European Journal of Applied Sciences 7 (5): 241-249, 2015
ISSN 2079-2077

DOI: 10.5829/idosi.ejas.2015.7.5.10171

Risk Factors and Management of Diabetes Mellitus in Pets

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Abstract: The knowledge of risk factors and management practice of diabetes mellitus in pets are very important to save the life of animals. Diabetes mellitus is a multi-factorial disease in origin, meaning that variety of factors play a role in the disease process. Genetic and environmental factors play an important role in feline and canine diabetes. Genetics in feline include the overrepresentation of cats with diabetes and environmental risk factors in cat include advancing age, obesity, gender, neutering, drug treatment, physical inactivity and indoor confinement. A genetic basis and altered immune response have a role in the pathogenesis of canine diabetes. Seasonal effects on the diagnosis indicate that there is an environmental influence on disease progression. At least 50% of diabetic dogs have IDDM diabetes due to immune destructions of β-cells. The primary goal of treating diabetic pets is to control clinical signs without causing clinical hypoglycemia as well as other complications and to maximize the chance of achieving a diabetic remission. Identification and treatment of concurrent disease plays an integral role in the successful management of the diabetic pets. lente is the insulin of choice in cats to maximize their chance of going in to diabetic remission and for dogs Ultraletne is preferable.

Key words: Diabetes Mellitus · Management · Pets and Risk Factors

INTRODUCTION

Diabetes mellitus is derived from the Greek word diabetes meaning siphon to pass through and the Latin word mellitus meaning honeyed or sweet. This is because in diabetes excess sugar is found in the blood as well as in the urine. It was known in the 17th century as the pissing evil and was probably coined by Apollonius of Memphis around 250BC. It was first recorded in England, in the form of diabetes in medical text written around 1425. In 1675 Thomas Willis added the word mellitus to the word diabetes and got its full name diabetes mellitus. This was because of the sweet test of the urine [1].

Diabetes is a multiple organ affecting disorder characterized by chronic carbohydrate, fat and protein metabolism failure in the body, especially insulin responsive organs. It results due to a deficiency or absolute lack of insulin secretion by β-cells of the pancreas or decreased number or resistance of cellular insulin receptors. It occurs not only in humans but also in pets with the prevalence of dogs and cats is 1:100 and 1:50 respectively. Based on the degree of β-cell insulin production failure diabetes mellitus divided in to two. These are Insulin Dependent Diabetes Mellitus (IDDM) and Non Insulin Dependent Diabetes Mellitus (NIDDM). The former is frequently seen in dogs while the latter is common in cats [2].

Among the factors that contribute to the development of diabetes mellitus are genetic, immune and environmental factors. Although all breed of dogs are affected; mixed and large breed dogs are more susceptible to the disease, while in cats there is no breed predilection. However Burmese cats are frequently affected than the other [3].

Even though diabetes mellitus is non curable disorder; it is easily and successfully managed that requires a committed effort by the veterinarian and client. Treatment of the diabetes mellitus is a combination of art and science, due to parts of many factors that affect the diabetic state and the animal's response. Each animal needs individualized, frequent reassessment and treatment that may be modified based on the response [4].

Treatment includes use of oral hypoglycemic drugs, exogenous insulin injection, dietary supplement and exercise which are the first choice of treatment, but if the disease is severe, fluid and bicarbonate therapy are also recommended [2].

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Hence, the objective of the paper was: to provide information regarding to the risk factors as well as management practice of diabetes mellitus in pets.

General Consideration of Diabetes Mellitus

Pancreas and its Endocrine Hormone Production: Pancreas is a small vital organ located in abdominal cavity near to small intestine which is a dual functional gland, having feature of both endocrine and exocrine functions. The exocrine part secrets pancreatic fluid which contains digestive enzymes that passes to small intestine. These help to further break down the carbohydrate, proteins and lipids or fats [5].

