Diabetes Mellitus in Feline Patients: How Sweet It Isn't (or is it…)

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Atlantic Provinces Veterinary Conference
April 19-21, 2024

According to ALIVE criteria, diabetes mellitus (DM) is a heterogeneous group of diseases characterized by hyperglycemia due to inadequate insulin secretion, action or both. DM is then subdivided based on an absolute lack of insulin (Type 1 or juvenile diabetes) or a relative lack of insulin (Type 2 or insulin resistant DM). Although there is no real test in feline medicine to know if a patient is a Type 1 or Type 2 diabetic, it is estimated that 95% of newly-diagnosed diabetic cats are Type 2.

Clinically, feline caregivers are aware when their cat has developed diabetes even if they are unable to verbalize the disease that matches their concerns. A diabetic cat will manifest hyperglycemia by multiple clinical signs including:

- Polydipsia ("My cat sure is drinking a lot of water")
- Polyuria ("I sure have to clean out that litterbox of urine more than ever before")
- Alterations in appetite ("My cat is picky" or "My cat is always hungry")
- Sarcopenia ("My cat feels skinny/now I can feel their spine")
- Poor coat quality ("Why is my cat starting to get matts?")
- Ddiabetic neuropathy ("Why is my cat limping")
- The ADR patient ("Something is wrong with my cat, I know it!")

It is important to appreciate a client's observations as these clinical signs will reverse with appropriate treatment. We can use this reversal/improvement of clinical signs as a means of monitoring treatment success (what the speaker calls "hands off monitoring"). Conversely, a decline in patient status can alert us that our treatment plan is not appropriate and we can take action before it comes an emergency (i.e. catching a cat in ketosis rather than full diabetic ketoacidosis/DKA).

With appropriate control of blood sugars (to reverse beta cell damage) and resolution of the underlying disease that contributed to the diabetes in the first place (e.g. resolving obesity) it is possible for a Type 2 diabetic to go into remission or a non-insulin dependent state. With poor glucose regulation, chronic hyperglycemia can cause irreversible damage to the beta cells and the feline patient transitions from a Type 2 to a Type 1. Type 1 diabetics have undergone beta cell destruction and will always be in an insulin dependent DM state. DM type is very important when it comes to treatment as many treatments used in Type 2 DM (such as oral hypoglycemics) would be contraindicated in a Type 1 individual.

Once we have a DM diagnosis, what are our pharmaceutical options for treatment? In the early 2000's, the human Type 2 DM sulfonylureas drug class (e.g. Glyburide, Glipizide) were used in the cat with very limited success. This led to feline practitioners shying away from oral hypoglycemics and using insulin as the pharmaceutical of choice to regulate a diabetic feline. Insulin choices for use in cats have changed over the decades. Currently, there are two licensed veterinary insulins for cats: Prozinc® (Boehrigner-Ingeelhem) and Caninsulin/Vetsulin® (Merck). The human-licensed insulin Glargine (Lantus®, Sanofi) has also been used with considerable success. No study has shown one insulin to be better at achieving remission than another. Thus, selecting a starting insulin will largely come down to practitioner preference, product availability, and patient response. Cats can have concurrent endocrinopathies including hyperadrenocorticism and hypersomatotropism (acromegaly) that can greatly impact an individual's response to insulin.

In 2024, Boehringer-Ingelheim launched the first SGLT2 inhibitor for use in Canada in cats with Type 2 DM under the product name Senvelgo® (Vexagliflozin). The launch of SGLT2 inhibitors makes 2024 an exciting time to manage DM in cats as it gives us an effective oral option to achieve euglycemia in our feline patients.

