Effect of hyperthermia and acidosis on equine skeletal mitochondrial function

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Introduction

Exercise demands an increased rate of ATP production. ATP is produced in the mitochondria through the combustion of oxygen and substrates to produce a proton gradient which is used to drive ATP synthesis in a process termed oxidative phosphorylation (OXPHOS). Horses undergoing strenuous exercise have muscle hyperthermia, up to 44°C and skeletal muscle acidosis of pH 6.5. Hyperthermia induced membrane permeability could cause increased non-phosphorylating respiration (LEAK), fatigue and rhabdomyolysis. The effect of acidosis on OXPHOS has not been studied, though acidosis has been suspected in decreased mitochondrial function. The aim of this study was to test the hypothesis that hyperthermia leads to increased mitochondrial LEAK, and decreased OXPHOS with acidosis.

Materials and methods

All procedures approved by the Oklahoma State University IACUC. Fresh skeletal muscle biopsies were obtained from 6 healthy unconditioned TB geldings. Skeletal muscle mitochondrial function was measured using high resolution respirometry at 38°C, 40°C, 42°C, and 44°C (pH 7.1) to assess the effects of temperature, and pH of 6.1, 6.5 and 7.1 (38°C) to assess the effects of pH on mitochondrial oxygen consumption.

Results

Temperature had no effect on OXPHOS at 44°C compared to 38°C. LEAK supported by Complex I increased from 12 to 27% of Complex-specific OXPHOS at 38°C and 44°C (p = 0.0048). LEAK supported by Complex II increased from 21 to 73% at 38°C and 44°C (p = 0.0001). OXPHOS was preserved through Complex I when pH was lowered to 6.5, reduced when pH was lowered to 6.1 and OXPHOS through Complex II was also decreased, but less profoundly.

Discussion and Conclusion

This study concludes hyperthermia increased LEAK but physiologic acidosis (pH = 6.5) does not decrease OXPHOS. The increased membrane permeability caused by hyperthermia represents partial consumption of the proton gradient used to create ATP. As leak increases, increasing amounts of oxygen must be consumed to maintain ATP production and muscle contraction causing more heat and consequently more leak. OXPHOS was maintained at low pH, indicating acidosis may not have a deleterious effect on exercising equine skeletal muscle. Conditioning is thought to improve an athlete’s ability to withstand strenuous exercise. Next step is to condition horses under a specific regime, collect muscle biopsies from conditioned horses and subject them to the same protocols and look for a decrease in LEAK at higher temperatures. Decreased LEAK during hyperthermia would indicate better OXPHOS efficiency in conditioned horses.