

Time to Administration of Anticonvulsant Medications in Status Epilepticus and Seizure

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BACKGROUND

A seizure is defined as an abnormal surge of electrical activity in the brain that can lead to convulsions or a loss of consciousness. Any seizure lasting longer than 5 minutes or continuous seizure activity without an interictal period is defined as status epilepticus (SE).¹

SE is a neurological emergency that needs immediate medical attention. Anticonvulsants are used to stop seizures and to treat SE. Guidelines recommend that anticonvulsants should be administered within the first 5 minutes of seizure onset.² A delay in treatment for SE can result in increased morbidity and mortality.

In the SENSE registry, only 32% of the patients received treatment within 30 minutes.³ Factors such as the time needed for the preparation of intravenous piggyback (IVPB) anticonvulsant and pharmacy order verification may delay anticonvulsants administration.⁴

OBJECTIVE

The objective of this study was to quantify the time from order entry to administration of intravenous (IV) fosphenytoin and levetiracetam in the intensive care unit and analyze the associated safety outcomes.

METHODS

Adult patients who had an order for IV levetiracetam or fosphenytoin in the Neuro-Intensive Care Unit (Neuro-ICU) at Weill Cornell Medical Center between January 1, 2017 and December 31, 2019 were screened for inclusion.

Inclusion criteria:

- Documented or presumed status epilepticus or seizure

Exclusion criteria:

- Received the IV anticonvulsant for seizure prophylaxis
- Received first IV anticonvulsant dose outside the hospital

Data collection: age, gender, documented home anticonvulsant, admission and discharge Glasgow Coma Scale (GCS), admission diagnosis, etiology of SE/seizure, benzodiazepine and dose administered, ICU/hospital length of stay, IV anticonvulsant and dose administered, and time from order entry to administration of IV anticonvulsant.

Patients were still included if they experienced SE or seizure outside the hospital, if all other criteria were met.

RESULTS

Table 1: Baseline Characteristics

| | Status Epilepticus (n=15) | Seizure (n=12) | Total (n=27) |
|--------------------------------------|---------------------------|----------------|--------------|
| Age, median (range) | 65 (26-87) | 72 (27-85) | 70 (26-87) |
| Male Gender | 6 (40%) | 7 (54%) | 13 (48%) |
| Home Anticonvulsant | 4 (27%) | 1 (8%) | 5 (19%) |
| Confirmed Event | 17 (100%) | 8 (67%) | 23 (85%) |
| Admission GCS, median (range) | 13 (3-15) | 13 (4-15) | 13 (3-15) |
| Discharge GCS, median (range) | 11 (4-15) | 15 (4-15) | 13 (3-15) |
| Etiology | | | |
| • Brain Trauma | 0 (0%) | 1 (8%) | 1 (4%) |
| • Infection | 1 (7%) | 1 (8%) | 2 (7%) |
| • Non-Adherence | 0 | 0 | 0 |
| • Stroke | 5 (33%) | 7 (58%) | 12 (44%) |
| • Cardiac Arrest | 0 | 0 | 0 |
| • Other | 7 (47%) | 3 (25%) | 10 (37%) |
| • Unknown | 2 (13%) | 0 | 2 (7%) |
| Benzodiazepine | 12 (80%) | 6 (50%) | 18 (67%) |
| Benzodiazepine Agent | | | |
| • Lorazepam | 11 (92%) | 6 (100%) | 17 (94%) |
| • Midazolam | 1 (8%) | 0 (0%) | 1 (6%) |
| IV Anticonvulsant Agent | | | |
| • Levetiracetam | 9 (60%) | 10 (83%) | 19 (70%) |
| • Fosphenytoin | 6 (40%) | 2 (17%) | 8 (30%) |

All values are expressed as the number (%), unless otherwise specified.
 Because of the small sample size, medians rather than means were used to represent the central values.

Table 2: Primary Endpoint

| | Status Epilepticus (n=15) | Seizure (n=12) | Total (n=27) |
|--|---------------------------|----------------|--------------|
| Time (Minutes) to Administration of IV Anticonvulsant | 24.5 (6-91) | 69 (0-158) | 44 (0-158) |
| Time (Minutes) to Administration of IV Anticonvulsant, By Agent | | | |
| • Levetiracetam | 24.5 (8-87) | 69 (0-158) | 33.5 (0-158) |
| • Fosphenytoin | 26 (6-91) | 90.5 (39-142) | 33.5 (6-142) |

All values are expressed as median (IQR).
 Because of the small sample size, medians rather than means were used to represent the central values.

Table 3: Secondary Endpoints

| | Status Epilepticus (n=15) | Seizure (n=12) | Total (n=27) |
|---|---------------------------|----------------|------------------|
| Mortality | 5 (33%) | 3 (25%) | 8 (30%) |
| Documented Infusion Site Reactions | 0 (0%) | 0 (0%) | 0 (0%) |
| ICU Length of Stay (Days), median (range) | 16.0 (2.4-73.9) | 3.5 (1.2-9.9) | 6.5 (1.2-73.9) |
| Hospital Length of Stay (Days), median (range) | 27.6 (7.4-136.5) | 5.9 (1.7-36.2) | 17.5 (1.7-136.5) |
| Received IV Anticonvulsant Within 30 Minutes | 10 (67%) | 3 (25%) | 13 (48%) |
| • Levetiracetam | 6 | 3 | 9 |
| • Fosphenytoin | 4 | 0 | 4 |

All values are expressed as number, (%), unless otherwise specified.

DISCLOSURES

All authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation.

DISCUSSION

Because of the retrospective nature of the study, there are many limitations in providing an accurate picture of the time to administration of anticonvulsants for status epilepticus and seizure patients.

The limitations of this study are:

- Small sample size
- Documented administration times may not always be accurate.
- Patients limited to those who were administered IV levetiracetam and fosphenytoin.
- Inconsistency in documentation of GCS and whether or not patients were on an anticonvulsant at home.
- Only included IVPB levetiracetam and fosphenytoin, so may not be generalizable to all IV anticonvulsants used for SE and seizure.

CONCLUSION

Overall, it took greater than 30 minutes for most patients to receive the first dose anticonvulsant for seizure or status epilepticus. The time to administration was much shorter in the SE group than the seizure group, perhaps due to the emergent nature of SE. Future studies should evaluate changes in administration time with IV push dosing of anticonvulsants.

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