Effect of Acute Hyperglycemia on Intra-Renal Oxygenation as Estimated by BOLD MRI in Rats

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INTRODUCTION

Recent studies suggest that renal tissue pO2 is significantly lower in diabetic rats [Diabetologia. 2003;46:1153-1160], and that hypoxia of the kidney plays a major role in the development of acute [N Engl J Med. 1995 Mar 9;332(10):647-55] and chronic renal failure [Clin Exp Pharmacol Physiol. 2006 Oct;33(10):989-96]. It was also recently shown that blood oxygenation level dependent (BOLD) MRI technique can detect kidney hypoxic changes in streptozotocin (STZ) induced rat diabetes model as early as 2 days after administration of STZ [Invest Radiol 2007; 42:157-162]. Here, we wanted to study how much (if any) hyperglycemia directly contributes to the observed hypoxia. We used an animal model recently described by Saha *et.al* who showed that a bolus administration followed by continuous infusion of glucose could produce immediate and sustained hyperglycemia in rats [J. Pharmacology & Experimental Therapeutics. 2006, 316 (3):1159-1164].

MATERIAL AND METHODS

The study protocol was approved by the Institutional Animal Care and Use Committee. Four male rats (319±16 grams, three Sprague-Dawley, one Wistar Furth, Harlan Laboratories, Madison, WI USA) were anesthetized using Inactin (100 mg/kg *i.p.*, St. Louis, MO, USA). The femoral vein was catheterized for infusion of glucose.

Imaging was performed on a 3.0T scanner (CV/i, GE, Milwaukee, WI, USA) using a multiple gradient recalled echo sequence (TR/TE/flip angle/bandwidth/FOV/slice thickness/NEX =95ms/2.9-36.5ms /30/62.5kHz/10cm/2mm/12) to acquire eight T2* weighted images. The in-plane spatial resolution is 0.39mm. The rat kidney was positioned in the middle of the standard knee coil. One transverse slice was selected in the middle of the kidney. Three sets of T2*-weighted images and blood glucose measurement (One Touch Ultra, LifeScan, USA) were acquired for baseline. 20% Glucose solution was then administered starting as a bolus (0.6ml) followed by a 90' continuous infusion *via* an infusion pump (Genie Plus, Kent Scientific, Litchfield, CT , USA). Further sets of T2*-weighted images were obtained every 3 minutes and blood glucose was monitored every 10 to 20' minutes.

The signal intensity *vs.* echo time data were fit to a single decaying exponential function to generate R2* map. ROIs were chosen on the maps to obtain values for the mean and standard deviation of R2* in the renal medulla and cortex. The readings during first 60 minutes glucose infusion were averaged as post data. The statistical significance of the differences between pre- and post-glucose R2* values was assessed using the two-tailed paired Student's t-test.

RESULTS

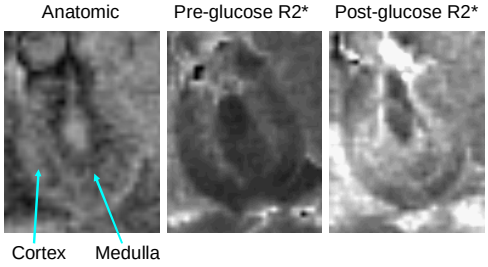

Figure 1 (left): Pre- and post-glucose R2* maps from one representative rat. The relatively brighter medulla in the post-glucose R2* map as compared to pre-glucose map, signifying a decrease in medullary oxygenation. The window and level settings for both the maps are exactly the same.

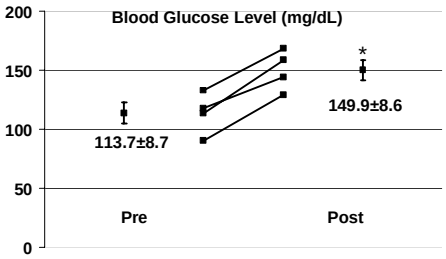

Figure2 (middle): Summary of individual changes in blood glucose level before and after glucose infusion. A statistically significant increase in post-glucose was observed.

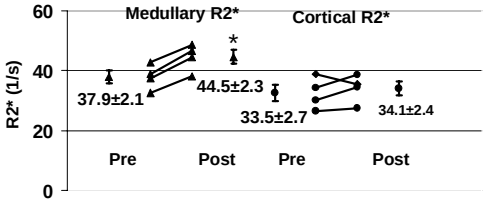

Figure3 (right): Summary of individual changes in medullary and cortical R2* before and after glucose infusion. A statistically significant increase in post-medullary R2*was observed.

CONCLUSION AND DISCUSSION

The preliminary results presented here demonstrate that intra-renal oxygenation as evaluated by BOLD MRI does decrease immediately following acute hyperglycemia. The increase in R2* is modest compared to the previous report with the STZ model (even at the 2 day time point). This could be partly due to the much higher level of hyperglycemia in the STZ model (~400 mg/dL *vs.* 149 mg/dL). While the measured blood glucose levels we observed are significantly higher than the baseline values, the magnitude of change is much less compared to the previous report [J. Pharmacology & Experimental Therapeutics. 2006, 316 (3):1159-1164]. The disparity could be in part due to a different anesthetic agent used in this study, and our animals not being fasted. .

ACKNOWLEDGEMENT

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