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Treatment of Diabetes Mellitus in Dogs Using Isophane Insulin Penfills and the Use of Serum Fructosamine Assays to Diagnose and Monitor the Disease

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Thoresen, S. I. and F. H. Lorenzen: Treatment of diabetes mellitus in dogs using isophane insulin penfills and the use of serum fructosamine assays to diagnose and monitor the disease. Acta vet. scand. 1997, 38, 137-146. – The objectives of the study were to test the use of a prefilled insulin syringe (*Insulatard® Novolet®*, isophane insulin, 100 IU/mL) in treating diabetic dogs and to test the clinical usefulness of serum fructosamine measurements in diagnosing and monitoring diabetes mellitus in dogs. For this study 15 dogs from throughout Norway with newly diagnosed diabetes mellitus were included and treated over a period of 180 days. All 15 dogs showed pretreatment hyperglycaemia. Of the 13 dogs tested, all showed elevated pretreatment serum fructosamine values. Within 2 weeks, 3 of the 15 included dogs had dropped out of the study. In 8 of the 12 remaining dogs, the clinical signs ceased within this period. Within a month, another dog was euthanised and one had died. Seven of the 10 remaining dogs were clinically normal. Three dogs had normal serum fructosamine concentrations, while in 6 dogs moderately or highly elevated serum fructosamine concentrations persisted. In one case serum fructosamine was not measured at this time. Increase in serum fructosamine concentration seemed to reflect hyperglycaemia and deteriorated clinical condition. Decrease in serum fructosamine concentration seemed to reflect improved glycaemic status and clinical condition. During the study period the owners did a total of approximately 3500 injections on their dogs. No reports of injection difficulties were received. This study documents that *Insulatard® Novolet®* is easy and safe to use in treating diabetic dogs and that serum fructosamine reflects long-term glucose concentrations in dogs. Serum fructosamine measurements provided a simple and easy way to diagnose persistent hyperglycaemia and monitor the treatment in diabetic patients.

persistent; hyperglycaemia.

Introduction

Traditionally, the diagnosis of diabetes mellitus is based on a case history of polyuria and polydipsia followed by ascertainment of persistent hyperglycaemia and glucosuria (*Nelson* 1995). Several other causes may produce similar findings, such as severe stress, renal failure or primary renal glucosuria (*Bush* 1993). Particularly if only a single determination of blood glucose is performed, persistent hyperglycaemia cannot be ruled out. Therefore, alternative clinical chemical parameters have been investigated. It has been known for many years that several proteins, including haemoglobin and serum proteins, are glycated by an irreversible non-enzymatic reaction that mainly depends on the glucose concentration (*Maillard* 1912, *Arm-*

bruster 1987). Determination of glycated haemoglobin has frequently been used to evaluate blood glucose control in humans (*Jovanovic & Peterson* 1981). In dogs, determination of glycated haemoglobin has also been used for monitoring glucose status and the effectiveness of insulin therapy (*Wood & Smith* 1980). Recently, simple spectrophotometric assays for determining glycated serum proteins ("fructosamine") have become available (*Staudacher* 1990). The main difference between glycated haemoglobin and serum fructosamine as analytes is the length of their respective presence in blood, which is about 120 days for glycated haemoglobin compared with 8-10 days for glycated serum proteins (fructosamine). Because of the shorter half-life, fructosamine can be used to evaluate the mean blood glucose concentration over a period of 1-2 weeks compared with 6-8 weeks using glycated haemoglobin (*Mahaffey et al.* 1984).

The need to improve the diagnostic and follow-up procedures for canine diabetic patients is apparent. *Doxey et al.* (1985) report that the major reasons for euthanasia after stabilisation were unwillingness of the owner to continue treatment or "old age". Other reasons for euthanasia associated with the diabetic state were blindness, vomiting and severe polydipsia. Simplified follow-up procedures and introducing improved diagnostic and monitoring tools might therefore increase the chance of survival for the canine diabetic patient.

