Diabetes Mellitus (Feline)

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Synonyms

Sugar diabetes

Disease Description

Definitions

Diabetes mellitus (DM) is an endocrine disorder of dogs and cats that is characterized by absolute or relative deficiency of insulin.[1]

Three types of diabetes mellitus have been identified:

1) **Type I** (i.e. insulin-dependent) arises when lack of insulin production results in an absolute deficiency of insulin and dependence on external insulin supplementation. Type I DM is the most common form of DM in dogs and may occur from autoimmune destruction of the insulin-secreting pancreatic beta cells.[2,3] Although uncommon in cats, chronic pancreatitis is the most common cause in cats.[2,3] Islet amyloidosis can also lead to type I DM.[2,3]

2) **Type II** (i.e. noninsulin-dependent) is characterized by impaired insulin secretion from beta cell dysfunction, and/or by peripheral insulin resistance. Total insulin secretion may be normal or increased; however, the amount of insulin is insufficient to prevent hyperglycemia. Abnormal insulin secretion combined with insulin resistance leads to stable reregulation of blood glucose levels at a higher concentration.[2] Type 2 DM is sometimes reversible, so the disease can go into remission. Type II DM occurs in cats but not dogs. It is the most common form, affecting 80-95% of cats with DM.[1,4,5]

3) **Type III** (i.e. gestational, hormone-induced) occurs when insulin resistance develops in association with high concentrations of progesterone (e.g. megestrol acetate) or other diabetogenic hormones (e.g. cortisol, epinephrine, growth hormone, glucagon). Type III DM has been reported in dogs and cats.[34,35]

Pathophysiology

Effects of Insulin

Insulin primarily targets liver, muscle, and fat cells. Its main function is to promote storage of glucose as glycogen, amino acids as protein, and fatty acids as fat. Insulin also promotes glycogen synthesis, decreases gluconeogenesis, and decreases hepatic enzyme activity that is involved in the conversion of amino acids into glucose. Insulin increases lipid synthesis while inhibiting lipid degradation. Insulin promotes a positive nitrogen balance by stimulating protein synthesis while inhibiting protein degradation.[1]

Effects of Insulin Deficiency

When either absolute or relative insulin deficiency occurs, reduced glucose entry into the liver, muscles, and adipose tissue occurs. Furthermore, the liver produces more glucose via increased gluconeogenesis and glycogenolysis, which leads to hyperglycemia. Glucose is lost through the urine once the renal capacity for reabsorption of glucose is overcome, which causes osmotic diuresis. With insulin deficiency, decreased protein synthesis, and increased protein catabolism occurs. These effects result in loss of muscle mass and negative nitrogen balance. Finally, lipid metabolism becomes deranged. Increased levels of non-esterified fatty acids are transported to the

liver, leading to hepatic steatosis and hyperlipidemia. Increased production of ketone bodies eventually leads to ketoacidosis.[1] For more information on ketoacidosis, see the Feline VINcyclopedia chapter on Ketoacidotic Diabetes Mellitus.

Acute hyperglycemia stimulates insulin secretion and glucose utilization; however, chronic hyperglycemia (glucose toxicity) can impair insulin secretion. One study of 5 cats showed that chronic hyperglycemia suppressed insulin secretion and caused normal cats to have insulin levels consistent with type 1 DM within 5 days.[1] Only 3-7 days of blood glucose (BG) levels ≥480 mg/dL (≥26.64 mmol/L) resulted in almost complete insulin suppression in normal cats.[4] Other studies have demonstrated degeneration of islet cells and permanent hyperglycemia in normal cats given large doses of glucose.[2] Lipotoxicity refers to the negative effects of fatty acids on beta cells. Glucose toxicity and lipotoxicity can lead to increased apoptosis of beta cells and increased glycogen deposition.[8]

