Polish Journal of Veterinary Sciences Vol. 19, No. 2 (2016), 387–391

DOI 10.1515/pjvs-2016-0048

Original article

Influence of various carbohydrate sources on postprandial glucose, insulin and NEFA concentrations in obese cats

A. Mori[1], K. Ueda[1], P. Lee[2], H. Oda[1], K. Ishioka[1], T. Sako[1]

[1] School of Veterinary Nursing and Technology
[2] School of Veterinary Medicine, Faculty of Veterinary Science, Nippon Veterinary and Life Science University, 1-7-1 Kyonancho, Musashino, Tokyo 180-8602, Japan

Abstract

Carbohydrate is an important source of energy, which can significantly affect postprandial blood glucose and insulin levels in cats. In healthy animals, this is not a big concern; however, in obese and diabetic animals, this is an important detail. In the present study, the impact of four different carbohydrate sources (glucose, maltose, corn starch, and trehalose) on short-term post-prandial serum glucose, insulin, and non-esterified fatty acid (NEFA) concentrations was investigated with four obese cats. Each of the carbohydrate sources was added to a commercial wet food diet for feeding the animals. A significant difference was observed in postprandial glucose, insulin, and NEFA area under the curve (AUC) values between each carbohydrate source in obese cats. Furthermore, glucose and maltose induced the highest postprandial glucose and insulin AUC values, whereas trehalose induced the lowest postprandial glucose and insulin AUC value amongst all carbohydrate sources, respectively, in obese cats. However, trehalose has a higher risk of inducing side effects, such as diarrhea, as compared to other carbohydrate sources. As such, different carbohydrate sources appear to have a very significant impact on post-prandial glycemia and subsequent insulin requirement levels in obese cats. These results might be useful when selecting a prescription diet for obese or diabetic cats. In addition, maltose appears to be capable of inducing experimentally evoked postprandial hyperglycemia in obese cats, which may serve as a good tool for use to check the impact and effectiveness of newly developed oral hypoglycemic drugs or supplements for cats in future experiments.

Key words: cat, carbohydrate, diet, glucose, insulin

Introduction

Obesity is common amongst privately owned cats. Since the cat is carnivorous by nature and would normally consume prey high in protein, with moderate amounts of fat, and a minimal amount of carbohydrate, in a natural environment, cats are metabolically adapted for greater metabolism of proteins and lower utilization of carbohydrates, as compared to omnivores. As such, carbohydrate amounts and sources can

Correspondence to: A. Mori, e-mail: amori@nvlu.ac.jp

be important contributing factors influencing postprandial hyperglycemia in cats (de-Oliveira et al. 2008). Therefore, the objective of this study was to investigate and evaluate whether different carbohydrate sources (corn starch, glucose, maltose, and trehalose) can influence the degree of induced hyperglycemia and postprandial glucose parameters [postprandial serum glucose, insulin and non-esterified fatty acid (NEFA) concentrations] in obese cats. Inducing postprandial hyperglycemia is far easier to perform and observe in obese cats as compared to lean cats (Martin et al. 2010, Coradini et al. 2011).

Materials and Methods

Four obese (3 castrated males and 1 spayed female; 4.7-7.9 kg of body weight (BW); 4-5 body condition score (BCS); 2-6 years old) adult domestic cats, which were originally derived from animal facility (AQS Co Ltd, Narita, Japan) and subsequently maintained in our laboratory for research, were used in this study. The BCS was determined on a five point scale: 1, thin; 2, lean; 3, optimal; 4, obese; and 5, gross. Obese cats were fed on the commercial dry diet (C/D dry , Hill's Colgate, Tokyo, Japan) twice daily and caloric intake was set at half of 1.0 × Resting Energy Requirement (RER) ($BW^{0.75} \times 70$). Approval for the work was given by the Nippon Veterinary and Life Science University Animal Research Committee.

The study was carried out over a 5 week period consisting of 5 1-week periods, consisting of a 1 day washout period in between (last day of each 1-wk periods), in which cats were fed the Select Protein Duck and Rice wet diet (Royal canine Japon, Tokyo, Japan), and caloric intake was set at half of 0.75 × RER ($BW^{0.75} \times 70$) following a 24 h fast.