The part of the pancreas with endocrine function is made up of approximately a million of cell clusters called islets of Langerhans. The islets comprise four types of cells; α-cells that secrets the hormone glucagon, the β-cells, which release insulin, the δ-cells that secret somatostatin and γ-cells responsible for pancreatic polypeptide [5].

Insulin is 51 amino acid hormone produced by the β-cells of the pancreas and plays central role in regulation of carbohydrate, fat and protein metabolism in the body. It causes cells in the liver, skeletal muscles and fat tissue to absorb glucose from the blood. In the liver and skeletal muscles, glucose is stored as glycogen and in fat cells (adipocytes) it is stored as triglycerides [6].

Classification of Diabetes Mellitus: There exist varies types; the most common types of classification however is based on degree of β-cell injury as $type_1$ and $type_2$ diabetes [4].

$Type_1$ diabetes mellitus also called insulin dependent diabetes mellitus (IDDM) is characterized by destruction of β-cells of the pancreas and complete loss of insulin secretion. This type occurs most commonly in dogs, to certain extent also in cats. In this types of diabetes loss of β-cells is irreversible as result the chance of developing Diabetic Ketoacidosis (DKA) is higher than that of $type_2$ for this reason lifelong insulin therapy is mandatory [3]

$Type_2$ or non insulin dependent diabetes mellitus (NIDDM) appears to be the most common form of diabetes in cats. Destruction of β-cell is not predominant pathologic alteration in NIDDM rather development carbohydrate intolerance in cats with NIDDM result due to impaired insulin secretion by β-cells; insulin resistance in insulin responsive tissue and acceleration of hepatic glucose. β-cells have ability to secret insulin, however, the secretory response to stimulate is delayed and the total amount of insulin secretion is abnormal [2].

In addition to this two major types of diabetes, also other forms exist that account for a smaller proportion of total diabetic case. Gestational diabetes, for example, though it has not been reported in cats, it has been documented in dogs during pregnancy and diestrus [4].

Pathophysiology: When glucose concentration is higher than 110mg/dl, insulin is secreted and blood glucose concentration lowers to normal range. Further decreasing of blood glucose below 60mg/dl, depressed insulin secretion and stimulate α-cells to release glucagon which increases blood glucose level back into normal physiological range [7].

Relative or absolute deficiency of insulin secretion by β-cells results in decreased tissue utilization of glucose, amino acids and fatty acids that cause accelerated hepatic glycogenolysis and glucogenesis and accumulation of glucose in circulation results in hyperglycemia. As blood glucose concentration increases, the concentration in the renal tubular cells become beyond renal threshold to reabsorb glucose from the glomerular ultrafiltration and result in glucoseuria. A glucoseuria creates osmotic diuresis causing polyuria, which leads polydipsia in order to prevent dehydration, diminished peripheral tissue utilization of ingested glucose results in weights loss, as the body attempts to compensate for perceived starvation that is why diabetic patients are said to be polyphagia (excessive eating) [2].

Clinical Manifestation and Diagnosis: The most clinical manifestations of diabetes mellitus are polydipsia, polyuria, polyphagia, weight loss and glucoseuria. Untreated or improperly regulated diabetes, may lead to change in the acidity of blood (DKA) with dehydration, vomiting, depression, coma and finally death [3].

Diagnosis of diabetes mellitus is based on clinical findings and measurements of glucose in blood and urine. It is primarily diagnosed by demonstration of persistent glucoseuria and fasting hyperglycemia. The normal fasting value for blood glucose in dogs and cats is 75-120mg/dl [8].

The urine of diabetic animal is more viscous than normal and often has a sweet odor and also urine specific gravity elevates when blood glucose level increases. Large amount of glucose is excreted through urine because it's beyond the renal threshold capacity. The renal threshold capacity of dog is 180mg/dl while that of the cat is 240mg/dl [4].

Complications Associated with Diabetes Mellitus: Untreated or improperly regulated diabetes, may lead to different complications. Among several complications, some of these are; neuropathy, nephropathy, cataract and ketoacidosis diabetes [9].

