Levetiracetam for seizure prophylaxis after cerebrovascular surgery

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Background

- Cerebrovascular surgery is the operative treatment of blood vessel disease that affects circulation to the brain[1]

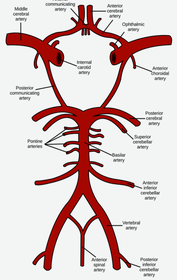


Image 1. Circle of Willis

- Cerebrovascular diseases include aneurysms, arteriovenous malformations (AVM), cavernous malformations, and occlusive vascular diseases
- Type of surgery: elective (no hemorrhage) versus emergent surgery (hemorrhage)

Image 2. Unruptured aneurysm

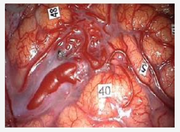


Image 3. AVM

- Incidence of early seizures after cerebrovascular surgery is 2.3%[2]
  - Risk of seizures may be associated with[2,3,4]:
    - Aneurysmal subarachnoid hemorrhage (aSAH)
    - Location of ruptured aneurysm: middle cerebral artery (MCA) or anterior communicating artery (ACoA)
    - Hemorrhage extending to the brain parenchyma or intraventricular space
- Seizure prophylaxis after cerebrovascular surgery
  - Initiating an antiepileptic medication for *primary prevention* of seizures:
    - No history of seizures or antiepileptic medication use ≤ 6 months prior to surgery
  - Variable practices for initiating prophylaxis after cerebrovascular surgery with limited evidence
  - At UCSF, levetiracetam (LEV) is preferred over other antiepileptic medications if prophylaxis is initiated
    - Drug level monitoring is not required and fewer drug interactions
    - Usual dose: LEV 500 mg-1000 mg IV or PO twice daily for ≥ 7 days after surgery

Purpose

To evaluate and establish the standard of care for seizure prophylaxis after cerebrovascular surgery at UCSF Medical Center

Methodology

Study Design:

- Retrospective cohort study from August 1st, 2013 to July 31st, 2015 (N=160)
- Patients ≥ 18 years old admitted for cerebrovascular surgery were reviewed and screened for exclusion criteria
  - Surgical procedure reports were generated, electronic medical records and medications were reviewed

Exclusion Criteria:

- Past medical history of seizures
- Preoperative or intraoperative seizures
- Antiepileptic medications prior to surgery
- Antiepileptic medications besides LEV for prophylaxis

Statistics Analysis: Chi-square test and student's t-test

Primary Outcome: Seizure occurrence in the early (≤ 7 days) postoperative period

Secondary Outcomes: Characteristics or potential risk factors in patients who experienced seizures or were initiated on LEV

Table 1. Baseline demographics

	No LEV n=115	LEV n=45	P-value
Male (%)	34 (30)	20 (44)	0.439
Female (%)	81 (70)	25 (56)	0.577
Age (Mean ± SD)	54 ± 15.8	52 ± 15.9	0.503
Height (cm, mean ± SD)	165 ± 10.6	167 ± 11.1	0.320
Weight (kg, mean ± SD)	76 ± 19.8	75 ± 21.1	0.754

SD = standard deviation; LEV = levetiracetam

Table 2. Seizure occurrence

	No LEV n=115	LEV n=45	P-value
Total Seizures (%)	2 (1.7)	0 (0)	0.373
Unruptured aneurysm (elective surgery)	1	0	-
Ruptured aneurysm (aSAH)	1	0	-

Patient Characteristics

Table 3. Aneurysmal subarachnoid hemorrhages

Type	No LEV n=115	LEV n=45	P-value
aSAH	4	2	0.400
aSAH + IVH	12	2	-
aSAH + IVH + IPH	0	5	-

aSAH=aneurysmal subarachnoid hemorrhage; **IVH**=intraventricular hemorrhage; **IPH**=intraparenchymal hemorrhage

Figure 1. Type of procedure

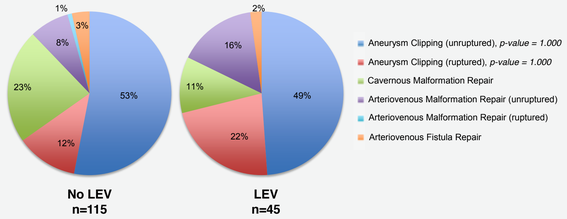


Figure 2. Estimated blood loss from procedure

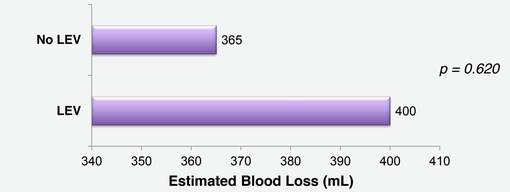
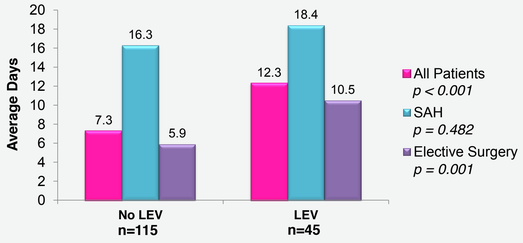


Figure 3. Length of stay



Results

- Of 160 patients who underwent cerebrovascular surgery, only 45 (28%) were started on LEV
- Although seizure occurrence did not reach statistical significance, out of 115 patients who did not receive LEV, only 2 (1.7%) patients experienced early postoperative seizures
- Patients started on LEV in the elective surgery group had a significantly longer length of stay
- There was no correlation between seizure occurrence and aSAH, type of procedure, or blood loss
- Of the aSAH patients, only 1 had early postoperative seizure and the hemorrhage did not extend into the IVH or IPH

Conclusions

- It is possible that cerebrovascular surgeries have a low incidence of early postoperative seizures, where prophylaxis with LEV may not be necessary in lower risk patients, but further studies are needed
- Patients who are initiated on LEV may have prolonged length of stay

Discussion

Study Limitations

- Single-center study, retrospective, small sample size
- Many confounding factors that may contribute to prolonged length of stay
- Seizure occurrence beyond 7 days or after hospital discharge was not captured

Future Directions

- Increase sample size and duration of the study to meet power
- Case-control study design or prospective, randomized, placebo-controlled trial with adequate postoperative follow-up
- Consider other patient characteristics that may increase concern for seizure occurrence after surgery to incorporate into standard guidelines for initiating seizure prophylaxis
  - Location of aneurysm, altered mental status, neurological deficits, edema

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Approved by the UCSF Committee on Human Research