

Title: PET evaluation of hemorrhagic shock and resuscitation

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Abstract

In the USA, trauma kills approximately 150,000 people each year. Despite such an impact on health care, fluid resuscitation in trauma continues to be a debatable issue. Crystalloids or colloids are commonly used and these fluids augment O₂ delivery only by increasing preload. The only fluids that can increase both O₂-carrying capacity and preload are hemoglobin based products. Thus, the long-term goal of this research is to develop encapsulated hemoglobin as a complete and universal resuscitative fluid to address multifaceted pathophysiology of hemorrhagic shock. Liposome encapsulated hemoglobin (LEH), as well as other hemoglobin-based O₂ carriers (HBOCs), have undergone extensive evaluation. But, an efficient O₂ carrier is not necessarily an efficient O₂ delivery vehicle. PET has the capability to visually, quantitatively and noninvasively assess O₂ delivery and metabolism in response to resuscitation. HYPOTHESES 1) LEH delivers O₂ to the brain in the same fashion as RBCs, 2) cerebral O₂ delivery from LEH is sustained for a longer period of time than the unencapsulated HBOCs, and 3) LEH encapsulating high-affinity hemoglobin delivers more O₂ to the brain than LEH containing low-affinity hemoglobin in severe blood loss. SPECIFIC AIMS are: 1) Develop and validate image-derived cardiac time-activity curve as an arterial input function in MicroPET investigation of rat cerebral oxygen metabolism (CMRO₂). 2) Investigate the effect of oxygen affinity of hemoglobin in LEH on cerebral oxygen metabolism after resuscitation in a rat model of hemorrhagic shock. 3) Evaluate the improvement in CMRO₂ and energy metabolism after LEH resuscitation against standard resuscitative fluids in a rat model of hemorrhagic shock. We will perform microPET imaging with O-15 radiotracers (O₂ gas, CO gas and H₂O) to determine CMRO₂ and CBF. A rat model of hemorrhagic shock will be resuscitated with LEH, whole blood, Ringer's lactate solution and 5% albumin. Cerebral energy metabolism will be established by tissue markers of aerobic metabolism.

This is an innovative proposal that utilizes state-of-the-art imaging technology in a small animal model. The study will not only address important issues pertaining to oxygen metabolism in shock and resuscitation, it may also be useful in evaluation of other artificial oxygen carriers undergoing preclinical and clinical trials.