Journal of Emergency Medicine Case Reports

J Emerg Med Case Rep 2018; 9: 61-2 | DOI: 10.5152/jemcr.2018.2173

Reversal of Isoniazid-Induced Status Epilepticus Following Pyridoxine

Necmi Baykan[1], Polat Durukan[2]

[1]Clinic of Emergency Medicine, Nevşehir State Hospital, Nevşehir, Turkey
[2]Department of Emergency Medicine, Erciyes University School of Medicine, Kayseri, Turkey

Cite this article as: Baykan N, Dorukan P. Reversal of Isoniazid-Induced Status Epilepticus Following Pyridoxine. J Emerg Med Case Rep 2018; 9: 61-2.

ABSTRACT

Introduction: Intoxication caused by anti-tuberculosis drugs is a rare event in the modern era of medicine. However, high doses of isoniazid may cause convulsion, metabolic acidosis, lactic acidosis, rhabdomyolysis, coma, and eventually death.

Case Report: Sixteen-year-old female patient of foreign nationality with no history of systemic disease or drug use was admitted to the emergency department with decreased level of consciousness. Glasgow Coma Scale was 6; pupils were isochoric; and pupillary light reflexes were bilaterally equal. Metabolic acidosis with high anion gap was detected. Following this, a generalized tonic–clonic seizure occurred. These clinical signs and symptoms led to orotracheal intubation. Metabolic acidosis was treated using NaHCO3. After 10 mg of intravenous diazepam injection, the seizure was stopped.However, three additional convulsions occurred and midazolam was intravenously administered. And finally invtravenous pyridoxine (50 mg/kg/day) infusion was started. The patient gained consciousness after 30 minutes.

Conclusion: Isoniazid intoxication may be successfully treated with early intervention and the administration of pyridoxine, which is the sole treatment modality.

Keywords: Isoniazid intoxication, coma, pyridoxine

Received: 25.10.2017 **Accepted:** 07.02.2018

Introduction

Intoxication cases caused by anti-tuberculosis drugs occur rarely. Isoniazid (INH) is an effective and economically advantageous drug option in the treatment and prophylaxis of tuberculosis (1). Isoniazid (true) inhibits glutamic acid decarboxylase activity, which is dependent on pyridoxal phosphatase and blocks the production of gamma amino butyric acid (GABA). Convulsions occur as a result of these processes (2). In addition, isoniazid reduces the amount of nicotinamide dinucleotide (NAD). Lactate dehydrogenase that converts lactate into pyruvate requires NAD as a cofactor, and decreased levels of NAD levels lead to lactate accumulation and acidosis, which further leads to lactic acidosis accompanied with convulsions in the patient (3).

High doses of INH are associated with metabolic acidosis, convulsions, rhabdomyolysis, lactic acidosis, coma, and even may cause death if not properly treated. The best treatment for INH intoxication-related convulsions is pyridoxine (vitamin B6) administration. Herein we present a case of a patient admitted to the emergency department after intractable seizures and metabolic acidosis with high anion caused by INH intoxication.

Case Report

A 16-year-old female patient of foreign origin weighing approximately 60 kg with no clinical history of systemic disease or drug use was admitted to the emergency department after decreased level of consciousness. Her relatives described that the event

Address for Correspondence:
Necmi Baykan, Clinic of Emergency Medicine, Nevşehir State Hospital, Nevşehir, Turkey
E-mail: drnecmibaykan@gmail.com

occurred 15 minutes prior to admission. Neurological examination findings revealed that Glasgow Coma Scale (GCS) was 6 and pupils were isochoric with bilateral equal pupillary light reflexes. Vital parameters were as follows: blood pressure 96/45 mmHg; pulse rate 138/minute; and oxygen saturation 85%. Findings of biochemical laboratory analysis revealed glucose levels 195 mg/dl; urea 17 mg/dl; creatinine 0.65 mg/dl; sodium 139 mEq/L; potassium 2.8 mEq/L; chlorine 106 mEq/L; calcium 9.3 mg/dl; AST 24 U/L; ALT 12 U/L; CPK: 594 U/L. White blood count was 27100 µ/L. Blood gas values in venous blood were as follows: pH: 6.84, pO_2:66 mmHg, pCO_2: 49 mmHg, HCO_3: 4.3 mEq/L, BE: -25.5 mmol/L, SO_2: 69 mmHg, and lactate:15. The patient was orotracheally intubated due to metabolic acidosis with high anion gap, which was treated using $NaHCO_3$. Subsequently, three times generalized tonic-clonic convulsions occurred and they were treated with a total dose of 15 mg diazepam IV. Computed tomography of the head showed no pathology of acute origin. Urine testing revealed no drug abuse. We have realized that she did not ingest any other drugs. However, relatives of the patient affirmed that the patient ingested approximately 20 tablets of INH (each tablet 300 mg; total estimated 6 grams). We also learnt that this overdose intake was intentional. Gastric lavage was performed and 50-g activated charcoal was administered through a nasogastric tube. Slow intravenous infusion of pyridoxine of 50 mg/kg/day was commenced. Patient gained consciousness after 30 minutes and the patient's GCS score increased. Blood gas values in venous blood at first hour were as follows: pH: 7.14, pO_2:38 mmHg, pCO_2:50 mmHg, HCO_3:12.4 mEq/L, BE:-11.6 mmol/L, and SO_2:78 mmHg. The patient was followed up for another 2 hours in the emergency room and transferred to the intensive care unit, wherein the patient was kept intubated for 20 hours. The vitals were stable when the patient was under mechanical ventilation, and extubation was performed after consciousness unfolded. After extubation, the patient was discharged with in full health and results of biochemical testing were normal. A total duration of 12 hours of $NaHCO_3$ therapy was administered to the patient while the patient was in ED and intensive care unit. In the intensive care unit, general supportive treatment was applied in addition to $NaHCO_3$. The patient's written consent has been obtained for use in a scientific publication using patient's data.

