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Research Article

EVALUATION OF SERIAL BLOOD GLUCOSE CURVE FOR MANAGEMENT OF DIABETES IN DOGS

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ABSTRACT

The present study was aimed to evaluate clinical application of blood glucose curve monitoring and insulin therapy for diabetes mellitus in dogs. The overall incidence of diabetes mellitus was 1.48% and prominent clinical signs were polydipsia, polyuria, polyphagia, weight loss and lethargy. The mean fasting blood glucose in diabetic dogs at the time of diagnosis was 22.37 ± 1.78 µmol/L (402.7 ± 32.0 mg/dL). Dogs were divided into two groups (group-I: >19.43 µmol/L (350 mg/dL) and group-II: < 19.43 µmol/L (350 mg/dL)) depending upon blood glucose level. Hemato-biochemical findings revealed markedly increased alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) cholesterol, triglyceride, high-density lipoprotein (HDL)-cholesterol, amylase and lipase. Urine examination revealed hypersthenuria, glycosuria, variable ketonuria, and leukocytes in the urine sample of diabetic dogs. Oral hypoglycemics were found ineffective in diabetes management. Insulin treatment was initiated at the dose rate of 0.5 IU/kg body weight in group-I and 0.25 IU/kg body weight in group-II and adjustments were made according to blood glucose fluctuations in individual animals. Serial blood glucose curve was generated for both groups before (day 0) and after beginning of treatment (post seven days and twenty-eight days). Insulin therapy along with continuous glucose monitoring through blood glucose curve at regular intervals showed good glycemic control after one month of regular monitoring and improvement in overall quality of life in all diabetic dogs.

Keywords: Canine, Diabetes mellitus, Glucose curve, Insulin therapy, Monitoring

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Diabetes mellitus (DM) is the most commonly diagnosed endocrinopathy in companion animals with prevalence estimated to be between 0.0005% and 1.5% in dogs (Catchpole *et al.*, 2005). Clinical signs in DM are attributed to persistent hyperglycemia and glucose intolerance, either due to insulin deficiency or due to the impaired effectiveness of insulin's action, or a combination of both. Initially cases are rarely reported because clinical signs can be very subtle and most patients are presented later with diabetic ketoacidosis with systemic signs of illness such as anorexia, vomiting, dehydration, and occasionally acute blindness secondary to cataract formation (Hess *et al.*, 2000). The primary goal of therapeutic management of diabetic dogs is to eliminate owner-observed clinical signs and to prevent the complications of poorly controlled diabetes (Ettinger and Feldman, 2010). Diagnostic and therapeutic protocols for diabetes mellitus in dogs have evolved significantly over the last few years. However, there has been great variation between therapy strategies adopted by clinicians for insulin therapy and dose adjustments. This is mainly attributed to variation in an individual's response to insulin therapy and inaccurate glucose monitoring protocols adopted in various clinical settings. The present study was conducted to provide detailed clinical appraisal, haemato-biochemical and urine chemistry alterations, blood glucose fluctuations, glucose curve for glycemic monitoring and also to provide better insights into insulin therapy and its duration of glycemic control in diabetic dogs.

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MATERIALS AND METHODS

The study was carried out in the department of Veterinary Medicine, Dr. G C Negi College of Veterinary and Animal Sciences, CSKHPKV Palampur (H.P) from February 2018 to June 2019,with IAEC permission.

Animal selection: Preliminary screening of 1212 dogs for diabetes mellitus was done based on patient history, clinical signs, random blood glucose concentrationusing an on-site glucometer andurine analysis. Dogs having random blood glucose concentration above 6.1 µmol/L (110 mg/dL) were subjected to fasted blood glucose estimation using glucose kit based on GOD-PAP method (Liquichek blood glucose kit, AGAPPE) (Trinder, 1969). Dogs having persistently fasted blood glucose above 8.9 mmol/L (160 mg/dL) along with persistent glycosuria were confirmed with diabetes mellitus. Ten healthy dogs who were presented for vaccination or routine general examination were included in the study as control group. Normal clinically healthy dogs have a fasting blood glucose concentration within a range of 3.3 µmol/L (60 mg/dL) to 6.1 µmol/L (110 mg/dL). The study included 18 confirmed cases of diabetes mellitus.

