DIABETES MELLITUS IN CATS

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Categories : Vets

Date : May 26, 2014

KERRY E SIMPSON BVM&S, CertVC, FANZCVSc, PhD, MRCVS looks at how treatment and management of diabetes mellitus in cats has progressed and has suggestions for approaches to stabilising difficult cases

DIABETES mellitus (DM) is a common endocrinopathy in cats. The management of feline diabetes has evolved in the past decade as we have come to better understand the unique feline physiology and metabolism. With this understanding has come new recommendations with regard to diet, feeding, monitoring and insulin administration, along with a new appreciation for the importance of underlying disease.

This article aims to highlight the recent advances in the management of the feline diabetic, discussing the management of these cases, and investigations that might be considered in cases where stabilisation proves difficult.

What is diabetes mellitus and why does it occur?

DM describes a state when the body is either not able to produce enough insulin or not able to respond appropriately to the insulin that is produced (or a combination of both).

In a non-diabetic, insulin is produced from the pancreatic beta cells. These cells are adapted to respond to the amount of glucose in the blood and release insulin whenever the glucose is elevated. Insulin allows other cells to take up the glucose and use it for energy or store it for use later.
Different forms of diabetes are described in people, namely type-one and type-two diabetes.

Type-one diabetes is caused by the immune system attacking the pancreatic beta cells and destroying them: this form of diabetes is rare in cats.

Type-two diabetes is caused by a combination of decreased insulin production and insulin resistance. It isn’t known which of these problems occurs first, but the pancreas no longer produces an appropriate amount of insulin in response to elevated blood glucose levels, and the cells are no longer able to respond appropriately to the insulin and take up glucose and process it in a normal manner. This leads to a high blood glucose level, which in turn causes a condition known as “glucose toxicity”. This further decreases the function of the pancreatic beta-cells, worsening the problem.

In people, type-one diabetes is sometimes known as insulin-dependent diabetes\(^1\), and type-two diabetes known as non-insulin dependent diabetes; however, these terms are not applicable in cases of feline diabetes.

In addition, some conditions can stop the cells in the body being able to respond to insulin or alter the production of insulin by the pancreas (or both). These conditions include over-production of steroid hormones by the adrenal glands (hyperadrenocorticism), and over-production of growth hormone from a pituitary (acromegaly; Figure 1). When these conditions occur they can block the body’s response to insulin and the production of insulin by the pancreas and, therefore, result in diabetes mellitus as a consequence of the underlying disease process (this is known as secondary diabetes mellitus).

Diabetes mellitus is the second most common endocrinopathy in cats, with an incidence of approximately one in 200\(^2\). The majority of cats diagnosed with diabetes mellitus have type-two diabetes, although secondary diabetes mellitus is also seen.

Certain risk factors have been identified that increase the likelihood of developing type-two diabetes. These include genetics (Burmese cats are five times more likely to develop diabetes compared to other breeds of cat, and male cats have a higher risk than female cats), obesity, indoor lifestyle\(^3\) and certain medications, such as corticosteroids or some hormones (megestrol acetate or ovarid)\(^4\).

These risk factors can dramatically increase the chance of a cat developing diabetes. For example, it is known a 50 per cent gain in weight (an average sized cat that would typically weigh 4kg, but weighs 6kg) decreases the response to insulin by 50 per cent – this means the pancreas has to work twice as hard to control the circulating blood glucose levels, simply because the cat is overweight\(^5\).

In obese people, early diagnosis of type-two diabetes can negate the immediate need for insulin
injections. Unfortunately, this is not the case in cats – by the time they show clinical signs of the problem (drinking and urinating more; Table 1) they are already suffering from glucose toxicity and, therefore, require insulin (at least initially) to decrease the glucose and allow any remaining beta cell function to recover.

Management

The aim of therapy for DM is to eliminate the signs of disease so the cat can have a good quality of life. The mainstay of treatment is insulin administration; the effects of injectable insulin are far superior to those of any oral medications at decreasing glucose toxicity and increasing the chance of diabetic remission.

Several types of insulin are available, but, in the UK, only one that is licensed. This insulin has an intermediate level of duration (typically around 12 hours) and needs to be given by subcutaneous injection twice daily, at approximately 12-hour intervals.

