EVALUATION OF SEVERE ANEMIA BY QUANTITATIVELY MEASURING MULTI-ORGAN OXYGEN USING \(^{19}\)F MRI IN A RAT MODEL

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Introduction: Banked red blood cells are frequently transfused in anemic patients to improve oxygen delivery and provide adequate oxygenation of tissues. Unfortunately, blood transfusions carry risks of disease transmission, fatal immunogenic reactions, and a decrease in immune function. Prior human studies from our institution have demonstrated that increasing the amount of dissolved oxygen in the blood, although known to only be a small fraction of the total oxygen content, reverses the decline in cognitive function and decreased energy level associated with acute, severe, isovolemic anemia (1). Although previous models have evaluated global effects of severe anemia such as changes in cardiac output, blood pressure, lactate levels, and cellular injury, changes in tissue oxygen levels (the endpoint of interest), in multiple organs have not been examined. A quantitative method using fluorine-based (\(^{19}\)F) MRI (2,3) allows direct measure of regional dynamic oxygen pressure (pO\(_2\)) changes, is minimally invasive and previously validated. This method uses the linear relationship between longitudinal relaxation rate (R\(_1\)) of hexafluorobenzene (HFB), and pO\(_2\). The R\(_1\) of HFB has minimal temperature dependence, and is not significantly influenced by pH or CO\(_2\). We successfully used the method in a rat model to compare tissue oxygen pressures (pO\(_2\)) in multiple organs under normal and hyperoxic conditions (4,5).

Methods: Sprague-Dawley rats (n=3) were anesthetized with isoflurane and ventilated via tracheostomy. A femoral arterial line was placed for blood pressure monitoring and arterial sampling. Rats were kept euthermic and eucapnic throughout the study. HFB (50 \(\mu\)l) was injected into each organ of interest using a 33 ga. needle. The FiO\(_2\) was randomly selected as 0.3 or 1.0. An FiO\(_2\) of 0.3 was used in place of air in order to produce pO\(_2\) values of hemoglobin saturation near 100% and thereby isolate the effects of increasing dissolved oxygen alone with the increase in FiO\(_2\) to 1.0 (oxygen).

After equilibration, the rat was rescanned at FiO\(_2\) = 1.0 or 0.3. After the set of scans as previously described. Alternated relaxation delays with variable acquisitions (ARDVARC) were used to reduce clearance effects. T\(_2\) was calculated voxel by voxel (1x1x5 mm) with a three-parameter fit. PtO\(_2\) was calculated using a linear calibration curve of pO\(_2\) vs. R\(_1\). Spin echo proton images were acquired as a reference. After the scan, the inspired gas was changed to the other value (FiO\(_2\)=1.0 or 0.3). After equilibration, the imaging procedure was repeated. Each rat then underwent continuous hemodilution by simultaneously withdrawing 45 ml/kg of arterial blood while infusing an equivalent volume of colloid (Hextend, BioTime Inc., Berkeley, CA) via the tail vein over 40 min. After equilibration, the rat was rescanned at FiO\(_2\) = 1.0 and 0.3, with arterial samples taken before and after the set of scans as previously described.

Results: Mean pO\(_2\) was 117.7±27.8 mmHg (FiO\(_2\)=0.3) and 498±27.5 mmHg (FiO\(_2\)=1.0) before hemodilution. Mean Hb was 12.0±0.8 g/dL before hemodilution, 108.7±31.5 mmHg (FiO\(_2\)=0.3) and 492.0±34.7 mmHg (FiO\(_2\)=1.0) after hemodilution. Mean Hb was 12.0±0.8 g/dL before hemodilution, and 4.2±0.6 g/dL after hemodilution. All organ PtO\(_2\) values were increased by the increase in FiO\(_2\) from 0.3 to 1.0 under both normal and anemic conditions. All organ PtO\(_2\) values at FiO\(_2\) of 0.3 were decreased by hemodilution, although only by a small amount.

Discussion: The \(^{19}\)F MRI method allows quantitative measurement of decreases in oxygen levels in multiple organs during severe anemia. Although the small number of rats (n=3) did not allow adequate power for statistical analysis, all organs had a decrease in PtO\(_2\) at FiO\(_2\)=0.3 with severe isovolemic anemia. This decrease was more than reversed by increasing the FiO\(_2\) (dissolved oxygen). These preliminary findings suggest the value of supplemental oxygen in increasing organ oxygen levels may be greater than the small amount of increase in arterial oxygen content. In addition, this \(^{19}\)F MRI method may have value in assessing the effectiveness of artificial blood substitutes and other resuscitation fluids and protocols.

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