Valproic Acid for Treatment of Hyperactive or Mixed Delirium in ICU

Study Protocol

NCT02343575

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VPA as an Adjunct Treatment for Hyperactive/Mixed Delirium Study

Medication adjustment protocol:

<u>Adjustments can take place every 24 hours according to the below schedule:</u>

If study physician decides based on the below criteria that medications need to change, they notify RA/pharmacy

	Placebo arm	VPA arm
1. start	➢ **Placebo PO BID** ➢ **Rescue: HAL IV 1-5 mg Q4hr PRN**	➢ **VPA PO 500 mg BID** ➢ **Rescue: HAL IV 1-5 mg Q4hr PRN**
2. If ICDCS = or > 4, RASS = or > 1 and patient cont to meet criteria for hyperactive/mixed delirium, consider increasing meds according to protocol	➢ **Placebo PO BID** ➢ **Rescue: HAL IV 1-5 mg Q4hr PRN**	➢ **VPA 500 mg PO q am, 1000 mg PO QHS** ➢ **Rescue: HAL IV 1-5 mg Q4hr PRN**
3. If need to increase	➢ **Placebo PO BID** ➢ **Rescue: HAL IV 1-5 mg Q4hr PRN**	➢ **VPA 500 mg PO q am, 1500 mg PO QHS** ➢ **Rescue: HAL IV 1-5 mg Q4hr PRN**
4. If need to increase	➢ **Placebo PO BID** ➢ **Rescue: HAL IV 1-5 mg Q4hr PRN**	➢ **VPA 500 mg PO Q am, 2000 mg PO QHS** ➢ **Rescue: HAL IV 1-5 mg Q4hr PRN**

- **Blinded physician evaluates patient daily: clinical exam, ICDSC, DSM V criteria for delirium, EPS, primitive reflexes**
- **Research Assistant daily collects CBC (esp platelets), CMP (esp LFTs), INR, QTc, EPS side effects**
- **If QTC increases by 20% from initiation of medication or equals 500 or above, LFTs increase (ALT > 150, AST> 80) or platelets decrease by 30% or are below 150, research assistant consults with affiliated physician (#2). Physician #2 carefully examines situation and decides whether any of these changes can be due to study medication.**
    - **If No → note is taken, study continues as designed, no unblinding necessary.**
    - **If Yes →study physician #1 is informed and unblinded and the best clinical decision for the patient is taken**
- **Patients will be in the study for total of 7 days or until resolution of delirium (ICDSC < 4 plus 24 hours), whichever is shorter time. If patients need continued treatment after the study resolution, they will be followed by the regular psychiatry consult team.**