The objectives of the study were to test the use of a prefilled insulin syringe (*Insulatard® Novolet®*, isophane insulin, 100 IU/mL) in treating diabetic dogs and to test the clinical usefulness of serum fructosamine measurements in diagnosing and monitoring diabetes mellitus in dogs.

Materials and methods

Patients

Through an announcement in the Norwegian Journal of Veterinary Medicine small animal practitioners were invited to participate in this study if they had patients and owners fulfilling the following specified criteria:

a) Diagnosis of canine diabetes mellitus confirmed by case history, clinical examination and laboratory analyses; b) weight >6 kg; c) the owner was motivated to perform the injections, feed the dog according to the instructions, exercise it regularly and record the dogs' general behaviour, injection times and any difficulties related to daily treatment throughout the study period.

Dogs showing signs of acute or chronic kidney disease, pyometra or hyperadrenocorticism, in ketoacidotic coma, in oestrous or under cortisone or depot-progesterone treatment were excluded from the study.

Veterinarians from 14 clinics participated in the investigation. They reported on the physical examination, treatment, control and follow-up on 15 diabetic dogs (Table 1). The dogs came from throughout Norway. All included dogs had a history of polydipsia, polyuria, polyphagia and weight loss, and a thorough clinical examination supported the diagnosis diabetes mellitus. The average age at the time diabetes mellitus was diagnosed was 9.1 years. The age, sex, weight and breed distribution are given in Table 1.

Laboratory analyses

At each follow-up visit to the veterinarian, either scheduled or unscheduled, blood samples were drawn, centrifuged, and analysed within 3 days at the Central Laboratory, Norwegian College of Veterinary Medicine (NCVM). Besides serum fructosamine measurements and a complete blood count, a standard biochemistry profile (AST, ALT, ALP, CK, amylase, lipase, pro-

Table 1. Data for diabetes mellitus dogs participating in the study. Four of the 8 female dogs were castrated after diagnosis.

Dog no.	Breed	Age when diagnosed	Weight (Kg)	Sex	Castrated
1	Toy Poodle	11y[1] 3m[2]	8.7	Male	No
2	Hamilton Stövare	8y 2m	23.0	Female	No
3	Miniature Poodle	6y 8m	6.2	Male	No
4	Miniature Poodle	11y 5m	11.0	Male	No
5	Toy Poodle	10y 10m	15.5	Female	No
6	English Setter	10y 1m	29.0	Male	No
7	Drever	9y 7m	12.0	Female	Yes
8	Miniature Poodle	7y 2m	9.0	Female	Yes
9	Labrador Retriever	6y 5m	60.0	Female	No
10	Samoyed	11y 11m	26.0	Female	Yes
11	Welsh Corgi	6y 9m	13.0	Female	Yes
12	Labrador Retriever	10y 9m	49.0	Male	No
13	English Setter	10y 8m	19.0	Female	No
14	Fox Terrier (Wire)	7y 7m	14.0	Male	No
15	Rottweiler	7y	35.0	Male	No

[1]: y = years [2]: m = month(s).

tein, albumin, urea, creatinine, bile acids, bilirubin, cholesterol, glucose, phosphate, calcium, sodium, potassium) was performed. The analytical methods are specified in *Thoresen et al.* (1992).

Serum fructosamine assay and reference range

Fructosamine in serum was assayed with a Technicon RA-1000™ system[1] using an automated method evaluated for use in canine serum samples (*Jensen* 1992). This assay is based upon the reducing ability of glycated serum proteins in alkaline solution[2] and the reference range for non diabetic dogs is 250-320 μmol/l (Central Laboratory, NCVM).

Treatment and follow-up

The owners received detailed oral and written instructions from their veterinarian concerning the disease, injection procedures, dosages, diet, exercise demands, and signs of hypoglycaemia and necessary treatment. To monitor the treatment and dosage adjustments, the owners agreed to bring the dog to the clinic at least 6 times within the next 6 months after the first insulin injection had been given.

The dogs were then followed during a six-month treatment period based on the information from the individual patient recordings, the type of dog joining the study, signs of the disease and the laboratory results obtained. Castration of intact bitches was strongly recommended.