To investigate the effect on postprandial glucose parameters, we randomly added 1) no carbohydrate (Control); 2) corn starch (Corn) (Kawamitsu Bussan Co., Ltd, Tokyo, Japan); 3) glucose (Glucose) (D(+)-Glucose, Wako Pure Chemical Industries Ltd, Osaka, Japan), 4) maltose (Maltose) (Maltose Monohydrate, Wako Pure Chemical Industries Ltd, Osaka, Japan), and 5) trehalose (Trehalose) (Hayashibara Co., Ltd, Okayama, Japan) into the diet for each cat. We added 0.25 × RER ($BW^{0.75} \times 70$) of each carbohydrate source with wet food [5g for each cat, Select Protein Duck and Rice wet diet (Royal canine Japon, Tokyo, Japan)], since carbohydrate sources are powder. This dose of carbohydrate was previously referenced in a human study (van Can et al. 2009). We confirmed that over 50% and 100% of all the food was eaten within 30 min and 2 hours, respectively, for all four obese cats. Additionally, we checked for side effects of each type of carbohydrate supplementation (gastrointestinal problem) in all four cats, for up to three consecutive days after the initial day of feeding.

Blood samples were collected by bleeding 1.5 ml from the jugular vein of cats, 30 min prior to and 0.5, 1, 2, 4, 6, 8 and 10 hours post-feeding of the diets. Blood samples were collected into polypropylene tubes and allowed to clot at room temperature for 10 min. Subsequently, blood samples were centrifuged (1700 × g) at 4°C for 10 min to separate the serum. After centrifugation, the serum samples were immediately stored at -80°C until further use. Serum glucose and NEFA concentrations were measured by an enzymatic method using an Iatro LQ GLU kit (Mitsubishi Kagaku Iatron, Tokyo, Japan) and Iatro tech NEFA kit (Mitsubishi Kagaku Iatron, Tokyo, Japan), respectively, and processed by a Hitachi autoanalyzer 7180 (Hitachi High-Technologies Corporation, Tokyo, Japan). Serum insulin (immunoreactive insulin) concentration was measured using an ELISA kit (Morinaga Institute of Biological Science, Kanagawa, Japan) according to the manufacturer's instructions (The intra-assay CV and inter-assay CV were ≤ 6% and ≤ 10%, respectively) (Nakaya et al. 2009).

Data are presented as the median [min, max]. Total area under the curve (AUC) was estimated as the post-prandial summary variable and calculated by the trapezoidal rule in units of concentration × hours. Significance was determined using Friedman repeated measures ANOVA on ranks and Student-Newman-Keuls Method for pairwise multiple comparison procedures for comparison of AUC or temporal analysis of glucose, insulin and NEFA concentrations between the Control and four carbohydrate sources. The significance level was set at $p<0.05$ and all tests were run in Sigmaplot 11.0 (Build 11.2.0.11, Systat Software Inc., CA, USA).

Results

Temporal analysis of post-prandial glucose concentrations with each type of carbohydrate diet revealed no significant differences over time as compared to the Control diet (Fig. 1a). However, significant differences were observed in median glucose [min, max] AUC values among the treatment groups (Friedman repeated measures ANOVA on ranks, $p=0.015$). The Trehalose diet rendered the lowest glucose AUC value (738.13 [714.50, 1,108.50] mg/dL hr^{-1}) amongst all diets examined. The Glucose (893.75 [805.5, 1,277.25] mg/dL · hr^{-1}) and Maltose (861.13 [824.75, 1.154.25] mg/dL · hr^{-1}) diets had significantly higher glucose AUC values than the Trehalose diet (Pairwise multiple comparison procedures (Student-

