MANAGEMENT OF FELINE DIABETES MELLITUS: MAXIMIZING REMISSION

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MANAGEMENT OF FELINE DIABETES

Therapy for diabetes should be instituted as soon as possible after diagnosis with the main goal being remission; euglycaemia without the need for insulin therapy. For cats not achieving remission the goals are resolving clinical signs and avoiding hypoglycemia. Insulin and dietary modification are the principal therapies used for management of diabetic cats.

Feeding

Diets low in carbohydrates and high in protein reduce post-prandial hyperglycaemia and insulin concentrations in healthy cats. Initial data in diabetic cats suggests these diets result in better clinical control, reduced insulin requirements and increased rates of diabetic remission. Thus a commercial low carbohydrate diet should be used in diabetic cats, unless contraindicated by other disease.

Obesity in cats reduces insulin sensitivity, and hence obese cats should be fed an energy restricted diet so they lose 1-2% body weight per week.

Insulin therapy

Long-acting insulin is the preferred treatment to achieve remission. Achieving good glycaemic control with intermediate acting potent insulins such as NPH and lente is often difficult. Long-acting insulins glargine and detemir provide better glycaemic control, reduced risk of clinical hypoglycaemia and a significantly higher probability for remission when given twice daily with a low carbohydrate diet.

Cats presented with diabetic ketoacidosis can be treated with glargine intramuscularly or intravenously, as when injected this way it acts like regular insulin and can be used for initial stabilization.

Glargine

Glargine is a long-acting human synthetic insulin analogue. It should not be mixed or diluted. In cats once daily administration produces a similar mean daily glucose concentration and area under the 24hr glucose curve as PZI, and both had significantly lower values than lente insulin. Glargine produced a glucose nadir later than PZI or lente, and had longer duration of action (22hrs) than lente.

However, glargine has a longer effect if administered BID compared to once daily. Once daily administration produces similar remission rates to twice daily dosing of lente insulin. Twice daily dosing is recommended as excellent glycaemic control facilitates remission, and glycaemic control is superior if glargine is injected twice daily.

Glargine can be safely instituted at 0.5U/kg bid and serial blood glucose curves should be obtained daily for 3 days. When using glargine, it is often more useful to assess pre-insulin glucose concentration rather than the nadir glucose as it often takes 3-5 days for a good glucose-lowering effect to be seen. This may be due to the long duration of action and carry-over effect of glargine. Almost all cats will need to have their initial dose reduced within 2 weeks and many will achieve remission within 4 weeks. Glargine can also be used intramuscularly in combination with subcutaneous insulin for treatment of ketoacidosis.

Detemir is a new long-acting synthetic insulin analogue which can be diluted with saline or water prior to injection. Detemir results in similar remission rates and time to remission as glargine, but the median maximum dose used (1.75 IU/cat BID) is less than with glargine (2.5 IU/cat BID)

Monitoring and adjusting insulin dose when using glargine or detemir should be based on pre-insulin and nadir glucose concentration, water intake, urine glucose concentration and clinical assessment (Table 1). Pre-insulin glucose concentrations measured at home are an excellent tool for modifying daily doses of glargine or detemir. Cats treated with glargine should have a negative, 1+ or 2+ urine glucose (scale 0-4+) and a value of 3+ or 4+ suggests a dose increase is required.

The good glycaemic control achieved when using glargine or detemir likely reverses glucose toxicity of B-cells, facilitating endogenous insulin production and a reduced requirement for exogenous administration. Insulin dose may be reduced sequentially as indicated by blood glucose concentration, urine glucose and water intake, until the dose is ½-1U/cat SID prior to Insulin may then be withdrawn, and the cat monitored to ensure continued remission. Even if normoglycaemic, it is recommended that insulin is not withdrawn within 2 weeks of commencement of therapy. Newly diagnosed diabetic cats that have good glycaemic control within the first few weeks of therapy, are very likely to go into diabetic remission. Cats that have been long-term diabetics eg >6 months are less likely to go into remission, probably because of progressive B-cell loss associated with glucose toxicity.

In conclusion, glargine and determir are safe and effective in treating feline diabetes and are the preferred insulins in newly diagnosed diabetic cats. Long-term diabetic cats should be changed to glargine or detemir if there is poor glycaemic control or owners wish to pursue once daily injections. High remission rates are expected in newly diagnosed cats when combined with a low-carbohydrate diet and twice daily injections.

