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Review Article

Pathological Evaluation of Hypoglycemia and Hyperglycemia in Canines and Felines

Shubham Sharma*

M.V.Sc Scholar, Veterinary Pathology, Ranchi Veterinary College, Kanke, Jharkhand, India

***Corresponding Author:** Shubham Sharma, M. V. Sc Scholar, Veterinary Pathology, Ranchi Veterinary College, Kanke, Jharkhand, India.

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Abstract

Glucose homeostasis refers to the processes involved in the production, storage and release of glucose from Storage. Glucose is derived by the ingestion, digestion and absorption of carbohydrates, and blood glucose is maintained within tight limits by several different mechanisms. In addition, in processes particularly important in cats, gluconeogenesis and glycogenolysis allow glucose to be made within the body from other substrates. Reference ranges vary according to the laboratory and testing method but 3.0-6.5 mmol/l in dogs and 3.1-7.2 mmol/l in Cats are generally acceptable glucose concentrations that are unlikely to cause clinical signs in most animals. Hypoglycaemia is a life-threatening condition generally defined by a blood glucose lower than 3 mmol/l. Clinical Signs are not always apparent at a blood glucose level of 3 mmol/l, although a rapid fall in blood glucose, for example following an accidental insulin over-dose in a diabetic patient, may lead to clinical signs at a higher blood glucose concentration if there has not been sufficient time for counter-regulatory mechanisms to take effect. Hyperglycaemia is most commonly encountered in stressed animals and in patients with diabetes mellitus. Canine diabetes is usually the result of insulin deficiency and a classification scheme has been described. Diabetic ketosis is another complication due to hyperglycaemia , Fatty acid mobilization and ketone body formation resulting in ketosis. NKHS is another syndrome but with absence of ketone in it.

Keywords: Homeostasis; Diabetes Mellitus; Ketosis; NKHS

Introduction

Hypoglycaemia

Hypoglycaemia is a life-threatening condition generally defined by a blood glucose lower than 3 mmol/l. Clinical signs are not always apparent at a blood glucose level of 3 mmol/l, although a rapid fall in blood glucose, for example following an accidental insulin over dose in a diabetic patient, may lead to clinical signs at a higher blood glucose concentration if there has not been sufficient time for counter-regulatory mechanisms to take effect. Similarly, a slow fall in glucose may allow an animal to appear clinically well with a blood glucose between 2 and 3 mmol/l. Hypoglycaemia can result in permanent neurological damage if not recognized and managed quickly and is far more common in dogs than cats. Fasting in healthy dogs and cats does not normally lead to hypoglycaemia.

Clinical signs of hypoglycaemia

Where seen, the majority of clinical signs are neurological in origin and are commonly exacerbated by the accompanying adrenergic response. Glucose cannot be made or stored in the brain, so the central nervous system is entirely dependent on blood glucose for provision of energy and is very vulnerable to permanent damage during prolonged hypoglycaemia. Although glucose

transport into the majority of neurons is not insulin dependent, a concentration gradient is still required for facilitated diffusion and hypoglycaemia leads to a serious condition called neuroglycopenia.

Causes of hypoglycaemia and their recognition

Excess utilization of glucose

Sepsis

Sepsis is a common cause of hypoglycaemia, and is particularly associated with bacterial infection and certain parasitic infections such as Babesia spp. infections. In sepsis a state of increased glucose consumption develops which may be exacerbated by reduced food intake.

Mechanisms thought to underlie septic hypoglycaemia

- Production of inflammatory mediators
- Decreased blood pressure
- Tissue perfusion
- Hypoxaemia-induced anaerobic metabolism

Common scenarios for hypoglycaemia associated with sepsis are pyometra and peritonitis, and clinical signs of the underlying disease usually predominate. Laboratory diagnosis involves evaluation of a complete blood count, where a neutrophilia with or without a left shift is expected.

Pregnancy

Pregnancy, dominated by progesterone, tends to cause insulin resistance, which suppresses the intra cellular transport of glucose and increases blood glucose concentration. However, late in pregnancy (days 40-63), to ensure a constant supply of glucose to the growing fetuses, the normal multisystemic responses to hypoglycaemia are reduced. The metabolic demands of late pregnancy may also lead to ketosis in the presence of hypoglycaemia, but this is usually reversible with treatment [12,13]. The presence of ketones can be detected in blood or urine. When testing urine for ketones it is important to use as fresh a sample as possible and to read the dipstick at the exact time interval indicated. In addition, the clinician must be aware that urine dipsticks test only for acetoacetate, rather than beta-hydroxy butyrate, which can be the predominant ketone in blood, so false negative results may be obtained.

