkish Society of Medical and Surgical Intensive Care Medicine and 2nd Euro-Asian Critical Care Meeting 27-30 November, 2013 İstanbul.

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