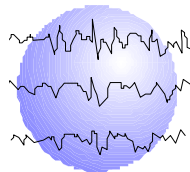


**REVIEW OF OVER 400 INTRAVENEOUS
LEVETIRACETAM ADMINISTRATIONS IN
PEDIATRIC PATIENTS AGES NEWBORN
THROUGH 11 YEARS OF AGE**

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ABSTRACT

RATIONALE: Levetiracetam (LEV) is a widely prescribed antiepileptic drug in adult and pediatric patients. The availability of the intravenous (IV) formulation, approved in adults, provides a continuum of care when oral is not an option. Little information is available on IV LEV in pediatric patients. We investigated the usage, administration technique and tolerability of IV LEV in pediatric patients under 12 years old.

METHODS: With IRB approval, a list of children who initiated IV LEV between August 2006 and April 8, 2007 at Children's Hospitals and Clinics - St. Paul was generated through computer inquiry. A chart review was performed on all children meeting age criteria. Data collected included demographics, dosing, administration procedures, reason for use and discontinuation and adverse effects (AE).

RESULTS: 48 pediatric patients (25 males, 23 females) under 12 years of age (range: 1day-11 yrs,10 mo; median: 22 months) including 7 newborns received a combined total of 401 doses of IV LEV. Two patients received 32.1% of the doses (66 and 63 doses respectively). Single doses ranged from 3.24-51.47 mg/kg/dose (median: 11.9). IV LEV was diluted with either NS or D5W, prepared as a piggyback or in a syringe and administered via pump. The mean IV LEV concentration was 27.8 mg/ml (median: 30 mg/ml; range: 3.66-34 mg/ml). 59.4% of doses were administered via peripheral line (vs. central line) and 94.9% of 399 doses were infused over 15 minutes (range: 10-60 min). For two doses, line type and infusion time were unknown. There were no infusion related AEs except one isolated mild phlebitis rating in the patient receiving 63 total doses. Ten patients had 11 AEs reported and deemed by the treating physician as possibly due to IV LEV: one each for confusion, ataxia, fussiness, chorea and 7 sleepiness/fatigue. 3/10 discontinued IV LEV due to AEs, 6/10 continued IV LEV or transitioned to oral LEV and 1 patient returned to the home AED regimen. Routine vital signs were not required with IV LEV infusions at this institution and therefore were not assessed. Four patients died during IV LEV treatment. No death was deemed by the treating physician as secondary to drug treatment. 25% (12/48) received IV LEV as a continuation of their home oral LEV use for use while unable to take oral. 75% initiated LEV treatment as IV LEV for new onset seizures (29/36) and in patients with known seizures disorders, as an attempt to change from the home AED regimen (5/36) or in place of home oral AED regimens while unable to take oral (2/36). 36/44 (81.8%) patients discharged from the hospital on oral LEV maintenance treatment. 3 discontinued due to side effects, 3 changed back to the original home regimen and 2 discontinued due to lack of acceptable seizure control.

CONCLUSION: Our investigation shows that an average 30 mg/ml IV LEV concentration infused over 15 minutes in patients ages newborn through 11 years of age is easy to administer and well tolerated in both patients exposed to oral LEV or in patients initiating LEV for the first time.

Introduction:

Levetiracetam (LEV) is FDA approved in children ages 4 years and older as adjunctive treatment for partial onset seizures with or without generalization. It is also approved in older children for treatment of myoclonic jerks associated with Juvenile Myoclonic Epilepsy. Experience since 2000 supports LEV as a broad spectrum antiepileptic drug (AED). This benefit as well as its tolerability has resulted in LEV being widely prescribed. An added benefit of LEV is the availability of an alternative route of administration with the FDA approval of the injection formulation in 2006. IV LEV provides a continuum of care when oral administration is not an option. Current published data on IV LEV is in the adult population, however, given the use of oral LEV in children seen at our hospital, use of IV LEV in this population was expected. We investigated the usage, administration technique and tolerability of IV LEV in pediatric patients under 12 years of age.