Effects of Risk Factors

One of the major risk factors for DM in cats is obesity, which is very similar to what occurs in people. Obese cats are approximately 3.9 times more likely to develop DM than cats of optimal weight.[1] Adipose tissue in lean people secretes high levels of the adipocytokine adiponectin. Adiponectin has anti-inflammatory actions and increases insulin sensitivity.[2] Adiponectin levels decrease in obese cats, and obese cats have decreased glucose effectiveness.[6,7] Furthermore, as adiponectin levels decrease, adipose tissue increases secretion of leptin and other pro-inflammatory cytokines.[5,7] Decreased expression of the glucose transporter, GLUT4, occurs in muscles and fat of obese cats. Overall effect is impaired insulin signaling and enhanced insulin resistance.[1] In one study of cats offered free access to an energy dense diet, their body weight increased by 44% and insulin sensitivity decreased by >50%.[8]

Amylin is also an important factor in the development of insulin resistance in cats. Amylin is a hormone co-secreted with insulin from the pancreas. Chronic insulin hypersecretion occurs along with insulin resistance in conditions such as obesity, glucocorticoid administration, certain infections, and acromegaly. Increased insulin secretion leads to increased amylin deposition in islet cells in the form of amyloid. Amyloid is toxic to beta cells and causes increased apoptosis and decreased insulin secretion.[9] Pancreatic amyloid deposition occurs in 65-90% of cats with DM.[2]

Disease Description in This Species

Diagnosis

History/Physical Examination Findings: Cats with DM typically have a history of polyuria (PU), polydipsia (PD), and polyphagia. Weight loss and lethargy may also be noted.[2,3] Dehydration, poor haircoat, and hepatomegaly secondary to hepatic lipidosis may also be noted. Approximately 10% of diabetic cats have signs of diabetic neuropathy, with hindlimb weakness, difficulty jumping, and a plantigrade posture.[1] Cats with concurrent diseases (e.g. pancreatitis, acromegaly, hyperadrenocorticism) may have additional clinical signs.

Complete Blood Count (CBC): Abnormalities may include mild anemia and a stress leukogram.[1]

Biochemistry Panel: The hallmark abnormality is persistent hyperglycemia. Diagnosis can be made with the documentation of persistent hyperglycemia and glucosuria, in combination with characteristic clinical signs.[2,3] DM must be differentiated from stress-induced hyperglycemia. In one study of 106 cats with stress-related hyperglycemia, 21 cats had glucose levels of >270 mg/dL (>14.98 mmol/L).[1]

Other abnormalities may include hypercholesterolemia, azotemia, and elevated alanine aminotransferase (ALT) and alkaline phosphatase (ALP). Azotemia may be pre-renal from dehydration or represent concurrent chronic kidney disease (CKD). In one study, CKD was a significant comorbidity in 7/16 diabetic cats.[10]

Urinalysis: Glucosuria is present in cats with DM. Glucosuria and clinical signs of DM typically do not occur until BG levels exceed the renal threshold (>250-300 mg/dL, >13.88-16.65 mmol/L).[3] Other causes of glucosuria may include administration of ketamine, CKD, and postobstructive (urethral) diuresis.[2] Glucosuria is uncommon or intermittent with stress-induced hyperglycemia. Evaluation for glucosuria on urine specimens collected at home can be performed to help determine if hyperglycemia is stress related or persistent.[2]

Other changes on urinalysis may include proteinuria, ketonuria, pyuria, and hematuria. A urine culture is commonly performed since urinary tract infections (UTIs) are common in diabetic cats.[3] One study found that 13.2% of diabetic cats had a UTI.[1]

Fructosamine Assay: Fructosamine levels can be used to confirm the diagnosis and help to determine if hyperglycemia is stress related.[3] Fructosamine is formed from the irreversible binding of glucose to amino groups in plasma proteins. Fructosamine levels reflect mean BG concentration over the last 1-2 weeks. Most newly-diagnosed diabetic cats have fructosamine levels 7.21 mg/dL (>400 µmol/L). Fructosamine levels are unaffected by stress. Cats with recent onset of DM (<1-2 weeks) and only mild DM may have normal fructosamine levels. Furthermore, diabetic cats with concurrent hyperthyroidism or hypoproteinemia may have normal fructosamine levels due to lower plasma protein levels and rapid protein turnover rates.[1] Fructosamine measurements are unreliable in cats with concurrent hyperthyroidism.[2]

