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Therapeutic management on diabetes mellitus in canine

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Abstract
The present study was conducted to estimate various blood/serum biochemical parame ters in diabetic canines along with therapeutic management in Jaipur region, of Rajasthan during June, 2020 to December, 2020. A total of two hundred canines of different age group, sex and breed with the history of polydipsia, polyphagia, polyuria, obesity, rapidly developing bilateral cataracts, rapid weight loss or in combination thereof were screened. Diabetic canines were managed well with intermediate-acting insulin (Caninsulin) @ 0.25 IU/kg body weight subcutaneously after meal twice a day resulted significant decrease in blood glucose levels over the period of time. Supportive therapy, balanced diets rich in high fiber, complex carbohydrates, high quality protein content and a low restricted fat along with regular, scheduled feeding always at same amount twice daily and regular exercise should also advised on daily basis.

Keywords: Caninsulin, Jaipur, Complex carbohydrates, Diabetes Mellitus

Introduction
The word 'diabetes' is derived from the Greek word "Diab" (meaning to pass through, referring to the cycle of heavy thirst and frequent urination); 'mellitus' is the Latin word for "sweetened with honey" (refers to the presence of sugar in the urine). Greeks had the knowledge of a disease accompanied by polyuria and wasting of body, whereas Arelacus of Cappadocia mentioned a disease characterized by thirst and polyuria. From the Middle East, the knowledge of diabetes mellitus had spread to Spain as a disease characterized by polyuria, polydipsia with sugary flavoured urine. With the discovery of sugar in urine and its detection by laboratory test, the knowledge permeated into the 18th century (Patel *et al.*, 2012) [17].

Diabetes mellitus is complex disease to treat as it is a multi-organ affecting problem. The primary goal of diabetes mellitus treatment is maintenance of patient's blood glucose levels as close to normal as possible i.e. 100 mg/dl. This can be achieved by proper insulin administration, diet, regular exercise regimes, oral hypoglycemic drugs and avoidance or control of concurrent illness that may complicate the animal's diabetic state (Rheal *et al*., 2003) [19].

Sidhu and Randhawa (2019) [21]. Concluded that management of diabetes mellitus is achieved by insulin administration, diet, regular exercise and oral hypoglycaemic drug. Alternate therapies like use of encapsulated islet, gene therapy ete. are being evaluated for its clinical application in efficient management of diabetes mellitus.

The IU-40 pork lente (porcine zinc insulin suspension) has been the first choice recommendation for dogs. The duration of action is close to 12 hours in most dogs and the amorphous component of the insulin helps to minimize postprandial hyperglycemia (Monroe *et al*., 2005) [15].

Materials and Methods
The present research work entitled "Clinical Studies on Diabetes Mellitus in Canine" has been carried out at the Department of Veterinary Medicine, Post Graduate Institute of Veterinary Education and Research (PGIVER), Jaipur. The animals taken for study, were canines brought to the Veterinary Clinical Complex (VCC) of PGIVER, Jaipur and

Government Veterinary Polyclinic Hospital, Panchbatti, Jaipur during June, 2020 to December, 2020. In the present investigation entitled "Clinical studies on diabetes mellitus in canine" a total of two hundred canines (dogs) were included on the basis of clinical manifestations, having history of polydipsia, polyphagia, polyuria, obesity, rapidly developing bilateral cataracts, rapid weight loss or in combination thereof.

These canines were screened for blood glucose by using on-site glucometer. The animals showing random blood glucose level above 140 mg/dl, were tested again for fasting blood glucose next day after 12 hours of fast (Deepa, 2014 and Jatav, 2015) [6, 11]. Based upon the results eleven canines were diagnosed as diabetic. Ten healthy canines (dogs) were also included for healthy control group in the study.

Collection of blood and serum

In order to study haemato-biochemical alterations in diabetic canines, blood samples were collected from all canines following all the aseptic precautions. Using 22 or 24 gauge sterilized needle and 10 milliliter (ml) disposable syringe, total 7 ml of blood was collected from the cephalic or saphenous vein.

Out of this, 2 ml blood was collected in sterilized test tubes containing disodium salt of ethylene diamine tetra acetic acid (EDTA) @1 mg/ ml of blood) as an anticoagulant while remaining 5 ml blood was collected in another sterilized test tube without any anticoagulant for the separation of serum and thereafter blood slants were made and incubated for one hour at 30 ºC. Then the tubes were refrigerated for some time (allowing retraction of clot) and centrifuged at 2500 rhythm per minute (rpm) for 30 minutes in order to separate serum. On separation, serum was immediately transferred into sterilized screw capped vial; a drop of Merthiolate solution (1:10,000) was added and stored in deep freeze at -40 ºC until used for biochemical estimations. The blood samples were also collected from 10 healthy canine (Healthy control group) as described above and subjected for the estimation of haematological and biochemical values.

Therapeutic Management

The following common therapeutic treatment was given for diabetic canines as per requirement.

A) Insulin Therapy: The positive cases of diabetes mellitus were treated with Insulin @ 0.25 IU/kg body weight subcutaneously after meal at every 12 hours interval. Regular monitoring of blood glucose by using on-site glucometer was also done to avoid any complications.

(B) Supportive Therapy: therapy consisting combination of: Syrup containing L-Carnitine, L-Arginine and Taurine @ 5 ml twice a day under 15 kg body weights and @ 10 ml twice a day over 15 kg body weights orally.

Syrup containing Calcium, Vitamin D3 and Phosphorous @ 5 - 10 ml twice daily for pups and small breeds and @ 10 - 20 ml twice daily for adults and large breeds orally.