Methods:

IRB approval was obtained from Children's Hospitals and Clinics of Minnesota to complete a retrospective review of IV LEV use at St. Paul Children's Hospital. A list of all children who received IV LEV between August 2006 and April 8, 2007 was generated through computer inquiry. A chart review was performed on all children who were under 12 years of age. Data collected included demographics, dosing, administration procedures, reason for IV LEV use and its discontinuation, and adverse effects (AE).

Results

Forty-eight pediatric patients under the age of 12 years were identified as receiving at least one dose of IV LEV in the review period. 25 males and 23 females ranging in age from 1 day to 11 years, 10 months received a combined total of 401 doses of IV LEV. 50% of patients were under the age of 2 years including 7 newborn babies (Figure 1). 14/48 patients received a one time dose of IV LEV while 34/48 received multiple IV LEV administrations ranging from 2 to 66 total administrations per patient. 32.1% of the total 401 IV LEV doses were administered in 2 patients: 63 total doses and 66 total doses respectively.

Individual administered doses ranged from 3.24 – 51.47 mg/kg/dose with a median administered dose of 11.9 mg/kg (Figure 2). Each IV LEV dose was diluted with either normal saline or dextrose 5% in water and prepared as a piggyback or in a syringe and administered via pump. The final diluted concentration of each IV LEV dose ranged from 3.66 – 34 mg/ml with a mean and median final concentration of 27.8 mg/ml and 30 mg/ml respectively. Line type and infusion duration were identified in 399/401 IV LEV doses. 59.4% of 399 doses were administered via peripheral line. Infusions of IV LEV ranged in duration from 10 – 60 minutes, however 94.9% were infused over 15 minutes.

The 7 newborn patients received a total of 78 IV LEV doses. Individual doses ranged from 3.24 mg/kg to 51.47 mg/kg (Figure 3). 75.6% of IV LEV doses were diluted to a concentration of 30 mg/ml (range 3.66 – 34 mg/ml) and 97.4% were infused over 15 minutes.

Adverse reactions were minimal. Routine vital signs were not required with IV LEV infusion at this institution and therefore were not assessed. In the 401 IV LEV doses, there was only one isolated mild phlebitis rating associated with one individual IV LEV dose administration. This was documented in the patient receiving a total of 63 IV LEV doses. Ten patients had a total of 11 adverse effects reported and attributed by the treating physician as possibly due to IV LEV (Table 1). Of the ten patients reporting adverse effects, 3 discontinued IV LEV due to the adverse effects, 1 patient discontinued IV LEV to return to the home AED regimen, and 6 continued IV LEV or transitioned to oral LEV.

Four patients died during IV LEV treatment. No death was deemed by the treating physician as secondary to drug treatment. Deaths were attributed due to 1) irreversible brain damage after status epilepticus, 2) withdrawal of life support in a patient with shaken baby syndrome with subdural hemorrhage and ischemic brain injury, 3) cardiac arrest resulting in hypoxic injury, and 4) a massive infarct in a pneumococcal meningitis patient.

The reasons for IV LEV use are identified in Figure 4. 81.8% (36/44) of patients discharged from the hospital on oral LEV. Of the twelve of 48 patients which transitioned from home oral LEV to IV LEV while inpatient, all returned back to oral LEV except one patient who died. Of the 36 patients who initiated LEV treatment for the first time as IV LEV, 3 patients died and 3 patients discontinued IV LEV due to adverse effects. Two patients (newborns) discontinued LEV treatment due to lack of acceptable seizure control. Finally 3 patients transitioned back to their home oral AED regimen. Two had only used IV LEV in place of their oral home AED regimen while inpatient and receiving nothing by mouth. The third patient attempted a change from the oral home AED regimen, required IV AEDs during initial hospitalization, but transitioned to another AED as a result of the epilepsy work-up.

Conclusions:

Our investigation suggests that IV levetiracetam, diluted to an average 30 mg/ml concentration and infused over 15 minutes, in patients ages newborn through 11 years of age is easy to administer and well tolerated in both patients exposed to oral LEV or inpatients initiating LEV for the first time.