Thyroid Hormone Measurement: Measurement of T4 level is indicated because signs of DM and hyperthyroidism are similar, and the diseases can be present concurrently.[3]

Feline Pancreatic Lipase Immunoreactivity (fPLI): Because pancreatitis in cats may be associated with DM, fPLI assay may be considered. Chronic pancreatitis can diminish beta cell function and lead to loss of beta cells through fibrosis.[9] One study of 29 diabetic cats and 23 nondiabetic cats showed affected cats had significantly higher serum fPLI levels.[11]

Ultrasonography: Abdominal ultrasonography may reveal a diffusely, homogeneous hyperechoic liver with hepatic lipidosis. If pancreatitis is present, the pancreas may be hypo- or hyperechoic, and peripancreatic fat may be hyperechoic because of inflammation.

Prevalence and Risk Factors

Diabetes mellitus is one of the more frequent endocrine diseases of cats. Approximately 0.5-1.2% of cats in private practice have DM.[1,12-14] The incidence of feline DM in the United States has increased from 0.08% in 1970 to 1.2% in 1999.[1] This increase may be attributed to an increase in risk factors.[1]

Obesity is a major risk factor for the development of DM in cats because obesity can lead to insulin resistance.[2,7,13,15] In one study, approximately 50-60% of diabetic cats were overweight.[2] Other risk factors include physical inactivity, glucocorticoid administration, increasing age, pregnancy, systemic infection, pancreatitis, acromegaly, hyperadrenocorticism, CKD, and being male.[1,3,10,14]

Signalment

A strong sex predisposition for DM exists in the cat, with 70-80% being male.[1,2] Male cats have lower insulin sensitivity compared to females.[1,2] However, one study of 1,128 cases did not report a significant association of sex with DM.[13] Peak incidence of DM occurs is between 10-13 years of age.[8] Some studies have reported a higher incidence the Burmese, Tonkinese, and Norwegian forest cats.[1,8,13,14]

Clinical Signs

Common signs include PU, PD, polyphagia, weight loss, lethargy, poor haircoat, abdominal pain, dehydration, and abdominal distension from hepatomegaly.[1,7] Signs of concurrent diseases (e.g. hyperthyroidism, pancreatitis, hyperadrenocorticism, acromegaly) can also be present.[1,3,11] Approximately 80% of cats with hyperadrenocorticism and nearly all cats with acromegaly have concurrent DM.[1]

Laboratory Profile

Sodikoff's Laboratory Profiles of Small Animal Diseases: Diabetes Mellitus, Hyperosmolar Syndrome
Sodikoff's Laboratory Profiles of Small Animal Diseases: Diabetes Mellitus, Secondary
Sodikoff's Laboratory Profiles of Small Animal Diseases: Diabetes Mellitus, Uncomplicated
Sodikoff's Laboratory Profiles of Small Animal Diseases: Hyperglycemia, Stress Induced
Sodikoff's Laboratory Profiles of Small Animal Diseases: Hyperlipidemia, Secondary

Etiology

Acromegaly
Diabetogenic hormones
Glucagon excess
Glucocorticoids
Growth hormone
Hyperadrenocorticism
Megesterol acetate
Obesity
Pancreatitis
Pregnancy
Progesterone

Breed Predilection

Burmese
Norwegian forest cat
Tonkinese

Sex Predilection

Male

Age Predilection

Mature, middle-aged
Old

Clinical Findings

Abdominal distention
Abdominal pain
AFEBRILE
Anorexia, hyporexia
ASCITES OR ABDOMINAL DISTENTION
Cervical weakness
Cervical, neck ventroflexion
Coma, unconsciousness
Dehydration
Depression, lethargy
GAIT ABNORMAL OR LAMENESS
Hair coat poor
Hepatomegaly
Hindlimb muscle atrophy
Hindlimb weakness
Hyporeflexia
Mucous membranes pale
MUSCLE ATROPHY
Nausea
Overweight, obese
PARALYSIS OR PARESIS
Paraparesis, paresis
Plantigrade posture
Polydipsia
Polyphagia, increased appetite
Polyuria
Stupor
VOMITING
Weakness: Asthenia or Paresis
Weight loss
ZZZ INDEX ZZZ