Examination: The blood samples were collected from the

radial or a recurrent tarsal vein in sterile vials containing disodium salt of ethylenediamine-tetra acetic acid (EDTA 1mg/ml) for haematology and in heparanized vials for biochemical examination.The haemato-biochemical examination was done by using an automatic hematology analyzer (BC-2800VET, MINDRAY) for haematological parameters (complete blood count (CBC) and Microlab 300 Clinical Chemistry Analyser (by Merck Limited, Mumbai) for biochemical parameters (alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), cholesterol, triglyceride, high-density lipoprotein (HDL)-cholesterol, amylase and lipase). Furthermore, 5 ml of midstream urine samples were collected by catheterization for routine urine urinalysis in a semiautomatic urine analyzer (Uriscan Optima-YD Diagnostics Corp. Korea).

Therapy: All the cases diagnosed with diabetes were divided into two groups depending upon the level of hyperglycemia and the therapeutic protocol adopted (Table 1). The insulin used for the treatment protocol was a combination of fast-acting human recombinant insulin and intermediate-acting NPH (Neutral Protamine Hagedorn) also known as Isophane (Human Mixtard 30/70®). Out of 6 dogs in group II,4 dogs had blood glucose concentration below 13.88 µmol/L (250 mg/dL), so they were initially treated with oral hypoglycaemic drug glibenclamideat the dose rate of 0.2 mg/kg body weight BID along with dietary modification for twenty-eight days. The owner was asked to feed the dog twice a day with 2 meals coinciding with morning and evening insulin injections. The diet consisted of slow releasing carbohydrate, high-quality protein and high-fiber with water ad-lib. Owner was asked tomake aone-daymealconsisting amixture of chapati made of multigrain flour, chicken breast or eggs, kidney beans (who do not feed chicken), high-fiber vegetableslike broccoli, carrots or cucumber; all ingredients in equal parts and the meal was split into two equal halves. The dogs were fed twice with equal quantity of meal at fixed timings. The dogs which were accustomed to 3 times feeding, were fed withhigh-fiber meal in the afternoonlike apple, banana, pumpkin etc.

Monitoring: Serial blood glucose sampling was carried out every 2 hours and glucose curve was generated on day 0, day 7 and day 28 after beginning of treatment to evaluate the response to the treatment and insulin dose adjustment. Days when animal was not brought to the hospital, home monitoring was advised to the owners.

The data obtained were subjected to statistical analysis by using computer software Instat from Graphpad software, 2008. The mean values of different parameters between the control and diseased group; control, pre, and post-treatment were compared at 1% and 5% level of significance using "t" test and "ANOVA" as described by Park (2009).

RESULTS AND DISCUSSION

Out of 1212 dogs presented from February 2018 to June 2019, 18 cases were diagnosed with diabetes mellitus with an overall incidence rate of 1.48%. Age-wise highest incidence i.e., 55.55% (10/18) was recorded in old dogs (>5 years), followed by adults (1-5 years) with an incidence of 33.33% (6 /18) and minimum incidence was recorded in young dogs (<1 year) i.e., 11.11% (2 /18). Similarly, many researchers reported that the incidence was found to increase with advancing age and the highest incidence occurring in dogs of 10 to 15 years age group (Fall *et al.*, 2007). All eighteen diabetic dogs were divided into two groups depending on the level of hyperglycemia. Clinical observation and haemato-biochemical profile were recorded on day 0, day 7 and day 28 post treatment (Table 2 & 3). Four dogs were initially treated with glibenclamide for twenty-eight days. However, there was no improvement in the blood glucose levels and clinical signs of polydipsia, polyphagia and polyuria were persisting, therefore these animals were also treated with insulin at the same initial dose rate of 0.25 mg/kg body weight SC BID.

