

# Hallucination: A rare complication of levetiracetam therapy

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## ABSTRACT

Levetiracetam is a new antiepileptic drug. In addition to epilepsy, it is also used for treating anxiety disorders and dystonia as well as tardive dyskinesia associated with the use of levodopa and neuroleptic drugs. Phenytoin therapy in a 10-year-old boy with convulsions was discontinued following cardiac rhythm impairment. The patient was then started on levetiracetam. However, visual and auditory hallucinations were observed on the 1st day of levetiracetam therapy. Levetiracetam was discontinued and replaced with sodium valproate, and the hallucinations resolved. The purpose of this report was to remind physicians that hallucinations are one of the rare complications of levetiracetam.

*Keywords: Adverse events; child; levetiracetam.*

Levetiracetam (LEV) is an S-enantiomer pyrrolidine-type antiepileptic. In addition to epilepsy, it is also used for treating anxiety disorders and dystonia as well as for treating tardive dyskinesia associated with the use of levodopa and neuroleptic drugs. It is widely used because of its safe drug profile and pharmacokinetic properties and low hepatic metabolism [1].

We describe a patient started on LEV therapy for epileptic seizure, which was discontinued because of hallucination and subsequent clinical improvement was observed.

## CASE REPORT

We learned that a 10-year-old male patient referred to our clinic had been intubated because of loss of consciousness following syncope, extubated within 24 h, and started on iv phenytoin therapy following convulsion. At physical examination, his body weight was 20 kg, height was 130 cm, body temperature was 36.6°C, pulse was 98 min, and respiration rate was 20/min. His Glasgow Coma Score was 13. Physical examination revealed no meningeal signs, pupils were normal and reactive, and there was normal muscles tone. He was confused and opened

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his eyes on verbal warning. The respiratory system and abdomen were all normal. The antibiotic and antiepileptic treatment that the patient was receiving was maintained. Electrocardiography revealed rhythm irregularity in the form of ventricular extrasystoles, and phenytoin was discontinued. The ventricular extrasystoles resolved during monitoring. Following recurrence of generalized tonic-clonic seizure, the patient was started on LEV (Keppra, 500 mg/5 ml vial) at a dose of 20 mg/kg per day as recommended by the pediatric neurology department. Seizures were controlled, but the patient began experiencing visual and auditory hallucinations (e.g., my mother is calling, a snake is coming, it is going to bite me, and catch the snake) 3–4 times a day. Laboratory investigations, i.e., complete blood count, serum electrolyte levels, and renal and liver function tests were normal. Cranial magnetic resonance imaging and electroencephalography (EEG) were normal. Hallucinations were provisionally attributed to the antiepileptic therapy, and LEV was discontinued and replaced with sodium valproate. There was no history of head injury or psychiatric disorder in the past or in any other family members. Developmentally, he was normal. The patient recovered from his hallucinations within 48 h, and he was transferred to the pediatric ward.

## DISCUSSION

The new antiepileptic drug LEV is an S-enantiomer of piracetam. Levetiracetam partially blocks N-type high-voltage activated calcium channels, thus reducing calcium release from intraneuronal stores and reversing negative allosteric effects of gamma amino butyric acid and glycine. It has no effect on Na<sup>+</sup> or T-type Ca<sup>2+</sup> channels. Levetiracetam is completely absorbed by the gastrointestinal system following oral administration and is eliminated unchanged with urine [2, 3].

Levetiracetam is a powerful and generally well-tolerated antiepileptic drug in children. Levetiracetam-related side-effects are observed at a level of 17.2%–51.3% and generally appear within the first 5 months of treatment [4]. Side-effects most commonly affect the central nervous system and are

generally mild. A study by Idris et al. [5] evaluating the effectiveness of LEV in refractory epilepsies reported side-effects of irritability in 11% patients, somnolence in 7.5%, confusion in 5.6%, impaired gait in 3.7%, decreased perception in 1.8%, speech impairment in 1.8%, lethargy in 1.8%, and enuresis in 1.8%. Coppola et al. [6] reported mild and transient side-effects in 17.2% children with refractory epilepsy; these effects were mostly observed in the first 4 weeks of treatment and these findings decreased with dose reduction.

Studies have reported that irritability, somnolence, confusion, and gait impairment are observed at doses >30–40 mg/kg per day; these side-effects completely resolve when the dose is decreased or the drug is discontinued; and these side-effects are not observed when the dose is gradually increased [7]. However, in a study on 200 children with refractory epilepsy, Peake et al. [8] showed that side-effects were not dose-dependent. They reported emotional and behavioral changes in 24% cases; these side-effects were observed in the first 5 months of treatment and the drug was discontinued in 4% cases and side-effects spontaneously resolved in other cases.

Emphasis has been on various risk factors potentially capable of increasing the probability of LEV use-related psychotic symptoms. These risk factors include febrile convulsion, a history of psychiatric disease in the patient or the family, and existing mental abnormalities [9, 10]. One review of 13 studies, performed in 2014, reported a 2.18-fold higher risk of behavioral side-effects in pediatric patients using LEV compared with the placebo [11].

Shakya et al. [12] reported auditory hallucinations in the 3rd week of LEV use in a 32-year-old patient with refractory epilepsy and that these symptom resolved 3 days after drug discontinuation. Aksoy et al. [13] determined hypokalemia and hypomagnesemia 1 month after LEV use in a 23-year-old male patient and reported that this electrolyte imbalance resolved after gradual drug discontinuation. Other rare side-effects of LEV are skin lesions and hair loss [14].

Levetiracetam is widely used for treating epilep-

sies in pediatric intensive care units. The purpose of this report was to remind physicians that hallucinations are one of the rare complications of LEV.

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