

Feline diabetes: maximizing your treatment results

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The primary goal of management of a newly diagnosed diabetic cat has changed from just controlling clinical signs and avoiding clinical hypoglycaemia, to one where the primary goal is to achieve diabetic remission, and in some cats, a cure for diabetes. Preliminary data show that about 25-30% of cats that achieve remission, have no evidence of glucose intolerance on a glucose tolerance test, meaning essentially that they are cured. The remaining 70% have various levels of impaired glucose intolerance, and hence should be classified as pre-diabetic.

With appropriate therapy, remission is achievable in approximately 90% of newly diagnosed diabetic cats, that is, cats are able to maintain euglycaemia without the need for insulin therapy. However, remission rates are substantially lower in cats with long-standing diabetes where hyperglycaemia has been inadequately controlled because of inappropriate insulin type or dose adjustments, or because underlying disease such as acromegaly precludes achieving excellent glycaemic control. Typically, long-term, poorly controlled cats referred for management of their diabetes, have remission rates of 30% or less, because there are inadequate numbers of functioning beta cells remaining to maintain euglycaemia without exogenous insulin therapy.

Whatever the underlying cause of diabetes in an individual cat, chronic hyperglycaemia causes glucotoxic and lipotoxic damage to beta cells which initially is reversible but later irreversible. Therefore, therapy needs to be aimed at rigorously controlling blood glucose and should be instituted as soon as possible after diagnosis. Early institution of rigorous glycaemic control results in remission rates of > 80%, whereas waiting 6 months or longer to institute the same rigorous control results in substantially lower remission rates, which are in the order of 30%. The key factors in achieving high remission rates in newly-diagnosed diabetic cats are firstly, use of long-acting insulin, secondly, feeding a low carbohydrate diet and thirdly, frequent monitoring, ideally home monitoring, together with appropriate adjustment of insulin dose. For those cats not achieving remission, the goals are to resolve clinical signs and avoid hypoglycaemia.

Insulin therapy

The long-acting insulins glargine and detemir remain the preferred treatment for diabetes mellitus in cats to maximize the probability of remission. Their effectiveness and safety is enhanced when combined with a low-carbohydrate diet. Achieving good glycaemic control and hence remission with intermediate-acting potent insulins such as NPH and lente is often difficult, and increases the risk of clinical hypoglycaemia. Published data suggests that the long-acting insulins glargine and detemir provide better glycaemic control and reduced risk of clinical hypoglycaemia when given twice daily and combined with a low-carbohydrate diet. More importantly, their use results in a significantly higher probability for remission.

Cats presented with diabetic ketoacidosis can be treated with subcutaneous glargine during stabilisation. When used intramuscularly or intravenously, glargine acts like regular insulin and can be used for initial stabilisation in place of regular insulin.

Glargine can be safely instituted at 0.5 IU/kg q12h and serial blood glucose curves should be obtained daily for 3 days either in hospital or at home. When evaluating the blood glucose curve using glargine, it is often more useful to assess pre-insulin glucose concentration rather than the nadir glucose. We have found it often takes 3--5 days for a good glucose-lowering effect to be seen in the glucose curves, possibly because of 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 4-6 weeks.

In contrast to glargine, detemir is a newer synthetic insulin analogue with long duration of action through modification of the insulin molecule via addition of an acylated fatty acid chain. This modification facilitates reversible binding to plasma proteins, particularly albumin, from where it is released slowly into plasma. The modification also prolongs self-association in the injection depot, which prolongs absorption from subcutaneous tissue at the injection site and contributes to the long duration of action.

Detemir results in similar remission rates and time to remission as glargine. The same dosing protocol as for glargine can be used. Although, the median maximum dose reported from one study (1.75 IU/cat q12h) was approximately 30% less than with glargine (2.5 IU/cat q12h) for a similarly designed study, this might be because the cats on detemir were older and had higher rates of concurrent renal disease, which might have decreased the renal clearance of detemir. This is unlike the situation in dogs, where the dose of detemir is approximately ¼ of that for glargine. The advantages of detemir is that it can be diluted with a special diluting medium supplied by the manufacturer (although it appears to be difficult to obtain from the manufacturer in USA) and that the duration of action might be longer and more predictable than with glargine. The advantage of glargine is that when administered intramuscularly or intravenously, it has a similar action profile to regular insulin and can be used in the treatment of cats with diabetic ketoacidosis.

