

Gallium compounds for treatment of TBI

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Gallium compounds, which are non-steroids, have been studied for various cancer treatments in animals and humans and found to be effective in a number of trials. In fact, the use of gallium nitrate (GN) is FDA approved for the treatment of hypercalcemia (bone calcium loss) in cancer patients. Also, the anti-inflammatory and neuropathic pain blocking properties of gallium compounds have been studied and are relevant to the treatment of TBI. Gallium compounds have not been studied (except in my study) for the treatment of concussion or traumatic brain injury although the hypercalcemia and neuropathic pain blocking processes are very similar to other applications. The chemical cascade of calcium, resulting from brain damage, occurs rapidly after an injury and gallium compounds can be administered immediately following an injury to reduce the tissue damage. I have not yet commercialized this technology, but patent US Patent 9205108 B2 on "Treatment of Traumatic Brain Injury by Using Gallium Compounds to Reduce Oxidative Stress Levels" was Issued on 12/8/2015 for concussion and traumatic brain injury treatment in my name.

Background:

Giza, C.C. and Hovda, D.A. The Neurometabolic Cascade of Concussion. *J. Athletic Training*. 2001, 36(3), 228-235, describe the series of events following a concussion, including the associated chemical pathways. Immediately following the injury there is a sudden intracellular efflux of potassium and an influx of calcium ions producing a hypercalcemia condition in the brain. The calcium accumulation can lead to cell death and disrupt neurofilaments and microtubules. The calcium accumulation is seen within hours of a concussion and persists for two to four days after an event. Additionally, cerebral swelling as a result of calcium and sodium influx occurs post concussion and further exposes the patient to additional risk.

According to National Institute of Neurological Disorders and Stroke (NINDS), "Discussion on Traumatic Brain Injury: Hope through Research", April 15, 2011, "One area of research that shows promise is the study of the role of calcium ion influx into the damaged neuron as a cause of cell death and general brain tissue swelling".

Product Description:

Gallium compounds are FDA approved to treat hypercalcemia in cancer patients and have also been shown to reduce pulmonary, arthritic and other forms of inflammation. The chemical cascade resulting from brain damage occurs rapidly after an injury and gallium compounds can be administered rapidly through a variety of methods, including transdermally, immediately following an injury to reduce the tissue damage. The FDA-approved GN product called Ganite® has been used for cancer treatment applications.

I conducted a mouse study with researchers at Eastern Kentucky University using a moderate TBI and a dose of gallium nitrate (GN) that is nearly the same as the FDA daily dose approved for hypercalcemia in cancer patients and one that has been used in other applications on animals and on humans. We ran sham, saline and GN treated mice and looked at oxidative stress as a marker for TBI. Western blot assays were run in duplicate for carbonyl oxidation as an overall marker and 3-nitrotyrosine (3-NT) for protein nitration. Even though it is not yet known if oxidative stress is causal in TBI it is a well documented indicator of damage. What we found was, as expected the saline treated mice induced oxidative stress as measured by assay. In the carbonyl assay the GN mice showed a 15% oxidative reduction $p=0.10$ (90% significance) relative to saline and in the 3-NT assay a 96% reduction $p=0.01$ (99% significance) compared to saline in oxidation. These are positive results since they are totally independent markers for concussion damage reduction. Furthermore, gallium nitrate is an oxidizing agent, not an anti-oxidant so one would have expected the opposite oxidation effect aside from the therapeutic benefit. Also, this was the first attempt on the timing of treatment, dose and choice of chemical form for gallium so there is much to do. The study showed no difference in the activity level of any of the classes of mice.

Application:

A gallium compound can be administered to a human or animal who has suffered a concussion or other brain trauma by the most convenient method, with oral, nasal inhalation or transdermally being the preferred methods, to reduce the immediate release of calcium in the brain. The timing of the gallium therapy is very important to stop tissue damage. The potential use of gallium compounds to reduce excess tissue calcium and prevent hypercalcemia in concussion or other brain trauma is the same approach as used in treating cancer patients for hypercalcemia. The additional benefit of rapid edema reduction makes concussion therapy with gallium compounds a good choice for sports related or military injury since it can be administered rapidly immediately following a TBI to reduce or eliminate the potential damage.