Diagnostic Procedures

Diagnostic Procedures:	Diagnostic Results:
Complete blood count (hemogram)	ANEMIA Neutrophilia
Urinalysis	Bacteriuria, urine bacteria increased Glucosuria, glycosuria Ketonuria Proteinuria, albuminuria Pyuria, white blood cells increased Red blood cells present in urine Urine specific gravity decreased
Fructosamine assay on serum	Fructosamine >400 µmol/L
Ocular examination	Retinal blood vessels tortuous RETINAL CHANGES Retinal hemorrhages
Serum biochemistries	Alanine aminotransferase (ALT) increased Alkaline phosphatase (ALP) increased Aspartate aminotransferase (AST) increased Azotemia/uremia Blood urea nitrogen (BUN) increased Hypercholesterolemia Hyperglycemia Hypernatremia Hypokalemia Hyponatremia Hypophosphatemia Lipemia, lipids increased
Ultrasonography of abdomen	Hyperechoic liver Pancreas hyperechoic Pancreas hypoechoic Peripancreatic fat hyperechoic
Pancreatic lipase immunoreactivity	Feline pancreatic lipase immunoreactivity elevated

Treatment / Management

SPECIFIC THERAPY

Goals of therapy are to revert a transient diabetic into a state of remission (if possible); maintain BG levels below renal threshold for as much of a 24-hour period as possible; avoid hypoglycemia; and improve clinical signs.[3]

Oral Hypoglycemic Agents

Oral hypoglycemic agents are not routinely used in cats. Sulfonylureas are the most likely oral hypoglycemic to be tried in cats. These drugs stimulate insulin secretion but need functional beta cells to work. Glipizide can be used in cats that are not ketotic and have mild to moderate signs of DM. Glipizide only works in 30-40% of cats and may accelerate beta cell loss.[1,3] Glipizide is given at 2.5 mg per cat PO q 12 hrs with a meal for 2 weeks.[1] The dose may then be increased to 5 mg per cat PO q 12 hrs, if no adverse side effects occur.[1] If no response is noted within 4-6 weeks, then insulin therapy is indicated. Glipizide is not used in conjunction with insulin. Glipizide is typically only recommended in cats in which owners refuse to administer insulin or are considering euthanasia.[1,16]

Alpha-glucosidase inhibitors inhibit intestinal glucose reabsorption and reduce post prandial hyperglycemia. Acarbose has been used in conjunction with insulin and dietary therapy in cats. It is not beneficial as a sole therapeutic agent.[3]

Insulin Therapy

Administration of insulin is the treatment of choice for feline DM. Several types of insulin are available:

Lente: Porcine zinc lente insulin is a mixture of short-acting, amorphous and long-acting, crystalline insulin. Vetsulin/Caninsulin® is a porcine zinc lente insulin that has been licensed for use in cats. Various studies have demonstrated good glycemic control and the potential for remission with this type of insulin.[1,5] However, blood glucose nadir occurs 2-12 hours after administration. The AAHA Diabetes Management Panel does not recommend the use of porcine zinc lente insulin as initial treatment for DM in cats because of its potentially short duration of action and poor control of clinical signs.[3]

Vetsulin/Caninsulin® is a U-40 insulin and only appropriate U-40 insulin syringes should be used for administration.[12] Initial dose is 0.25-0.5 U/kg SC q 12 hrs. One study reported that 7/25 cats treated with lente insulin went into diabetic remission during the 12 months of the study.[5] In another report, 23/41 cats treated with lente insulin went into diabetic remission.[2]

An insulin pen containing porcine zinc insulin (VetPen®) has been approved for SC injection of insulin in cats in some countries. In a study of 37 cats that were already being treated for DM with porcine zinc insulin, the insulin pen was well tolerated and effectively controlled DM in 34 of the cats.[19]