Neoplasia (non-beta cell tumour)

In theory, any neoplasm may cause hypoglycaemia as it consumes glucose during a phase of rapid growth. In reality, certain large tumours are more likely to have this effect, such as hepatomas, hepatocellular carcinomas, leiomyomas and leiomyosarcomas [2]. In addition, other types of tumour may cause hypoglycaemia either by increased consumption of glucose or an alternative mech such as the release of insulin-like peptides or a detrimental effect on gluconeogenesis.

Seizure activity

While seizures may be a clinical sign of hypoglycaemia, it is also important to note that a fall in blood glucose concentration may arise as a consequence of prolonged seizure activity. Hence the detection of mild hypoglycaemia in a patient after a long period of seizuring does not necessarily confirm that the primary cause of the seizure was hypoglycaemia. While the sympathetic nervous system tends to elevate blood pressure and blood glucose as a compensatory mechanism at the time of a seizure tonic-clonic seizure activity may increase glucose consumption in muscle and in turn act to reduce blood glucose.

Leucocytosis and polycythaemia

In any condition where there is an increased number of glucose-consuming red or white blood cells in the circulation, spurious hypoglycaemia may arise. Other clinical signs may be apparent, such as hypertension or nosebleeds in the case of polycythaemia or pyrexia in patients with elevated white blood cell counts. For this reason, a complete blood count is recommended for hypoglycaemic patients.

Exercise-induced/working dog hypoglycaemia

Exertional hypoglycaemia is a diagnosis of exclusion and is seen in lean, healthy dogs who undertake periods of intense physical activity such as hunting. Clinical signs may range from mild weakness with muscle tremors to profound signs of hypoglycaemia resulting in seizures and coma.

Decrease in glucose production

Hepatic disease

Most animals with liver disease will remain euglycaemic until around 70% of liver function is lost but

- Portosystemic shunts
- Hepatic fibrosis
- Glycogen storage diseases

Copper Storage Disease are among the many conditions affecting the liver that may lead to hypoglycaemia.

Liver disease may be accompanied by a fall in plasma albumin and urea concentrations, and in some cases liver enzymes and/or total bilirubin may also be elevated. In the non-jaundiced animal, a bile acid stimulation test will help to evaluate liver function or detect portosystemic shunting.

Hypoadrenocorticism

In the fasting dog or cat, glucocorticoids such as cortisol help to preserve normoglycaemia by increasing lipolysis and gluconeogenesis while decreasing peripheral glucose utilization.

Lack of cortisol in both typical and atypical hypoadrenocorticism can lead to hypoglycaemia, which may occur in the absence of classical electrolyte abnormalities (hyperkalaemia and hyponatraemia) in atypical disease.

Suggestive clinical signs accompanying hypoglycaemia in hypoadreno corticism include

- Vague anorexia
- Inability to cope with stress (e.g. cattery or kennels)
- Gastrointestinal disturbance
- Lack of a stress leucogram on a complete blood count, due to hypocortisolaemia.

Diagnosis is usually straightforward because patients with both atypical and typical hypoadrenocorticism fail to show a cortisol response on an adrenocorticotropic hormone (ACTH) stimulation test. The disease is much more common in dogs but has also been reported in a number of cats.

Neonatal hypoglycaemia

Hypoglycaemia is common in young puppies and kittens secondary to a combination of an

- Immature liver
- High energy requirements
- Inadequate substrate availability for gluconeogenesis and glycogenesis.

Neonatal hypo glycaemia is avoided by ensuring that all puppies or kittens are fed either by their mother or by hand every 2-3 hours and are kept in a warm environment. Puppies usually grow out of this tendency by 12-20 weeks, but some toy breeds remain susceptible to hypoglycaemia throughout their lives.

Presence of excess insulin or a hypoglycaemic agent

- Insulin overdose
- Insulinoma (pancreatic beta cell neoplasia)
- Toxicity: The artificial sweetener xylitol, commonly found in ‘sugar-free’ products such as chewIng gum, may also cause signs of hypoglycaemia by stimulating the release of insulin from beta cells [9].

