

Medical and Nutritional Management of Feline Diabetes Mellitus

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Although diabetes mellitus is a common endocrinopathy in cats, there is still much that we do not understand about this complex and interesting disease. To date, much of our current knowledge about the management of feline diabetes mellitus (DM) has been extrapolated from the practices used to manage humans with DM. Recently, some of the familiar concepts and treatments that have been co-opted from human medical literature have come under scrutiny by veterinary researchers. It turns out that the cat, with its unusual nutrient requirements and unique metabolism, makes for an interesting diabetic.

Medical management of feline DM. Medical management in the form of daily insulin injections is the cornerstone of therapy for most diabetic cats. Other drugs that have been investigated for possible use as sole or adjunctive agents for DM management include glipizide (a sulfonylurea drug), chromium, vanadium, metformin, acarbose, and troglitazone. Veterinary experience with almost all of the latter drugs (glipizide is the exception) is extremely limited. All of our current information about these drugs is derived from just a few small clinical studies or anecdotal observations.

Insulin. Insulin is required to control glycemia in most diabetic cats, although there are exceptions to this rule. Several insulins are available for use in the cat; these include regular, lente, NPH, PZI, and ultralente insulins. The principal indication for regular insulin is for the emergency treatment of diabetic crises, such as diabetic ketoacidosis. Regular insulin generally has no role in the long-term management of DM. Longer acting insulins, such as lente, NPH, and PZI, are common first choices for feline DM. The author prefers to initiate insulin therapy with NPH at a dose of 0.25 to 0.5 U/kg. Initially, NPH is given just once daily (in the morning) and the effects monitored at home by the owner. Ultimately, the majority of DM cats require twice daily NPH dosing. If NPH is ineffective, lente or PZI can be substituted and may work better than NPH for some cats. In the author's hands, ultralente insulin has not been efficacious in cats and I generally do not recommend its use.

A major complication of insulin use is hypoglycemia, which can be difficult to detect clinically in cats. Hypoglycemic episodes tend to occur most often when "tight" glucose control is attempted and, for this reason, glycemic control of cats is based on the presence or absence of clinical signs rather than strict monitoring of blood glucose. The practice of using the presence of clinical signs as an indication of glycemic control has been supported by several studies. Most owners and veterinarians subjectively determine a cat to be a well controlled diabetic when polyuria and polydipsia resolve and the cat eats well and gains weight. Laboratory measures of glycemic control, such as fructosamine, correlate well to subjective assessments based only on clinical examination in many cases. Hypoglycemia is a common reason that cats with so-called "transient diabetes" are presented to the veterinarian. Hypoglycemia that occurs after the cat receives an appropriate pharmacologic insulin dose should immediately raise a suspicion that the cat's insulin requirement has decreased. In the author's experience, daily or EOD urine monitoring has proven useful for reducing the incidence of hypoglycemia. Owners are instructed to test the morning urine for glucose and ketones but do not make insulin adjustments based on the test results. The owners are instructed to call for advice if the urine is negative for glucose or positive for ketones, otherwise the prescribed insulin dose is given. Monitoring in this manner is not perfect but does help to avoid giving insulin to cats that might have been normo- or hypoglycemic most of the preceding several hours.

Glipizide. Glipizide is a sulfonylurea drug that directly enhances insulin release from pancreatic islets. It is indicated for use in non-ketotic diabetic cats with mild to moderate hyperglycemia and characteristics of Type II DM of humans. It is reported that up to 30% of diabetic cats may have a form of DM that resembles human Type

II DM. However, the number of cats that have a favorable clinical response to glipizide appears – anecdotally – to be much less than 30%. A number of factors may be responsible for the apparent discrepancy, including, among others, the patient population characteristics (primary versus referral patients), disease stage at the time of diagnosis, and the presence of other influences (e.g., glucose toxicity) on the therapeutic response. A concern about the use of glipizide is the potential for hastening beta cell loss as a result of chronic stimulation of insulin release and a concomitant increase in pancreatic amyloid deposition. Experimental studies have indicated that this concern may be valid. The key to successful management of DM with glipizide is patient selection. Unmitigated failure would be expected if glipizide therapy were prescribed for all diabetic cats at the time of diagnosis. With proper patient selection, glipizide can be very effective for relatively short-term glucose control. The ideal candidate is mildly hyperglycemic (< 300 mg/dl) and non-ketotic; frequently, these cats are obese. Unfortunately, although some cats do well on glipizide for long periods, most eventually require insulin to achieve sufficient glycemic control.

Chromium and vanadium. Chromium and vanadium are trace metals with insulinomimetic properties that have received attention as a possible adjunct therapies for feline DM. These minerals have multiple effects to decrease insulin resistance, increase insulin peripheral action, and favorably alter glucose metabolism. The efficacy of these compounds for the treatment of DM is questionable. Currently, neither mineral is recommended for routine use in humans with DM, except when a deficiency is demonstrated.

Some investigations have shown beneficial effects in normal and diabetic cats supplemented with chromium and vanadium but the role of these compounds in the management of feline DM remains to be determined. In normal, non-obese cats, chromium supplementation improves fasting glucose and glucose tolerance but does not alter insulin concentrations. However, in other studies, chromium supplementation had no effects on glucose tolerance tests in obese and non-obese cats.