Protamine Zinc: Protamine zinc insulin (PZI or ProZinc®) is a combination of protamine and zinc insulins.[8] It has a longer duration of action than lente insulin.[9] Studies using protamine zinc insulin have shown good glycemic control in 85% of cats after 45 days of therapy using a mean dose of 0.59 U/kg SC q 12 hrs.[9] The BG nadir typically occurs at 5-7 hours.[9] In one study, hypoglycemia was experienced in 22% of cats given this type of insulin.[2] Another study of 185 cats treated with protamine zinc insulin had a remission rate of 56.2%, and only 5.4% became clinically hypoglycemic.[14] In a study comparing glargine and protamine zinc insulin in newly-diagnosed diabetic cats, remission rate was 23% (5/22) for the Prozinc group.[17] No significant differences in mean BG, fructosamine levels, and quality of life score were noted between the treatment groups.[17]

Prozinc is a U-40 insulin and only the appropriate U-40 insulin syringes should be used for administration.[12] The starting dose is 0.25-0.5 U/kg SC q 12 hrs. Average starting dose is 1-2 U per cat. Ideal body weight is used to calculate insulin dosages, not actual weight. Cats should not be started on >2-3 U, even if they are very large.[2-4]

Glargine: Glargine (Lantus®) is a U-100, long-acting human analogue insulin. It is slowly released from the site of injection. Although considered a peakless type of insulin in people, cats have a long, less prominent BG nadir.[3,9] Initial dose for cats with BG levels >360 mg/dL (>19.98 mmol/L) is 0.5 U/kg SC q 12 hrs. Initial starting dose for cats with BG levels <360 mg/dL (<19.98 mmol/L) is 0.25 U/kg SC q 12 hrs. Average initial dose is 1-2 U per cat, with dosages calculated on ideal body weight. Starting doses should not exceed 2 U. Once daily administration can be effective in some cats.[2,3,4] Some studies have reported a higher rate of remission in cats given glargine compared to cats treated with other types of insulin (cats were also fed low carbohydrate diets).[2] One study reported that 21/29 (72%) cats treated with glargine achieved remission.[2] However, other studies have reported that cats fed low carbohydrate diets had similar remission rates regardless of the type of insulin administered.[2,17]

Detemir: Detemir (Levemir®) is another U-100, long-acting insulin analogue. Remission rates of newly diagnosed diabetic cats on detemir have been reported at >80%.[4] Detemir may have a longer duration of action and less variability than glargine in some cats. Initial dosing is similar to glargine.[4] In one study of 14 diabetic cats, 13 achieved moderate or excellent control of clinical signs within 3 months, including 5 cats that were treated previously with other types of insulin.[18] Three cats achieved remission.[18] Only two episodes of clinical hypoglycemia were reported.[18]

Insulin Pump: Implantable insulin pumps have been used to manage diabetic cats. One report details a cat that achieved remission after use of an insulin pump implanted subcutaneously and filled with a rapid-acting recombinant insulin.[20] The pump was controlled telemetrically with a smart phone, and insulin dose was adjusted based on a continuous blood monitoring system (CGMS).[20] In another study, pumps filled with glargine were investigated in 10 normoglycemic cats to

determine their effectiveness.[36] The pump was well tolerated but failed due to technical reasons in 4 cats and 1 cat became hypoglycemic when insulin leaked into SC tissues.[36] Further studies are warranted to determine their applicability to clinical patients.

SUPPORTIVE THERAPY

Dietary Therapy

Dietary modification is an important component of therapy. A high-protein, low-carbohydrate diet is recommended. Higher protein levels maximize metabolic rate, prevent lean muscle mass loss, and improve satiety. Carbohydrates can contribute to hyperglycemia and glucose toxicity in cats.[3,16] High-carbohydrate diets increase insulin demands, while high-protein, low-carbohydrate diets can improve insulin sensitivity and contribute to loss of fat.[7] High-protein diets are defined as protein providing >40% metabolizable energy (ME). It is recommended that cats receive a diet with carbohydrates providing <12% ME. High-fiber diets are not recommended.[3]

Cats eating a low-carbohydrate diet often have significantly lower fructosamine levels than cats eating high-carbohydrate diets.[20] High-protein, low-carbohydrate diets may improve chances of remission and reduce insulin requirements.[1,4,5,9] Remission rates for cats fed a diet of 12% ME from carbohydrates was 68% compared to 41% of those receiving a diet with 26% ME from carbohydrates.[4]