Neuropathy: It is most common complication of diabetes in cats with prevalence of 10% in cats with diabetes, but it is also recognized in diabetic dogs. The pathogenesis is unknown with the most clinical findings of hind limb weakness, impaired ability to jump, a plantigrade posture with the cat hock touch the ground when it walks and muscle atrophy. Currently there is no specific therapy for diabetic neuropathy in pets [10].

Nephropathy: Renal insufficiency and diabetes are common geriatric diseases that often occur currently especially in older cats. Abnormal renal insufficiency may result from the deleterious effect of diabetic state (i.e. diabetic nephropathy) or may be independent problems that develop in conjunctions with diabetes in the geriatric pets. The pathogenic mechanism is unknown. The most clinical signs are protienemia and albuminuria. It has also no specific treatment [2].

Cataract: It is the most common complication of canine diabetes, when the lens of the eye become opaque, blindness results in the affected eyes. It is in dogs with diabetes are seen far more often than cats with diabetes [3].

High blood glucose level (hyperglycemia) causes change in the lens of the eyes. Water diffuses in to the lens causing swelling and disruption of the lens structure that result in the opacity the eye. If cataract is present it is advisable to remove the lens surgically [11].

Steatosis: Liver is enlarged considerably deep yellow to orange and extremely friable which is susceptible to destruction leading to intra abdominal hemorrhage. The accumulation of fat in the liver is the result of increase fat metabolism. If accumulation of lipid in the liver is extensive and long standing a sequel may be nutritional cirrhosis [9].

Diabetic Ketoacidosis: It is a serious complication of diabetes mellitus which must be regarded as true medical therapy. This develops as a result of an increase of the production of ketone bodies to compensate for the underutilization of blood glucose [3].

It is caused by a lack of insulin or an insufficient amount of insulin. Since a lack of insulin means that glucose is not able be to used as result the body searches a new source of energy. In this condition, the diabetic patient breaks down body fat (lipolysis) to use as energy. During lipolysis waste products called ketones are produced which are eliminated in the urine. Under normal conditions the body can tolerate and eliminate ketones. But, in diabetic ketoacidosis, fats are being broken down at such a high rate that the body can-not eliminate ketones fast enough and they build up in the blood. In high amounts; ketones are toxic to the body which causes the acid-base balance to change and serious electrolyte and fluid imbalances occurred [10].

Risk Factors of Diabetes Mellitus: A number of factors predispose pets to develop diabetes mellitus. These includes genetics, environmental factors; such as age, gender, weight, diet and concurrent illness, an inflamed pancreas and long-term use of progesterone like drugs or steroid drugs and autoimmune factors [8].

Genetic Factors: In diabetic cats, insulin resistance is largely the result of genotype, but it is worsened by environmental factors such as obesity. If these cat gain weight some will no longer be able to secret enough insulin to compensate for the additional deterioration in insulin resistance that accompanies weight gain. In this situation, decompensation of glucose metabolism occurs and impaired glucose tolerance develops [12].

Tyep$_1$ (IDDM) diabetes is principally a disease of dogs and the major genetic susceptibility is linked to a major histocompatibility complex allele on the leukocyte antigen gene on chromosome 6 paired, although many other gene contribute. Breed and familial predisposition is reported in Samoyed, miniature poodles and Rottweiler dogs. Preliminary sequence analysis of dog leukocyte antigen (DLA) gene in a heterogeneous population of canine diabetics revealed that one haplotype is over represented. This haplotype has major histocompatibility complex allele associated with susceptibility to type$_1$ diabetes. Dogs with DLA haplotype are three times more likely to develop diabetes than dogs with other haplotypes. The association between canine diabetes and the major histocompatibility complex in a heterogeneous population strongly suggested that both a genetic predisposition and the immune response have a role in the pathogenesis of diabetes in dogs [13].