Hyperglycaemia

Hyperglycaemia is most commonly encountered in stressed animals and in patients with diabetes mellitus; common causes of this condition.

Clinical signs of hyperglycaemia

In dogs and cats, glucose is usually freely filtered at the glomerulus and entirely reabsorbed in the proximal tubule of the kidney, only appearing in the urine when the renal threshold is exceeded (10-12 mmol/l in dogs and 12-16 mmol/l in cats). The presence of glucose in the urine leads to an

- Osmotic diuresis
- Polyuria
- Secondary polydipsia

When elevations in blood glucose concentration are severe and chronic, clinical signs can progress to altered behaviour and even coma as the osmotic effect of glucose in the blood results in the movement of water from other body compartments, causing interstitial dehydration.

Causes of hyperglycaemia

Stress hyperglycaemia

Stress hyperglycaemia in cats is an especially common phenomenon, with stress hormones such as adrenaline and cortisol potentially driving glucose higher than 16-20 mmol/l (19) (20) . Stress hyperglycaemia in cats has also been related to lactate release, associated with a cat struggling against restraint for blood sampling. 'Stress' hyperglycaemia can also be caused in critical illness by mechanisms that are not fully understood, but the potential consequences of hyperglycaemia in this situation include

- Dehydration (via osmotic diuresis)
- Depressed immune function
- Excessive inflammatory responses
- Oxidative stress
- Prothrombotic effects.

Stress hyper glycaemia may also be seen in dogs, but is generally less dramatic, raising blood glucose to around 10-12 mmol/l. In both dogs and cats, stress hyperglycaemia is usually distinguished from chronic hyperglycaemia by fructosamine measurement

- Diabetes mellitus
- Obesity

There is strong evidence for obesity causing peripheral insulin resistance in cats, which can progress to diabetes mellitus [9]. In dogs, there is evidence for obesity-associated insulin resistance but it is less clear [16].

Hormonal antagonism

Hyperglycaemia can also arise as a result of the presence of hormones that antagonize insulin, causing peripheral insulin resistance.

- **Glucocorticoids:** Excess glucocorticoids, such as cortisol, may elevate blood glucose in dogs or cats either iatrogenically or in the presence of a cortisol-secreting adrenal tumour (adrenal-dependent hyperadrenocorticism) or an ACTH-secreting pituitary mass (pituitary-dependent hyper adrenocorticism).
- **Growth hormone:** Growth hormone (GH) can also antagonize insulin and cause insulin resistance. Acromegaly in the cat, caused by excess GH from a pituitary macro adenoma, is an increasingly commonly recognized cause of hyperglycaemia and diabetes mellitus in cats [18]. The disease is most commonly found in male cats over the age of 10 years, and in addition to insulin resistance may be characterized by a change in facial features, organomegaly, widened inter dental spaces and eventually signs of hypertension and renal failure.

Acromegaly is exceptionally rare in the dog; however, during the progesterone-dominated phase of dioestrus in entire females, in a physiological phenomenon unique to this species, GH is released into the circulation from the mammary glands. Thus, bitches in dioestrus may be susceptible to hyperglycaemia and even diabetes mellitus because both progesterone and GH will contribute to peripheral insulin resistance.

Pancreatitis

Acute and chronic pancreatitis can affect beta cell function, making animals more susceptible to hyperglycaemia. In addition, hyperglycaemia itself can worsen pancreatitis, and also damage the islets further - a phenomenon sometimes referred to as 'glucose toxicity'. Signs of acute pancreatitis in dogs and cats may include inappetence, vomiting, abdominal pain, diarrhoea and depression, but it can be especially difficult to detect acute pancreatitis clinically in cats because the signs may be very vague. In addition, in both dogs and cats, chronic pancreatitis may lead to only minor clinical signs while having a significant effect on endocrine and/or exocrine pancreatic function. Usually a combination of clinical signs, testing for markers of pancreatic inflammation such as canine or feline pancreatic lipase immunoreactivity, and diagnostic imaging such as pancreatic ultrasonography is sufficient to achieve a diagnosis [15,23].

