GLUCOSURIA IN CAPTIVE OKAPI (OKAPIA JOHNSTONI)


Abstract: Eighteen of 38 captive okapi housed in the United States were found glucosuric by dipstick analysis. To confirm these findings, urine glucose concentrations of captive okapi from one collection (n = 10) were analyzed by two methods: urine dipstick analysis and quantitative analysis. Seven of these urine samples were positive for glucose by dipstick, with comparable glucose measurements by quantitative analysis. For a presumed normal control, okapi (n = 10) held in captivity within their native home range were tested for glucosuria by urine dipsticks; all were negative. Serum fructosamine (221–362 μmol/L) and insulin (9–45 pmol/L, 1.17–5.85 μU/ml) concentrations were determined from okapi (n = 6) with and without glucosuria with the use of results considered within normal limits for other ruminants. We conclude that glucosuria is a true finding in many apparently healthy captive okapi in the United States.

Key words: Glucosuria, kidney, okapi, renal disease, urine glucose.

INTRODUCTION

Recent observations suggested that glucosuria is present in a number of otherwise clinically normal okapi (Okapia johnstoni) in captive collections of the United States, Europe,23 and Japan. A recent survey conducted by the American Zoo and Aquarium Association (AZA) Species Survival Plan (SSP) of North American okapi determined that 86 okapi in this program are held in 24 institutions (Sarah Long, pers. comm.). Eighteen of 38 captive okapi were glucosuric by urine dipstick analysis. Glucosuria is abnormal in mammals and can have an infectious, metabolic, inherited, or familial etiology. In domestic ruminants, glucosuria is infrequently diagnosed and not present unless the serum glucose renal threshold of 100–160 mg/dl (5.59–8.94 mmol/L) has been reached.23

To validate the accuracy of urine dipsticks for measuring urine glucose and to confirm the presence of glucosuria in okapi, results from urine dipsticks were compared with quantitative laboratory analysis of urine for glucose concentration.

MATERIALS AND METHODS

Free-catch, midstream urine samples were obtained from captive okapi (n = 10) at the White Oak Conservation Center (WOCC; Yulee, Florida 32097, USA). Each sample was collected into a sterile urine cup and labeled with animal accession number and time of day. All samples were collected between 0700 and 0800 hours during the first urination of the day. The urine was applied to the glucose dipstick (CS; Chemstrips®; Roche Diagnostics Corp., Indianapolis, Indiana 46256, USA; range undetectable to 1,000 mg/dl) within 15 min of collection. A portion of the same urine sample was submitted to Baptist Health Laboratories (Fernandina Beach, Florida 32034, USA) for quantitative glucose and creatinine analysis (Synchron LX20 chemistry analyzer, Beckman and Coulter Inc., 200 S. Kraemer Boulevard, Brea, California 92822, USA) with the oxidase and alkaline picric acid test. Urine glucose:creatinine were calculated to reduce effects of urine concentration.

As presumed normal controls, okapi (n = 10) held captive within their home range of Epulu, Democratic Republic of the Congo, had free-catch, midstream urine samples collected at first light between 0630 and 0700 hours. Each sample was collected into a sterile urine cup and labeled with animal accession number and time of day. The samples were then tested for glucosuria with CS within 15 min of sampling.

Serum samples for insulin, glucose, and fructosamine concentrations were collected from the jugular vein of okapi anesthetized with xylazine (0.14 mg/kg, Xyla-ject®, Phoenix Pharmaceuticals, St. Joseph, Missouri 64503, USA) and carfentanil (0.004 mg/kg, carfentanil citrate, Wildlife Pharmaceuticals, Fort Collins, Colorado 80522, USA) during routine examinations in two collections: WOCC and Disney’s Animal Kingdom.

On the basis of these results, a survey of the North American okapi population for glucosuria was undertaken by the okapi SSP. Of the total population of 86 individuals, 38 animals in 11 institutions with an equal sex distribution (12.16.10) were sampled for urine glucose (Sarah Long, pers. comm.).
Table 1. Urine glucose determination by dipstick and quantitative methods in captive okapi (n = 10).