(C) Dietary Modification: Diet containing high fiber with complex carbohydrates, high quality protein content and a low restricted fat along with regular and scheduled feeding, always the same amount twice daily. Regular exercise was also advised on daily basis.

In the study diabetic canines were treated with Insulin @ 0.25 IU/kg body weight subcutaneously after meal at every 12 hours interval. The insulin chosen for treatment protocol was intermediate-acting insulin also known as Caninsulin. Caninsulin is a combination of highly purified porcine insulin (40 IU/ml) consisting of 35% amorphous zinc insulin and 65% crystalline zinc insulin “Lente” type. (Behrend *et al.* 2018) [3].

Palm *et al*. (2009) [16]. Opined that problems with short duration of insulin effect despite twice a day administration are more common than problems with prolonged duration of insulin effect, especially with NPH insulin. For this reason, porcine source Lente insulin was considered the initial insulin of choice for the treatment of diabetes in dogs.

Most diabetic dogs suffer from insulin deficiency and require exogenous insulin. Oral insulin would be highly advantageous but is poorly absorbed. The main reason for low absorptivity is the hydrolysis of insulin by enzymes in the gastrointestinal tract (Chen *et al*., 2018) [4]. Most diabetic dogs may require twice daily administration of Caninsulin for satisfactory glycaemic control (Horn and Mitten, 2000) [10].

Carnitine helps peripheral tissue for utilization of glucose (Ferannini, 1988) [8]. Carnitine also plays an important role in diabetes mellitus complications, it may prevent occurrence of chronic diabetes mellitus complications (Silig, 1999) [22].

Arginine appears to exert modestly beneficial effects on glucose metabolism; L-arginine has been shown to decrease fasting blood glucose, improve glucose control during the oral glucose tolerance test increase insulin sensitivity and increase glucose disposal and decrease endogenous glucose production in diabetes mellitus patients (Piatti, 2001) [18]. Arginine has also been shown to improve healing of diabetic ulcers and may have averted the need for amputations (Arana, 2004) [2].

The possible role of taurine in the regulation of glucose metabolism the amino acid seems to increase glyconeogenesis, glycolysis and glucose oxidation and glucose uptake in the liver and heart. It also increases insulin activity (Hansen, 2001) [9].

Vitamin D is important for prevention of islet cell death and improves insulin production (Norman, 1980). Vitamin D3 restores the suppressor cells, decreases Th1 cytokine production responsible for β-cell death and shifts the immune response toward Th2 pathway, leading to benign insulitis (Khoo, 2011) [12].

The movement of calcium is vital to the function of any cell type but has a special role to play in pancreatic β-cells due to its importance in the process of insulin release. Insulin production and subsequent release from these cells is controlled by multiple players, including glucose, neurotransmitters, peptide hormones and other compounds (Alfa, 2015) [1].

Calcium has a significant role to play in physiological insulin release from islet β-cells. Glucose, acting as the main stimulus of these cells, actually serves to control calcium concentrations across many compartments of the cell, including the endoplasmic reticulum, mitochondria, nucleus and cytosol, among others (Klec, 2019) [13]. Phosphorous also affect insulin status and play an important role in regulating postprandial (pp) blood glucose (Soltani *et al*., 2007) [23].

The goals of dietary therapy were to optimize body weight with appropriate protein and carbohydrate levels, fat restriction, and calorie and portion control. Weight loss in obese patients and stopping DM associated weight loss were

treatment goals for diabetic patients (Behrend *et al*., 2018) [3].

Diets lower in carbohydrates result in lower pp blood glucose levels. Ideally, carbohydrates used should be complex with a low glycemic index as these release glucoses more slowly and further reduce the pp hyperglycemia which is so damaging to diabetics. Dietary management should be instituted at the same time as insulin therapy in the diabetic dogs. The goal of dietary therapy is to minimize pp fluctuations in blood glucose and to potentiate the action of insulin. They support the feeding of a high complex carbohydrate (> 50% dry matter), high fiber diet (> 10% dry matter) to dogs with DM. Diets containing increased amounts of soluble fiber (fruits, legumes and oats) delay gastric emptying alter intestinal transit time and potentiate the actions of insulin in tissues. Increased amounts of insoluble fiber (cellulose, vegetables and grains) alter intestinal transit time and slow starch hydrolysis (Elliott *et al.*, 2012) [7].

Physical activity includes all movement that increases energy use, whereas exercise is planned, structured physical activity. Exercise improves blood glucose control in diabetes mellitus, reduces cardiovascular risk factors, contributes to weight loss and improves well being (Chen *et al*., 2015 and Lin *et al*., 2015) [5, 14].

Conclusions

Diabetic canines were managed well with intermediate-acting insulin (Caninsulin) @ 0.25 IU/kg body weight subcutaneously after meal twice a day resulted significant decrease in blood glucose levels over the period of time. Supportive therapy, balanced diets rich in high fiber, complex carbohydrates, high quality protein content and a low restricted fat along with regular, scheduled feeding always at same amount twice daily and regular exercise should also advised on daily basis. It was observed that, handheld glucometer for estimation of blood glucose could be helpful for an easy and quick diagnosis of diabetes mellitus under field conditions.

Out of 11 diabetic canines, 4 canines (36.36%) having fasting blood glucose level below 250 mg/dl were treated with insulin therapy only for five days and remaining 7 canines (63.63%) having fasting blood glucose level above 250 mg/dl were treated with insulin therapy for seven days. After treatment, blood glucose level became within normal range in all canines. Supporting treatment along with dietary modification was followed for four to six weeks. All the dogs were presented for follow up.

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