SGLT2 or Sodium-Glucose Transporter 2 are transporters found in the proximal tubule of the kidney. Their role, along with SGLT1, is to actively move glucose from filtrate (a low glucose solution) to blood (a high glucose solution). In a diabetic, the blocking of SGLT2 allows for the "dumping" of excess glucose via the urinary system and euglycemia to be achieved. As SGLT2 works independent from insulin, and the body still needs insulin to survive/not go into DKA, SGLT2 inhibitors are contraindicated in a patient with absolute insulin deficiency (i.e Type 1 DM). As we are unable to know the exact insulin production of a cat, there is a risk of a patient becoming DKA on these medicines, so they must be closely monitored for ketone production. Cats that went DKA on SGLT2 inhibitors were likely to do so within the first 14 days of starting these medications; making this the time-period where more aggressive monitoring is required. Cats that had previously been on insulin and then were switched to a SGLT2 inhibitors had an approximately 3x greater chance of becoming DKA. This increased risk is likely due to these cats having more beta cell damage (and thus lower insulin production) than a newly diagnosed DM cat. As SGLT2 inhibitors are going to achieve euglycemia regardless of ketone production, these patients may manifest with a normal blood glucose despite being in DKA (i.e. euglycemic DKA). Cats that are acting unwell on SGLT2 inhibitors, or are trending into DKA based on blood ketones, should stop this drug immediately and be transitioned onto insulin.

Ketones in cats can be monitored via blood or urine. Handheld ketone monitors, similar in appearance and use to a glucometer, are readily available. If monitoring via blood, it is important to note that newly diagnosed diabetic cats can have mild elevations in blood ketones consistent with being in ketosis. Blood ketone levels >2.4mmol/L yields a DKA diagnosis sensitivity and specificity of 100% and 87% respectively.

SGLT2 vs Insulin: where to start? As with any treatment plan, patient selection is going to be the key to success. If we ever have concerns about how a patient is doing, it is always essential to look at how the cat is first and glucose numbers/curves second. The most basic questions we should be asking caregivers and ourselves at every visit and for every cat are:

Are we hydrated?
Are we eating?
Are we holding weight/muscle mass?
Are we a "happy" diabetic?

References/resources:

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Wild Rose Cat Clinic of Calgary

April 21 2024

Insulin start plan for Miss Kitty-Kat

Based on in clinic spot sugars and clinical signs, we are tentatively diagnosing Miss Kitty-Kat as diabetic as her blood sugars were 29.8mmol/dL (cat normal is 4 – 9 mmol/dL) and Kitty-Kat had lots of sugar in her urine (a process called glucosuria) ☹ Full lab work has been sent to the lab to confirm no other funny business is present with results due back in a few days.

Most cats are diabetic because they are "type 2" or have insulin resistance. With careful control of sugar levels through insulin, we can give the pancreas a rest and reverse the damage done to the insulin producing cells thus pushing a cat towards a non-insulin dependent diabetic state (i.e. remission can be the ultimate goal).

A rare but worrisome form of diabetes in cats is a condition called "diabetic ketoacidosis". DKA cats are often acutely sick with vomiting, severe dehydration and anorexia. In cats at high risk for DKA, we can use ketone monitors in the same way we use a glucometer. Kitty-Kat's ketones levels today were 0.3mmol/L (our goal is always to be less than 1)

Treatment plan for MISS KITTY-KAT:

1) **Start Insulin**: We start our diabetics on insulin as their bodies are saying "we need more" than the body can make. By supplementing with insulin, the pancreas is under less stress and can start to heal. There are many types of insulin available. We start cats on long-acting insulins (both human and veterinary). Picking a starting insulin is based on veterinarian preference, availability, and the life-realities around administration. For MISS KITTY-KAT, we are starting her on the human insulin Lantus (Glargine) as this insulin can **sometimes** be dosed at once a day in cats ☺ Lantus is dosed at a value of 0.25 – 0.5 unit/kg once to twice a day or 3 – 7 units but we always start lower than theory as we do not know Kitty-Kat's sensitivity.