On day 0, clinical signs observed in diabetic dogs were polydipsia and polyuria (16/18, 88.88% each), polyphagia (13/18, 72.22%), weight loss (12/18, 66.66%), lethargy (10/18, 55.55%), constipation and dehydration (7/18,38.88%) and 27.77% (5/18) of dogs were anorectic. Only 3 out of 18 (16.66%) dogs showed vomiting and one only one (5.55%) had diarrhoea. Eight dogs (44.44%) developed ocular changes like cataract and uveitis and abnormal gait was observed in 2 dogs only. These clinical manifestations have been attributed to persistent hyperglycemia and alterations in glucose, protein and fat metabolism (Hume *et al.*, 2006). Systemic signs like vomiting and anorexia can develop due to ketosis and metabolic acidosis (Fleeman and Rand 2001). The onset of diabetic cataract involves several factors like osmotic changes in the lens, glycosylation of structural proteins and a decreased concentration of antioxidants (Kumar *et al.*, 2014). After twenty-eight days of initiation of insulin therapy, there was complete remission of the clinical signs in all the dogs of both the groups.

All the hematological parameters had no significant variation between healthy, pre- and post-treatment group (Table 2). In both the groups, the blood glucose values decreased significantly after seven days and further

Table 1. Therapeutic protocol in different groups of diabetic dogs

Group	Plasma Glucose (mmol/L)	Treatment protocol	No. of animals
Group I	> 19.43 mmol/L	Insulin @ 0.5 IU/kg bwt sc bid + dietary modification	12
Group II	< 19.43 mmol/L	Insulin @ 0.25 IU/kg bwt scbid + dietary modification	6

decreased after twenty-eight days of treatment. But even after twenty-eight days of treatment the blood glucose values were significantly higher than the healthy group. In group-I, the ALT value decreased significantly after twenty-eight days of treatment and the values were comparable to the healthy group. In group-II there was no significant decrease in the value of ALT after twenty-eight days as compared to the value on day 0. The values of AST in group-I and group-II on day 0 differed significantlyfrom healthy group and in both groups values of AST showed a non-significant decrease after seven days and twenty-eight

Table 2. Pre and post treatment haematological parametersin diabetic dogs

S. No.	Parameters	Healthy group (N=10)	Group I (N=12) II (N=6)	Pre-treatment values (Day 0) (Mean±S.E.)	Post treatment values (Day 7) (Mean±S.E.)	Post treatment values (Day 28) (Mean±S.E.)
1	Hb (g/dl)	14.97±0.65	Group I	13.61±1.27	13.24±0.80	14.04±0.76
			Group II	14.92±2.85	16.10±2.77	14.80±1.90
2	PCV (%)	43.1±2.69	Group I	42.27±3.61	39.99±2.40	43.64±2.24
			Group II	46.47±8.31	47.03±7.42	45.60±4.76
3	TEC ($\times 10^{12}$/L)	7.38±0.20	Group I	6.45±0.50	6.65±0.42	6.52±0.27
			Group II	6.86±1.19	7.00±1.09	6.96±0.69
4	TLC($\times 10^{9}$/L)	12.29±1.07	Group I	15.4±2.73	14.25±1.24	10.63±0.84
			Group II	11.4±3.18	25.03±14.50	10.38±1.81
5	Lymphocytes (%)	21.79±3.92	Group I	18.02±4.53	24.56±4.61	27.09±3.65
			Group II	22.7±2.99	16.35±4.74	26.55±3.89
6	Monocytes (%)	3.74±0.25	Group I	2.82±0.41	2.64±0.26	3.41±0.36
			Group II	4.47±0.46	3.53±0.67	5.05±1.40
7	Granulocytes (%)	74.47±4.12	Group I	79.15±4.76	72.80±4.66	69.25±3.86
			Group II	72.82±3.18	80.13±5.28	68.40±4.38
8	MCV (fl)	58.78±3.16	Group I	65.58±1.82	58.49±5.60	62.86±1.35
			Group II	67.5±2.64	67.50±3.38	61.98±0.52
9	MCH (pg)	20.18±0.44	Group I	20.73±0.73	25.93±4.96	22.21±0.54
			Group II	21.5±1.04	22.90±2.22	20.25±0.59
10	MCHC (g/dl)	35.61±2.29	Group I	32±0.47	32.99±1.40	32.22±0.58
			Group II	31.8±0.46	33.80±2.24	32.05±0.23
11	RDW (%)	13.45±0.34	Group I	14.86±1.01	14.65±0.85	13.47±0.62
			Group II	12.77±0.51	12.98±0.97	13.50±0.29
12	Platelet ($\times 10^{9}$/L)	336.2±36.2	Group I	313.62±67.33	315.13±48.40	347.88 ±31.54
			Group II	344±110.46	368.25±66.38	295.75±63.71

