

## **Synergistic Effect Of Aminoguanidine And Hypertonic Saline Combination As A Neuroprotective Agent After Lateral Fluid-Percussion Brain Injury In The Swine Model**

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### **Purpose**

Neuroinflammation plays a key role in secondary traumatic brain injury (TBI). Inducible nitric oxide synthase (iNOS) is uniquely produced in large amounts, causing neuronal death through glutamate toxicity and oxidative damage. Aminoguanidine (AG), a specific iNOS inhibitor, had been shown in small animal models to reduce ischemic lesion volume as prophylaxis and treatment in traumatic brain injury. We hypothesize that AG and hypertonic saline (HTS), when administered in combination (COUPLER solution), is superior to either agent alone in neuroprotection after TBI.

### **Materials and Methods**

48 swines were divided into 5 treatment groups (controls, no treatment, AG treated, HTS treated, COUPELR treated). Lateral fluid percussive brain injury was induced under general anaesthesia. General and invasive parameters including arterial pressure, intracranial pressure and brain oxygenation/tissue perfusion were recorded. A portion of animals from each treatment group was sacrificed and underwent perfusion plus immunohistochemistry at 2.5 hours, 1 day and 3 days post-injury.

### **Results**

COUPLER was more effective than AG or HTS alone in reducing intracranial pressure, and conferring neuroprotective effects as evidenced by the extent of iNOS production and neuronal apoptosis at various time points post-injury, with no adverse effects on systemic blood pressure. This study is novel in the use of a large animal model to evaluate the effects of an AG containing solution in TBI.

### **Conclusion**

COUPLER solution has a potential role as an early resuscitative fluid in severe traumatic brain injury.