(Sources for funding include a grant from UCB Pharma)

Figure 1

Age Demographics

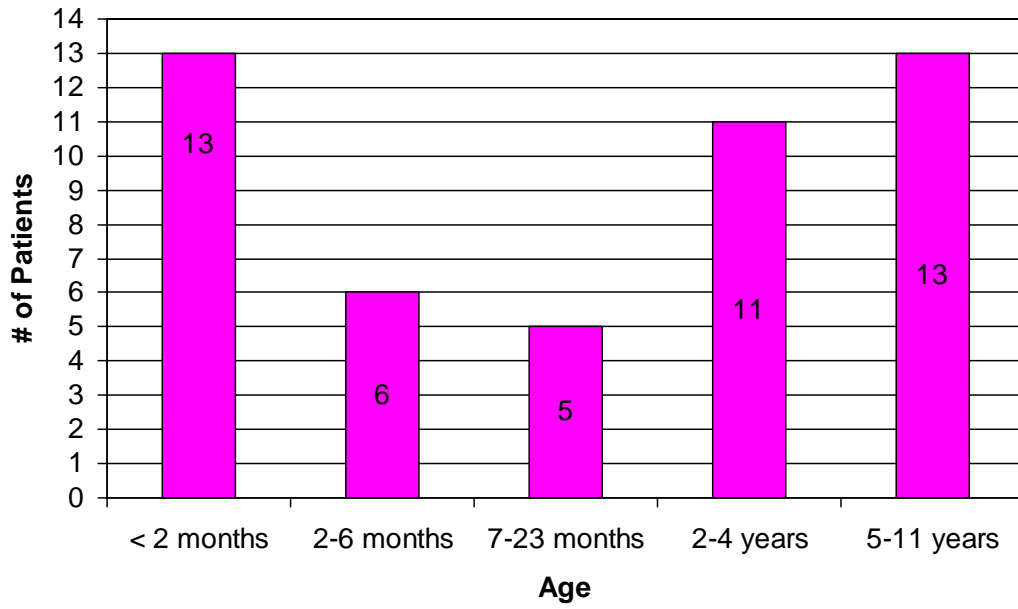


Figure 2

Range of Individual IV LEV Dosages

(N=401)