days of treatment. There was a non-significant decrease in the value of ALP after seven days and a further decrease after twenty-eight days of treatment. Liver is a primary organ susceptible to diabetes-induced oxidative stress, leading to liver tissue injury. Similar findings were recorded by Valilou and Lofti (2012) and Senthilkumar and Subramanian (2007) where activities of serum ALT, AST and ALP were significantly increased in diabetic animals. In diabetes mellitus there is alteration incarbohydrate, protein and fat metabolismresulting in hepatic lipidosis (Kumar *et al.*, 2014; Qadri *et al.*, 2015).

In group-I, there was a significant decrease in the values of triglyceride after twenty-eight days of treatment but they were still significantly higher than values of healthy dogs. A similar trend was observed in group-II animals but after twenty-eight days of treatment values were comparable to the healthy dogs. On day 0, the mean value of cholesterol in both groups was significantly higher than the healthy group andthe values decreased significantly after twenty-eight days of treatment and were comparable to the healthy group. In group-I, HDL-cholesterol value decreased non-significantly after seven

Table 3. Pre and post treatment biochemical profile of diabetic dogs

S. No.	Parameters	Healthy group (N=10)	Group I (N=12) II (N=6)	Pre-treatment values (Day 0) (Mean±S.E.)	Post treatment values (Day 7) (Mean±S.E.)	Post treatment values (Day 28) (Mean±S.E.)
1	Glucose (mmol/L)	4.81 ± 0.22^{a}	Group I	26.16 ± 0.67^{b}	18.61 ± 1.03^{c}	9.59 ± 0.49^{d}
			Group II	15.62 ± 1.51^{b}	12.28 ± 1.06^{c}	8.66 ± 0.31^{d}
2	ALT (IU/L)	41.1 ± 5.11^{a}	Group I	140.50 ± 21.66^{b}	110.00 ± 15.86^{bc}	63.75 ± 13.30^{acd}
			Group II	46.00 ± 9.91^{a}	47.50 ± 8.10^{a}	40.00 ± 7.90^{a}
3	AST (IU/L)	48.8 ± 4.19^{a}	Group I	85.50 ± 14.67^{ab}	70.10 ± 15.68^{ab}	55.00 ± 15.15^{ab}
			Group II	38.75 ± 2.75^{ab}	37.50 ± 6.74^{ab}	28.00 ± 1.73^{b}
4	ALP (IU/L)	86.7 ± 4.5^{a}	Group I	220.00 ± 53.14^{b}	172.00 ± 40.89^{ab}	103.50 ± 15.43^{ab}
			Group II	347.0 ± 157.07^{a}	282.7 ± 125.03^{a}	105.75 ± 32.89^{a}
5	Total Bilirubin (µmol/L)	4.96 ± 0.51^{a}	Group I	10.60 ± 5.30^{a}	5.82 ± 1.20^{a}	5.30 ± 1.20^{a}
			Group II	4.96 ± 1.37^{a}	3.76 ± 0.68^{a}	3.25 ± 0.68^{a}
6	Direct Bilirubin (µmol/L)	1.03 ± 0.24^{a}	Group I	2.91 ± 2.05^{a}	1.88 ± 0.51^{a}	1.88 ± 0.51^{a}
			Group II	1.37 ± 0.68^{a}	1.03 ± 0.17^{a}	1.37 ± 0.34^{a}
7	Indirect Bilirubin (µmol/L)	3.59 ± 0.68^{a}	Group I	6.50 ± 3.42^{a}	3.93 ± 0.68^{a}	3.93 ± 0.68^{a}
			Group II	3.08 ± 0.68^{a}	2.74 ± 0.51^{a}	3.08 ± 0.34^{a}
8	Total Protein (g/L)	63.00 ± 1.70^{a}	Group I	62.30 ± 3.60^{a}	63.10 ± 2.40^{a}	65.00 ± 2.30^{a}
			Group II	66.00 ± 2.30^{a}	64.00 ± 2.20^{a}	62.50 ± 3.80^{a}
9	Triglycerides (µmol/L)	0.35 ± 0.02^{a}	Group I	2.18 ± 0.29^{b}	1.93 ± 0.27^{b}	1.13 ± 0.16^{c}
			Group II	1.94 ± 0.60^{b}	1.75 ± 0.54^{b}	1.20 ± 0.19^{ab}
10	Cholesterol (µmol/L)	3.65 ± 0.27^{a}	Group I	6.39 ± 0.51^{b}	5.81 ± 0.47^{b}	4.09 ± 0.46^{a}
			Group II	6.75 ± 1.74^{b}	5.49 ± 1.04^{ab}	4.04 ± 0.22^{ab}
11	HDL-Cholesterol (µmol/L)	1.83 ± 0.10^{a}	Group I	3.53 ± 0.30^{b}	3.20 ± 0.28^{b}	3.20 ± 0.28^{b}
			Group II	3.18 ± 0.69^{a}	3.18 ± 0.51^{a}	2.66 ± 0.58^{a}
12	BUN (µmol/L)	9.03 ± 0.95^{a}	Group I	11.01 ± 1.51^{a}	8.46 ± 0.67^{a}	7.74 ± 0.40^{a}
			Group II	9.85 ± 1.16^{a}	8.56 ± 0.60^{a}	7.06 ± 0.30^{a}
13	Creatinine (µmol/L)	81.33 ± 9.72^{a}	Group I	109.62 ± 17.68^{a}	92.82 ± 15.03^{a}	75.14 ± 7.96^{a}
			Group II	108.73 ± 21.22^{a}	70.72 ± 13.26^{a}	60.11 ± 6.19^{a}
14	Amylase (U/L)	654.04 ± 21.71^{a}	Group I	1019.45 ± 55.17^{b}	979.65 ± 48.91^{bc}	833.9 ± 44.08^{cd}
			Group II	828.05 ± 89.03^{a}	792.95 ± 90.78^{a}	733.13 ± 93.54^{a}
15.	Lipase (U/L)	46.806 ± 5.3^{a}	Group I	141.49 ± 31.44^{b}	122.21 ± 23.22^{b}	99.89 ± 12.36^{ab}
			Group II	107.72 ± 27.76^{ab}	109.28 ± 30.41^{b}	89.45 ± 11.09^{ab}

