

Can High-Dose Levetiracetam Be Safe? A Case Report of Prolonged Accidental High-Dose Levetiracetam Administration and Review of the Literature

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Abstract: Levetiracetam is an antiepileptic drug that has been used both as adjunctive therapy and monotherapy in pediatric patients with epilepsy. We report a patient with cerebral palsy and epilepsy who took 200 mg/kg per day of levetiracetam for 55 days with no apparent adverse effects. Four other cases of accidental overdose were found in the literature; none of these was associated with any apparent adverse effects. These findings suggest that, in at least some cases, levetiracetam doses much higher than the recommended maximum of 60 mg/kg per day can be administered without apparent adverse effects.

Key Words: levetiracetam overdose, epilepsy, children

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Levetiracetam is an antiepileptic drug that has been used both as adjunctive therapy and monotherapy in pediatric patients with epilepsy. It has become one of the most frequently used antiepileptic drugs because of a favorable pharmacokinetic profile and a low incidence of adverse effects.¹ The most commonly reported adverse effects at recommended dose include somnolence, dizziness, asthenia, nervousness, and irritability.² We report a 7-year-old girl in whom there were no apparent adverse effects after 200 mg/kg per day of levetiracetam was administered for 55 days. The usual maximum levetiracetam dosage is 60 mg/kg per day.

CASE REPORT

A 7-year-old girl with spastic diplegia who had been followed up in our child neurology from the age of 1 was prescribed levetiracetam because of refractory seizures after treatment with traditional antiepileptic medications. On 10 occasions, her mother accidentally administered the recommended dose of levetiracetam. She remained on this dose for 55 days at which stage she was admitted to hospital, when the error was discovered.

On examination, she was conscious and oriented. Her blood pressure was 90/50 mm Hg; pulse, 84bpm; respiratory rate, 20 breaths per minute; and temperature, 37.6°C. General examination revealed no abnormality. Examination of the central nervous system revealed increased deep tendon reflexes in the lower extremities, positive babinski sign, and ankle clonus. No additional examination abnormality was detected in addition to previous findings before levetiracetam was prescribed.

Laboratory investigations showed normal values of blood counts, chemistry, electrolytes, and thyroid functions tests. We

could not measure the serum concentration of levetiracetam, because of the lack of analysis of serum levels in our hospital.

The patient was hospitalized for observation of levetiracetam adverse effects. The drug was immediately administered at the correct dose (40 mg/kg), and no additional adverse effects were observed. The patient was discharged after 5 days with her correct dose of levetiracetam. No seizure recurrence was seen in either hospital follow-up or 1-year follow-up.

DISCUSSION

Levetiracetam is a novel antiepileptic drug with a favorable efficacy-tolerability ratio and a unique mechanism of action.³ There are limited published data on accidental high-dose levetiracetam administration in young children, and there is uncertainty about what levels are likely to be toxic. The maximum recommended dose of levetiracetam in children aged 4 to 16 years is 60 mg/kg per day.⁴ We report a patient who was inadvertently treated with a dosage of 200 mg/kg per day of levetiracetam for 55 days without any apparent adverse effects.

We performed a PubMed search with the terms “levetiracetam overdose” and “children,” including all English and Spanish articles in our search. We found only 4 pediatric case documents on long-term use of high-dose levetiracetam. The cases are summarized in Table 1.

Recently, a study published by Lewis et al,⁵ which was a review of levetiracetam ingestions in children younger than 6 years report to a poison center, the most common symptoms were drowsiness and ataxia. In this review, only 2 patients admitted to hospital included a 2-month-old infant who was accidentally given a dose 10 times that of her usual dose and a 3-year-old child who was lethargic on arrival to the hospital given an unknown dose. Of all the cases, only 1 patient had moderate adverse effects. No patients died as a result of following unintentional ingestion of levetiracetam.

Similarly, in another study, Bodmer et al⁶ reported no serious adverse effects and 1 moderate outcome in 74 children aged 6 years or below. The moderate outcome was described by the authors as showing symptoms and signs as a consequence of the exposure that were more pronounced or more systemic in nature than minor symptoms, but were not life threatening and there was no residual disability. Furthermore, in this study that reported that most cases received unintentional ingestions of levetiracetam, only 27 cases received intentional ingestions of levetiracetam with a range of dose 750 mg to 4750 mg, respectively.

Özkale et al⁷ described a 10-month-old female infant who was given 10 times the recommended dose of levetiracetam for 35 days; no adverse effects were observed. Awaad⁸ reported 2 patients who were unintentionally administered high doses of levetiracetam. A 2-year-old girl was accidentally given a dose 10 times the recommended dose. The other patient was a 5-year-old child who received 4 times the recommended dose. The author stated that levetiracetam treatment was terminated immediately

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TABLE 1. Demographic and Clinical Data of 4 Patients With Long-Term Levetiracetam Overdose

Patient Number	Age, mo/Sex	The Amount and Duration of the Received Levetiracetam	Underlying Disease	Clinical Sequelae
1*	24/F	10× recommended dose, 1 wk	CP + epilepsy	None
2†	60/F	10× recommended dose, 4 wk	Epilepsy	Mild itching
3‡	N/A	71.4 mg/kg per day, 4 wk	Epilepsy	None
4§	10/F	10× recommended dose, 5 wk	Ohtahara syndrome	None

*Awaad, 2007.

†Awaad, 2007.

‡Glauser, 2002.

§Özkale, 2014.

CP, cerebral palsy; F, female; N/A, not available.

and resumed after 10 days in both patients, and no serious adverse effects were observed during the observation in the hospital.

The clinical findings in our case were similar to those reported in the literature, with spontaneous recovery and no evident adverse effects, even at the highest doses reported typically 10 times the recommended dose.

In conclusion, the clinical course of our patient is consistent with the cases reported in the literature of children who were inadvertently administered or ingested high-dose levetiracetam. In no case was any serious adverse effects reported. However, further studies are necessary to determine thresholds for levetiracetam toxicity.

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