Examined diabetes rates in thousands of American dogs found that over all mixed breed dogs were more prone to diabetes than purebreds. Among purebreds, breeds varied greatly in their susceptibility with dogs, miniature poodles and dachshunds have high incidence of diabetes; but no cat breeds are genetically predisposed to develop diabetes i.e. all breed of cats are affected [14].

Autoimmune Factors: Autoimmune response occurs when something goes wrong in immune system. In autoimmune disorders; the immune system fails to distinguish between what is self and non-self and starts to attack its own cells. The location where the attack occurs determines the type of immune disease. When this attack occurs on the β-cells of the pancreas, it causes $type_1$ diabetes [15].

$Type_1$ diabetes develops because the body mistakenly identifies the β-cells of the pancreas as being foreign, or non-self. This results due to several factors such as viral infections and early introduction of cow's milk. The immune system targets and ultimately destroys the, β-cells resulting in absence of insulin and the subsequent diagnosis of diabetes [16].

Among viruses; particularly Coxsackie virus B_4 is the most popular risk factor of IDDM. But, virus is not by itself much important risk factor of diabetes rather it initiates autoimmunity. Scientists believe that regions of the Glutamic Acid Decarboxylase (GAD) molecules, a protein made by the β-cells in the pancreas, is identical to that of the virus known as coxsackie B_4. Hence, after a pancreas infected by the coxsackie B_4 virus, T-cells that destroys the foreign invaders, might identify the similar protein regions in the coxs1ackie virus protein and GAD protein and destroys both coxsackie virus and β-cells of the pancreas [16].

Early introduction of cow's milk before 3or 4 months old may play an active role in the development of $type_1$ diabetes due to autoimmune response. A research showed that newly diagnosed bitches with $type_1$ diabetes had large amount of antibodies that recognizes a specific protein in cow's milk ''Bovine Serum Albumin'' and a protein that sometimes appears on the surface of β-cells after illness. So the theory is that after an illness, autoimmune response of the body mistakenly identifies the transient protein that appears on the insulin producing as β-cells foreign invader and destroys it [16].

Environmental Factors: In feline species, the one mostly seen is $type_2$ diabetes (NIDDM). This relates to life style changes such as physical inactivity and obesity, as well as other factors including; sex, age, drugs and disease. Data largely from domestic short and long-haired cats in North America and Burmese cats in Australia identified obesity, advanced age; male gender, being neutered and drug treatment are as environmental risk factors [17].

In canine species $type_1$ diabetes (IDDM) is common so multiple environmental factors are likely to initiate β-cells autoimmunity, which, once begun, proceeds by common pathogenic pathways. This may be due to environmental influences, interestingly, a highly significant seasonal incidence of diagnosis of canine diabetes also exists and the incidence peaks in winter. The gut and the pancreas are probably immunologically as well as anatomically linked and influenced by environmental risk factors such as intestinal microflora, infections and dietary factors. Two of environmental risk factors that are frequently implicated in $type_1$ diabetes are; enteroviral infections and exposure to cow's milk protein, in which both triggers to the gut immune system [18].

Obesity and Diet: In feline species the major acquired risk factors for NIDDM is insulin resistance associated with obesity. Therefore, obesity is a significant risk factor for diabetes in cats. This increased risk is the result of obesity induced insulin resistance and hyperinsulinemia. A study showed that free access to a highly palatable, energy-dense diet resulted in cats increasing their body weight by mean of 1.9 kg or 44.2%. Insulin sensitivity was reduced by more than half with weight gain in these cats. In fact, in two third of the cats, insulin sensitivity fell below the range of previously reported of normal cats. Importantly, after weight gain, 25% of the cats in study had an insulin sensitivity value that lay within range of previously reported of diabetic cats [19].

Fasting hyperinsulinemia in lean cats is the greatest single risk factor for the development of impaired glucose tolerance with obesity. Some experts go so far as say that feline diabetes is man-made disease because it results due to improper feeding style. The pattern of fat deposition in obese cat also influences the severity of insulin resistance. In general, central obesity (abdominal obesity) in cat is associated with greater insulin resistance and risk of diabetes than peripheral obesity [19].

