Journal of Equine Veterinary Science 34 (2014) 465–470

Contents lists available at ScienceDirect

Journal of Equine Veterinary Science

journal homepage: www.j-evs.com

Original Research

Assessment of Insulin and Glucose Dynamics by Using an Oral Sugar Test in Horses

Amy Schuver DVM [a,1], Nicholas Frank DVM, PhD, DACVIM [b,*], Kelly A. Chameroy PhD [a], Sarah B. Elliott MS [a]

[a] Department of Large Animal Clinical Sciences, College of Veterinary Medicine, University of Tennessee, Knoxville, TN
[b] Department of Clinical Sciences, Tufts Cummings School of Veterinary Medicine, North Grafton, MA

ARTICLE INFO

Article history:
Received 7 May 2013
Received in revised form 3 September 2013
Accepted 9 September 2013
Available online 1 November 2013

Keywords:
Hyperinsulinemia
Insulin resistance
Glucose
Laminitis
Equine metabolic syndrome

ABSTRACT

Straightforward testing procedures are needed to facilitate the diagnosis of insulin dysregulation in horses because hyperinsulinemia and insulin resistance are associated with laminitis. Results of an oral sugar test (OST) were compared with those of the intravenous glucose tolerance test (IVGTT). We hypothesized that OST and IVGTT area under the curve values for glucose (AUCg) and insulin (AUCi) would be closely correlated, as defined by a correlation coefficient value $\geq$0.90. Both tests were performed in 10 horses meeting the criteria for equine metabolic syndrome (EMS) and 8 Quarter horse crossbred mares from a university teaching herd (control group). The OST was also performed in 21 Quarter horse crossbred mares from the same herd, and test repeatability was evaluated in 8 of these horses. All testing was performed under fasting conditions. Median AUCg and AUCi values were 1.3- and 9.0-fold higher, respectively, for the IVGTT and 1.3- and 6.8-fold higher, respectively, for the OST in the EMS group than those in the control group. AUCg (Spearman correlation coefficient [r_s] = 0.58; $P = .012$) and AUCi ($r_s = 0.90$; $P < .001$) values for the two tests were positively correlated. Mean ± SD coefficients of variation for repeated tests in 8 mares were 6.4% ± 3.1% and 45.1% ± 36.2% for AUCg and AUCi, respectively. We conclude that OST and IVGTT insulin results are closely correlated, so the OST warrants further consideration as a field test for insulin dysregulation in horses.

1. Introduction

Straightforward testing procedures are needed to facilitate the diagnosis of insulin dysregulation because hyperinsulinemia and insulin resistance (IR) are associated with laminitis in equids [1-4]. The general term “insulin dysregulation” is used to refer to alterations in insulin metabolism. Current screening for insulin dysregulation includes measurement of resting glucose and insulin concentrations and calculation of glucose-to-insulin and insulin-to-glucose ratios [1]. Proxy measures of insulin sensitivity and secretion, such as the reciprocal of the square root of insulin and modified insulin-to-glucose ratio, respectively, are also calculated from glucose and insulin values [1,2]. If further evaluation is required, dynamic testing is performed by conducting a euglycemic–hyperinsulinemic clamp, a frequently sampled intravenous glucose tolerance test, or a combined glucose–insulin tolerance test [1]. These procedures provide more direct measures of insulin sensitivity but often require hospitalization, have a higher cost, and take several hours to complete.

Measurement of resting insulin concentrations under fasting conditions is currently recommended as a screening test for insulin dysregulation, with detection of hyperinsulinemia in the fasting state supporting a diagnosis of IR [3]. However, a dynamic test is necessary for the diagnosis

* Corresponding author at: Dr. Nicholas Frank, DVM, PhD, DACVIM, Tufts Cummings School of Veterinary Medicine, 200 Westboro Road, North Grafton, MA 01536.
E-mail address: nicholas.frank@tufts.edu (N. Frank).
[1] Dr. Schuver’s present address is PO Box 826 Washington, OK 73093.

0737-0806/$ – see front matter © 2014 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.jevs.2013.09.006

of insulin dysregulation when fasting insulin concentrations are within reference ranges. The ideal dynamic test would be easy to perform on the farm and take only a short time to complete. An oral sugar test (OST) was therefore developed by our research group to try and meet these goals. In a pilot study, corn syrup (Karo light corn syrup; ACH Food Companies, Inc, Memphis, TN) was administered orally to horses in different quantities, and glucose and insulin concentrations were measured. Corn syrup was selected because it is readily available for purchase and can be easily administered to horses by owners. The syrup is administered orally by using a dose syringe and is very palatable. Once an OST was developed, we sought to compare results of this test with those of a conventional intravenous glucose tolerance test (IVGTT). We specifically hypothesized that OST and IVGTT area under the curve values for glucose (AUCg) and insulin (AUCi) would be closely correlated, as defined by a correlation coefficient value (CV) of >0.90. Other objectives of this study were to examine OST results from a herd of healthy Quarter Horse crossbred mares and assess test repeatability. A corn syrup containing glucose, maltose, and starch, but not fructose, was selected.