Values with at least one different superscript in a row differs significantly ($p<0.05$)

days of treatment but was still higher than the healthy group. A similar trend was observed after twenty-eight days of treatment. In group-II the pre-treatment and post-treatment values varied non-significantly. The values of BUN and creatinine decreased non-significantly after twenty-eight daysof treatment in both groups. These results were in agreement with the previous studies (Ismail *et al.*, 2015) where minor alterations in the biochemical parameter like total protein, BUN, and creatinine were found whereas, a significant increase was seen only in cholesterol and triglycerides. Increase in blood cholesterol and triglyceride level was also recorded earlier by Hess *et al.* (2000) in 33% diabetic dogs. The reason for increase in the values of lipid profile in diabetic dogs is related to a decrease in lipoprotein lipase activation which occurs secondary to a decrease in insulinsecretion (Durocher *et al.*, 2008).

On day 0, the mean value of amylase and lipase in group-I was significantly higher than healthy group. The values of amylase after twenty-eight days of treatment decreased significantly but were still significantly higher than the healthy group. The values of lipase decreased non-significantly but were comparable to the healthy group after twenty-eight days of treatment. In group-II the pre- and post-treatment values of amylase and lipase varied non significantly than that ofthe healthy group. Similar finding was recorded by Steiner (2003) in pancreatic inflammation and by Catchpole *et al.* (2005) in diabetic dogs. Amylase