Discussion

High doses of INH may lead to metabolic acidosis, rhabdomyolysis, convulsions, lactic acidosis, coma, and eventually death (1). The therapy regimen consists of supportive treatment and high doses of pyridoxine as the dose should be increased parallel to the doses of INH intake. INH intoxication with 20 mg/kg may lead to light poisoning in the acute phase; doses over 30 mg/kg may cause generalized convulsions; doses over 80 mg/kg may cause drug-resistant and repeated convulsions, lactic acidosis, and coma which may lead to death.

Signs of acute intoxication, such as tachycardia, vomiting, rash, severe ataxia, speech difficulties, peripheric neuritis, vertigo, grand-mal seizures, coma, emerge within 30-120 minutes after INH intake (1). Our patient presented with tachycardia, metabolic acidosis with high anion gap, repeat convulsions, lactic acidosis, and loss-of-consciousness with GCS 6.

INH intoxication causes drug-resistant convulsions by decreasing GABA levels in central nervous system which leads to lower seizure threshold. Convulsions, specifically resistant to barbiturates, are treated more efficiently if antiepileptic drugs are administered together with pyridoxine (4). Therefore, we administered midazolam with pyridoxine.

Muscle contractions during convulsions may rarely lead to rhabdomyolysis, which may be lethal. Moreover, rhabdomyolysis may slow beta-hydroxy-butyric acid metabolism, thus contributing to metabolic acidosis (5). Studies have shown that INH intake over 2.4 grams is directly associated with CPK increase (4). In the present case, CPK levels were increased as a sign of rhabdomyolysis but renal functions were normal; thus, no emergent dialysis was indicated.

Conclusion

Tuberculosis is a still-active disease in our country. INH intoxication cases may occur and may cause death if not properly and urgently treated. Therefore, in emergency departments, the differential diagnosis should include INH intoxication in cases with convulsions with unknown origin and resistant to commonly used antiepileptic drugs, metabolic acidosis with high anion gap, and coma. The only specific antidote for treatment is pyridoxine administered parenterally in equal doses with INH intake.

Informed Consent: Written informed consent was obtained from who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - N.B.; Design - P.D.; Supervision - P.D.; Resources - N.B., P.D.; Materials - N.B.; Data Collection and/or Processing - P.D.; Analysis and/or Interpretation - P.D.; Literature Search - N.B.; Writing Manuscript - N.B., P.D.; Critical Review -P.D.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors have no conflict of interest to declare.

References

1. Lheureux P, Penaloza A, Gris M. Pyridoxine in clinical toxicology: review. Eur J Emerg Med 2005; 12: 78-85. [CrossRef]
2. Coban EK, Dogan VB, Dirik A. A Cause of Status Epilepticus in Turkey: Isoniazide Intoxication. Dusunen Adam: The Journal of Psychiatry and Neurological Science; 2013; 26: 395-7. [CrossRef]
3. Özçeker D, Haşlak F, Yetim A, Çıtak A, Baş F, Tamay Z. A bactericidal agent used with suicidal intent: isoniazid. Journal of the Child 2014; 14: 78-80.
4. Okutur SK, Borlu F, Paksoy F. Acute Isoniazid Intoxication: Convulsion, rhabdomyolysis and metabolic acidosis. Turk J Med Sci 2006; 36: 397-9.
5. Altun D, Çetingök H, Eren GA, Çukurova Z, Hergünsel O. Acute isoniazid intoxication: case report. Medical Journal of Bakırköy 2015; 11: 36-9. [CrossRef]