



Alpha-lipoic acid intoxication in an adolescent girl: Case report and review of the literature

Ergen kız hastada alfa lipoik asit zehirlenmesi: Olgu sunumu ve dizin incelemesi

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The known about this topic

Alpha-lipoic acid is a widely used antioxidant and is also used for the treatment of many diseases such as diabetic neuropathies, autoimmune and neurodegenerative disease, hepatic disorders, and cancer. Although alpha-lipoic acid demonstrates a wide and safe therapeutic range in adults, there is no reported safety dosage in the pediatric population.

Contribution of the study

Alpha-lipoic acid intoxication is a very rare condition in the pediatric population, this is the fifth case reported in the pediatric literature. This patient developed a seizure and coagulopathy emerging with the lowest known dose of alpha-lipoic acid ingestion.

Abstract

Alpha-lipoic acid is a widely used medication that does not need a prescription. Although it is safely used in adults, hitherto no safe dose for children has been reported, and there is no known antidote. The medical literature provides four reports of alpha-lipoic acid intoxication in the pediatric population to date. This case-report is the lowest known dose of alpha-lipoic acid intake leading to poisoning in a teenager.

Keywords: Alpha-lipoic acid, coagulopathy, convulsion, intoxication, teenager

Öz

Alfa-lipoik asit, reçeteleme gerektirmeyen, yaygın olarak kullanılan bir ilaçtır. Yetişkinlerde güvenle kullanılırken çocuklar için güvenli doz aralığı belirlenmemiştir ve bilinen bir antidotu yoktur. Dizinde dört adet alfa lipoik asit zehirlenmesi olgusu sunulmuştur. Şu ana kadar çocuklarda adet alfa lipoik asit zehirlenmesine neden olan en düşük dozu olgumuzla bildirmektediriz.

Anahtar sözcükler: Adolesan, alfa lipoik asit, koagülopati, zehirlenme, konvülsiyon

Cite this article as: Polat S, Kılıçaslan Ö, Turan Sönmez F. Alpha-lipoic acid intoxication in an adolescent girl: Case report and review of the literature. *Turk Pediatri Ars* 2020; 55(3): 328–30.

Introduction

Alpha-lipoic acid (ALA), first defined by Reed et al. (1) in 1951, is a widely used antioxidant. Taking advantage of its effect on terminating free radicals, chelating metal ions, increasing cytosolic glutathione and vitamin C levels, ALA has been described as a potent biologic antioxidant and a detoxification agent in the treatment of heavy metal exposure, alpha-amanitin, and acetaminophen intoxications (2–4). Alpha-lipoic acid is also used for the dietary

supplement, treatment of many diseases such as diabetic neuropathies, autoimmune and neurodegenerative disease, hepatic disorders, and cancer (3, 4).

The preparation is not needed to be prescribed in many countries. It is known to have a broad and safe therapeutic range in adults; the most common adverse effect of ALA is gastrointestinal adverse effects, which emerge over 2400 mg/day of ALA intake (3, 4). Hitherto, no safety data regarding dosage in children have been reported.

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Received/Geliş Tarihi: 11.03.2019 **Accepted/Kabul Tarihi:** 06.12.2019

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DOI: 10.14744/TurkPediatriArs.2019.66564

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Table 1. Review of features and clinical presentation of ALA intoxication cases

Features of the cases	Ozçetin, M. (2012)	Karaaslan, U. (2013)	Hadzik, B. (2014)	Tolunay, O. (2015)	The present case (2017)
Age	10 months	20 months	14 years	14 months	16 years
Weight	Not specified	10.5 kg	40 kg	Not Specified	60 kg
Dose of ALA	Not specified	226 mg/kg	150 mg/kg	Not Specified	30 mg/kg
Symptom onset	4 hours	4 hours	Not Specified	2 hours	2 hours
Symptoms on admission	Convulsion	Lethargy, vomiting, involuntary movements	Convulsion	Lethargy, vomiting, involuntary movements	Lethargy, vomiting, involuntary movements
Severity of convulsion	Status, resistant to antiepileptics	Status, resistant to antiepileptics	Status, resistant to antiepileptics	Status, resistant to antiepileptics	Non-status
Coagulopathy	None	None	Severe	None	Moderate
MODS	None	None	Developed	None	None
Hospitalisation	8 days	5 days	Exitus	8 days	5 days

ALA: Alpha-lipoic acid; MODS: Multiple organ dysfunction syndrome

Animal studies provide extensive data; the lethal dose (LD50) level in dogs is reported as between 400–500 mg/kg. Also, hepatic and renal failure following overdose ALA exposure has been reported (3, 4). There is no known antidote for ALA intoxication.

We present a case of a teenage girl presented with seizures and coagulopathy after ALA intake of about 30 mg/kg. This case is the fifth ALA intoxication report found in the pediatric literature, and as far as we know, ALA intoxication after ingestion of the lowest dose reported.