Table 4. Pre and post treatment urine analysis of diabetic dogs

S. No.	Parameter	Healthy group (N=10)	Group I (N=12) II (N=6)	Pre-treatment values (Day 0) (Mean±S.E.)	Post treatment values (Day 7) (Mean±S.E.)	Post treatment values (Day 28) (Mean±S.E.)
1.	Blood (RBC/µl)	absent	Group I	0	0	0
			Group II	0	0	0
2.	Bilirubin (µmol/L)	absent	Group I	7.35±6.33	3.08±2.22	0
			Group II	0	0	0
3.	Urobilinogen (µmol/d)	absent	Group I	0.64±0.31	0.64±0.31	0
			Group II	0.42±0.42	0.42±0.42	0
4.	Ketones (µmol/L)	absent	Group I	3.12±1.22	0.86±0.23	0
			Group II	0.65±0.41	0.22±0.22	0
5.	Proteins (mg/dl)	Nil	Group I	27.5±15.89	2.5±1.63	0
			Group II	27.5±24.28	0	0
6.	Nitrite	absent	Group I	0	0	0
			Group II	0	0	0
7.	Glucose (µmol/L)	absent	Group I	90.19±10.16	36.77±9.14	3.47±1.02
			Group II	69.38±13.88	18.04±12.49	0.14±0.14
8.	pH	6.2±0.2	Group I	5.88±0.18	5.63±0.13	5.44±0.20
			Group II	5.50±0.35	5.50±0.35	5.38±0.38
9.	Specific gravity	1.02±0.001	Group I	1.03±0.001	1.03±0.001	1.02±0.01
			Group II	1.03±0.001	1.03±0.001	1.02±0.01
10.	Leucocytes (WBC/µl)	absent	Group I	10±3.65	8.12±2.97	0
			Group II	11.25±5.15	7.5±2.5	0
11.	Clarity	Clear	Group I	Clear	Clear	Clear
			Group II	Clear	Clear	Clear

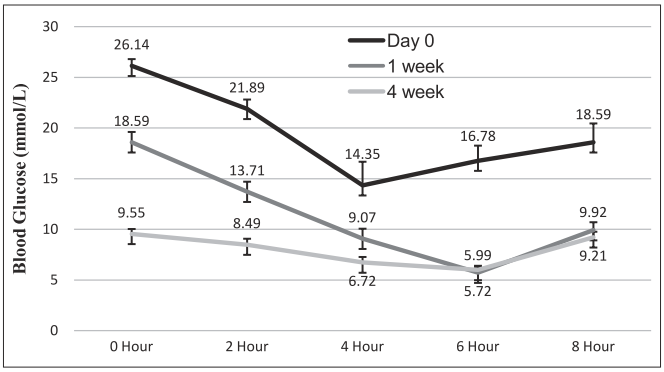

Fig. 1. Mean Serial blood glucose curve for group I

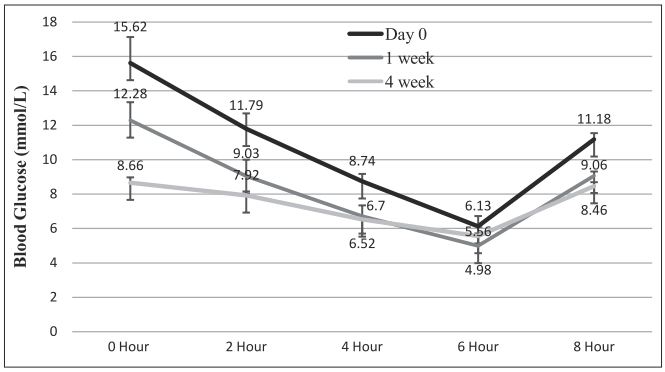

Fig. 2. Mean Serial blood glucose curve for group II

and lipase are commonly, but not invariably, found raised in the presence of pancreatitis. Chronic pancreatitis is a common histological finding in diabetes cases, although its role as a cause or effect of diabetes mellitus is yet not clear (Davison, 2015).