<table>
<thead>
<tr>
<th>Sample No.</th>
<th>Chemstrip (mg/dl)</th>
<th>Quantitative glucose analysis [mg/dl (mmol/L)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>positive (250 range)</td>
<td>220 (12)</td>
</tr>
<tr>
<td>2</td>
<td>positive (1,000 range)</td>
<td>868 (49)</td>
</tr>
<tr>
<td>3</td>
<td>positive (1,000 range)</td>
<td>810 (45)</td>
</tr>
<tr>
<td>4</td>
<td>positive (500 range)</td>
<td>442 (25)</td>
</tr>
<tr>
<td>5</td>
<td>positive (250 range)</td>
<td>230 (13)</td>
</tr>
<tr>
<td>6</td>
<td>positive (100 range)</td>
<td>27 (2)</td>
</tr>
<tr>
<td>7</td>
<td>positive (250 range)</td>
<td>300 (17)</td>
</tr>
<tr>
<td>8</td>
<td>negative</td>
<td>not submitted</td>
</tr>
<tr>
<td>9</td>
<td>negative</td>
<td>not submitted</td>
</tr>
<tr>
<td>10</td>
<td>negative</td>
<td>not submitted</td>
</tr>
</tbody>
</table>

RESULTS

The urine of the initial 10 captive okapi tested by CS determined that urine glucose ranged from undetectable to 1,000 mg/dl of glucose, with seven okapi positive for glucosuria (Table 1). CS results were compared with the quantitative analysis completed on the same urine samples, with the seven positive CS results also positive by automated analysis. The quantitative analysis was compared with the appropriate corresponding ranges of the CS and had a standard deviation of 316 mg/dl. Urine glucose:creatinine on glucose-positive samples appeared elevated, ranging between 1 and 20, with <1 assumed within normal concentration and values >1 indicative of high urine concentration. This finding is consistent with work completed in Belgium, where urine glucose:creatinine on a single okapi ranged between 6.32 and 13.56.24

Of the 10 captive in situ okapi tested for glucosuria with CS, none had any detectable urine glucose. Each of these 10 okapi was tested on multiple occasions.

Table 2. Serum glucose, insulin, and fructosamine concentrations for okapi with glucosuria (n = 3) and without glucosuria (n = 3).

<table>
<thead>
<tr>
<th>Okapi</th>
<th>Serum glucose [mg/dl (mmol/L)]</th>
<th>Serum insulin [pmol/L (μU/ml)]</th>
<th>Serum fructosamine [μmol/L]</th>
<th>Urine glucose [mg/dl]</th>
<th>Urine glucose quantitative analysis [mg/dl (mmol/L)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 WOCC</td>
<td>130 (7.27)</td>
<td>21 (2.70)</td>
<td>219</td>
<td>positive 1,000 range</td>
<td>868 (49)</td>
</tr>
<tr>
<td>4 WOCC</td>
<td>150 (8.38)</td>
<td>45 (5.85)</td>
<td>217</td>
<td>positive 500 range</td>
<td>442 (25)</td>
</tr>
<tr>
<td>5 WOCC</td>
<td>180 (10.06)</td>
<td>15 (1.95)</td>
<td>121</td>
<td>positive 250 range</td>
<td>230 (13)</td>
</tr>
<tr>
<td>A DAK</td>
<td>140 (7.80)</td>
<td>27 (3.51)</td>
<td>243</td>
<td>negative</td>
<td>not submitted</td>
</tr>
<tr>
<td>B DAK</td>
<td>124 (6.93)</td>
<td>9 (1.17)</td>
<td>236</td>
<td>negative</td>
<td>not submitted</td>
</tr>
<tr>
<td>C DAK</td>
<td>140 (7.80)</td>
<td>21 (2.73)</td>
<td>231</td>
<td>negative</td>
<td>not submitted</td>
</tr>
</tbody>
</table>

4 DAK, Disney’s Animal Kingdom; WOCC, White Oak Conservation Center.

5 Normal concentration, 100 ± 6 (ISIS, 1999).

Of the AZA okapi population, 47% were glucosuric by CS. Of the 11 facilities that reported results, five had no okapi with glucosuria and six had both negative and positive animals in the same collection. One institution reported 131 urine samples from a single pregnant female okapi analyzed by CS both pre- and postparturition. Samples were negative for glucose in 12% (16 of 131) of the samples during pregnancy but were negative for glucose in 50% (65 of 131) of the postparturition samples.