In addition to insulin, it has been shown cats with diabetes mellitus respond best to a low-carbohydrate, high-protein diet (this may not be appropriate for those with renal insufficiency). The diet does not need to be given and then insulin dosage altered depending on the portion eaten because cats have a slow postprandial alteration in blood glucose, and their cellular release of glucose is mediated predominantly by hexokinase, meaning alterations in blood glucose with diet are much slower than other species.

A low-carb diet further decreases the rise in blood glucose after eating and helps keep glucose in a stable range. Studies have shown by feeding such a diet and administering insulin twice daily, many cats can become “transient diabetics”

Not all cats will stabilise on twice-daily insulin injections – this may be because another condition is leading to insulin resistance. Any other disease process can participate in this, the most common of which include urinary tract infections (present in approximately 16 per cent of diabetic cats despite no overt signs of cystitis), pancreatitis, acromegaly or hyperadrenocorticism. Another is because the cat makes antibodies to the insulin (it is a porcine product and while it is similar to feline insulin it does have some slight differences that occasionally cats can make antibodies to).

Alternative off-licence insulins are available. The most commonly used are synthetic ultra-long acting human insulins. These products have been developed to slowly lower blood glucose and keep it lowered for prolonged periods of time. Their structure is slightly different to naturally occurring insulins, and the monitoring is different, in that although they are very long acting, twice-daily administration is still advised to allow an accumulation of the insulin. These insulins accumulate over five to seven days and, therefore, the dose should not be increased more than once per week.
Once the insulin level is stable the aim is to maintain the blood glucose within or near to the normal range. This decreases glucose toxicity and is thought to improve the probability of a cat becoming a transient diabetic – in fact, studies using these insulins along with a diabetic (low-carb) diet, have shown very good responses in cats, with the majority of cases becoming transient diabetics (Figure 2).\(^7\,^8\)

Monitoring blood glucose is imperative. Cats that are receiving too much insulin can have one of two responses: they can develop hypoglycaemia, which can be fatal if severe/not treated; alternatively, if the blood glucose drops rapidly or too low, the body can react by producing “stress hormones”, such as adrenaline, noradrenaline and corticosteroids. These hormones block the effect of insulin and the glucose will bounce back to a high level and remain there until the stress hormone levels decrease (a somogyi can last up to three days in a cat). This will make the cat appear as if it is not responding to insulin on a spot check, when, in fact, it has responded previously and developed a short-term insulin resistance as a result of too much insulin.

As a diabetic cat is stabilised it is important to monitor the effect of the insulin dose to see at what level the individual cat’s blood glucose is controlled and remains in or just above the normal range throughout the day. This varies between cats, depending on the individual’s residual pancreatic reserve and the amount of insulin resistance, and can vary with time as the effects of glucose toxicity decrease. Unfortunately, prolonged elevations in glucose are life-threatening and can lead to development of acidosis, imbalances in the breakdown and storage of fat, protein and various metabolites and, ultimately, can prove fatal. Therefore, diabetic cats should be monitored to ensure the blood glucose is neither too high nor too low.

The most effective way of monitoring the cat’s blood glucose is to monitor it in the home environment, as this will more accurately reflect the “normal” daily variations. Studies have shown that at home monitoring better reflects the cat’s response to insulin than monitoring in a veterinary practice, where cats are stressed and their blood glucose will vary.\(^9\) While in some cases in-practice monitoring is useful (particularly in the initial stages), putting the cat on a regular regime of at-home monitoring can be best. Either glucometers intended for human patients or specialised veterinary glucometers can be used to monitor cats. While the veterinary devices are more expensive they have been made specifically for cats/dogs and are potentially more accurate and use less blood. The human machines aren’t quite as accurate, but it is the general trend – and ensuring the blood glucose hasn’t dropped too low – that is most important and for both of these applications using a human glucometer is preferable to not measuring at all.

At-home glucose monitoring can be achieved in the majority of cats (own information sheets on diabetes and how to monitor at home are available as free downloads from www.felineexpert.co.uk).

Other ways of monitoring a cat’s response to insulin include monitoring fructosamine levels and using implantable glucose monitors\(^10\). Fructosamine is a protein that becomes elevated with
prolonged elevations in blood glucose and can give an idea of the average blood glucose over the preceding three to six weeks. This is useful in the diagnosis of diabetes mellitus, but is less useful in monitoring the response to insulin, as cats that are on too much insulin and spending the majority of their time in a somogyi over-swing, will have an elevated fructosamine.