Isophane insulin is recommended for the treatment of diabetes mellitus in dogs (*Gordon* 1967, *Lorenzen* 1992), and included patients were treated with *Insulatard® Novolet®*. *Insulatard® Novolet®* is a prefilled dial-a-dose insulin syringe containing 100 IU human isophane insulin per ml in prefilled syringes of 1.5 ml. The syringe is intended for human use and able to deliver 2-58 IU of isophane insulin in increments of 2 units. The veterinarians instructed

[1] Technicon Instruments Corporation, Tarrytown, New York, USA.

[2] Fructosamine Test Plus, F. Hoffmann-La Roche & Co., Switzerland.

the owners to store the syringes in the refrigerator before use, and at room temperature when in use.

The dosage of insulin

The veterinarians were free to fix the insulin dose in each individual case. It was proposed that a large diabetic dog should initially be injected with 0.3-0.4 IU/kg twice daily with a 12-h interval and with feeding (Fig 1). For smaller dogs a dose of 0.5-0.7 IU/kg twice a day was proposed (Fig 1). The dose had to be injected subcutaneously *in regio colli dorsalis* just cranial to the scapular region. If the dog became acutely febrile or should undergo major surgery, the owners were instructed temporarily to halve the dose.

Diet and exercise

The owners agreed to feed their dogs with a constant daily amount of food that was rich in fibre and had a low content of easily digestible carbohydrates. Sweets, chocolate, sweet fruits etc. were to be avoided.

The dogs received a fairly constant amount of physical exercise every day.

Hypoglycaemia signs

The owners were informed by their veterinarians about signs of hypoglycaemia (stupor, incoordinated gait, salivation, convulsions and unconsciousness). If signs of hypoglycaemia occurred, the owners were instructed to give the dog 1-2 tablespoons of glucose dissolved in temperate water, and to contact their veterinarian if the signs had not disappeared within 10-15 min. Such episodes and other observed side effects of the treatment were to be recorded and presented to their veterinarian.

Follow-up procedures

The owners were asked to make daily recordings in predesigned forms of the dogs' general behaviour, injection times and any difficulties related to treatment. These data were collected and reviewed by the veterinarian at each follow-up. The participating veterinarians were asked to examine the diabetic dogs on a regular basis scheduled as days 8, 15, 30, 60, 90, and 180 following diagnosis. On these occasions the participating veterinarians performed a clinical examination of the dog and took blood samples.

Based on the information obtained by the clinical examinations and laboratory results, the veterinarians made appropriate adjustments in the treatment. Results from the clinical and laboratory examinations were recorded in predesigned forms. These data and the data recorded by the owners were sent to the principal investigator for evaluation.

Results

Dropouts

According to the research protocol an extensive physical examination was performed on each dog prior to inclusion to secure correct diagnosis of diabetes mellitus and to exclude other disorders. Despite this, 4 of the included dogs died during the observation period for reasons presumably not related to diabetes mellitus. Dog no. 2 was euthanised on the owners request a few days after inclusion in the study. Dog no. 4 was euthanised 3 weeks after inclusion due to a severely deteriorated clinical condition. Necropsy revealed adrenal hyperplasia and endocardiosis. Dog no. 7 underwent removal of the anal glands on day 63. Recovery was uneventful and insulin treatment continued until the dog died 7 weeks later (day 114) of unexpected heart failure. Necropsy was not performed. Dog no. 13 died suddenly 2 weeks after inclusion for unknown reasons. Necropsy was not performed.

