Increasing use of, but under-dosing with levetiracetam in benzodiazepine refractory convulsive status epilepticus. Emergency clinicians need updated guidance on alternatives to phenytoin pending trial evidence

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Background

Newer alternatives to phenytoin, levetiracetam and valproate, for established convulsive status epilepticus (CSE) are attractive1, though comparative efficacy and safety is not yet certain pending the outcome of a large trial now underway2. We set out to establish the extent to which current practice in a UK regional neuroscience centre adhered to national/international guidance3, and current evidence in this context.

## Methods

From 133 episodes of SE identified prospectively by coding over 18months, retrospective notes review identified 47 adults (≥16years) with CSE. Patients with postanoxic SE, who arrived intubated, or with missing records were not included. Data on demographics, clinical SE features, treatment and outcomes were collected, and quality assured by the senior investigator. Adequate minimum dosing for each agent was defined ≥90% of the recommended mg/kg (levetiracetam 40; valproate 30; Phenytoin 20), with average UK adult weights used where this had not recorded.

## Results

Benzodiazepines were the initial treatment in all patients. Of 34 patients treated with a 2nd line AED, 1(3%) received Valproate, 18(53%) levetiracetam and 15(44%) phenytoin. Where the dose could be identified, this was most commonly 1000mg for levetiracetam and phenytoin, irrespective of weight. 82% of patients treated with levetiracetam had been under-dosed (mean dose 66%+/- SD29%), and 60% with Phenytoin( 78+/- 22%). 68% were admitted to ICU (mean stay 5 days), of whom 58% had received Levetiracetam and 42% phenytoin (not significant by drug or dose).

## Conclusions

Levetiracetam is being increasingly used in CSE, despite not being licensed nor recommended in most guidance, and in advance of RCT evidence. Valproate is rarely used despite a comparable evidence base1. Phenytoin, and especially levetiracetam are frequently under dosed, despite a conservative threshold for levetiracetam (up to60mg/kg is recommended by some2). Under treatment is likely to affect patient outcomes, and may contribute to high ICU rates in this study. As alternatives to phenytoin are increasingly used, emergency clinicians need urgent guidance for appropriate dosing pending further evidence2.

1. Yasiry, Z and SD Shorvon, Seizure, 2014: **23**(3), p167-174.

2. Bleck, T*, et al.*, Epilepsia, 2013. **54**: p. 89-92.

3. Unterberger, I, Journal of Clinical Neurophysiology, 2016: **33**(1), p10-13.