FELINE DIABETES MELLITUS: WHAT DIET SHOULD I CHOOSE & HOW DO I MANAGE PROBLEM CATS

Jacquie Rand BVSc DVSc Dip ACVIM; Rhett Marshall BVSc, MACVS,
Centre for Companion Animal Health, School of Veterinary Science,
The University of Queensland, Brisbane Australia

Article modified October 2008 from: *RAND JS, Marshall R Feline diabetes mellitus: which insulin do I choose and how do I adjust the dose. Proceedings of the American college of Veterinary internal medicine forum, May 2006 Kentucky, USA*

Feeding

While the ideal combination of macronutrients (protein, fat and carbohydrate) to feed diabetic cats is not known, diets low in carbohydrates and high in protein reduce post-prandial hyperglycemia and insulin concentrations in healthy cats. Initial data from diabetic cats also suggest that low carbohydrate-high protein diets result in better clinical control, reduced insulin requirements and increased rates of diabetic remission. Thus a commercial low carbohydrate should be used in diabetic cats, unless contraindicated by other disease. During the first few weeks of treatment, diabetic cats may have a reduced appetite, and if they refuse these low carbohydrate diets, they should be offered any palatable food.

Care should be taken with cats diagnosed with advanced end-stage renal disease, as diets high in protein may have a deleterious effect. For these cats, dietary management of renal disease using a restricted protein diet should take precedence over dietary management of diabetes. Twice daily administration of the oral hypoglycemic agent acarbose may help to reduce glucose absorption in cats which for health reasons are on a high carbohydrate diet.

Obesity in cats markedly reduces insulin sensitivity and hence calories should be restricted so weight loss occurs in obese cats at a rate of 1-2% loss of body weight per week. Because of the decreased postprandial hyperglycemia with a low carbohydrate diet, it is suggested that diets with less than 20% of calories from carbohydrate (eg. Hills m/d, Purina DM) should be used for obese diabetic cats during the calorie restriction phase. Currently, most feline weight loss diets are low fat, high carbohydrate diets. Weight loss improves insulin sensitivity, and may reduce insulin requirements. In some cats, diabetic remission is obtained after weight loss and short-term insulin or oral hypoglycemic therapy.

Acarbose

The α-glucosidase inhibitors (eg acarbose) reduce intestinal glucose absorption (Greco 1999) and are generally not effective in the treatment of feline diabetes alone, but can be used in conjunction with insulin and/or other oral agents to gain better glycaemic control. Cats given acarbose and fed a high carbohydrate diet had a reduced postprandial glucose concentrations,, but similar results were achieved feeding a low carbohydrate diet alone (Singh et al 2006).

Problem cats

When cats treated with insulin fail to stabilise, a number of underlying causes and approaches to treatment should be considered. It is important to remember that many cats take 1 to 4 months to stabilise. It is unrealistic to expect excellent control after only 2 to 4 weeks of treatment, except in cats going into early remission.

For intermediate acting insulin, the most common problems resulting in poor control are excessive dose, miscalculation of dose, too short duration of insulin action, or poor absorption of insulin. Some cats are mistakenly labeled problem cats when the clinical signs are well controlled, but blood glucose measurements are less than ideal. This usually occurs when there are unrealistic goals for glycaemic control when using lente, NPH or ultralente. If the glucose nadir is below 10 mmol/L (182 mg/dL) after each insulin injection, peak action occurs >3 hours after administration, and hypoglycaemia is not occurring, glycaemic control is usually adequate. These cats usually have good clinical control (stable body weight, good coat condition, active, alert, water drunk <100ml/kg/24h). Swapping to a longer acting insulin such as glargine will usually improve glycemic control.

For long-acting insulin such as glargine and detemir the most common problems resulting in poor control are insulin resistance of unknown cause or associated with growth hormone excess (acromegaly).

Problem cats have persistent clinical signs including polydipsia (water drunk > 100 mL/kg/24h), low body condition score, polyphagia, lethargy, and a poor hair coat; an insulin dose higher than normal (1.5 – 2 or more IU/kg/injection); and either a nadir glucose> 180 mg/dL (10 mmol/L) or hypoglycemia. For problem-solving in problem cats, it is important to first rule-out administration problems. Expired insulin, heat affected insulin (eg. left in a car in summer), poor mixing of suspensions, failure of administration (eg. injecting through the skin pinch onto the hair-coat), and the presence of air bubbles in the syringe causing a lower administered dose, all occur regularly in practice. Insulin syringes can be difficult to manage for elderly owners with arthritic hands and poor vision. These owners are often better able to cope with insulin pens. Misunderstandings between the owner and veterinarian regarding the number of units to be administered can occur when using 40-IU/mL insulin in a 100-IU/mL syringe, because the cat is only getting 40% of the dose indicated by the markings on the syringe. Watch the owner administer the insulin. If it is an old bottle of insulin, change to a new one. If the cat has been treated for at least 8 to 12 weeks and insulin is being correctly administered but poor control is still evident, measure water intake over consecutive days at home (measure fructosamine concentration if water intake cannot be measured), and obtain a blood glucose curve. Home monitoring of blood glucose concentrations is invaluable for helping to characterize the problem.

