

## **Adrenergic Blockade Increases Intracellular Na<sup>+</sup>/K<sup>+</sup> Ratio and Decreases Lactic Acid in Skeletal Muscle During Hemorrhage**

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### **Background:**

Following severe trauma and blood loss, skeletal muscle increases production of lactate, dramatically increasing circulating lactate concentrations. High blood lactate levels are commonly interpreted as evidence of tissue hypoperfusion and anaerobic glycolysis.

However, occurs under well-oxygenated conditions, epinephrine increases glycolysis linked to increased Na<sup>+</sup>, K<sup>+</sup>-ATPase activity in skeletal muscle. Combined α- and β-adrenergic blockade blocks the increase in lactate during hemorrhage. We investigated the effect of in vivo adrenergic receptor blockade on skeletal muscle intracellular Na<sup>+</sup> and K<sup>+</sup> following hemorrhage.

### **Hypothesis:**

Pre-treatment with α- and β-adrenergic antagonists prior to hemorrhage will result in a significantly increased intracellular Na<sup>+</sup>/K<sup>+</sup> ratio and decreased lactic acid content in skeletal muscle through reduced Na<sup>+</sup>/K<sup>+</sup> ATPase activity.

### **Methods:**

Male Sprague Dawley rats weighing 40-60 gms were anesthetized with pentobarbital. The left carotid artery and right jugular vein were cannulated for continuous blood pressure monitoring, withdrawal and reinfusion of shed blood, and drug infusion. Propranolol (0.5mg/kg, ip) and phenoxybenzamine (2mg/kg, iv) were used for α- and β-receptor blockade. Rats were hemorrhaged to a MAP of 40 mmHg for 1 hr. The EDL and soleus muscles were harvested bilaterally for determination of Na<sup>+</sup> and K<sup>+</sup> concentration. Intracellular lactate and glycogen concentrations were determined enzymatically.

### **Results:**

Adrenergic receptor antagonists significantly reduced muscle lactic acid content in both EDL and soleus. In addition, muscles from animals treated with adrenergic blockers had higher intracellular Na<sup>+</sup>/K<sup>+</sup> ratio. ATP levels in blocker-treated animals were significantly higher than in untreated, shocked animals.

### **Conclusions:**

Lactate production following hemorrhagic shock is directly related to the increase in Na<sup>+</sup>, K<sup>+</sup>-ATPase activity stimulated by epinephrine in well-oxygenated tissue. These observations challenge the traditional teaching of anaerobic glycolysis as the source of this lactate and may have an impact on future treatment strategies for victims of severe trauma or hemorrhage.