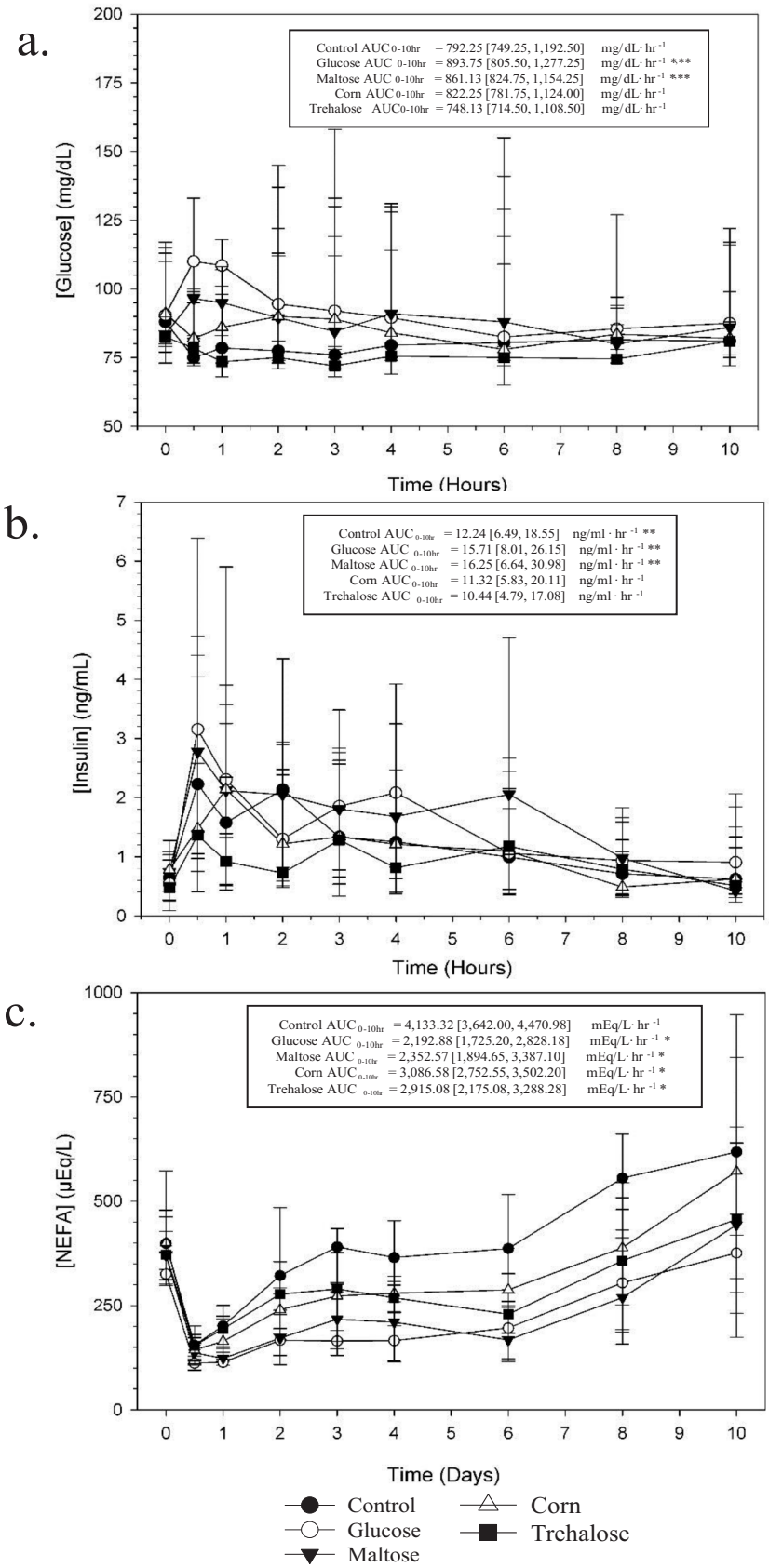

Fig. 1. Median temporal changes in post-prandial serum (a) glucose, (b) insulin, and (c) non-esterified fatty acid (NEFA) concentrations, under different diet regimens in obese cats (n=4). Results are expressed as median [min, max]. Total area under the curve (AUC) results are presented in the graph inset. Asterisk indicates significance [$p<0.05$; Pairwise multiple comparison procedures (Student-Newman-Keuls Method)] when compared with the Control diet. Double asterisk indicates significance [$p<0.05$; Pairwise multiple comparison procedures (Student-Newman-Keuls Method)] when compared with the Trehalose diet.

-Newman-Keuls Method) , $p<0.05$). Whereas Control (792.25 [749.25, 1,192.50] mg/dL · hr^{-1}) and Corn (822.25 [781.75, 1,124.00] mg/dL · hr^{-1}) diets had slightly higher glucose AUC values than the Trehalose diet.

