

IRON STATUS OF HYPERINSULINEMIC/INSULIN RESISTANT HORSES

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Introduction

Hyperinsulinemia unrelated to recent high soluble carbohydrate feeding and disproportionate to blood glucose levels, indicating insulin resistance, is well known to occur in equine pituitary pars intermedia dysfunction (PPID, Cushing's disease), has been described in ponies and miniatures, and is receiving increasing attention as an underlying problem in horses prone to obesity and laminitis. In humans, several studies have identified iron overload as both a risk factor for the development of insulin resistance, and a consequence of insulin resistance. The purpose of this study was to determine if insulin resistant horses and ponies also show blood indices indicative of iron overload.

Materials and Methods

The insulin resistant (IR) study group was composed of adult horses and ponies from several breeds, known to be hyperinsulinemic. Horses with active infections or laminitis were excluded to avoid false elevations of ferritin (McLean, 1987; Smith et al, 1984). This group was further divided into horses receiving mineral supplementation, based on forage analysis (including a maximum Fe:Cu of 10:1 and Fe:Z of 3.3:1, Johnson et al, 2004) and those on unsupplemented diets. Controls were adult horses and ponies free of obvious disease. Hyperinsulinemic horses were on diets of low NSC forage only, or forage and beet pulp with small amounts of rice bran and flax. Control horses were on diets of forage only or forage plus concentrate or beet pulp. No horses in any group were receiving supplemental iron with the exception of what may have been added to commercial concentrate mixes. Serum iron, total iron binding capacity (TIBC) and ferritin were analyzed by the Comparative Hematology Laboratory at Kansas State Veterinary Medical Center by methods previously published by the founder of that laboratory (Smith et al, 1984). Transferrin saturation index (TSI) was calculated by the equation:

$$\text{TSI} = (\text{serum iron}/\text{TIBC}) \times 100$$

Data was analyzed by ANOVA and Student's T.

Results

Serum iron, TIBC, and ferritin values in control horses were similar to those previously reported for normal horses and well within the observed ranges used by the testing laboratory. There was no significant difference between groups for TIBC. There was no significant difference between IR balanced and unbalanced diets for serum iron ($P = 0.12$), or between IR balanced diets and normal ($P = 0.22$), but a significant difference between IR unbalanced and normal ($P = 0.0031$). For TSI and ferritin, there were no significant differences between IR horses on balanced diets and normal controls, but highly significant differences ($P < 0.0001$) between IR on unbalanced diets and both the control and IR on balanced diets.

TABLE I
SERUM IRON INDICES OF CONTROL VERSUS INSULIN RESISTANT HORSES ON
MINERAL BALANCED ON UNBALANCED DIETS

<i>Serum Values</i>	<i>IR – balanced diets</i>	<i>IR – unbalanced diets</i>	<i>Control</i>
Iron ug/dl	155 +/- 38.3 N = 10	181 +/- 48.9* N = 32	135 +/- 40.0 N = 18
TIBC ug/dl	381 +/- 73.6 ^a N = 10	347 +/- 65.2 ^a N = 32	351 +/- 60.1 ^a N = 18
TSI %	40.3 +/- 5.29 ^a N = 10	53.1 +/- 14.5 ^b N = 32	36.5 +/- 5.33 ^a N = 18
Ferritin ng/ml	116 +/- 57.8 ^a N = 10	313 +/- 99.9 ^b N = 38	139 +/- 43.9 ^a N = 27

• Significant difference from controls but not when compared to IR on balanced diet

a,b Different superscripts represent significant differences within a row (P<0.05)

Discussion

Risk factors for equine insulin resistance have not been completely identified but likely represent an interaction between genetic predisposition, underlying disease states and the environment. Since genetic factors are beyond our control and drug therapy for PPID does not necessarily lead to resolution of IR, identifying external factors has the potential to improve control. The role of iron overload as a risk factor for IR (Fernandez-Real et al, 2002; Jehn et al, 2004), and therapeutic effect of lowering body iron levels (Fargion, 2005; Piperno, 2004), has been documented in man. Ferritin has been shown to be highly correlated with hepatic iron stores in horses (Smith et al, 1984). This study has documented a highly significant elevation of body iron in insulin resistant horses on uncontrolled mineral intakes. This elevation is believed to be real, and not the result of occult inflammation, since transferrin saturation in these horses was also elevated and serum iron was not depressed (McLean et al, 1987). Animals on mineral balanced diets had normal TSI and ferritin levels, and improvement in their insulin resistance, but since other measures were undertaken concurrently (e.g. reduction in NSC of the diet), the effect of the mineral balancing per se could not be determined. More extensive prospective and intervention to treat studies are necessary to clarify the role iron might play in equine IR

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