

Prophylactic AEDs after Aneurysmal SAH

- Question: Does treatment with AED therapy following aneurysmal SAH prevent:
 - Subsequent seizures
 - Development of epilepsy
 - Improvement cognitive outcome

Background

- Aneurysmal SAH is associated with seizures, development of post-SAH epilepsy, and cognitive dysfunction
- Current practice is empiric with neurosurgeons treating with AEDs if they were trained to.
- AEDs may have adverse effects
- No randomized data to support either treating or not treating prior to the first seizure

Justification

- Attempt for evidence-based care
- Unclear risk-benefit for treatment prior to vs. after first seizure
- Unclear impact of AEDs on quality of life

Conceptual Approach

- Phase 3 RCT
- Adaptive design potential with different AED arms collapsing to a single best agent
- Treat in ED ASAP after SAH diagnosed (< 12 hrs)
- Hunt-Hess grades 1-4
- No prior sz hx
- Exclude: trauma, isolated peri-mesencephalic SAH, Hunt-Hess grade 5, already on AEDs at time of event

Interventions

- Randomization to intravenous:
 - Placebo
 - Keppra
 - Phosphenytoin
- Adaptive design to lead to single AED
- To maintain double blind – sham AED levels to be titrated along with real levels
- Would EFIC be appropriate?

Outcomes

- Time/occurrence of first seizure (probably cannot justify continuing placebo if a seizure occurs)
- Quality of life measures at 3, 6, & 12 months
- EEG for epileptiform activity
 - 72 hours after start of study drug
 - 3 & 12 months