**Cats Are Not Small Dogs- Things to Consider When Treating Feline Diabetes**

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**Insulin Therapy in Cats**

The long-acting insulin preparations are recommended in cats because the ideal glycemic control achieved with these preparations is superior to the glycemic control achieved with intermediate-acting insulin preparations (e.g., NPH, Vetsulin®) in most cats. Improved glycemic control has been associated with higher diabetic remission rates.

**Currently Available Long-acting Insulin Preparations**

- Lantus® (insulin glargine 100 U/ml)
- Levemir® (insulin detemir 100 U/ml)
- ProZinc® (protamine zinc insulin 40 U/ml)
- Toujeo® (insulin glargine 300 U/ml)

Currently available formulations that are routinely used in cats include insulin glargine (Lantus®), PZI (ProZinc®), and insulin detemir (Levemir®). The recommended starting dose for these long acting formulations is 1-2 U/cat every 12 hours. The majority of cats will have acceptable glycemic control at a dose of 1-6 U/cat every 12 hours. Twice daily insulin administration is recommended and is more likely to result in ideal glycemic control. If it is not possible to administer insulin twice daily, once daily administration of Levemir® or Toujeo® (starting dose: 1-2 U/cat) may provide acceptable clinical control and decrease the occurrence of complications associated with untreated diabetes mellitus. Toujeo® has been studied in healthy cats, but there is limited information about clinical use in diabetic cats.

**Dietary Recommendations**

- Low carbohydrate diet (Purina DM, Hill's Prescription Diet m/d)
    - Associated with better clinical control, reduce insulin requirements, and increased remission rates
- Meal feeding is ideal, but eating does not need to be coordinated with insulin administration (grazing is allowed)
- Recommend weight loss in obese cats
    - 1-2% loss of body weight per week
- The author has had success with Hill's Prescription Diet Metabolic when cats gain weight or fail to lose weight with high protein/low carbohydrate diets.

**Goals of Therapy**

- Resolution of clinical signs
- Normal activity level and good quality of life
- Stable body weight
- Possible to achieve ideal glycemic control in most cats with long-acting insulin
- Diabetic remission

## Monitoring and Insulin Dosage Adjustment

### Continuous Glucose Monitoring

The FreeStyle Libre continuous glucose monitoring system provides a readily available, cost-effective way to continuously assess glycemic control over a 14-day period. This system does not require calibration, so the owner does not have to obtain blood samples from the pet to check the blood glucose concentration. Continuous glucose monitoring is the recommended assessment method for any challenging diabetic and could replace the blood glucose curve in most diabetics. It can be challenging maintain the glucose sensors on cats for the 14-day period.

### Home Blood Glucose Curve Protocol

- Use a hand-held glucometer that has been designed and validated for use in cats
- Blood glucose before food and insulin administration
- Feed and administer insulin
- Blood glucose 1 hour after food and insulin, then every 4 hours in cats receiving long-acting preparations until the next dose of insulin

Increases in the insulin dosage should be based on the presence of clinical signs combined with an objective assessment of glycemic control (continuous glucose monitoring, blood glucose curves, fructosamine concentration, and HbA1c). Routine blood glucose monitoring allows for assessment of glycemic control as well as detection of subclinical hypoglycemia. This is especially important in cats because of the possibility of diabetic remission (return to a noninsulin-dependent state). If it is not possible to use a continuous glucose monitor (FreeStyle Libre) or perform a blood glucose curve, a combination of urine glucose and HbA1c or fructosamine can be used for monitoring. The insulin dose is typically increased by 0.5-1 unit/dose.

### Reasons for Poor Regulation

- **Insulin therapy**
    - Underdosing
    - Time-action profile is not appropriate (using intermediate-acting insulin)
    - Handling issues and/or inactivation
    - Administration issues

- **Insulin resistance**
    - Hypersomatotropism- recommend screening all diabetic cats 6-8 weeks after initiating insulin therapy (see below)
    - Urinary tract infection
    - Pancreatitis
    - Renal disease
    - Hyperthyroidism
    - Hyperadrenocorticism

### Hypersomatotropism

Hypersomatotropism is a state of excessive production and secretion of growth hormone (GH). Acromegaly is the phenotype or clinical syndrome that develops as a result of chronic exposure to excessive amounts of GH and Insulin-like Growth Factor 1 (IGF-1). The phenotypical changes of acromegaly are slow to develop and may not be present in all cats at the time hypersomatotropism is diagnosed. For this reason, it is more appropriate to refer to the presence of increased concentrations of GH as hypersomatotropism rather than acromegaly, especially when the clinical syndrome is not present.

