Cytoprotective Effects of Antioxidants on Articaine-Induced Astrocyte Toxicity

Shilpa Jhol, MS

Richard White, PhD, FAHA
Harry Komiskey, PhD

Abstract

INTRODUCTION:

As the push to reduce clinic wait times and healthcare spending costs are on the rise, administration of local anesthesia is becoming a popular option in a vast majority of surgical procedures. Anesthetic drugs are thought to mainly target neurons in the brain by suppressing synaptic activity. However, the direct effects of local anesthetics on astrocyte signaling remain largely unknown. Antioxidants such as N-acetylcysteine (NAC) and ubiquinol, may reduce astrocyte reactive oxidative species (ROS) and improve mitochondrial respiration.

In the current study, we propose to investigate the cytoprotective effects of these antioxidants on astrocytes co-treated with articaine and understand articaine's direct effect on astrocyte Kir4.1 channels.

METHODOLGY:

Embryonic rat hippocampal tissue (E18) was obtained and cultures were grown until they reached 80% confluence. Cells were treated with NAC (30uM, 100uM, 300uM) or ubiquinol (30nM, 100nM, 300nM) in a dose-dependent manner for 24 hours and co-treated with articaine (10uM) for an additional 24 hours. Cellular potassium currents were also measured directly via whole-cell patch-clamp technique at a holding potential of -50 mV. Mitochondrial biogenesis was examined using immunofluorescence.

CONCLUSIONS & SIGNIFICANCE:

Both NAC and ubiquinol increased cell viability significantly and reduced the amount of glial fibrillary protein (GFAP) released from rat embryonic astrocytes. Whole-cell readings revealed an inward-rectifying current with a reversal potential of -40mV- -50mV. Addition of barium or articaine attenuated inward-potassium currents. Cells treated with NAC and ubiquinol also showed an upregulation in mitochondrial biogenesis. A novel cellular transduction mechanism may contribute to articaine's toxic effects on astrocytes and thereby decrease astrocyte-neuron signaling. Comparative studies need to be performed to understand articaine's influence on astrocyte-neuron signaling.

Biography

Shilpa Jhol has a Master of Science degree from the Georgia-Philadelphia College of Osteopathic Medicine. Under the direction of her advisor, Dr. Komiskey, Shilpa's current thesis research focuses on how antioxidants and local anesthetics affect astrocyte behavior. Shilpa's passion to understand astrotoxicity stems from her interest in learning about neurological diseases. Shilpa attained her bachelors of science in Neuroscience and Behavioral Biology at Emory University in 2015 and is currently waiting on admittance to medical school.

Email: shilpajh@pcom.edu