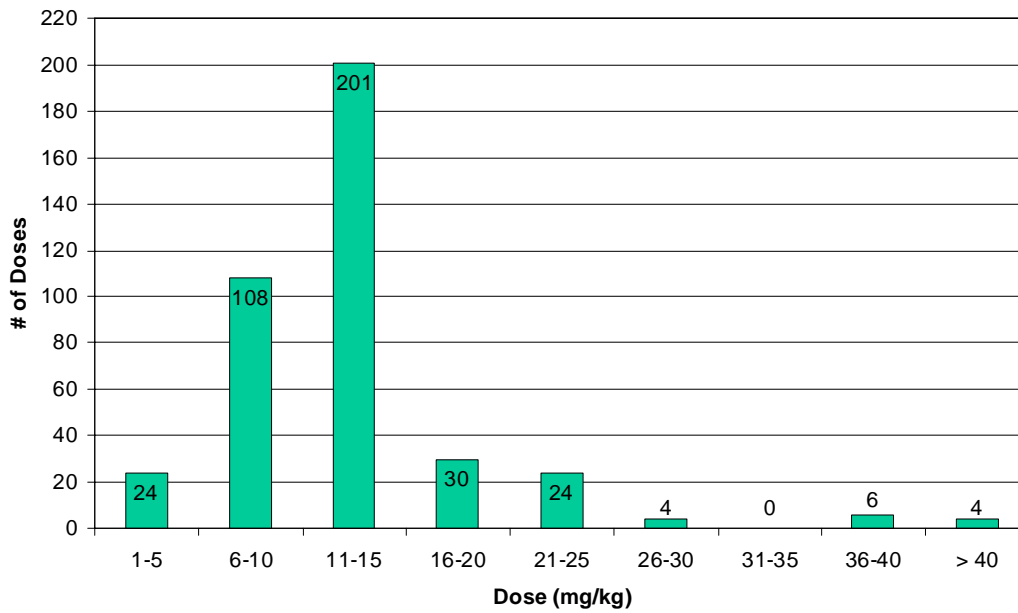


Figure 3 **Range of Individual Newborn IV LEV Dosages**

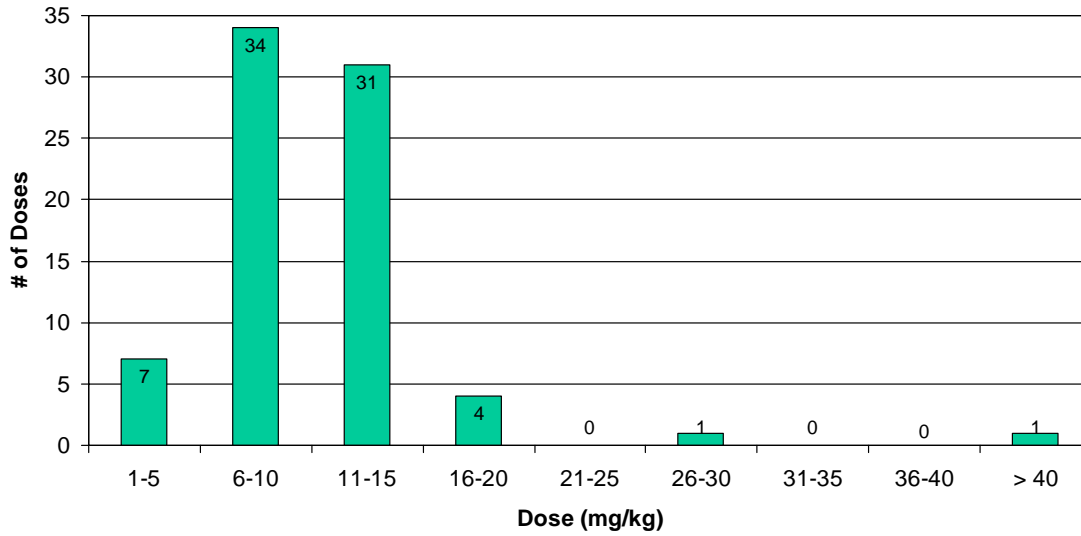


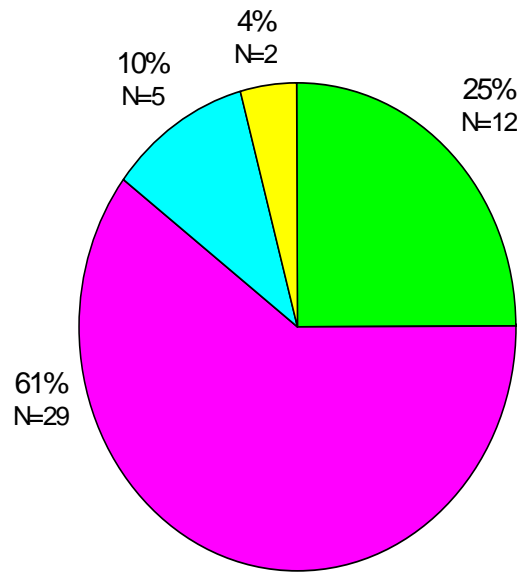
Table 1

Adverse Events

Pt.	Adverse Effects	LEV Naïve?	Age	LEV Duration	# LEV Dose	Dose Range (mg/kg)	LEV Discontinued due to AE?
1	Confusion	Yes	5 yrs, 3 mos	4 days	8	4.9 – 14.7	Yes
2	Severe Ataxia	Yes	7 yrs, 6 mos	1 day	1	9.84	No
3	Sedation	Yes	11 yrs, 10 mos	5 days	13	11.65 – 17.48	Yes
4	Sedation	Yes	4 mos	9 days	23	8.88 – 10	No
5	Sedation	No	3 yrs, 7 mos	2 days	2	5.71	No
6	Lethargy	Yes	8 days	3 days	7	10.03 – 21.27	No
7	Sedation, Fussy	Yes	5 mos	1 day	1	37.09	No
8	Sedation	Yes	Newborn	5 days	7	8.58 – 19.6	No
9	Lethargy	Yes	Newborn	4 days	9	3.24 – 10	Yes
10	Chorea	Yes	4 yrs, 2 mos	2 days	4	9.55 – 17.2	No

Figure 4

Reason for IV LEV Use



- Continuation of Home Oral LEV Regimen
- New Onset Seizures
- Attempt to Change Treatment from Home Regimen in Known Seizure Patient
- Inplace of Home Oral AED Regimen While Unable to Take Oral