2. Materials and Methods

2.1. Animals

Ten adult horses with equine metabolic syndrome (EMS) were compared with 8 healthy adult mares (control group). Criteria for inclusion in the EMS group were based on American College of Veterinary Internal Medicine consensus statement recommendations [3] and included obesity, defined by a body condition score (BCS) of $\geq$7/9 according to the scoring system of 1 to 9 developed by Henneke et al [4] and/or regional adiposity in the form of an enlarged neck crest (subjective assessment); and combined glucose–insulin test or frequently sampled IVGTT results consistent with IR within the past 6 months. All horses in this group had histories of bilateral forelimb lameness consistent with laminitis. The control group contained 8 adult Quarter Horse crossbred mares selected from a university teaching herd. Horses in the EMS group were not tested for pituitary pars intermedia dysfunction, but clinical signs of this condition were not evident at the time of testing. Criteria for inclusion in the control group included a normal medical history for the previous 12 months, a BCS of <7, normal physical examination findings, absence of regional adiposity, and no history of laminitis. Median (range) age was 14.4 years old (7-21 years old) for the EMS group and 9 years old (7-15 years old) for the control group. Four mares and 6 geldings were included in the EMS group, with Arabian (3), Tennessee Walking Horse (2), Paso Fino (2), Morgan (1), Azteca (1), and Missouri Fox Trotter (1) breeds represented. Quarter Horse crossbred mares were included in the control group. Body weight ranged from 445 to 507 kg in the control group and from 418 to 559 kg in the EMS group. Body condition scores ranged from 4/9 to 5/9 and from 6/9 to 8/9 in the control and EMS groups, respectively. Horses with EMS were housed individually in stalls (2.75 m $\times$ 3.5 m) with attached outdoor dry lots (3.7 m $\times$ 10 m; n = 6) or were housed in pairs in dirt paddocks (15 m $\times$ 55 m; n = 4), while control group mares (n = 8) were housed on pasture as part of a larger herd. Approximately 12 months later, 21 adult nonobese Quarter horse crossbred mares from the same teaching herd of 25 animals housed on pasture underwent an OST. Criteria for inclusion in this group were a BCS of <7, absence of regional adiposity, and no history of laminitis. Eight mares from the first study were retested 24 hours later to assess repeatability. Both studies were completed in the month of July.

2.2. Study Design

For the comparison between EMS and control groups, horses were transported to the teaching hospital 2 days before testing and given time to acclimate to their surroundings. Each animal then underwent an IVGTT and an OST on consecutive days in random order. Testing was performed under fasting conditions by leaving only one flake of hay, weighing approximately 4 lbs, with each horse at 9:00 PM the night before and then withholding feed until testing was completed. Approximately 24 hours before the first test was performed, catheters (14-gauge, 5.5-inch polypropylene jugular catheter; Abbott Laboratories, North Chicago, IL) were inserted into jugular veins. Patency of IV catheters was maintained thereafter by infusing 5 mL of saline solution containing heparin (4 IU/mL) every 6 hours until the second test was completed and catheters were removed.

When the herd of 21 mares was evaluated, mares were tested in groups of 4 or 5; 13 mares underwent a single OST, and 8 mares underwent repeated testing on consecutive days and returned to pasture between tests. The 8 mares that underwent repeated testing differed from those in the first study. Horses were brought in from pasture at 4 PM and housed on a dry lot overnight with water provided ad libitum. Hay was fed to the group as normal at 5 PM, and then feed was withheld until after testing was completed the following day at approximately 12 PM. Horses undergoing testing on consecutive days were turned out to pasture at 12 PM and then returned to the dry lot at 4 PM. A single IV catheter was placed the afternoon before testing, and patency was maintained overnight by infusing 100 IU heparin in solution. Catheters were maintained for 2 days in 8 horses that underwent repeat testing. All protocols were approved by the University of Tennessee Institutional Care and Use Committee.

2.3. Intravenous Glucose Tolerance Test

Dextrose 50% (wt/vol) solution (Dextrose 50% injection; Abbott Laboratories) was infused at a rate of 50 mg/kg of body weight (bwt) within 1 minute, immediately followed by 20 mL of heparinized saline. Blood samples were collected before and at 15, 30, 45, and 60 minutes after dextrose infusion. Blood was collected in tubes containing a glycolytic inhibitor (potassium oxalate/sodium fluoride) and tubes without anticoagulant, and then 5 mL of heparinized saline was infused after each blood collection. Plasma and sera were harvested via centrifugation