The opportunistic serum samples were analyzed for glucose, insulin, and fructosamine concentrations as tests commonly used in association with hyperglycemia and diabetes mellitus (Table 2). Insulin concentrations in both glucosuric (n = 3) and nonglucosuric (n = 3) okapi were within the normal range of cattle (Bos sp., 20–150 pmol/L) and domestic small carnivores (14–43 pmol/L; K. R. Refsal, pers. comm.). Corresponding serum glucose concentrations in glucosuric animals were normal to high-normal and high-normal in nonglucosuric animals. Serum fructosamine concentrations in both glucosuric and nonglucosuric okapi were comparable to reported concentrations in horses (Equus caballus, 197–317 μmol/L) and half-breed Zebu calves (Bos sp., 215–232 μmol/L).21

DISCUSSION

Differential diagnoses for glucosuria in mammals can include acute and chronic renal disease, diabetes mellitus, infectious disease, and renal tubule disorders.3 From this study, it appears that the high incidence of glucosuria in ex situ captive okapi is a true finding. This observation was first reported in 1977 from Europe, where five captive okapi were glucosuric on both urine chemistry dipsticks and quantitative analysis.11 Because renal disease can produce glucosuria, it was considered a differ-
ential explanation. However, acute and chronic renal disease appears rare in the North American okapi population, with only two aged okapi in recent years presenting lesions of chronic renal disease concurrent with multiple systemic organ failure (Scott B. Citino, pers. comm.). In contrast, the European Endangered Species Breeding Programmes (EEP) population reported that 16 of 98 okapi post-mortem over a 50-yr span reported chronic tubulointerstitial nephropathy.12 These renal lesions resembled those in pigs (Sus scrofa) and humans (Homo sapiens) caused by the fungal toxin ochratoxin A. However, this toxin is unlikely the cause of renal damage in okapi because it is usually degraded in the rumen.18,20 In six other necropsies, lesions similar to those of humans diagnosed with chronic nonsteroidal analgesic nephropathy were identified from a single European collection.13 Although the increased capillary thickness beneath the renal pelvis and mucosa of the urethra and urinary bladder were seen in these okapi, the hallmark of nonsteroidal anti-inflammatory nephropathy, papillary necrosis was not seen in the okapi. Interestingly, all six okapi were fed browse from the willow family (Salix sp.), which contains salicylic acid.13 Unfortunately, no urine samples were available from these okapi for analysis. Salix sp. browse was not reported in the diet of okapi in North American zoos and has not been used in feed at WOCC, although anecdotal reports confirm that it is used in North American zoos.

To date, there have been no reports in the EEP or SSP of an okapi with clinical diabetes mellitus. However, diet has been implicated for many years in development of diabetes mellitus in other mammalian species, so it could play a role in the pathogenesis of glucosuria in okapi.2 The okapi held in Epulu are fed a natural browse diet of over 100 species of plants. It is estimated that each of these okapi consumes approximately 23 kg of leaves a day.14 Wild okapi have only been seen feeding on leaves and, in some cases, only the tip of the leaves. It has been reported that both European and U.S. zoos feed their okapi a variety of produce, pelleted diets, hay, and selected cuttings from trees (browse).5,6,19,23 However, the variety of browse species and absolute browse quantity cannot be provided to the extent available in situ. European zoos feed larger amounts of produce, generally five times as much as North American zoos, and less roughage on average than North American zoos.19,23 Guidelines for feeding okapi established by the SSP and EEP suggest a diet (by weight) of 50% roughage (e.g., good-quality alfalfa hay), 25% concentrate, and 25% produce.5,6 Diets at WOCC contain 50% hay, 20% pellets, 10% produce, and 20% browse, although seven of 10 okapi are glucosuric with this feeding regime. In any case, it appears that captive diets do not reflect the same nutritional composition of wild diets.14