Vanadium is thought to decrease insulin resistance and enhance glucose utilization via direct actions to enhance the activity of insulin signaling pathways, although the exact mechanism of action is not known. Vanadium supplementation is generally well tolerated by cats and beneficial effects on glycemic control have been reported. Although an eventual role may be found for these compounds, the current knowledge does not allow for a general recommendation for their use in diabetic cats to be made.

Metformin, acarbose, and troglitazone. A number of drugs have been used successfully to manage glycemia in humans with DM; some of these, such as metformin, acarbose, and troglitazone, have been suggested as potential therapy for feline DM. When used in clinical patients, the results have been less-than-spectacular. Metformin reduces hepatic glucose production and may also decrease insulin resistance. Metformin pharmacokinetics have been determined in cats and have found to be similar to those determined in humans. Clinical experience with metformin in diabetic cats, although scant, has not been promising. Acarbose is an alpha-glucosidase inhibitor that modulates blood glucose by its action to decrease glucose absorption from the gastrointestinal tract. Experience with its use in feline DM is limited and anecdotal; reports indicate that the drug has inconsistent effects on feline blood glucose. Troglitazone was a promising drug for treatment of human DM, but was removed from the market due to unacceptable side effects. Troglitazone was well tolerated when administered to normal, healthy cats in a pharmacokinetic study. The pharmacokinetic parameters of troglitazone in the cat were similar to those described for other species, including humans. The effects of troglitazone on glucose tolerance and insulin sensitivity in cats have not been determined.

With the exception of insulin, the use of the discussed drugs, including chromium and vanadium, as therapy for feline DM is essentially unexplored. Thus, before we dismiss these drugs entirely based on the findings of small studies or anecdotal reports, there should be a call issued for large, prospective studies to fully evaluate the efficacy of these drugs as DM treatments.

Dietary Therapy. The role of diet to control DM has been the subject of numerous investigations. The principles of diet therapy for diabetic cats have been distilled from the human medical literature. Species differences in the composition of the normal diet, nutrient metabolism, and perhaps even the pathogenesis of DM, complicate extrapolation of dietary recommendations from one species to another. Species-specific investigations are preferred when possible. Fortunately, the current focused effort in this area of research is likely to generate helpful knowledge about dietary management of feline DM.

The goals of dietary therapy are not uniform for all diabetic cats. Obese diabetics may benefit from weight loss. Mild to moderate caloric restriction is appropriate when weight loss is the goal. Weight gain may be desirable for diabetics that are underweight at the time of diagnosis. In this case, the caloric requirements for the desired weight can be determined and the ration adjusted accordingly. The nutrient composition of the diabetic cat's diet may be varied to optimize the caloric content or to gain an advantage over glycemic management. The schedule of feeding may impact on glycemia and the efficacy of injected insulin. It is important to allow the cat to adhere to its usual feeding schedule whenever possible. For example, if the cat was offered free choice before DM was diagnosed, it should be allowed free choice as a diabetic. The insulin protocol should be molded around the cat's feeding pattern rather than vice versa.

Fiber. The role of dietary fiber in the management of glycemia is still not entirely known, despite being recommended as adjunctive management for feline DM for several years. Fiber reduces glycemia in humans by modulating the post-prandial absorption of glucose from the intestinal tract. A similar mechanism is thought to be at work in the cat although species differences in the normal magnitude of the postprandial rise in blood glucose may make this a moot comparison. However, there were several studies that indicated that diabetic control was improved in cats that received a high fiber diets compared with controls, suggesting that other factors might be at play in fiber fed cats.

Protein. The carnivorous nature of cats is familiar to everyone. Physiologically, cats are obligate carnivores, with a natural diet that is high in protein and low in carbohydrate. Recent investigations into the effects of dietary protein content on DM management have yielded interesting results. Owned, diabetic cats treated with insulin and a high fiber diet were allowed to continue on insulin therapy but the diet was changed to a high protein-low carbohydrate diet (~15% and ~2%, respectively). The high protein diet was associated with reduced insulin requirements in nearly all cats studied. The reduced insulin requirement was not associated with a loss of glycemic control and fructosamine levels did not change in the high protein group. Diets that are high in protein may more closely mimic a cat's natural diet than diets that contain large amounts of glucose. Diets containing lots of glucose (~35%) produce postprandial hyperglycemia in cats, but diets with a lower glucose content or with a different carbohydrate do not.

Traditionally, dietary therapy for DM has generally been used in conjunction with some form of medical therapy, usually insulin, to control glycemia. Dietary therapy alone would not usually be expected to result in normalization of glycemia. However, the author has noted rapid resolution of hyperglycemia and clinical signs of DM in a number of cats that received insulin and a high protein diet as initial therapy for DM. Insulin could eventually be discontinued in some of these cats and they were maintained on the diet alone. Although anecdotal, these observations reflect information available in the literature regarding the efficacy of high dietary protein for controlling hyperglycemia and suggest the potential usefulness of this approach.