Two Cases of Levetiracetam Overdose Without Any Serious Side Effects

Ciddi Bir Yan Etki Olmadan Yüksek Doz Levetirasetam Alan İki Olgu

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ABSTRACT

We present two pediatric cases of levetiracetam overdose. The first case was a 3-year-old girl who was, by her family, accidentally given levetiracetam at 115 mg/kg/day for one-month duration. The second case, a 3-month-old girl who accidentally used 300 mg/kg/day dose about one month. We didn't observe remarkable severe side effects in our patients.

Key Words: Overdose, levetiracetam, epilepsy, children

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ÖZET

Yüksek doz levetirasetam alımı olan 2 vaka sunulmuştur. İlk vaka; 3 yaşında kız hasta, 1 aydır levetirasetamı 115 mg/kg/gün dozda almıştı. 2. vaka olan 3 aylık kız hasta ise levetirasetamı 300 mg/kg/gün dozda 1 ay süreyle kullanmıştı. İzlemlerinde hastalarımızda yüksek doz kullanıma rağmen herhangi bir ciddi yan etki gözlenmedi.

Anahtar Sözcükler: Yüksek doz, levetirasetam, epilepsi, çocuk

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INTRODUCTION

Levetiracetam is a new generated antiepileptic drug that is one of the new choices for infants and young epileptic children with its efficacy, tolerability, and pharmacokinetic characteristics(1). New studies have suggested its wide spectrum efficacy against both partial onset, primary and secondary generalized epilepsies(2). The initial dose of levetiracetam is 1000 mg/day for adult patients. It can be increased to a maximum dose of 3000 mg/day in 2-weeks. Levetiracetam is prescribed as: 30/mg/kg/day, maximum dose: 60 mg/kg/day in children. The most common adverse effects are somnolence, dysphoria, nervousness, irritability, asthenia, and dizziness(3,4). We presented two pediatric patients who have taken overdose levetiracetam without any serious side effects.

CASE REPORT

Case 1

The first case was a 3-year-old girl who had been treated with carbamazepine for epilepsy. Levetiracetam was started as add-on therapy for 30 mg/kg/day due to her refractory seizures. When she came back to her regular clinic visit, we realized that she was given levetiracetam at 115 mg/kg/day for the last one-month duration. The patient was seizure-free, and no remarkable side effects were observed. The mother only complained about patient's nervousness. Her physical examination was normal. Laboratory testing revealed the following; hemogram parameters, liver and kidney function tests and serum electrolyte levels were within normal ranges.

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Levetiracetam serum concentration could not be assessed in our laboratory. The patient was closely followed, and levetiracetam was paused for two days. Subsequently the treatment was resumed to 30 mg/kg/day dose. No new complaints and findings were seen in the following days. However, patient's seizures recurred, and the drug therapy was rearranged.

Case 2

Three-month-old girl was admitted with new onset seizures. Levetiracetam was prescribed as 30 mg/kg/day dose. Family accidentally gave 300 mg/kg/day dose about one month. The patient's seizures decreased in fact, and she had one seizure at this period. Her parents observed no side effects. Her physical examination revealed normal findings. Laboratory testing revealed the following; hemogram parameters, liver and kidney function tests and serum electrolyte levels were normal. Levetiracetam serum concentration could not be assessed in our laboratory. The patient was closely followed, and levetiracetam doses were interrupted for two days. Subsequently treatment was resumed as 30 mg/kg/day dose. Any new complaint and findings were not seen, and seizure number was not increased following days.

DISCUSSION

Levetiracetam is water-soluble, rapidly and almost completely absorbed (96%) through oral administration. Mean time for maximum blood concentration is 1 -1.5 hours, with an elimination half-life of 6-8 hours in children and adults. It has minimal plasma protein binding, therefore; there is no significant interaction with other drugs for binding sites. The drug is excreted renally, and there is no hepatic metabolism(5,6). In a previous study, side effects profile of levetiracetam in children younger than four years were reported as irritability, somnolence, difficulty in sleeping, dizziness, rash, decreased appetite and hypertrichosis(2).

In the literature, two different forms of overdosing of levetiracetam has been reported. A part of reported cases are single intake of abundant levetiracetam doses and usually for suicide. The other parts of cases are accidental overdose takings of levetiracetam during longer periods. Children, as expected, are within the groups that are subject to drug unintentional. Only a few report of accidental overdose of levetiracetam in children have been presented in the literature to date. The clinical outcome was usually favorable in these children with only minimal adverse effects reported.

In a previous report, two patients at two years and five years age were given accidental overdose of levetiracetam caused no side effects. First patient was administered ten times the recommended dosage for one week, and second patient was administered four times the recommended dosage(7). In another case report which reported a ten-month-old who had Ohtahara syndrome, the child showed no side effects other than apathy after prescribing 300 mg/kg/day of levetiracetam for 35 days(8). Glauser et al. reported a child who received a dosage of 70 mg/kg/day instead of the target dosage of 40 mg/kg/day during the last four weeks with no notable adverse effects(1). Chayasirisobhon et al. reported a 41 years old male patient with epilepsy who intentionally took 126 levetiracetam tablets (500 mg) for suicide presented with mild blurred vision and mild ataxia. The symptoms subsided within one day, and the laboratory tests showed mild leucopenia and mild thrombocytopenia which returned to normal within two months(3).

The other reported 38-years-old woman patient arrived at the emergency department 6 hours after the 30 gr single dose levetiracetam ingestion. The patient was defined as 'obtunded' and had a Glasgow Coma Scale score of 8 and had respiratory depression. After the intubation, ventilation and supportive care her symptoms rapidly resolved, and she was extubated and discharged without any sequelae(8).

According to a record from UCB Pharma, a total of five patients with overdoses between 15 g and 50 g of levetiracetam were described. A patient with high dose intake of 50 g was comatose for two days; another patient with overdose of 27 g was aggressive and irritable. Transient leucopenia, thrombocytopenia and drowsiness arised in patients who ingested 15 grams of drug. None of the patients died because of overdose(9).

In a study from a poison centre, 222 cases who intentionally or unintentionally took single levetiracetam dose ingestions between 2000 and 2009 were reported. In 74 children aged six years or less, there were no major outcomes but one case (1.4%) who had a moderate outcome (not life-threatening and without any residual disability). This study suggested that the ingestion of levetiracetam in children six years age or younger is relatively safe(10).

We didn't see any obvious side effect in our patients. While this is an interesting result, the sample size of patients is very small. Hereby, it does not exclude the possibility of serious side effects in overdose -treated future patients. As pediatric patients who are exposed overdose levetiracetam increase in the literature, levetiracetam is going to be known how much harmless it is on high doses. Also, because we could not see levetiracetam levels in our patients, it is hard to conclude that overdoses of levetiracetam in children cause only minimal symptoms and adverse effects for now.

CONCLUSION

Similar to the previous reports we observed no severe side effects in our patients who received 115 mg/kg/day and 300 mg/kg/day levetiracetam for one month. We can suggest that accidental overdose of levetiracetam in children during the longer period is scarcely associated with serious side effects. However, it requires more reports than present for clear results.

Conflict of interest

No conflict of interest was declared by the authors.

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