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**Clinical Question:** Can Levetiracetam (Keppra) be used as effectively as an adjunctive treatment for refractory status epilepticus in pediatric patients, as has been demonstrated in adults.

**Citation:** Kim J, Ryu HW, Lim BC, et al. Effectiveness of Intravenous Levetiracetam as an Adjunctive Treatment in Pediatric Refractory Status Epilepticus. *Pediatric Emergency Care*. 2014 Aug; 30(8): 525-527.

**Introduction:** In cases of status epilepticus (SE) in pediatric patients, approximately 9% are refractory. Initial treatments of SE consist of benzodiazepines phenytoin or phenobarbital, or both. 10%-15% of cases of SE are refractory to these initial treatments. In such cases, additional drugs such as higher doses of the initial drugs, propofol, inhaled anesthesia and ketamine are considered. These drugs all can have severe side effects and result in negative cardiopulmonary effects. IV levetiracetam has fewer severe side effects and drug-to-drug interactions. It has been approved by the FDA for use in patients older than 16 as adjunctive therapy for SE. Few studies have assessed the effectiveness and safety of levetiracetam in pediatric patients with SE and even fewer in those with refractory SE.

### **Methods:**

DESIGN: Retrospective cohort

STUDY POPULATION: 14 patients; mean age was  $4.4 \pm 5.5$  years (range 4 days to 14.6 years); Patients were split into two age groups, Group A (0-2 y, 7 patients) and Group B (>2y, 7 patients) and these two age groups were compared; 10 of the patients were neurologically healthy prior to developing SE, while 4 had already been taking antiepileptics for an underlying diagnosis of SE. Four of the patients had nonconvulsive SE. Exclusion criteria included: "Where the medication was changed to an intravenous form from equivalent preexisting oral doses, the case was excluded from the study."

TREATMENT: Benzos as initial treatment, then, if seizure persisted, IV phenobarbital, phenytoin and/or valproate were used. The loading dose of levetiracetam was 20-30 mg/kg over 15 minutes, with an average loading dose of  $26 \pm 4.6$  mg/kg.

OUTCOME MEASURE: Complete termination of seizure, defined as complete stoppage of convulsive activities within 20 minutes of completion of the infusions and not recurring within the next 24 hours.

Termination of nonconvulsive SE was determined to be the regaining of consciousness or disappearance of epileptiform discharges on EEG.

**Results:** After administration of levetiracetam, 6 of the 14 (43%) patients showed termination of seizures. Five of the 10 (50%) with convulsive SE and 1 of the 4 (25%) with nonconvulsive SE had termination. An average of  $3.1 \pm 0.9$  IV antiepileptics were given before administering levetiracetam. In Group A (younger than 2), the average dose was  $25.6 \pm 5.2$  mg/kg which was similar to that in Group B (> 2 years), which was  $25.4 \pm 4.2$  mg/kg. 4 patients in Group A (57%) responded with seizure cessation. In Group B, 2 of the patients (28.6%) responded. There was no statistically significant difference between the two groups however; with a P-value of 0.592. The average number of IV antiepileptics given prior to administration of levetiracetam was  $2.7 \pm 1.0$  in Group A and  $3.6 \pm 0.5$  in Group B. None the patients involved experienced adverse events during or after administration of the levetiracetam.

**Discussion:** This study demonstrated a rate of termination of SE of 43%. Adult studies have demonstrated termination rates up to 57.5%. The authors point out that their rate of termination was lower than that of previous studies, which had looked at SE and not specifically refractory SE. While 43% termination rate does not seem significant, the safety and minimal adverse side effects of levetiracetam makes its use worth attempting. It should be noted that the results are limited by the small sample size.

**Limitations:** The retrospective cohort study design is not the ideal study format; RCT would be the better study design. Also, this study had a very small sample size. This study also did not account for the cause of seizure; 3 of the patients had seizures secondary to cardiac arrest, respiratory arrest or hypoxic-ischemic encephalopathy secondary to perinatal asphyxia.

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