Monitoring and adjusting insulin dose when using glargine or detemir should be based on a number of parameters, including pre-insulin and nadir glucose concentration, water intake, urine glucose concentration and clinical assessment as shown in Table 1. Cats treated with glargine or detemir should have a negative, 1+ or 2+ urine glucose (scale 0--4+) and a value of 3+ or 4+ probably indicates that a dose increase is required. Owners should be encouraged to do home glucose monitoring to facilitate tight glycemic control. Meters designed for use with feline blood are advantageous in achieving remission because the accuracy is greater than meters designed for human blood which tend to read lower than the blood glucose actual value. Owners performing home monitoring still need to return frequently for veterinary visits, ideally once a week, until remission is achieved, so the home log of glucose concentrations and insulin dose can be reviewed and dose adjusted as required.

New developments in management of human diabetes include GLP-1 agonists such as exenatide, which now exists in a once-a-week form, however, no clinical trial data have yet been reported from diabetic cats. This drug stimulates insulin secretion but only in the presence of glucose, so is not associated with severe clinical hypoglycaemia in the way that insulin therapy is. In addition it stimulates

beta cell regeneration. Another new development is a once-a-week insulin for human use, which potentially could provide a once-a-day or once-every-other-day therapy for cats.

Feeding: Low carbohydrate, restricted phosphorus diet

Diets low in carbohydrate reduce postprandial hyperglycaemia and insulin concentrations in healthy cats and are associated with increased remission rates in diabetic cats. Data from diabetic cats indicate that low-carbohydrate diets result in better clinical control, reduced insulin requirements and increased rates of diabetic remission. One study demonstrated a significantly higher remission rate using a diet with approximately 12% of energy from carbohydrate (Hills m/d) compared to 26% carbohydrate (Hills w/d); the protein contents were similar. In the first few days of treatment, if cats refuse these low-carbohydrate diets, they should be offered any palatable food. However, a commercial low-carbohydrate diet should be used in diabetic cats, unless contraindicated by other disease. When required, dietary management of renal disease using a restricted-protein diet should take precedence over dietary management of diabetes; acarbose can be used to reduce glucose absorption from the gastrointestinal tract. However, acarbose works well only in cats that consume their food within a short time after it is offered and is much less effective in cats which eat multiple small meals during the day, which is the feeding pattern more often observed in cats with IRIS stage 3 or 4 renal disease. Acarbose substantially decreases postprandial blood glucose in cats fed a high carbohydrate diet, but has no real benefit in cats eating a low carbohydrate diet.

Obesity in cats markedly reduces insulin sensitivity, and hence obese diabetic cats should be fed restricted energy so they lose 1--2% bodyweight per week. Weight loss improves insulin sensitivity, and may reduce insulin requirements. Although many diabetic cats achieve remission without substantial weight loss, achieving an ideal bodyweight is critical for maintenance of long-term remission. Due to the decreased postprandial hyperglycaemia with a low-carbohydrate diet, diets with less than 20% of energy from carbohydrate should be used for obese diabetic cats during the energy-restriction phase. In contrast to feline diabetic diets, most feline weight loss diets are low-fat, high-carbohydrate diets and are not recommended for newly diagnosed diabetic cats being managed to achieve remission.

There is increasing data now available linking renal disease to diabetes in cats. Therefore, given the frequency of renal disease in diabetic cats (17% in one study in 5-10 year old cats), attention should be paid to the phosphate content of the diet. Many grocery-line low-carbohydrate--high-protein feline maintenance diets are high in phosphate. Cats in stage 1 or 2 renal failure which do not require protein or phosphate restriction should be placed on a low-carbohydrate diet formulated for feline diabetics that is low in phosphate; high-phosphate, ultra low-carbohydrate diets are best avoided.

In conclusion, the principal goal of therapy has changed from controlling clinical signs to that of aiming for remission, and in some cases, cure of their diabetes. Key factors in achieving these goals are the use of the long-acting insulins glargine and detemir, low carbohydrate, restricted-phosphorous diets, and close monitoring, ideally with home monitoring, and appropriate dose adjustments. New therapies are emerging from human studies and they may have a future role in improving management of feline diabetes and reducing frequency of therapy.