Temporal analysis of post-prandial serum insulin concentrations, with each type of diet, indicated no significant differences in insulin secretion over time (Fig. 1b). However, significant differences were observed in median insulin [min, max] AUC values among the treatment groups (Friedman repeated measures ANOVA on ranks, $p=0.013$). With regard to insulin AUC, the Maltose (16.25 [6.64, 30.98] ng/ml · hr^{-1}) and Glucose (15.71 [8.01, 26.15] ng/ml · hr-1) diets demonstrated the greatest values amongst all carbohydrate sources, whereas Control (12.24 [6.49, 18.55] ng/ml · hr-1) and Corn (11.32 [5.83, 20.11] ng/ml · hr^{-1}) diets were very similar, and lastly, the Trehalose (10.44 [4.79, 17.08] ng/ml · hr^{-1}) diet rendered the lowest insulin AUC value amongst all the carbohydrate sources (Pairwise multiple comparison procedures (Student-Newman-Keuls Method), $p<0.05$) (Fig. 1b).

Temporal analysis of post-prandial serum NEFA concentrations revealed no significant differences over time between the Control and four carbohydrate sources (Fig. 1c). However, significant differences were observed in median NEFA [min, max] AUC values among the treatment groups (Friedman repeated measures ANOVA on ranks, $p=0.015$). With regards to NEFA AUC, all carbohydrate sources rendered a lower NEFA AUC value than Control (4,133.32 [3,642.00, 4,470.98] mEq/L · hr^{-1}) diet, but the Glucose (2,192.88 [1,725.20, 2,828.18] mEq/L · hr^{-1}), Maltose (2,352.57 [1,894.65, 3,387.10] mEq/L · hr^{-1}), Corn (3,086.58 [2,752.55, 3,502.20], and Trehalose (2,915.08 [2,175.08, 3,288.28] mEq/L · hr^{-1}) diets all resulted in a significantly lower NEFA AUC than the Control diet (Pairwise multiple comparison procedures (Student-Newman-Keuls Method), $p<0.05$).

Discussion

Overall, Glucose diet demonstrated the highest glucose AUC and mean postprandial glucose values (0.5-3 hours after feeding). This might be due to the fact that glucose is a monosaccharide, maltose is a disaccharide, and corn starch is a polysaccharide, thus rendering an increased digestion absorption rate according to each carbohydrate source. Trehalose diet induced the lowest glucose AUC values as compared to other carbohydrate sources examined, which was unsurprisingly since Trehalose has been reported to induce lower glycemic and insulinemic responses in obese men as compared with glucose (Maki et al. 2009). Moreover, feline intestinal trehalase activity may be non-existant and is significantly lower than that observed in humans (Hore and Messer 1968, Hietanen 1973, Galand 1989), therefore trehalose cannot be easily degraded in the feline intestine (Cowey et al. 1977, Coradini et al. 2011).

The insulin AUC results correspond with the glucose AUC results, which is expected. Glucose and maltose induced a high glycemic index in cats as in humans (Whelan 2004), and as such, higher postprandial glucose concentrations would tend to induce higher insulin secretion in cats. Surprisingly, the Trehalose diet rendered the lowest insulin AUC value, which was even lower than that found after feeding either Control or Corn diet. Trehalose loading induces lower insulin secretion than glucose loading in humans (Oku et al. 2000).

In normal human subjects, the rise in plasma insulin after an oral glucose load rapidly suppresses plasma NEFA. In our study, serum NEFA concentration decreased after feeding with all carbohydrate sources, but gradually increased thereafter, with all diets, especially the Control diet, which had the greatest increase in NEFA AUC. We speculate that this may have occurred because Control *diet's* total caloric count was lowest amongst all diets, therefore catabolization of body fat might have occurred resulting in subsequent increasing plasma NEFA.

Lastly, no side effects were observed in Control, Maltose, and Corn diets for three days after feeding. However, the Glucose diet induced mild side effects (loose stool and vomiting) in two of four obese cats immediately next morning, and the Trehalose diet induced severe diarrhea in all four obese cats for 2 days. This phenomenon might be related to high levels of enterobacteria utilization of carbohydrate or gastrointestinal osmotic pressure. As stated previously, cats may lack the ability to degrade trehalose in the intestine, allowing for undigested trehalose to pass into the large intestine, where microbial dysfermentation results in induced osmotic diarrhea and attendant discomfort triggering an aversion response. Since side effects were observed with all 4 cats with the Trehalose diet, perhaps the dose of trehalose used in this study may not be appropriate.

