

# Intravenous Levetiracetam in Refractory Status Epilepticus

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## Abstract

Refractory status epilepticus is defined as seizures, which last longer than 60 minutes despite treatment with a benzodiazepine and an adequate loading dose of intravenous antiepileptic drug. It has a high mortality and requires prompt management. Currently available drugs like midazolam, pentobarbital and propofol can cause hypotension and respiratory depression. We present control of Refractory status in three critically ill patients using intravenous levetiracetam, which has a unique drug profile.

## INTRODUCTION

Refractory status epilepticus (RSE) is defined<sup>1</sup> as seizures, which last longer than 60 minutes despite treatment with a benzodiazepine and an adequate loading dose of intravenous antiepileptic drug. Mortality ranges from 32-77%<sup>2</sup> and is compounded by other co morbid conditions and multiple organ dysfunctions in patients in the intensive care unit. RSE may cause irreversible brain injury.<sup>3</sup> The presently recommended drugs are midazolam, pentobarbital and propofol; which may necessitate ionotropic and ventilatory support.<sup>4</sup> Thus arises the need for early control of RSE using safer drugs. Levetiracetam (LEV) has a unique profile in lacking drug interactions as well as significant metabolism in the body<sup>5</sup> and may be a good alternative to the recommended drugs. We present three cases of RSE where Levetiracetam, given intravenously has been successful in abating RSE.

Case 1: A 35 year old male met with an accident involving blunt trauma to the abdomen. He presented to the hospital 1 day after injury with pain abdomen and disorientation. CT scan of the head was normal but CT of the abdomen revealed Liver injury grade 4. Vitals were stable. Patient was admitted to the Intensive Care unit and monitored closely. Apart from a serum bilirubin of 2.2 mg/dl, rest of the parameters were normal. On the 3<sup>rd</sup> day of injury patients had Refractory status epilepticus. Despite 12 mg lorazepam and a bolus of phenytoin it did not control. 500mg levetiracetam was given intravenously over 30 min. At 25 min the seizure stopped. Patient was continued on 500mg bd of the drug orally and was seizure free at 14 days.

Case 2: A 48-year-old woman was admitted to the ICU with a 3-day history of drowsiness, respiratory distress and intermittent fever. She had undergone repair for perforated duodenal ulcer 3 months back. At admission she had to be intubated and put on ventilatory support. She was suspected to have leak with peritonitis and sepsis. An exploratory laprotomy was performed with closure of the perforation and lavage. She was also tracheostomised. On 7<sup>th</sup> postoperative day she was put on a T piece as part of weaning when she developed R sided focal seizures with secondary generalizations. On reviewing the history she was found to have pregnancy induced hypertension 20 years back, history of seizures was doubtful; Mild head injury an year back. Despite 12 mg lorazepam, 4 mg diazepam and a loading dose of 800mg phenytoin seizure could not be controlled. Intravenous Levetiracetam was given dissolved in 100cc normal saline over 30 min, by this time the seizure had stopped. Patient was started on Levetiracetam 500mg bd. However after 48 hours she again had an episode of focal seizure. The dose of Levetiracetam was increased to 1500mg/day and carbamazepine 200mg added. Patient was seizure free at 14 days and successfully weaned of ventilator.

There were no signs of meningitis; CT Scan of the head was normal. Serum electrolytes and blood gases were normal. Cause of seizure was most likely tissue hypoxia.

Case 3: A 65-year man, presented with drowsiness of one-day duration. He had been diagnosed as Non Hodgkin's Lymphoma and undergone chemotherapy and radiotherapy. A CT scan revealed communicating hydrocephalus; VP shunt was done for the same, which relieved the symptoms.

However two days post operatively he developed right focal seizures, with secondary generalization. Phenytoin sodium was given as loading dose, preceded by diazepam. The seizure still continued till one hour. 1 gram of Intravenous levetiracetam was given over 15 minutes and by 30 minute the seizure had stopped. Leviteracetam 500mg twice a day was continued. Biochemical parameters, oxygenation was normal. Contrast MRI revealed a picture suggestive of infiltration of meninges of brain as well as the spinal cord. Ventricles were collapsed and shunt was in position Patient underwent radiotherapy again ad has been seizure free.

### **DISCUSSION**

The pharmacokinetics of levetiracetam were described by Pastalos. <sup>5</sup> He reported a bioavailability of 95% after oral ingestion, no protein binding, no hepatic or renal metabolism (34% dose metabolized 66% excreted unmetabolised in urine; metabolism is by hydrolysis in blood). There was no auto induction and no evidence of accumulation on multiple dosing. Moreover no clinically relevant interactions with other AED's were identified .He recommended the pharmacokinetics of levetiracetam as highly favorable and usage simple and straightforward. The successful use of oral LEV for RSE has been reported. <sup>6</sup> Ramel etal have demonstrated the safety and tolerability of intravenous LEV even at doses higher than those proposed. <sup>7</sup> The first clinical experience for intravenous LEV for status epilepticus was reported by Moddel etal. <sup>8</sup>

LEV merits larger trials for patients of refractory status epilepticus and can be of much help especially in critically

ill patients in the Intensive care where multiple factors may be causative for the seizure a drug with the features of LEV is well suited. In our patients also this unique profile of LEV led to it being used successfully in both the patients

### **CONCLUSIONS**

Levetiracetam, owing to minimal drug interactions, can be used to control refractory status epilepticus effectively, especially for patients in the ICU.

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