There are no well documented studies that convincingly demonstrate $type_2$ diabetes is a significant disease entity in dogs, although obesity causes insulin resistance in dogs. Dogs feed high amount of fat diet develop insulin resistance that is not compensated by increased insulin secretions, resulting in glucose intolerance [20].

The effects of dietary macronutrients were also evaluated in cats and dogs. Three test diets are used that are high in protein (46% of energy), fat (47% of energy) and carbohydrate (46%of energy). Pets which fed high carbohydrate diet had significantly higher mean and peak (23-32%) glucose concentrations and tended to have higher insulin concentrations than pets which fed either a high amount of protein or a high amount of fat diet. High amount of carbohydrate diets increase blood glucose and insulin levels and may predispose pets to obesity and leads to diabetes, while a diet of high amount of fat may contribute to pancreatitis (inflamed pancreas) and a risk factor for diabetes [13].

Sex and Age: Male cats have a greater risk for developing diabetes than female cats. The reason for this increased risk may be related to two factors. The first is the tendency of male cats to have lower insulin sensitivity value (37% lower) than females when they are lean, which deteriorates further with weight gain. Interestingly, only male cats had significantly increased basal insulin concentration after weight gain and the absolute concentrations tended to be higher than in obese female cats. Secondly, male cats are predisposed to obesity. The greater the fat mass, the less effective the insulin in reducing plasma glucose was observed. These findings of lower insulin sensitivity and higher insulin concentrations in mal cats may explain why male cats have a greater a risk of developing obesity and diabetes than female cats [21]. Increasing age in domestic dogs and cats are a greater risk factor for diabetes mellitus. So middle to old age pets are more affected than young pets [22].

Female dogs are more at risk than males because of the change in their reproductive hormones every time through a season. Reduced insulin sensitivity occurs in healthy bitches by day 30-35 of gestation and becomes more severe during late pregnancy. The diestrus phase of the non pregnant cycle of the bitches is similar in duration to the 9th weeks of pregnancy and it is generally agreed that the hormone profile during diestrus and pregnancy are essentially identical. However, the reduction in insulin sensitivity is more pronounced in pregnancy than diestrus. The alteration in the metabolic control of growth hormone during gestation may make pregnancy specific in dogs. Progesterone elevation causes glucose intolerance and overt diabetes during diestrus in bitches. It also stimulates the mammary gland of bitches to produce growth hormone which is potent inducer of insulin resistance. The periodic inducer of diestrus associated with insulin resistance may contribute to the increased risk for developing diabetes in females compared with male dogs [23].

Drug and Illness: Veterinarians can contribute to loss of insulin sensitivity by prescribing drugs that cause insulin resistance, especially if these medications are used for long term basis or if long acting forms are chosen. A wide variety of pharmacological agents such as corticosteroids are known to be diabetogenic in pets. Corticosteroids and progestins are the most commonly used drugs in cats that cause insulin resistance. Two or more treatments with corticosteroids in 2 years period pose a significant risk factor for diabetes in cats [24].

Dental disease was a significant risk factor for diabetes in pets as were chronic or recurring medical problems. Inflammation may also play pathogenic role in diabetes and periodontal disease and diabetes tend to promote one another [12].

Physical Inactivity: Physical inactivity increases the risk of diabetes both directly by decreasing insulin sensitivity and indirectly by an effect on body weight. In cats, being confined indoors and having low physical activity score were significant risk factors for diabetes. If the modern life style of an urban cat is compared with a feral cat that hunts to obtain all its food, urban cats are more susceptible [25].

Treatment of Diabetes Mellitus: Treatment of diabetes mellitus is a combination of art and science, due to the many factors that affect the diabetic state and animal's response. The primary goal of therapy for diabetic pets is to maintain blood glucose concentration as close to normal i.e. 100mg/dl as possible. This can be accomplished through proper insulin administration, diet, exercise, oral hypoglycemic medication and avoidance of or control concurrent illness [10].