Diabetes mellitus

Canine diabetes

Canine diabetes is usually the result of insulin deficiency . In some cases insulin deficiency may be preceded by a phase of insulin resistance, but by the time of diagnosis most dogs are unable to synthesize and secrete adequate amounts of endogenous insulin

from the pancreatic beta cells in response to hyperglycaemia. A small number of cases of canine diabetes mellitus (DM) are diagnosed when young animals (DM) are diagnosed when young animals (<6 months of age) become hyperglycaemic, and these are considered to be congenital in origin. As already discussed, the insulin resistance that precedes diagnosis in an estimated 20-40% of canine diabetic patients may be caused by exogenous corticosteroid or progestagen treatment, or endocrinopathies such as hyperadrenocorticism. Chronic hyperglycaemia in dogs has been shown to result in permanent beta cell damage and obesity may also con tribute to insulin resistance in dogs. In addition, diabetes associated with pancreatitis may account for 28-40% of cases of canine DM and is especially prevalent in DM cases with accompanying diabetic ketoacidosis (see later).

Insulin deficiency diabetes (IDD)

Primary IDD in dogs is characterized by a progressive loss of Pancreatic beta cells. The aetiology of beta cell deficiency/ destruction.

Processes are thought to be involved

- Congenital beta cell hypoplasia/abiotrophy
- Beta cell loss associated with exocrine pancreatic disease
- Immune-mediated beta cell destruction
- Idiopathic

Insulin resistance diabetes (IRD)

- Dioestrous/gestational diabetes
- Secondary to other endocrine disorders:
- Hyperadrenocorticism
- Acromegaly

Iatrogenic

- Synthetic glucocorticoids
- Synthetic progestagens
- Glucose intolerance associated with obesity

Feline diabetes

Feline DM appears to be more common with increasing age, and in certain breeds such as the Burmese [17]. The disease has a multifactorial aetiology which includes genetic factors and environmental influences such as obesity and physical inactivity, but the exact underlying cause is unclear because not all obese cats become diabetic. Other diseases can lead to diabetes in non-obese cats either directly via beta cell damage (e.g. pancreatic neoplasia or pancreatitis) or via insulin resistance (e.g. acromegaly or hyperadrenocorticism).

Overt DM in cats usually results from a combination of impaired insulin secretion from the pancreatic beta cells in addition to peripheral insulin resistance.

Most cats are thought to undergo a prediabetic glucose-intolerant phase before the islets are unable to keep up with the extra demand for insulin created by insulin resistance in the tissues.

Diabetic cats may also present with *'dropped hocks'* caused by a hyperglycaemia-associated peripheral neuropathy, which is often, gradually, reversible with treatment of the diabetes.

The phenomenon of a remission or '*honeymoon*' phase once a diabetic cat is treated with insulin occurs because, in contrast to dogs, who are unlikely to have any islets left at the time of diagnosis, feline diabetic patients usually have impaired islet function rather than absolute loss of beta cells at diagnosis. Hence diabetic remission, when it occurs, is the result of beta cell recovery as the blood glucose is controlled by exogenous insulin. Recent studies suggest that achievement of remission may be facilitated by a restricted carbohydrate diet and intensive insulin therapy to maintain blood glucose within tight limits.

Confirmation of a diagnosis of diabetes In both dogs and cats, the diagnosis of diabetes mellitus is confirmed by the

- Presence of appropriate clinical signs
- Persistent hyperglycaemia
- Glycosuria
- Elevated serum fructosamine concentration
- Persistent hyperglycaemia in a cat aged 7 years or older
- Obesity
- EPI
- Recent weight loss
- Polyphagia/Polydipsia

Should raise suspicion of diabetes mellitus and prompt measurement of serum fructosamine concentration.

Evaluation of glucose in a urine sample collected in a stress-free manner at home may also help to distinguish genuine insulin resistance from diabetes or prediabetes, because a lack of glycosuria implies a non stressed blood glucose concentration below 12-14 mmol/l.

Urinalysis in diabetic patients usually reveals glycosuria in addition to possible ketonuria. Urine sediment analysis may demonstrate evidence of urinary tract infection, although infection may be asymptomatic. Therefore, urine culture is recommended in all diabetic patients at diagnosis, because glycosuria predisposes to bacterial infection.

Urine specific gravity may be higher than expected in a polyuric diabetic patient because of the presence of a high concentration of glucose.

In addition to metabolic acidosis, most animals with diabetic ketoacidosis have total body sodium depletion, but serum sodium levels may be high (reflecting dehydration), normal or low (as a result of hyperosmolality causing water to shift into the vascular space, leading to dilutional hyponatraemia). Insulin deficiency and acidosis can also cause movement of potassium from the intra cellular to the extracellular fluid so diabetic animals, especially those with ketoacidosis, may be hyperkaliaemic prior to treatment, despite whole-body depletion of potassium. Many untreated diabetic patients are also hypochloraemic due to renal loss of chloride alongside hydrogen ions.