DOSE: We are starting Kitty-Kat on **1 unit once a day pending labs**

More insulin = lower sugar levels
Less insulin = higher sugar levels
****High sugar levels are not lethal in the short term but low sugar levels (hypoglycemic crisis) can be deadly****

2) **Patient monitoring**: We can make diabetes management in cats anywhere from very simple (monitoring of clinical signs) to more complicated (adjusting insulin doses based on blood sugar

levels/testing at home). For most of my patients, I prefer a mixture of approaches tailored to what MISS KITTY-KAT will let us get away with. On the monitoring side of things, looking at simple changes in her behaviour can tell us a lot about her sugar regulation.

Compared to a cat with unregulated diabetes, a well regulated kitty with have:

a. Improved coat quality: Diabetics tend to not groom as well, have greasy-dander coats
b. Improved mobility: Diabetic cats can have nerve issues making it seem they are walking on "pins and needles" or a slippery gait
c. Weight gain/weight stability especially with regards to muscle tone/muscle mass (so less boney along the spine)
d. Normal hydration
e. Less water intake and less urine output

3) **Blood sugar testing**: Blood glucose monitoring can be considered a more scientific/impartial way to monitor a response to insulin as it is checking our blood sugar levels at a given moment of time. We can use glucose monitoring to know if/how much insulin we need to give, how long is it lasting in the body, etc. That said, some general thoughts about home testing…

    a. Home glucose monitoring is my preferred method of insulin monitoring in cats as it avoids stress change that can be seen in clinic. We can also use other devices like urine glucose chips to measure progress in cats that are a challenge to take blood from. That said, <u>home testing is not going to work for every cat</u> in every circumstance so please do not stress if MISS KITTY-KAT is not going along with this part of the plan.

    b. If you are able to check glucose levels at home, then the tentative plan would be:
        i. Spot checking prior to insulin to make sure our numbers are not changing (i.e. we are not going into remission)
        ii. Curve: This would involve checking sugars before/at the time insulin is given and then again 4 – 6 hours after insulin and then once again before our next dose to give us an idea of how low we are going.

    c. So what is normal? Values to think about
        i. Normal range: 4 to 9mmol/dL
        ii. If less than 4, start giving sugar and call clinic ASAP. Do NOT give more insulin
        iii. If between 4 – 9 we are in normal range. DO NOT give insulin if it is the scheduled time. If sugar levels are at the low end, please monitor every few hours to ensure we are not going lower than 4.
        iv. If between 9 – 12, do NOT give insulin as Ms MISS KITTY-KAT may be going into remission. Please call/email the clinic as we may need to decrease his dose. Remember to check his b/g levels at his next scheduled insulin dose.
        v. If higher than 12, go ahead with 3 units or his current dose as per our testing results

4) **Ketone monitoring**: Ketone monitors are available on the human side and work very similar to a glucometer.

5) **Increase B12 to weekly for added pancreas support**. Low B12 can impact whole body health and delay our success in achieving remission. Please give 0.25ml (25 units) B12 weekly to MISS KITTY-KAT. B12 is also our go-to treatment to help with the symptoms of neuropathy in cats.

6) **Diet**: Wet food is our go-to as it is a high protein product. Diabetic dry foods exist that are high in protein, low in carbs (and variable in fat content). But Kitty-Kat is also a kidney cat and high protein diets can be harmful to her kidneys. The goal is striking a happy balance between these two conflicting nutrition requirements. When faced with a diabetic-kidney combination, my strategy is to manage the kidney change with diet and the diabetes with insulin as a happy balance between the two conditions

7) **Keep us posted**! When in doubt, skip the insulin and speak to myself or one of our technicians. If we are testing then I prefer to receive glucose readings via email or text. Our clinic email is info@catmd.ca.

8) **Follow-up**: Assuming all goes well we will plan to recheck in 1 week with the nurses to update our blood sugars. Any funny business before then please do not hesitate to call!

Thank you for your ongoing trust in us in caring for MISS KITTY-KAT!

Sincerely,

Dr. Liz Ruelle