Oral Hypoglycemic Drugs: The goals of oral hypoglycemic medications are to minimize glucose absorption by the intestine, minimize the conversion of glycogen to glucose in the liver and also help increase insulin secretion from the pancreas. The major groups of oral hypoglycemic drugs widely used for veterinary practice worldwide are; Sulfonylureas, Bigunide and Thiazolidinedione [26].

Insulin Therapy: Insulin therapy is the backbone of diabetic patient management especially in IDDM with the ideal goal of being maintaining blood glucose concentration around 100 mg/dl without complications [2].

Now days much commercially produced insulin is available and used for the long term management of diabetes mellitus. These commercially available insulin preparations include combination of beef and pork insulin which are relatively non antigenic for pets [27].

Thus different types of insulin are used for diabetic dogs and cats worldwide. These includes; regular or crystalline which is short-acting insulin, NPH and Lenten which are intermediate-acting while Ultrlente and PZI are long-acting insulin [28].

In general, cats and small dogs need insulin injections more frequently, usually twice daily than larger breed of dogs that may only require one dose of insulin daily. But, the action of insulin varies in each individual and some large dogs will need 2 times insulin shots daily. The insulin needs of the individual animal are determined by collecting small amount of blood glucose (sugar) levels every 1-2 hours for 12-24 hours. This is called an insulin glucose response curve. When insulin treatment is first begun, it is often necessary to perform several insulin-glucose response curves to determine types of insulin use, dose of insulin, frequency of insulin administration and the time to feed the animal [3].

Dietary Therapy and Exercise: Dietary therapy should be correct obesity, maintain consistency in the timing and caloric contents of meal and furnish the diet that minimize postprandial fluctuation in the blood glucose. Soft moist food should be avoided due to hyperglycemic effect of disaccharides and propylene glycol found in moist soft feed. Diet containing high amount of fiber helps to promote weight loss, slow glucose absorption from intestinal tract and reduce postprandial fluctuation in the blood glucose, Hence control hyperglycemia. Although commercially available high fiber diets appear to be effective improving hyperglycemic control in diabetic pets discontinuation of insulin therapy is not recommended [29].

Once normal body weight has been attained, diet containing high amount of fiber content can be gradually changed to the prior's diet. The caloric intake should be calculated to maintain the pets nearest body weight and the daily caloric requirement of mature dog is 40-80kcal of metabolized energy per kilogram of ideal body weight. It is higher in smaller dogs and cats due to that the small animals have high metabolic rate. The feed schedule should be designing to enhance the action of insulin and minimize postprandial hyperglycemia. In case of cats multi-small meals are recommended to manage diabetes mellitus [30].

Chromium is an essential trace element that is required for normal carbohydrate and lipid metabolism. It improves glucose tolerance by increase insulin sensitivity with greater insulin effectiveness and blood glucose concentration decrease. Results demonstrated that the incorporation of chromium tripicolinate at 300 and 600 parts per billion in the ration of healthy cats produced a small but significant improvement in glucose tolerance. Chromium is an essential nutrient but, it is not a therapeutic drug [31].

Exercise is an important role in the maintenance of glycemic control by helping to promote weight loss and by eliminating insulin resistance induced by obesity. It also exerts glucose lowering effect by increasing the absorption of the insulin from the injection site, increasing blood flow hence, insulin delivery to exercise muscle, increasing glucose effectiveness but sporadic or strenuous exercise should be avoided. Insulin dose should be decreased in pets subjected with exercise on days of anticipated increases [2].

Bicarbonate Therapy: The clinical presentation of pets in conjunction with plasma bicarbonate or total venous Co_2 concentration is used for deciding the need for bicarbonate therapy or not. Bicarbonate therapy is not usually done when plasma bicarbonate or total venous Co_2 is 12 mili equivalents per litter or the patient is alert because alert patient has probably normal or nearly normal pH of cerebrospinal fluid. The acidosis in this patient is corrected through insulin and fluid therapy. The bicarbonate deficit (mili equivalents of bicarbonate) is given initially to correct acidosis to the critical level 12 mEq/L. When plasma bicarbonate is 11 mEq/L/kg, bicarbonate therapy should be initiated and corrected by administration of bicarbonate given initially 6 hrs. period of time. It should be never given in bolus infusion [2].