Formatted: Right: 18 pt

Poor control may result from an excessive dose of intermediate acting insulin, which may cause apparent insulin resistance (dose >1.5 – 2 IU/injection with persistent hyperglycaemia), or short duration of insulin action. In many cats treated with the intermediate-acting insulins such as lente and isophane, these potent insulins rapidly lower blood glucose. This stimulates counter-regulatory responses, even when blood glucose concentration is not in the hypoglycemic range. The resulting counter-regulatory response increases blood glucose concentration, and causes an apparent short duration of insulin action and insulin resistance. This can be very frustrating for veterinarians when managing diabetic cats. This response happens because of the action of the hypothalamic neurons that sense blood glucose concentration and initiate counter-regulation. The hypothalamic neurons control entry of glucose into their cytoplasm, and actively maintain a large concentration gradient with plasma glucose when blood glucose concentrations are high. When potent insulin such as lente insulin is given and blood glucose concentration decreases rapidly, the intracellular glucose concentration of the hypothalamic neurons decreases more quickly into the range perceived by the neurons as hypoglycemic and a counter-regulatory response is triggered, even before hypoglycemia develops. The resultant secretion of glucagon, epinephrine, cortisol and growth hormone increases blood glucose concentration, and causes an apparent short duration of insulin action. Because the glucose lowering effect of lente in cats is less than 8 hours, most diabetic cats have blood glucose concentrations of 360 to 430 mg/dl (20 to 24 mmol/l) at the time of the next insulin dose, predisposing them to premature counter-regulation. The result is that in some cats, lente and NPH insulins may only lower blood glucose for 2 to 3 hours. This inherent short duration of action of lente, NPH and ultralente insulins, coupled with the response of the hypothalamic neurons can be very frustrating for practitioners. It also is dangerous for diabetic cats, because their insulin dosage often is wrongly increased. The end result is that the effect of lente, NPH and ultralente is often too short to achieve good glycemic control, and insulin resistance and signs of hyperglycemia and hypoglycemia ensue. For this reason, the longer acting insulins glargine and detemir are first choice insulins in diabetic cats. PZI is a second choice insulin and lente insulin a third choice insulin. NPH is not recommended in cats except where no other insulin is available.

For cats on potent insulins such as lente or NPH, if the cat is polydipsic and insulin seems to have little effect, especially when previously it caused substantial lowering of glucose, or the duration of action seems to be short, there are two options. Either swap to glargine (recommended option) or first try lowering the dose of insulin to 0.3 to 0.5 IU/kg for 10-14 days to see if blood glucose or water intake improve towards the end of the period. If clinical control is not improved with a lower dose, check the glucose response to a standard dose of 0.5 IU/kg of insulin, to determine the duration of effect. If the glucose nadir occurs 2 – 3 hours after injection, switch to a longer acting insulin, or increase the frequency of administration to TID. Similarly with PZI, if the nadir occurs at <6 hours, change to BID administration, if the cat is receiving insulin once daily. With PZI or ultralente, if there is little response to insulin, try swapping to glargine and slowly increasing the dose until glycemic control is achieved, which may require a dose of 5-6+U/cat twice daily. If there is still polydipsia (water drunk>100ml/kg/24 h) and little glycaemic response after 1-2 months at a dose of 5-6U/cat twice daily, check the cat for hyperthyroidism, hyperadrenocorticism, acromegaly or other systemic disease such as renal failure, if there are clinical signs which suggest concomitant disease. We have seen improved glycaemic control in cats with periodontal disease, following dental surgery in combination with short-term antibiotics. In the meantime, increase the dose by 1 IU every 1-2 weeks until some glycaemic response is achieved. Control is achieved in most difficult cats, with the exception of cats with acromegaly, once glargine dose is 5-6 U/cat twice daily. Warn the owner that a severe hypoglycaemic episode can occur with this protocol, and to be particularly vigilant regarding the early signs of hypoglycaemia (lethargy, mental dullness, wobbliness, trembling and dilated pupils). In some cats which appear insulin resistant, but no cause can be found, admitting them to hospital for carefully observed intensive insulin therapy to normalize blood glucose for several days, may substantially reduce the subsequent insulin doses that achieve control. Most cats are eventually controlled on 1-3 U/cat BID of glargine, even if they required a dose as high as 5-6 U/cat BID in the first 1-3 months to control blood glucose.

KEYWORDS, feline diabetes, diabetic remission, insulin, glargine

Suggested reading:

Selected articles are available our website: www.uq.edu.au/ccah

Mazzaferro EM, Greco DS, Turner AS, Fettman MJ (2003) Treatment of feline diabetes mellitus using an α-glucosidase inhibitor and a low-carbohydrate diet, *Journal of Feline Medicine and Surgery* **5**(3), 183-189

Nelson RW (2005) Diabetes mellitus. *In* Ettinger SJ, Feldman EC (Eds.), *Textbook of veterinary internal medicine* (Vol. 2, pp. 1563): Elsevier Saunders

.Marshall RD, Rand JS. Comparison of the pharmacokinetics and pharmacodynamics of glargine, protamine zinc and porcine lente insulins in normal cats, *Journal of Veterinary Internal Medicine* 2002, 16(3):358.

Marshall RD, Rand JS. Comparison of the pharmacokinetics and pharmacodynamics of once versus twice daily administration of insulin glargine in normal cats, *Journal of Veterinary Internal Medicine* 2002, 16(3):373.

Formatted: Right: 18 pt

Marshall RD and Rand JS. Treatment with glargine results in higher remission rates than lente or protamine zinc insulins in newly diagnosed diabetic cats.*Proceedings 24th ACVIM Forum 2005*.

Rand JS and Marshall RD Diabetes mellitus in cats. Vet Clin North Am Small Anim Pract 35[1]:211-24 2005

Reference list provided on request

Formatted: Right: 18 pt