Canned food is preferred over dry food because it has lower carbohydrate levels; lower caloric density; increased water content; and portion control is easier.[3,9] In one study of 29 newly-diagnosed diabetic cats, feeding canned food was the only factor that was significantly associated with clinical remission.[22]

Control of Body Weight

Weight loss is recommended for obese cats since loss of fat can increase adiponectin levels, increase insulin sensitivity, and improve metabolic status.[6,7] Weight loss should occur at a rate of 1-2% of body weight per week. Energy requirements are calculated based on ideal body weight. Portion control of food is essential to achieve weight loss.[1,3]

Therapy of Concurrent Diseases

Concurrent diseases can contribute to insulin resistance and can make management of DM more difficult. Common concurrent diseases that can increase insulin resistance include acromegaly, hyperadrenocorticism, kidney disease, heart disease, pancreatitis, periodontal disease, and chronic infections (e.g. UTI).[1,5]

Glucagon-Like Peptide 1 Analogue: Glucagon-like peptide 1 (GLP-1) analogues can be used in conjunction with insulin to help achieve diabetic remission. Examples are exenatide immediate-release (Byetta®) and exenatide extended release (Bydureon®). GLP-1 analogues can stimulate insulin secretion; increase satiety, protect beta cells; and inhibit glucagon secretion.[3,23-25] Various studies have demonstrated that GLP-1 analogues in conjunction with insulin and diet therapy helped to achieve higher remission rates and better glycemic control compared to cats not receiving GLP-1 analogues.[23-25]

MONITORING

Goals

Primary goal is to control clinical signs of DM while avoiding hypoglycemia. Achievement of diabetic remission is also a reasonable goal.[2,3] Tight glycemic control is not necessarily realistic in cats like it is in people. Glucose levels are unlikely to normalize but most patients seem to be clinically well regulated if most BG results are <300 mg/dL (<16.65 mmol/L).[2] Control of clinical signs and avoidance of hypoglycemia is more imperative than individual BG levels. One study showed that control of DM as determined by owner observation of clinical signs was 5 times better than the degree of control as determined by monitoring of BG via laboratory testing. One study of 185 cats treated with a loosely-controlled approach using protamine zinc insulin reported a remission rate of 56.2%.[14] Hypoglycemic episodes occurred in 5.4% and diabetic ketoacidosis in 3.8% of the cats.[14]

Initial Monitoring

Hospitalization and monitoring via a BG curve may be considered on the first day of insulin therapy. By performing a BG curve, hypoglycemia following insulin administration can be identified. Do not increase insulin doses at this time even if hyperglycemia persists. Blood glucose levels are measured q 2-4 hrs following protamine zinc insulin and q 3-4 hrs after glargine insulin. Insulin

dosages are decreased by 0.5 U if BG drops below 150 mg/dL (8.32 mmol/L) during the initial glucose curve. After the first day of monitoring in the hospital, the cat can be discharged and re-evaluated in 7-14 days.[3]

Blood Glucose Curves
Performance of a BG curve is the most commonly used monitoring method for diabetic cats. Blood glucose curves can determine the glucose nadir and duration of action of insulin. BG curves can also detect clinically silent hypoglycemia, which allows insulin to be adjusted before clinical hypoglycemia develops. BG curves help determine if insulin doses and/or frequency of administration should be changed.[3] BG curves can be performed in the hospital, or at home using portable glucometers and a lancet.

