Impact of Exercise and Insulin on Microvascular PO$_2$ in the Diabetic Rat Soleus After Chronic Femoral Artery Ligation

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**Background:** Diabetes results in faster microvascular PO$_2$ (PO$_2_{mv}$) on-kinetics at the onset of muscle contractions reflecting an imbalance between oxygen delivery (QO$_2$) and oxygen utilization (VO$_2$). Femoral artery ligation as a model for vascular insufficiency elicits collateral growth and restoration of distal muscle flow. Exercise training enhances collateral growth after femoral ligation, while insulin should reduce the impact of diabetes.

**Aim:** To determine the effects of exercise training or insulin on the PO$_2_{mv}$ in the soleus muscle of diabetic rats after femoral artery ligation.

**Methods:** Female Sprague Dawley rats were randomly divided into three diabetic (streptozocin 50 mg/kg) groups: 1) Diabetic femoral artery ligated (DFL, n = 12), 2) Diabetic femoral ligated with exercise (DFLET, n = 14), and 3) Diabetic femoral artery ligated with insulin (DFLI, n = 12). Two wks later the left femoral artery was ligated in all rats. Exercise training and daily insulin glargine (1.6 U/100 g, sc.) were started one-week post-ligation and continued for 6 wks. After anesthesia, the soleus was exposed and stimulated (1 Hz, 6 V) over 3 minutes, while PO$_2_{mv}$ was measured at rest and during the rest-to-contraction transition using phosphorescent quenching and oxyphor G2.

**Results:** Insulin prevented the decrease in body weight (DFLI, 292 ± 7; DFL, 245 ± 8; DFLET, 234 ± 7 g) and soleus weight (DFLI, 176 ± 9; DFL, 143 ± 10; DFLET, 144 ± 7 mg). Glucose levels were elevated similarly in all three groups (>400 mg/dl). Resting PO$_2_{mv}$ and ΔPO$_2_{mv}$ during contractions was not different among the groups. The time delay in DFLI was shorter (8 ± 1 s) compared to DFL (15 ± 2 s) and DFLET (16 ± 1 s). Both DFLET and DFLI had faster time constants (16 ± 2; 15 ± 1 s) than DFL (30 ± 6 s). PO$_2_{mv}$ mean response time was faster in DFLET (32 ± 2 s) and DFLI (22 ± 2 s) compared to DFL (45 ± 5 s).

**Conclusion:** Despite receiving a suboptimal dose of insulin, the DFLI group maintained body and soleus weight without changes in blood glucose. While there is evidence for developing collateral circulation (high resting PO$_2_{mv}$) the faster PO$_2_{mv}$ kinetics in the DFLI and DFLET may reflect training and insulin associated maintenance of muscle metabolism (VO$_2$) in excess of the recovering oxygen delivery (QO$_2$). (Supported by Graduate Program Committee, KCOM – ATSU)

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