Monitoring of diabetes mellitus

- Water intake over 24 hours
- Urine testing

It is, however, important that urine glucose is assessed at the same time of day on each occasion, preferably in the morning, and that values are interpreted alongside other clinical data. A small amount of urine glucose in a morning sample is acceptable, but if the amount rises in a consistent pattern or ketones are also present, the owner should be instructed to seek veterinary advice. Conversely, if no glucose is detected in a morning urine sample, then it is possible that the dog or cat is at risk of hypoglycaemia and the insulin dose should be reviewed.

Urinary glucose measurements, however, must be interpreted in the light of other clinical findings and not used as the sole means of adjusting insulin dose because glycosuria may reflect inadequate duration of insulin activity rather than inadequate dose.

Glucose measurement

Ideally, in treated diabetic dogs, blood glucose should be maintained between 5 and 10-12 mmol/l, and in treated cats between 5 and 14-16 mmol/l, for the majority of the day.

Fructosamine measurement

High fructosamine concentration implies poor glycaemic control over the preceding 1-2 weeks, and low or normal fructosamine concentration may be consistent with periods of hypoglycaemia.

Investigation of unstable diabetes mellitus

The aims of therapy in canine and feline diabetes mellitus include

- Resolution of clinical signs (e.g. polyuria and polydipsia)
- Maintenance of a good appetite and stable bodyweight
- Owner perception that the patient has a good quality of life and is able to undertake a reasonable amount of daily exercise
- Minimal complications, such as ketosis, neuropathy hypoglycaemia, infections and cataracts.

History and clinical examination

The importance of an accurate and thorough history and clinical examination in the unstable diabetic patient cannot be overemphasized, in addition to a problem-orientated approach. No amount of laboratory testing or diagnostic imaging will substitute for a long and detailed conversation with the owner about the patient, the timing and reasoning behind dose adjustments, the clinical signs and the practically of insulin administration, insulin storage, feeding, exercise, administration of other drug treatments and potential clinical signs of other diseases.

Laboratory testing

Routine haematology and serum biochemistry, as well as urinalysis (including urine culture, since urinary tract infection may be a cause or consequence of poor glycaemic control) are useful in ruling out other causes of weight loss, polyuria or polydipsia and highlighting abnormalities which may be present as a result of other diseases, e.g. hypercalcaemia, neutrophilia and azotaemia.

Blood glucose curves [1,21]

- Whether the insulin is working consistently
- How long the insulin is lasting
- Whether the nadir concentration of glucose is dangerously low.