The mean values of urine analysis parameters are given in Table 4. The level of ketonuria and proteinuria which was variably present in most of the dogs, reduced to nil in all the dogs. The level of glycosuria reduced to either being absent or upto 5.55 µmol/L (100 mg/dL) in some dogs after twenty-eight days of treatment. Most diabetic dogs have glycosuria when blood sugar level exceeds the renal threshold (9.99 µmol/L; 180 mg/dL) (Bruyette, 2013; Kumar *et al.*, 2014). The value of urine pH non-significantly reduced in both groups and these values were comparable to the healthy group. Similarly, non-significant reduction in urine specific gravity values was observed in both the groups after twenty-eight days of treatment. As stated by many authors a high level of glucose in urine increases the specific gravity of urine and excessive solute load leads to polyuria which causes compensatory polydipsia. Due to nephrotic syndrome and shift in energy metabolism, diabetic dogs are often presented with proteinuria, ketonuria, and bilirubinuria

(Hess *et al.*, 2000; Hume *et al.*, 2006). The number of leukocytes also decreased from being variably present (up to 25 WBC/µl) to absent in all of the dogs after treatment. Many studies (Cook and Dip, 2012; Choudhary *et al.*, 2021) suggest that regular monitoring of glucose level in urine can be used for early detection of canine DM.

In this study the level of hyperglycemia was directly proportional to the degree of biochemical alterations, and after the initiation of insulin therapy, there was asignificant improvement in parameters like random blood glucose, alanine aminotransferase, aspartate aminotransferase, serum triglyceride, and cholesterol. These findings are similar to other studies (Monroe *et al.*, 2005; Fleeman *et al.*, 2009) suggesting that these parameters can aid in clinical monitoring of diabetic dogs.

Monitoring blood glucose through serial blood glucose curve

Group-I: Animals with fasting blood glucose value of more than 19.43 µmol/L (350 mg/dL) were included in this group. Insulin therapy was started with an initial dosage of 0.5 IU/kg body weight SC BID. The duration of action of insulin is close to 12 hours in most dogs and peak insulin activity is expected after four to six hours after administration (Rucinsky *et al.*, 2010). The blood glucose reading was taken every 2 hours for a period of 8 hours. The nadir (lowest glucose level) was achieved at the 4th hour on the first day and at the 6th hour onthe seventh day and twenty-eighthday. The comparative mean serial blood glucose readings were taken and curve was generated (day 0, day 7 and day 28) after initiation of insulin therapy (Fig. 1). Insulin dose was adjusted individually after generating glucose curve as blood glucose level at 6th hour had fallen below 5.0 µmol/L (90 mg/dL) in 3 dogs and up to 3.33 mmol/L (60 mg/dL) in 2 dogs suggesting hypoglycemia. If the nadir was within the range of 3.05 (55 mg/dL) to 5.0 mmol/L (90 mg/dL) and the pre-insulin values were less than 9.99 µmol/L (180 mg/dL), the insulin dose was decreased by 20% (Rucinsky *et al.*, 2010).

Group-II: For generating glucose curve for group-II, only those animals were taken which had fasting glucose value less than 19.43 µmol/L (350 mg/dL) and were kept on insulin at dose rate of 0.25 IU/kg body weight BID. The nadir was achieved at the 6th hour after insulin administration at all three instances. The comparative serial blood glucose readings were taken and curve was generated (day 0, day 7, day 28) after initiation of insulin therapy (Fig. 2). After twenty-eight days the pre-insulin fasting blood glucose value was 8.66±0.31 µmol/L (156±5.6 mg/dL) which is well below the highest safe pre-insulin value (11.10 to 13.88 µmol/L; 200 to 250 mg/dL) (Fleeman and Rand, 2001).

The initial goal of treatment is to maintain glucose levels below the renal threshold value and avoid symptomatic hypoglycemia. In our study, we have found that the insulin dose adjustment should not be done prior to 1-2 weeks after beginning of initial dose. Blood glucose curves are very useful while monitoring insulin therapy in diabetic patients as they can be used to make appropriate adjustments in insulin dose and identify hypoglycemia before clinical signs of hypoglycemia are noticed. It helps in determining lowest blood glucose levels (i.e. nadir) achieved after insulin therapy (Behrend *et al.*, 2018). If an acceptable nadir value is not achieved, the insulin dose should be adjusted. Once an acceptable nadir is achieved, the duration of action, roughly defined as the amount of time during which blood glucose is controlled, can be determined.

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