If a BG curve is performed at home, owners measure the first BG reading before the insulin injection, then q 2 hrs until the next dose of insulin for those cats on protamine or porcine zinc insulin. If glargine insulin is used, BG is measured q 4 hrs until the next insulin dose is given.[1,3] If BG falls below 150 mg/dL (8.32 mmol/L), then readings are done hourly.[3]

Stress hyperglycemia can falsely elevate BG when performing a curve. Stress can increase if the test is performed in the clinic.[1,3,12] For this reason, BG curves done at home are often preferred. It is important to note; however, that considerable day-to-day variation can occur in BG curves. One study of 7 cats that evaluated home BG curves taken on 2 consecutive days showed that evaluation of the 2 curves led to the same recommendation for insulin adjustment on only 6/14 occasions.[22]

Whenever possible, use a glucose meter calibrated for feline blood. Not all glucometers available at pharmacies are accurate in cats. They often give measurements that are 23-30% lower than reference laboratories.[4] The AlphaTRAK2™ has improved accuracy and is considered the optimal choice for monitoring feline diabetics.[3,4] In one study comparing 4 glucose monitoring systems, AlphaTrak™ and VetMate™ were the most accurate monitors.[26]

In a study comparing diabetic cats monitored at home versus non-home monitoring, the DIAQoL-pet score improved at all points in time in the home BG monitoring group compared to the non-home group. Remission occurred in 9/28 (32%) of the home group compared to 1/10 (10%) of the non-home group.[27]

Continuous Glucose Monitoring Systems
CGMs units have been evaluated in both dogs and cats. The Guardian REAL-Time® system is comprised of a sensor that is placed in subcutaneous tissue; a transmitter that transmits data over a distance of 3 meters to a monitor; and a pager-sized monitor that displays data. Interstitial glucose readings are collected q 10 seconds and a value is computed q 5 minutes.[28] In a study of cats comparing CGMS to a reference blood glucometer, CGMS was 100%, 96.1%, and 91% accurate at evaluating normal, high, and low blood glucose levels, respectively.[29] The Abbott Freestyle Libre™ glucose monitoring system was recently is available in the USA and can monitor for up to 14 days.[30]

Fructosamine Assay
Fructosamine levels can be used to monitor diabetic cats. Fructosamine levels increase when glycemic control worsens and they decrease when glycemic control improves. Fructosamine levels are unaffected by stress and food intake.[1] However, fructosamine levels cannot determine the insulin nadir or duration.[9] Cats with hyperthyroidism, hypoalbuminemia, or hypoglobulinemia can have decreased fructosamine concentrations.[3]

Urine Glucose Testing
Urine test strips can be placed in litterboxes to detect glucosuria. However, urine glucose strips cannot differentiate between hypoglycemia, normoglycemia, or mild hyperglycemia that may occur throughout the day. Urine test strips also do not reflect actual BG level. Variation in test strip quality exists, with glucosuria underestimated in some cases.[1] Urine glucose strips can be useful in detecting ketones and can be help determine if further laboratory testing is needed. Persistent glucosuria indicates inadequate glycemic control, so a BG curve may be needed.[1,3]

Monitoring of Clinical Signs

It is important for owners to evaluate and monitor clinical signs at home. PU and PD improve as glycemic control improves. Owners can also monitor appetite, body weight, and activity level.[3] Hypoglycemia is the most important complication of insulin therapy. Counsel owners on the signs of hypoglycemia. Signs of hypoglycemia can include weakness, ataxia, collapse, seizures, visual deficits, disorientation, and mental dullness.[1,9] Hypoglycemia can occur from insulin overdose; long duration of insulin activity resulting in overlap of doses; undetected diabetic remission; and increased insulin sensitivity subsequent to improvement in concurrent disorders.[1]

PROGNOSIS

Prognosis varies depending on a number of factors, including an owner's willingness to treat and monitor the cat appropriately; ability to achieve diabetic remission; response to insulin therapy; and presence of concurrent disease(s). In one study of 114 diabetic cats, median survival time (MST) was 516 days, with 25% of cats living >1,420 days.[31] Negative prognostic factors included hyperkalemia, concurrent diseases, and detection of ketoacidosis during follow-up.[31] Age, BG levels, fructosamine levels, and type of insulin administered were not associated with survival rates.[31] In another study of 185 diabetic cats undergoing loose-control of DM, MST was 1,488 days.[14] Cats not exclusively fed a low-carbohydrate diet were 50% more likely to have died during the study than cats exclusively fed a low-carbohydrate diet.[14]