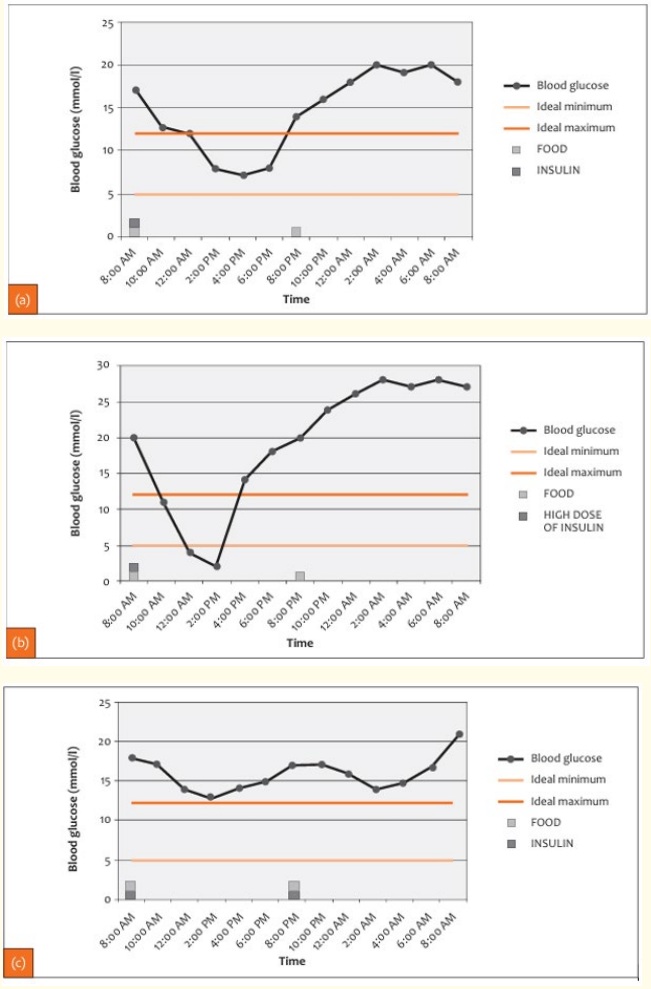

Figure a-c

Causes of diabetic instability

Management factors

Short duration of insulin action

An inadequate duration of action will be avoided by switching once-daily treated patients to twice-daily insulin if they appear to be unstable. Patients that would benefit from such a change can be usually be identified by their history of instability on once-daily insulin, frequent morning hyperglycaemia and glycosuria, and history of over night polyuria and polydipsia. In rare cases, insulin may last less than 8 hours and a long-acting PZI preparation may be required if treatment three times a day is not practical

Insulin-induced hyperglycaemia (Somogyi overswing)

Although owing to day-to-day variability in blood glucose curves, and the effects of hormones which counteract hypoglycaemia as discussed below, this phenomenon is not always apparent with serial blood samples.

The administration of a high dose of insulin (usually >1.5 IU/kg) once daily can lead to the phenomenon of a paradoxical insulin-induced hyperglycaemia. This occurs because of the rapid drop in blood glucose caused by the high insulin dose. The body's natural response to a low blood glucose (usually below 3.5 mmol/l), particularly if it has occurred rapidly, is to counteract this with the secretion of a combination of hormones and activate the sympathetic nervous system to antagonize the hypoglycaemic effect of insulin, often raising blood glucose to very high levels (>20 mmol/l) for several hours to days afterwards.

As this 'overswing' effect is not always apparent on blood glucose curves, other factors such as the history must also be used to determine whether this is the cause of instability in a patient.

If a Somogyi overswing is detected or suspected, then switching to 0.5 IU/kg insulin twice daily and making small adjustments every 3-5 days from that point is recommended.

Infection or inflammation

It is important to note that this type of pattern may also be seen early in the course of treatment, before the optimal insulin dose is reached, and does not necessarily require intense investigation if the insulin dose is still in the 0.5-1.0 IU/kg per injection range.

Infection and inflammation are very common causes of poor glycaemic control in diabetic dogs and cats. Any focus of infection or inflammation can result in insulin resistance in a diabetic patient and signs may be very obvious, e.g. a cat-bite abscess, or very subtle, e.g. a low grade urinary tract infection. Bacterial or fungal infection can result in a vicious circle because it causes insulin resistance and worsens hyperglycaemia, which in turn can exacerbate infection. Screening for infection or inflammation can include routine haematology, urinalysis (ideally collected by cystocentesis) and diagnostic imaging (e.g. thoracic radiography, abdominal ultrasonography), as well as other more specific tests if indicated by the history and clinical signs (e.g. blood culture, joint aspirates, pancreatic enzyme measurement, echocardiography, rhinoscopy). Pancreatitis is another common potential complication of canine and feline diabetes, and can cause 'brittle' glycaemic control. During the history taking, should there be any suggestion that the patient has 'off days' or has experienced any signs of abdominal pain, consideration should be given to assessment for pancreatitis.

In diabetic patients with pancreatitis, there is also a risk of the development of exocrine pancreatic insufficiency over time, which may also affect glycaemic control.

Hormonal antagonism

As already discussed, many hormones can antagonize the effect of insulin-

- Corticosteroids
- Growth hormone
- Progestagens
- Hypothyroid dogs

Can also suffer from insulin resistance. Excess hormone may be endogenously produced or administered exogenously - even topical treatment can destabilize an otherwise well con trolled patient. Hormonal antagonism usually leads to insulin resistance (defined as poorly controlled signs in a patient receiving an insulin dose of >2.2 IU/kg/injection where a Somogyi overswing has been ruled out (see above)). If insulin resistance is present along with signs of any endocrinopathy, as already discussed, appropriate further testing should be carried out such as an adrenocorticotropic hormone (ACTH) stimulation test for hyper adrenocorticism, thyroxine (T4)/thyroid-stimulating hormone (TSH) measurement for hypothyroidism or insulin-like growth factor (IGF)-1 measurement for acromegaly.

