

ABSTRACT #125

EFFECTS OF THE INSULIN SENSITIZING DRUG PIOGLITAZONE ON INDICES OF INSULIN HOMEOSTASIS IN HORSES FOLLOWING ENDOTOXIN ADMINISTRATION. JG Wearn¹, JK Suagee², MV Crisman¹, MW Hulver², BA Corl², DR Hodgson¹, RJ Geor², LJ McCutcheon¹. 1.Virginia-Maryland Regional College of Veterinary Medicine, Virginia Tech, Blacksburg, VA. 2.Virginia Tech, Blacksburg, VA.

Reducing insulin resistance may decrease the incidence of laminitis in horses with Equine Metabolic Syndrome. Pioglitazone, a thiazolidinedione class of anti-diabetic drug, modulates transcription of genes involved in glucose metabolism in humans. The ability of pioglitazone to influence insulin sensitivity and gene expression in equine tissues in an endotoxin-infusion model of induced insulin resistance was investigated.

Sixteen mature horses were randomly allocated to receive either 14 days of pioglitazone (1 mg/kg, orally, q24h, n=8) or control (n=8). On days 12 and 14 a frequently sampled intravenous glucose tolerance (FSIGT) test with minimum model analysis was performed and a skeletal muscle biopsy (middle gluteal) was harvested. Whole tissue RNA was extracted to determine, by qRT-PCR, the expression of insulin receptor and insulin responsive glucose transporter (GLUT4). On day 13, all horses received an endotoxin infusion (*Escherichia coli* 055:B5 lipopolysaccharide, 35 ng/kg, IV, over 30 min). Serial assessment of clinical and leukocyte parameters, indices of insulin homeostasis and gene expression were compared prior to, and following, endotoxin infusion.

Heart rate (HR) and rectal temperature (RT) increased and white blood cell count (WBC) decreased following endotoxin infusion ($P<0.001$), however maximal change from baseline did not differ between pioglitazone treated horses or their controls ($P=0.3719$, $P=0.6695$, $P=0.3611$ HR, RT, WBC, respectively). Twelve days of pioglitazone did not increase insulin sensitivity ($P=0.278$) nor protect against endotoxin induced insulin resistance ($P=0.241$). Pioglitazone increased insulin receptor ($P=0.018$), but not GLUT4 transcript levels in skeletal muscle. Endotoxin infusion reduced GLUT 4 transcript levels ($P=0.059$), but had no effect on insulin receptor ($P=0.396$) in both treated and control horses. Pioglitazone treatment had no effect on GLUT4 transcript levels ($P=0.418$) following endotoxin infusion.

Although no physiologic changes in insulin sensitivity were identified following pioglitazone treatment, the finding of increased insulin receptor expression may warrant investigation of either the effects of a longer treatment period or in horses with obesity-associated insulin resistance.