A preliminary PET evaluation of dodecafluoropentane emulsion effects on rabbit brain hypoxia in stroke

J.S. Nix1, A. Brown2, R.D. Skinner3, M. Berridge2, M. James2, P.K. Roberson4, W.C. Culp2; 1College of Medicine, University of Arkansas for Medical Sciences, Hope, AR; 2Radiology, University of Arkansas for Medical Sciences, Little Rock, AR; 3Neurobiology and Developmental Sciences, University of Arkansas for Medical Sciences, Little Rock, AR; 4College of Medicine Biostatistics, University of Arkansas for Medical Sciences, Little Rock, AR

Purpose: Dodecafluoropentane emulsion (DDFPe) has been shown in animal models to reduce brain infarct volume caused by ischemic stroke and is being studied as a potential neuroprotective drug. The mechanism of the tissue-saving effect of DDFPe remains uncertain, but increased oxygen transport has been shown in vitro. MicroPET scans were performed using Fluorine-18 Fluoromisonidazole (FMiso), a tracer that exhibits uptake proportional to hypoxia in viable tissue. The preliminary results suggest that DDFPe curtails hypoxia in the brain following stroke.

Materials and Methods: New Zealand White Rabbits (n=9) underwent angiographic embolization of the middle cerebral artery (MCA) using permanent injectable spheres, and intravenous FMiso was administered. PET scans evaluated the period 2 hours post FMiso injection, allowing the tracer time to distribute. Treatment group animals received IV 0.6 mL/kg of 2% w/v DDFPe within 2 hours of embolization, not exceeding 2.5 mL. Standardized uptake values (SUV) were calculated for stroked regions of interest (ROI) every 5 minutes over 30 minutes. In the case of unidentifiable stroke after treatment, an ROI was drawn in an area typical of MCA territory. Rabbit brains were harvested for histologic analysis.

Results: Three animals were excluded, 1 control that failed to have a significant infarct and 2 for procedural failures, leaving 3 controls and 3 treated. Mean ±SE SUVs ranged from 0.50 ±0.06 to 0.60 ±0.06 for DDFPe treatments and 1.06 ±0.15 to 1.30 ±0.17 for controls. The DDFPe group showed decreased hypoxia with P values less than 0.05 at each time point using Wilcoxon rank sum test.

Conclusion: The reduction of FMiso in stroked ROIs as indicated by lower SUVs shows the ability of DDFPe to alleviate hypoxia in areas of ischemia. Furthermore, the oxygenating effect persists beyond the DDFPe 2 minute blood half-life in rabbits. Further study is warranted.

Reference

Antioxidants taken orally 1 hour prior to radiation exposure can prevent DNA injury

K.J. Murphy, N. Velauthapillai, J. Barfett, D.M. Mikulis; Radiology, University health network, Toronto, ON, Canada

Purpose: Exposure to ionizing radiation with CT, X Ray or Angiography in diagnostic and therapeutic radiology and cardiology studies is known to cause DNA injury. Antioxidants are widely known to diminish the benefit of Radiation therapy. Our intent was to develop a simple cocktail of antioxidants to be taken orally prior to X-Ray exposures that can protect a patient’s DNA against radiation induced injury.

Materials and Methods: We performed a prospective randomized study in 10 patients undergoing TC MDP bone scans with identical doses. The patients received a preparation of Glutathione Vitamin C and Folate orally one hour prior to Tracer injection. The patients were randomized to premedication (5) or no premedication (5). Individual foci of DNA repair in cell nuclei were counted in 50 nuclei from each tube through 3D optical microscopy and computational histologic analysis.

Results: We performed a prospective randomized controlled trial with oral premedication vs none, with in vivo exposure from Tc MDP, the premedicated patients had far fewer breaks that the non medicated patients. Without prmedication there was an average of 70 percent increase in DNA breaks. There was no statistically significant increase in DNA breaks after premedication.

Conclusion: Premedication with our current formulation of antioxidants significantly reduced formation of γ-H2AX and 53BP1 foci after injection of a clinically standard radiation dose of Technetium 99 MDP for a bone scanning. 60 minutes prior to Tracer injection was adequate to achieve a significant reduction in foci. This is the first time that a protective effect has been shown after premedication and with In Vivo patient exposure to radiation. This has implications for diagnostic and therapeutic radiology, cardiology, and screening mammography.