Case

A previously healthy 16-year-old girl was admitted to the emergency department with confusion and vomiting. She weighed approximately 60 kg. She had no previous long-term medication history or epilepsy. She had a stable vital status but nystagmus and axial tremor on admission, shortly after admission she developed tonic-clonic seizures. The seizures were responsive to bolus midazolam and gradually stopped within several minutes.

In her medical history, we learned that approximately two hours before her admission, the patient took three pills, each of 600 mg ALA to self-treat her headache with intervals of half-an-hour. We calculated from the total 1800 mg of ingested drug the dose was about 30 mg/kg.

The laboratory examination revealed hyperglycemia: 163 mg/dL (N: 75–100), leukocytosis: 27800/mm³ (N: 3700–10 400) with negative CRP (complement reactive protein) value, normal hepatic and renal functions, and

normal serum iron levels. Coagulopathy was detected; PT: 20.7 sec, aPTT: 35.8 sec, INR: 1.74. Blood gas analysis revealed metabolic acidosis with a high anion gap (pH: 7.07; HCO₃: 13.3 mmol/L; BE: -14.2 mmol/L; and lactate: 10 mg/dL).

The patient was hospitalized and referred to the pediatric intensive care unit. Intravenous bicarbonate support was given for acidosis and coagulopathy was treated with vitamin K and fresh frozen plasma (FFP).

Cranial imaging (computed tomography and magnetic resonance imaging) performed for differential diagnosis showed no abnormality and so excluded possible underlying intracranial pathologies. The acidosis and coagulopathy resolved within 24 hours, again, neurologic symptoms were successfully treated. No further recurrence of the symptoms was observed. She was discharged without sequelae on the fifth day of follow-up.

Written informed consent was obtained from the parents of the patient for publication.

Discussion

Here, we reported a case of ALA intoxication in an adolescent girl, who initially presented with apathy, vomiting, followed convulsions, acidosis, and coagulopathy. To the best of our knowledge, this is only the fifth case reported in the pediatric literature about oral ALA intoxication. Moreover, the importance of this case is that our patient developed a seizure and coagulopathy emerging with the lowest known dose of ALA ingestion.

Alpha-lipoic acid is well investigated in animal studies; high-dose intake seems to be well tolerated. The LD50 was reported as 1130 mg/kg/day and 502 mg/kg/day for rats and mice, respectively (3, 4). Although ALA demonstrates a wide and safe therapeutic range in adults, there is no reported data on safety dosages in the pediatric population. Different studies conducted with a total of 1300 volunteers reported the adult safety dosage of ALA as 600–2400 mg/day (4, 5).

The half-life of ALA, when taken orally, is a mere 30 min. We performed gastric lavage, and probably this intervention prevented the further dramatic results that were observed in previous ALA intoxication cases (2, 4–7). Even though it was not performed in previous cases (6), it is evident that gastric lavage may bring benefit. In our case, we observed coagulopathy in the initial stage. The potential risks of organ damage and bleeding diathesis that ALA overdose could lead to (2) encouraged us to initiate vitamin K and FFP treatment immediately. Normalised coagulation values on follow-up proved our treatment strategy.

Our case is not the first ALA intoxication case that developed metabolic acidosis. ALA affects mitochondrial permeability via its prooxidant effect and this fact is ascribed to the resulting metabolic acidosis (4). Convulsions after ALA overdose has been reported before. Tolunay et al. (5) reported a case of patient with ALA intoxication presenting with seizures resistant to antiepileptic drugs and resulting with intubation. The effect of ALA on intense utilization energy in the central nervous system may be charged for seizures (5). Our patient also developed convulsions during follow-up in the emergency department but was successfully treated with bolus midazolam. A comparison of our case with previous ALA intoxication cases in literature is given in Table 1.

With this case, we aimed to emphasize that supplemental medications such as ALA have no safe dose for children and may lead to severe consequences. Easily accessible non-prescribed medicaments should be under the control of the family.

Informed Consent: Written informed consent was obtained from the parents of the patient for publication.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - S.P., Ö.K.; Design - S.P., F.T.; Supervision - F.T.; Funding - Ö.K.; Analysis and/or Interpretation - S.P.; Literature Review - S.P., F.T.; Writing - S.P., Ö.K.; Critical Review - F.T., Ö.K.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

Hasta Onamı: Hastanın ebeveynlerinden yazılı onam alındı.

Hakem Değerlendirmesi: Dış bağımsız.

Yazar Katkıları: Fikir - S.P., Ö.K.; Tasarım - S.P., F.T.; Denetleme - F.T.; Veri Toplanması ve/veya İşlemesi - Ö.K.; Analiz ve/veya Yorum - S.P.; Literatür Taraması - S.P., F.T.; Yazıyı Yazan - S.P., Ö.K.; Eleştirel İnceleme - F.T., Ö.K.

Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Mali Destek: Yazarlar bu çalışma için mali destek almadıklarını beyan etmişlerdir.

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