Fluid Therapy: Replacement and maintenance of normal fluid balance are important to ensure adequate cardiac output, blood pressure and blood flow to tissue and improvement in renal blood flow is especially critical. The type of fluid initially depends on the animal's electrolyte status, blood glucose and osmolality. Initial IV fluid choice is 0.9% NaCl with appropriate potassium

Table 1: Clinical properties of insulin preparation for diabetic dogs and cats

Type of insulin	Route of administration	Onset (hr)	Time of max. effect (hr)		Duration of effect (hr)	
			dogs	cat	Dog	cats
Regular crystals	IV	Immediate	½-2	½-2	1-4	1-4
	IM	1/6-1/2	1-4	1-4	2-8	3-8
	SQ	1/6-1/2	1-5	1-5	4-10	4-10
NPH	SQ	1-3	1-12	2-8	8-24	6-13
Lente*	SQ	½-2	3-12	2-8	8-24	6-14
Ultraletne**	SQ	2-8	6-16	-	8-24	-
PZI	SQ		-	6-16	-	6-24

Source: [6].

*primary choice of insulin for diabetic cats;**primary choice of insulin for diabetic dogs.

Table 2: Oral hypoglycemic drugs and their functions

Sub group	Generic Name (brand)	Route	Function
Biguanides	Metformin	Oral	Delay gastro intestinal absorption of ingested nutrient and promote the peripheral utilization of blood glucose
Thiazolidinediones	Rosiglitazone	Oral	Increase insulin sensitivity by acting on adipose muscle and liver tissue to increase glucose utilization and decrease glucose production.
Sulfonylureas	Glipizides		Stimulates insulin secretion by β-cells,
	Glibenclamide	Oral	direct action on liver to decrease hepato glucose output and the potentiation action of insulin on liver

Source: [15].

supplement. Most pet with DKA have significant deficit in total sodium ion which is best replaced with NaCl only if osmolality is greater than 35mg/dl. It should be hypotonic fluid i.e. 0.45% saline should be recommended [9].

Pets with severe DKA usually have develop Na^+ as result, no suffering from dramatic hyper osmolality despite elevation in plasma glucose and BUN. In addition to this hyper osmolality is readily corrected during 24-36 hrs. of treatment with appropriate fluid and insulin therapy. The initial volume and rate of fluid administration are determined by assessing degree of shock, dehydration, patient maintenance requirement and plasma protein concentration. Rapid replacement of fluid is not recommended unless there is shock [29].

Conclusions and Recommendation: In Ethiopia many instances; the policy of the country and lack of professional man power resource make minimal provision for health and care of small animals. Diabetes mellitus is multi factorial disorder which includes genetics, environment and autoimmune which is the most important predisposing factor. Middle to old age intact bitches are commonly affected and higher incidence results due to ovarian secretion of progesterone that is insulin antagonist which stimulates secretion of growth hormone which induce diabetes mellitus in bitches. Diabetes is a slow killer with no known curable treatment; however its complications can be reduced through proper awareness and timely treatment. It is important to keep the blood glucose level of patients under strict control for avoiding the complications. Although insulin is the back bone to manage diabetes mellitus, it leads to severe hypoglycemia unless it is used correctly.

Based on the above conclusion the following points should be recommended:

- Much attention should be given to small animal's health in universities, organizations and private sectors in Ethiopia.
- Further research should be conducted about diabetes mellitus in pets.
- Intact bitch should be spayed and male cats should not be castrated in order to prevent diabetes mellitus.
- Care should be taken during insulin therapy to avoid hypoglycemia or hyperinsulinemia development in the blood.

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