Monitoring therapeutic efficacy

Response to treatment can be evaluated using owner assessment, clinical signs, and changes in body weight and water intake. The pre-insulin glucose concentration is important when using glargine, detemir and PZI, as there is often a persisting effect from the previous injection. Nadir (lowest) glucose concentration limits the dose increase that can be made when nadir glucose concentration is in the lower end of the normal reference range.

When using other insulins (eg lente or NPH), dosage changes are usually based on nadir blood glucose. Pre-insulin glucose, time to nadir and the time to return to baseline are also used where appropriate (table 2).

Table 1. Parameters for changing insulin dosage when using insulin glargine or detemir in diabetic cats.

Parameter used for dosage adjustment	**Change in dose**
Begin with 0.5 U/kg if blood glucose (≥360 mg/dL (≥ 20 mmol/L) or 0.25/kg of ideal weight if blood glucose is lower. Do not increase in first week unless minimum response to insulin occurs or are using home blood glucose montoring, but decrease if necessary. Monitor response to therapy for first 3 days If no monitoring is occurring in first week, begin with 1 U/cat BID	
If pre-insulin blood glucose concentration >216mg/dL (>12mmol/L) provided nadir is not in hypoglycaemic range ***or*** If nadir blood glucose concentration >180mg/dL (>10mmol/L)	Increase by 0.25-1U
If pre-insulin blood glucose concentration 180<216mg/dL (≥ 10 - ≤12mmol/L) ***or*** Nadir blood glucose concentration is 90-160mg/dL (5-9mmol/L)	Same dose
If nadir glucose concentration is 54-72 mg/dL (3-4 mmol/L)	Use clinical signs, water drunk, urine glucose and next pre-insulin glucose concentration to determine if insulin dose is decreased or maintained.
If pre-insulin blood glucose concentration <180mg/dL (10 mmol/l) ***or*** If nadir blood glucose concentration < 54mg/dL (<3 mmol/l)	Reduce by 0.5- 1UU ***or*** if total dose is 0.5-1U SID, stop insulin and check for diabetic remission
If clinical signs of hypoglycemia are observed	Reduce by 30-50%
If blood glucose measurements are not available:	
If water intake is ≤20mls/kg on wet food or ≤60mls/kg on dry food	Same dose
If water intake is >20mls/kg on wet food or >60mls/kg on dry food	Increase dose by 0.5-1U
If urine glucose is > 3+ (scale 0 - 4+)	Increase dose by 0.5-1U
If urine glucose is negative	Decrease dose until 0.5-1 U SID and then check for diabetic remission

Table 2: Parameters for changing insulin dosage and frequency based on blood glucose measurements when using lente or NPH insulin in diabetic cats.

Blood Glucose Variable	**Recommendation**
Use an initial dose 0.5 U/kg of lean body weight BID if blood glucose is ≥ 360 mg/dL (> 20 mmol/L) and 0.25 U/Kg BID if glucose < 360 mg/dL (> 20 mmol/L).	
If pre-insulin blood glucose concentration is <210mg/dL (< 12mmol/L)	With-hold insulin and check for diabetic remission provided cat treated for a minimum of 2 weeks; otherwise reduce dose
If pre-insulin blood glucose concentration is 211-250mg/dL (13 - 16mmol/L)	Total dose should be no more than 1U/cat bid
If nadir blood glucose concentration is < 54mg/dL (<3mmol/L)	Dose should be reduced by 50 %
If nadir blood glucose concentration is 54-90mg/dL (3 – 5mmol/L)	Dose should be reduced by 1U if poor control of

	clinical signs of diabetes; dose should remain the same if exemplary control of clinical signs
If nadir blood glucose concentration is 91-180mg/dL(6 – 9mmol/L)	Dose should remain the same
If nadir blood glucose concentration is >180mg/dL(> 10mmol/L)	Dose should be increased by 1U
If nadir blood glucose concentration occurs within 3 hours of insulin administration, or blood glucose returns to baseline within 8 hours	Change to longer acting insulin (ie. Glargine, detemir or PZI)
If the nadir blood glucose concentration occurs at 8 hours or later	Once daily administration may be used, although twice daily administration at a reduced dose is preferred

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