Alternatively, implantable glucose monitors can be used to document the cat’s response to insulin over a two to three day period (Figure 3). These can be very useful in cats that are hard to stabilise; however, they require specialised equipment and need calibrating by measuring the blood glucose three times each day. They can be used in the veterinary clinic or home environment provided the owner can measure the blood glucose and calibrate the device.

Cats that are hard to stabilise

Some cats will prove very hard to stabilise. This may be because they have variable insulin requirements (often due to a degree of insulin resistance); their metabolism is faster than some cats and the insulin is not lasting the full 12 hours; the insulin is not being stored or injected correctly (or the owner is adjusting the dose himself or herself each day); the dose is wrong (typically because the insulin has been increased too quickly and the “stable point” has been missed); or the cat has true insulin resistance.

The author uses the monitoring methods outlined previously – having moved away from altering dosages based on urine dipstick curves. Cats have variable levels of glucosuria and the measurement doesn’t tell you if glucose is present because of a somogyi or lack of insulin.

The author’s approach to such cases is outlined in Figure 4. If a cat is insulin-resistant, then the author considers the differentials (Figure 5), and exclude those as appropriate, always bearing in mind a change of insulin may be needed if another cause cannot be found. The vast majority of cats stabilise well, but sometimes those with underlying disease that results in constant or varying resistance can be more problematic.

References


Figure 1a. A cat with hyperadrenocorticism. It presented with clinical signs of diabetes, but also a rotund abdomen and very thin skin (which developed a tear seen in image).
Figure 1b. A cat with acromegaly. It presented with unstable diabetes, but also had enlarged organs and enlargement of its skull, which led to a prominent jawline.
Figures 2a and 2b. Blood glucose curves demonstrating a “good response” to different types of insulin.
Figure 3. Placement of an implantable blood glucose monitor in a cat with unstable diabetes mellitus, allowing recording of blood glucose every five minutes for up to three days. This device is generally well tolerated by cats and can provide useful information regarding the response to insulin injections.

IMAGES: Sara-Ann Dickson.
Unstable DM

Check insulin
Is the owner storing it correctly?
Try a new bottle
Place vial inside sample pot to stop it falling over in fridge
(rubber bung can denature insulin)

Is the owner injecting it correctly?

Does the cat respond to insulin at all?

No
Assess whether the dose is appropriate
(most cats will stabilise on 0.5IU/kg to 1.0IU/kg or less)

Yes
Assess whether the dose is appropriate and try fine-tuning dosing interval or dosage
(some cats require tid dosing – if this isn’t possible changing to a longer acting insulin may be necessary)

If the cat is on a much higher dose but appears otherwise well, decrease to 0.25IU/kg and restart, increasing very slowly

If the cat is on an appropriate dose, or appears unwell, or you have never been able to stabilise the cat, treat as insulin-resistant
Figure 4. Approach to management of the unstable diabetic.
**Insulin resistance**

**Check for infections:**
Urinary tract infections are most common and will be clinically silent, other common infections include dental disease, but infection anywhere can lead to resistance.

**Assess for other diseases that may lead to resistance, or variable requirements:**
Full blood work to assess the general health profile of the cat should be collected, screening for hepatic or renal disease. Pancreatitis is very common in diabetic cats; fPLI should be assessed.

**Check for endocrinopathies:**
Cats with DM should have a mid-range or low T4. If the T4 is at the high end of normal, further testing should be performed. Acromegaly (excessive growth hormone) can be found in one out of three unstable diabetic cats (consider sending off an IGF-1 blood test). Hyperadrenocorticism in cats almost always leads to severe insulin resistance and therefore DM: low dose dexamethasone suppression +/- ACTH stimulation should be considered if clinical signs are appropriate (rare sex hormone diseases will present in a similar manner).

**Screen for other diseases such as neoplasia:**
Twenty per cent of diabetic cats seen in one referral population were found to have pancreatic carcinoma. Therefore, abdominal ultrasonography and thoracic radiography or CT is warranted.

*Figure 5. Approach to the cat with insulin resistance.*
<table>
<thead>
<tr>
<th>Symptom</th>
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<tr>
<td>Increased drinking</td>
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<td>Increased urinating</td>
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<tr>
<td>Weight loss</td>
</tr>
<tr>
<td>Increased appetite</td>
</tr>
<tr>
<td>Poor hair coat (often dull, but sticky)</td>
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<tr>
<td>Lethargy</td>
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Occasionally (10%) of cases will develop neurological changes, typically walking on their hocks and having problems jumping
Table 1. Clinical signs in cats with diabetes mellitus