Inadequate insulin activity

Insulin may be poorly absorbed subcutaneously, and assessment of the glycaemic response (every 30 minutes for 2-3 hours) to a test dose of 0.2 IU/kg neutral (soluble) insulin given by the intramuscular route may be useful. This is especially useful if the skin has become thickened at the site of insulin injection.

Recent research has shown that, although anti-insulin antibodies are present in the majority of dogs who have received heterologous bovine insulin therapy, they do not appear to be generally associated with instability or deleterious side effects [5-7] and such antibodies are rare in cats [8,9].

Diabetic ketosis, ketoacidosis and non ketotic hyperosmolar syndrome

Diagnosis of diabetic ketoacidosis

Diabetic ketoacidosis (DKA) is a serious and life-threatening complication of chronic hyperglycaemia due to diabetes. Insulin deficiency, cellular glucose starvation and an excess of diabetogenic hormones such as glucagon result in

- Hyperglycaemia
- mobilization of free fatty acids
- formation of ketones (acetoacetate and beta-hydroxy butyrate) as an alternative energy source for tissues. This results in ketosis and eventually progresses to acidosis. Ketones cause vomiting by direct stimulation of the
- chemoreceptor trigger zone
- ketonuria worsens osmotic diuresis, as well as promoting urinary loss of sodium and potassium. A ketotic episode in an otherwise stable patient is usually precipitated by either a treatment failure (e.g. missed insulin injections) or concurrent disease (e.g. pancreatitis, infection, renal disease), although DKA may be present at the time of initial diagnosis. Dogs and cats are susceptible to DKA, but the condition appears more common in dogs, most likely because cats often have some islet tissue remaining, which is able to secrete a small amount of 'protective' endogenous insulin.

Clinical signs of ketoacidosis include acute depression, weakness, dehydration, vomiting, tachypnoea (due to respiratory compensation for metabolic acidosis) and a smell of acetone.

- Ketonaemia
- Ketonuria (be aware, as previously mentioned, that urine test strips will detect acetoacetate but will not detect beta-hydroxybutyrate)
- Marked metabolic acidosis, with increased anion gap (blood pH of less than 7.10-7.15, and bicarbonate (HCO3-) values in the range 8-12 mmol/l)
- Non-regenerative anaemia, left shift neutrophilia, or thrombocytosis in 50% of cases [4,11].
- Occasionally marked red blood cell Heinz body formation (cats)
- Prerenal azotaemia (more common in cats than dogs)
- Initial hyperkalaemia (due to decreased renal excretion and acidosis), which may then develop into hypokalaemia as insulin treatment is instigated and potassium is driven into cells along with glucose [4,11].
- Hypophosphataemia may also develop with treatment, when phosphate shifts from the intracellular space to the extracellular space, and this increases the risk of haemolytic anaemia or seizures [22].

Measurement of beta-hydroxybutyrate (blood) and aceto acetate (urine) can be used to monitor the progress of the patient with DKA. In the early phase of treatment, an apparent increase in urinary dipstick ketones may actually be indicative of successful therapy as the most prevalent ketone, beta-hydroxybutyrate, is broken down to acetoacetate.

An important differential diagnosis for DKA is non ketotic hyperosmolar syndrome (NKHS), which appears very similar clinically and biochemically to DKA but there is an absence of ketones. NKHS is a complication of diabetes defined by extreme hyperglycaemia (>30 mmol/l), hyperosmolality (>350 mOsm/l), severe dehydration, central nervous system (CNS) depression, no ketone body formation and absent or mild metabolic acidosis [14]. Plasma sodium can be low, normal or high and the clinical signs are the consequence of an elevation in plasma solutes such as glucose, chloride and urea. Clinical management is broadly similar to that for DKA but it can be more challenging to monitor progress in the absence of detectable ketones to measure.

Conclusion

After all the above discussion, study and references, it can be concluded that glucose level alteration has multifactorial cause. There therapeutic treatment and balanced diet chart should be advised only after enough diagnostic test have been performed and root cause investigated. Improper diagnosis may worsen the above said situation and can have detrimental effect. Both Canine and Feline have different reasons of altered Glucose level and posses different aetiology and treatment protocols. Diabetic ketosis is another such effect, which should be kept in mind and investigated. Hence, with good diagnosis and proper treatment protocols, control over glucose fluctuations can be achieved and maintained, providing better quality of life to both Felines and Canines.

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