Feline hypersomatotropism is most commonly caused by a GH-producing pituitary gland adenoma, although cases of pituitary acidophilic hyperplasia and adenocarcinoma have been documented. The reported prevalence in diabetic cats based on an IGF-1 concentration >1000 ng/mL (131 nmol/L) is 26.1%, 21.3%, and 12.5% in the UK, Netherlands, and Switzerland, respectively. This is much higher than would be expected if the results were based solely on the presence/detection of an acromegalic phenotype (broad facial features, prognathia inferior, clubbed paws, organomegaly) and insulin resistant diabetes mellitus. It is also worth noting that acromegaly and hypersomatotropism were recently reported in multiple cats without diabetes mellitus. This is not necessarily surprising considering the slow and insidious disease process and that 2/3 of people with hypersomatotropism are not diabetic.

**Diagnosis**

The diagnosis is based on documentation of an increased serum IGF-1 concentration and evidence of pituitary enlargement with computed tomography (CT) or magnetic resonance imaging (MRI). Insulin-like growth factor 1 is a useful screening tool because validated assays are readily available, it reflects 24-hour GH secretion, and is a sensitive marker for GH excess. Further testing (cross-sectional imaging) is recommended if a cat is found to have an increased IGF-1 concentration. With regards to newly diagnosed diabetic cats, it is important to recognize that hepatic IGF-1 production is dependent on insulin in the portal circulation so screening for hypersomatotropism prior to insulin administration may result in a false negative result. It is recommended that screening be performed 4-6 weeks after initiating insulin therapy. An IGF-1 concentration >1000 ng/mL (131 nmol/L) is strongly suggestive of hypersomatotropism although this cutoff is arbitrary and may result in an underestimation of the true prevalence and underdiagnosis of mild or early forms. It is suggested that cats with classic clinical findings or those with an IGF-1 concentration between 800-1000 ng/mL (105 – 131 nmol/L) have cross-sectional imaging performed or be retested in the future. Based on prevalence studies in diabetic cats, it is recommended that an IGF-1 concentration be measured in all diabetic cats 4-6 weeks after initiating insulin therapy.

**Treatment**

Treatment can be divided into definitive (hypophysectomy, radiotherapy), targeted medical therapy (Signifor® [pasireotide], Novartis) and conservative. The conservative approach focuses on management of diabetes mellitus with insulin therapy and is reserved for cases in which definitive treatment is not available or is declined by the owner. The high insulin doses often required combined with fluctuations in insulin resistance predispose these cats to the development of hypoglycemic complications. For this reason, routine (before each dose of insulin) home blood glucose monitoring is recommended. This allows the insulin dose to be adjusted prior to each injection and also allows the owner to monitor for and confirm the occurrence of hypoglycemic episodes. Assessment of glycemic control should be based on the presence of clinical signs consistent with unregulated diabetes, blood glucose concentration curves and the fructosamine concentration. It is important to remember that most of these cats will not

lose weight despite unregulated diabetes and some cats may remain polyphagic even when glycemic control is acceptable.

**Targeted Medical Treatment**

A novel multi-receptor ligand somatostatin analog (Signifor® [pasireotide], Novartis) has shown promise in cats treated by researchers at the Royal Veterinary College. Pasireotide is a new drug that is manufactured and marketed for human use. Difficulty obtaining the drug and extreme cost has greatly limited the use of this drug in the United States.

**Hypophysectomy**

Transsphenoidal hypophysectomy is considered the treatment of choice for many cats with hypersomatotropism. With successful surgery, nearly the entire tumor is removed and there is rapid normalization of the GH concentration. This results in an overall reduction in insulin resistance and diabetic remission (non-insulin dependent state) in some cats. Unfortunately, this is a technically challenging surgery that has limited availability in the US. The limited availability, cost, and inherent risk of this procedure currently limit its utility in the US.

**Radiotherapy**

Despite limited availability in some locations, radiation therapy is the most widely available and frequently used treatment modality in the US. The goals of radiation therapy include reduction in GH and IGF-1 production as well as a reduction in tumor size.

**Prognosis**

The prognosis for feline hypersomatotropism can be quite variable and is influenced by the stage of disease at the time of diagnosis and treatment administered. Many owners elect to pursue the conservative approach rather than targeted therapy because of lack of availability, inherent risks, and the cost of these treatments. Regardless of the treatment chosen, early detection benefits both the cat and the owner because we are able to more effectively manage the associated complications and provide guidance through the decision-making process. Cats treated conservatively are managed until their quality of life is deemed unacceptable.

**Diabetic Remission**

- Noninsulin-dependent state
- Usually occurs within 3-4 months of initiating insulin therapy
- More common with rapid correction of hyperglycemia and ideal glycemic control
- Recommend a gradual reduction in the insulin dose to 0.5 – 1 U/cat every 12 – 24 hours before discontinuation
    - This may increase the likelihood of achieving remission
- Insulin therapy may be required in the future
    - ~25-40% of cats in remission will relapse

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