This study has a number of limitations. First, our results have low statistical power, being attributed to the small number of obese cats used. As such, due to the large biological variability amongst animals, the sample number used in our study is too small to accurately assess postprandial serum metabolites (eg. glucose, insulin and NEFA concentration) reliably. Second, side effects such as diarrhea occurred, since

carbohydrate sources were administered to cats. Any future study should make adjustments to the carbohydrate dosage, in particular with trehalose, since severe diarrhea was observed.

In conclusion, this study demonstrates that different carbohydrate sources can significantly affect post-prandial changes in the glucose and insulin response in obese cats. Out of all the carbohydrate sources examined, trehalose had the most minimal effect on post-prandial glucose and insulin AUC in obese cats. However, on the flip side, trehalose also produced the most severe side effects with severe diarrhea, at the dosage we used however. These results might be useful when choosing a prescription diet for obese or diabetic cats. Furthermore, maltose was able to experimentally induce postprandial hyperglycemia in obese cats without any serious side effects. As such, maltose might serve as a good tool for use to check the impact and effectiveness of newly developed oral hypoglycemic drugs or supplements for cats in obese cats, since post-prandial serum glucose and insulin concentrations in obese cats can be drastically changed and altered, as compared with healthy cats.

Acknowledgment

This work was supported by JSPS KAKENHI Grant Number 26850201.

References

Coradini M, Rand JS, Morton JM, Rawlings JM (**2011**) Effects of two commercially available feline diets on glucose and insulin concentrations, insulin sensitivity and energetic efficiency of weight gain. Br J Nutr 106 (Suppl 1): 64-77.

Cowey CB, Knox D, Walton MJ, Adron JW (**1977**) The regulation of gluconeogenesis by diet and insulin in rainbow trout (Salmo gairdneri). Br J Nutr 38: 463-470.

de-Oliveira LD, Carciofi AC, Oliveira MC, Vasconcellos RS, Bazolli RS, Pereira GT, Prada F (**2008**) Effects of six carbohydrate sources on diet digestibility and postprandial glucose and insulin responses in cats. J Anim Sci 86: 2237-2246.

Galand G (**1989**) Brush border membrane sucrase-isomaltase, maltase-glucoamylase and trehalase in mammals. Comparative development, effects of glucocorticoids, molecular mechanisms, and phylogenetic implications. Comp Biochem Physiol B 94: 1-11.

Hietanen E (**1973**) Interspecific variation in the levels of intestinal alkaline phosphatase, adenosine triphosphatase and disaccharidases. Comp Biochem Physiol A 46: 359-369.

Hore P, Messer M (**1968**) Studies on disaccharidase activities of the small intestine of the domestic cat and other carnivorous mammals. Comp Biochem Physiol 24: 717-725.

Maki KC, Kanter M, Rains TM, Hess SP, Geohas, J (**2009**) Acute effects of low insulinemic sweeteners on postprandial insulin and glucose concentrations in obese men. Int J Food Sci Nutr 60 (Suppl 3): 48-55.

Martin LJ, Siliart B, Lutz TA, Biourge V, Nguyen P, Dumon HJ (**2010**) Postprandial response of plasma insulin, amylin and acylated ghrelin to various test meals in lean and obese cats. Br J Nutr 103: 1610-1619.

Nakaya M, Kito Y, Matsuki N, Shibata H, Touhata Y, Tamahara S, Ono K (**2009**) A novel sandwich enzyme-linked immunosorbent assay for feline insulin. J Vet Med Sci 71: 1005-1007.

Oku T, Nakamura S (**2000**) Estimation of intestinal trehalase activity from a laxative threshold of trehalose and lactulose on healthy female subjects. Eur J Clin Nutr 54: 783-788.

van Can JG, Ijzerman TH, van Loon LJ, Brouns F, Blaak EE (**2009**) Reduced glycaemic and insulinaemic responses following trehalose ingestion: implications for postprandial substrate use. Br J Nutr 102: 1395-1399.

Whelan W (**2004**) The wars of the carbohydrates: part 3: maltose. IUBMB Life 56: 641.