Remission

Unlike dogs, cats can achieve diabetic remission. Cats in remission have normal to near-normal BG levels without administration of insulin or oral hypoglycemics.[4] Remission typically occurs 1-4 months after diagnosis but it is not necessarily permanent.[5,8] One study of 185 cats reported that 56.2% went into remission, with a median time to remission of 286 days.[14] Factors affecting the chance of remission include early diagnosis, extent of beta cell damage, diet, and effectiveness of insulin treatment.[5]

Several studies aimed at evaluating remission rates have been performed, using different insulin types. A study of 18 cats that were previously treated with other insulins showed a remission rate of 67% when the cats were switched to detemir.[33] However, these cats were also intensively monitored at home.[33]

One study of 24 newly diagnosed diabetic cats fed low-carbohydrate diets showed that all 8 cats treated with glargine achieved remission.[32] In contrast, only 3/8 treated with PZI and 2/8 treated with lente insulin achieved remission.[32] In this study, cats with lower mean 12-hour glucose levels by day 17 had a higher chance of remission.[32] Based on this study, glargine is sometimes recommended for newly-diagnosed diabetic cats.[12]

However, other studies have not shown an increase in remission using glargine. One small study of 13 cats fed low-carbohydrate diets showed that 43% of cats treated with lente insulin achieved remission while 17% of glargine-treated cats achieved remission.[2] A meta-analysis of data of diabetic cats fed low-carbohydrate, high-protein diets did not demonstrate a statistically significant difference in remission rates in cats treated with lente insulin (44.4%) or glargine (58.8%).[2] Another study reported that 8/24 (33.3%) of glargine-treated cats achieved remission, and 5/22 (23%) of protamine zinc-treated cats achieved remission.[17]

Feeding a low-carbohydrate, high-protein diet can increase the chance of remission. One report of 63 cats treated with a variety of insulins demonstrated that 68% of cats fed a low-carbohydrate diet achieved remission compared to 41% of cats fed a moderate-carbohydrate diet.[2,21] Another study of 29 cats showed that 16 cats achieved remission, and feeding canned food was the only factor that was significantly associated with remission.[22]

Other factors associated with remission include steroid-associated DM, lower mean BG levels during treatment, lower insulin levels during treatment, and lower glycemic variabilities.[14,24]

Insulin Resistance

Cats that have poorly-controlled DM despite being treated with >1.5 U/kg per dose have insulin resistance. In poorly-controlled diabetics, it is also important to rule out insulin administration errors. Observe the client's technique in administering insulin; confirm that proper insulin syringes are being used; confirm proper storage of insulin; and assess the appearance of insulin to determine if

it should be replaced (e.g. out of date, discolored). Also re-evaluate diet and weight loss plans. Laboratory and other diagnostic tests may be required to rule out other concurrent diseases that can contribute to insulin resistance.[3]

Special Considerations

Other Resources

Recent VIN Message Board discussions on diabetes mellitus
Recent VIN Message Board discussions on DM treatment
Recent VIN Message Board discussions on DM treatment monitoring
Recent VIN Message Board discussions on lente insulin
Recent VIN Message Board discussions on protamine zinc insulin
Recent VIN Message Board discussions on glargine insulin
Recent VIN Message Board discussions on detemir insulin
Recent VIN Message Board discussions on dietary therapy of DM

Recent Proceedings articles that discuss DM in cats
Recent VIN Rounds and Journal Clubs that discuss DM, its treatment and monitoring
2018 AAHA Diabetes Management Guidelines for Dogs and Cats
Client Handouts: Diabetes Mellitus Center

VIN Medical FAQs:
Managing Diabetes Mellitus in Cats
Dietary Management of Diabetic Cats
FreeStyle Libre Glucose Monitor
Discontinuation of Insulins by Eli Lilly
Discontinuation of PZI Insulin
Using Glargine in Diabetic Cats
Vetsulin Availability

Glucose Curve Calculator
Interactive Diabetic Case Challenge
Recent VIN News Stories on insulin and DM
Analysis of Prescription & Commercial Dry Diets for Diabetes Mellitus - 2010
Insulin Stability & Handling

Differential Diagnosis

Acromegaly
Hepatic disease
Hyperadrenocorticism
Hyperthyroidism
Neoplasia
Renal Disease

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