May 20th, 12:30 PM

Dantrolene for the Prevention and Treatment of Cerebral Vasospasm after Subarachnoid Hemorrhage – a Randomized Placebo-Controlled Trial to assess Safety, Tolerability and Feasibility

Susanne Muehlschlegel
*University of Massachusetts Medical School, Susanne.Muehlschlegel@umassmemorial.org*

Raphael A. Carandang
*University of Massachusetts Medical School, raphael.carandang@umassmemorial.org*

Wiley R. Hall
*University of Massachusetts Medical School, wiley.hall@umassmemorial.org*

*See next page for additional authors*

Follow this and additional works at: [http://escholarship.umassmed.edu/cts_retreat](http://escholarship.umassmed.edu/cts_retreat)

Part of the [Anesthesiology Commons](http://escholarship.umassmed.edu/cts_retreat), [Neurology Commons](http://escholarship.umassmed.edu/cts_retreat), [Surgery Commons](http://escholarship.umassmed.edu/cts_retreat), [Therapeutics Commons](http://escholarship.umassmed.edu/cts_retreat), and the [Translational Medical Research Commons](http://escholarship.umassmed.edu/cts_retreat)


[http://escholarship.umassmed.edu/cts_retreat/2014/posters/72](http://escholarship.umassmed.edu/cts_retreat/2014/posters/72)

This material is brought to you by eScholarship@UMMS. It has been accepted for inclusion in UMass Center for Clinical and Translational Science Research Retreat by an authorized administrator of eScholarship@UMMS. For more information, please contact Lisa.Palmer@umassmed.edu.
Presenter Information
Susanne Muehlschlegel, Raphael A. Carandang, Wiley R. Hall, Nisha Kini, Saef Izzy, I. Martijn VanDerBom, Thomas F. Flood, Matthew J. Gounis, John P. Weaver, and Bruce A. Barton

Comments
Abstract of poster presented at the 2014 UMass Center for Clinical and Translational Science Research Retreat, held on May 20, 2014 at the University of Massachusetts Medical School, Worcester, Mass.

Creative Commons License
This work is licensed under a Creative Commons Attribution-Noncommercial-Share Alike 3.0 License.

This is available at eScholarship@UMMS: http://escholarship.umassmed.edu/cts_retreat/2014/posters/72
Introduction:
Dantrolene is neuroprotective in animal models and may attenuate cerebral vasospasm (cVSP) after aneurysmal subarachnoid hemorrhage (aSAH) in humans. We evaluated safety/tolerability and feasibility of intravenous dantrolene (IV-D) after aSAH.

Methods:
In this single-center, randomized, double blind, placebo-controlled trial, 31 patients with acute aSAH were randomized to IV-D 1.25 mg IV every 6 hours x 7 days (n=16) or placebo (n=15). Primary endpoint was incidence of hyponatremia (sNa ≤ 134 mmol/L) and liver toxicity (% patients with ALT, AST and AlkPhos >5x upper limit of normal). Secondary safety endpoints included tolerability, systemic hypotension and intracranial hypertension. Efficacy was explored by clinical, transcranial Doppler (TCD) or angiographic cVSP occurrence, delayed cerebral ischemia (DCI) and 3-month modified-Rankin-Scale, Glasgow Outcome Scale and Barthel Index. Statistical analysis was performed using non-parametric tests, generalized estimating equations and mixed models.

Results:
Between IV-D vs. placebo, no differences were observed in the primary outcome (hyponatremia: 44% vs. 67% [p=0.29]; liver toxicity 6% vs. 0% [p=1.0]). Numerically more AEs and SAEs were seen in the IV-D group, but did not reach statistical significance (16 vs. 5 AEs, of which 5 vs. 2 were severe; RR 2.2; 95% CI 0.7-6.7; p=0.16). Three IV-D vs. two placebo patients reached stop criteria: one IV-D patient developed liver toxicity; two patients in each group developed brain edema requiring osmotherapy. No differences in angiographic, TCD, clinical cVSP, DCI, or 3-month functional outcomes were seen. Quantitative angiogram analysis revealed a trend towards increased vessel diameters in the IV-D group after the 7-day infusion-period (p=0.05).

Conclusions:
In this small trial, IV-Dantrolene after aSAH was feasible, tolerable and safe, but was underpowered to show efficacy or outcome differences.

Clinical Trial Registration Information: http://clinicaltrials.gov NCT01024972

Funding: American Heart Association (Scientist Development Grant 09SDG2030022, S.M.); Worcester Research Foundation (2010 Award, S.M.); University of Massachusetts Medical School (Faculty Scholar Award, S.M.); University of Massachusetts Center for Clinical & Translational Science/CTSA (UL1TR000161). The study drug dantrolene (Dantrium®IV) was donated by J.H.P. Pharmaceuticals (Parsippany, NJ). The study was entirely investigator-initiated and neither pharmaceutical company was part of the development, execution and analysis of the study or drafting of any publications.