

Case Reports

Disabling Resting Tremors Induced by the Short-term Infusion of Valproate: A Reversible Phenomenon

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Abstract

Background: Drug-induced tremors after long-term administration of anti-epileptics have been described in the literature. Such tremors are usually postural or action in nature with infrequent resting nature.

Case Report: A 23-year-old female presented in status epilepticus. Past and family histories were negative for seizures. She was managed per protocol with valproate. Within hours, she developed resting tremors. The tremors subsided on changing the anti-epileptic.

Discussion: Resting tremors have mostly been described in the literature as long-term side-effects of valproate. This case illustrates that even short-term infusion of valproate can cause resting tremors.

Keywords: Valproate, resting tremors, status epilepticus

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Introduction

Valproate is one of the most widely used first-line anti-epileptics in the management of epilepsy and status epilepticus. Tremors are one of the most common neurological side effects of valproate, and are thought to occur in 6–45% of patients. Approximately 25% of patients taking valproate are found to develop tremors within 3–12 months of initiating therapy.¹ The drug-induced tremors described with valproate are of mild severity and do not require treatment in 76.3% of cases.² Mostly, such tremors are postural or action in nature with infrequent resting tremors.^{1,2} Such resting tremors occur after long-term administration of valproate. To our knowledge, such resting type of disabling tremors after short-term infusion of valproate in the management of status epilepticus is a novel finding.

Case report

A 23-year-old female with no prior comorbidities presented as a neurologic emergency at the Institute of Human Behavior and Allied Sciences, Delhi, India, with generalized status epilepticus. The patient

was actively having generalized tonic–clonic seizures that had been going on for about 30 minutes prior to presentation. Her birth and childhood histories were uneventful. There was no prior history of fever, head injury, or loss of consciousness. She was not on any long-term medication or oral contraceptives. Also, there was no family history of seizures. On examination, there was no sign of injury. She was afebrile, stuporous, and responsive to pain. No meningeal or focal neurological signs were apparent. Her pupils were normal in size and reactive to light. Both sides displayed the extensor plantar reflex. She was treated according to the status epilepticus management protocol. After administration of intravenous lorazepam and sodium valproate in accordance with her body weight, generalized tonic–clonic movements subsided; however, she remained in a postictal drowsy state. The non-contrast computed tomography scan of the head, at this stage, was normal. Thereafter, she was moved to the Neurology Department Intensive Care Unit and was administered intravenous ceftriaxone, pantoprazole, and fluids. Two hours after infusion of valproate, she started to have generalized, large amplitude, resting



Video 1. Generalized, Large Amplitude, Resting Tremors all Over the Body at a Frequency of 4–6 Hertz Induced by the Short Term Infusion of Valproate for Status Epilepticus. The video demonstrates disabling resting tremors all over the body of the patient after infusion of valproate.

tremors all over her body at a frequency of 4–6 hertz (Video 1). The patient was clinically examined again in the ICU. She remained drowsy and afebrile but still there was no focal neurological deficit. There was no rigidity on examination. Additional signs of bradykinesia and the postural/action nature of the tremors could not be elicited, as the patient was in a postictal drowsy state. All the investigations including further neuro-imaging (brain magnetic resonance imaging), hematological, and biochemical tests of serum as well as cerebrospinal fluid were normal. A bedside electroencephalography (EEG) was done at this stage, which showed movement artifacts, but epileptiform discharges were absent. The patient could not be tested for entrainment or distractibility as she was not conscious enough for the tests.

A further dose of valproate was discontinued, and she was switched to levetiracetam. On the fourth day, the patient regained consciousness. She was evaluated clinically. Astonishingly, there were minimal tremors with no signs of entrainment or distractibility, no rigidity, bradykinesia, or sensory or cerebellar deficits. The EEG was non-revealing. Five days



Video 2. The Patient from Video 1 at Initial Follow-up. The video shows complete disappearance of resting tremors after 5 days of stopping valproate.

after the initial valproate infusion, the tremors subsided completely (Video 2). The patient was discharged in a stable and seizure-free state 10 days after admission. The patient has been under outpatient department follow-up since then.

Discussion

Tremors are one of the common side effects of certain anti-epileptics, commonly sodium valproate.³ Such drug-induced tremors are usually postural or action in nature, with infrequent resting tremors, which develop over a period of time.⁴ This case is unusual in three aspects: firstly, tremors were disabling and not mild; secondly, disabling resting tremors occurred after a short-term infusion of valproate for the management of status epilepticus; and, thirdly, such resting tremors are completely reversible within a short timespan, after switching to another anti-epileptic.

Physicians have to be aware of the appearance of valproate-induced tremors after a short-term infusion in the management of status epilepticus. Other common anti-epileptics, where tremors are reported, include lamotrigine and zonisamide.³ In our case, although the

seizures were controlled after the valproate infusion, she subsequently developed, as a side effect, large-amplitude rest tremors involving the whole body. She remained seizure and tremor free after switching to levetiracetam, another first-line antiepileptic in the management of status epilepticus and is doing well in the follow up.

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