Okapi have been classified as concentrate selectors on the basis of the mean particle/fluid retention time (MRT; 1.26–1.43) of the gastrointestinal tract, which is consistent with a browsing ruminant.15 Grazing ruminants have a longer MRT, which equates to a longer digestive interval because of increased degradation time required for the cellulose and hemicellulose of grasses.17 Certain specialized concentrate selectors (e.g., royal antelope, Neotragus pygmaeus; moose, Alces canadensis) might be able to bypass the rumen with higher quality food, such as fruits, allowing direct use of glucose.16 It has been reported that wild okapi do not consume fruit and should not have developed this adaptation.14 However, faster gastrointestinal transit time and rumen bypass could result in a transient hyperglycemia when okapi are fed a large proportion of carbohydrate-containing produce or concentrate.15,16 If this is the case, it is possible that the glucose renal threshold (100–160 mg/dl or 5.59–8.95 mmol/L for ruminants) could be reached, and excess glucose would be excreted in the urine.23 However, it appears unlikely that a persistent hyperglycemia resulting in glucosuria would be possible with the numerous okapi in this study. Additionally, during general anesthesia on numerous okapi at WOCC (n > 100), serum glucose concentrations rarely have been above 120 mg/dl, which is below the renal threshold for glucose in ruminant species. This concentration is confounded by the extensive use of xylazine in many okapi immobilizations; this α-2-agonist has been documented with transient hyperglycemia and glucosuria in domestic horses and white-tailed deer (Odocoileus virginianus) during anesthesia.1,22

Quantification of insulin concentrations was within the normal range for cattle. Glycosylated hemoglobin analysis was not available for this species because it is not validated for ruminants. Fructosamines are serum proteins that have undergone nonenzymatic, insulin-independent glycation that occurs proportionally to the glucose concentration over an extended time. Fructosamine concentrations can determine the average blood glucose levels over the past 21 days. Serum fructosamine concentrations in the okapi were within the normal ranges for Zebu cattle and horses. Consequently, it appears that hyperglycemia may not have been present in the evaluated okapi for the 21 days before immobilization.
Familial renal diseases resulting in glucosuria have been reported in dogs, cattle, and humans.\textsuperscript{7,9,10} Evaluation of the okapi SSP pedigree did not reveal familial overrepresentation of glucosuric animals, and inbreeding does not appear to be a factor within the North American okapi population at this time (Sarah Long, pers. comm.). Despite this, one of the most well-known familial renal diseases causing glucosuria is Fanconi syndrome, in which the kidneys have abnormal tubular reabsorption of many solutes such as glucose, phosphate, and amino acids. This defect results in glucosuria, aminoaciduria, and clinical signs including polyuria, polydipsia, rough hair coat, weight loss, dehydration, and weakness. None of these clinical signs were seen in okapi aside from glucosuria.\textsuperscript{7} A second familial defect is benign glucosuria in humans with three variations (A, B, and O) that result from an autosomal recessive dysfunction of renal tubules.\textsuperscript{1,10} The resulting glucosuria varies with each genotype but is caused by a reduction in glucose threshold, maximal glucose reabsorption rate, or a complete absence of glucose reabsorption. In humans, this benign condition does not cause clinical or physiologic problems. At this point in time, more research into okapi nephrology is needed to determine the etiology of glucosuria.

**CONCLUSIONS**

It appears that glucosuria is a true finding in many captive okapi in North America and Europe. Many etiologies have been evaluated; however, more information is needed to make definitive conclusions. Additional diagnostics such as urinary fractional excretion rates and serum insulin and fructosamine concentrations are needed. Research into okapi dietary requirements is needed because current captive dietary recommendations could play some role in producing glucosuria, inasmuch as okapi fed in situ diets do not have glucosuria.

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**LITERATURE CITED**


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