Two dogs (nos. 6 and 12) were euthanised due to treatment failure or complications related to

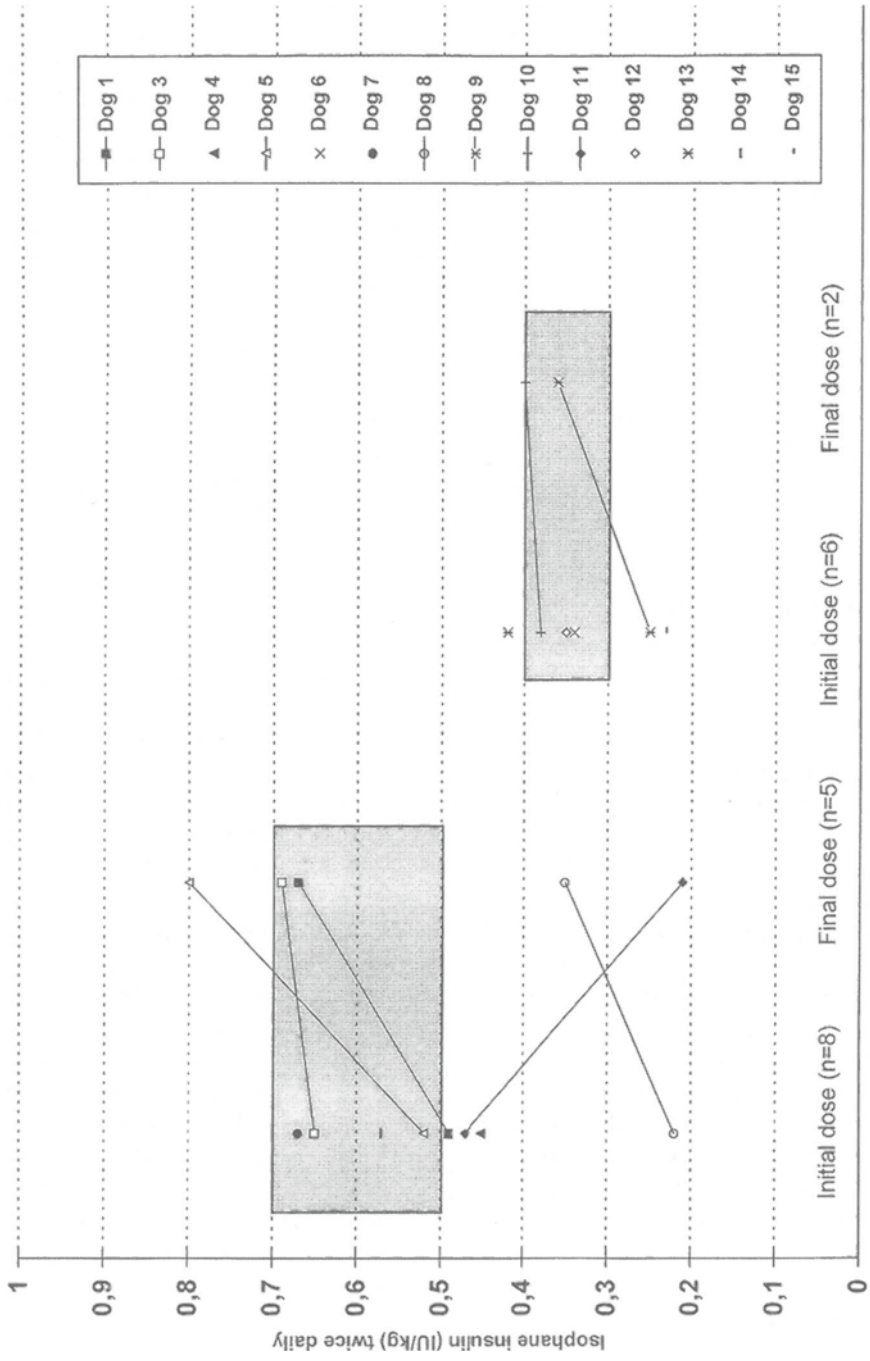

Figure 1. Insulin dose at the beginning and at the end of the study. Proposed insulin doses for small and large dogs are indicated by shaded rectangles.

diabetes mellitus. Dog no. 6 was euthanised 4 weeks after inclusion due to a severely deteriorated clinical condition after receiving *Test Medium Novolet®* (penfill for demonstration purposes only, does not contain insulin) for 2 weeks instead of isophane insulin. Dog no. 12 was euthanised 7 weeks after inclusion due to blindness.

One dog (no. 15) was excluded from the study due to lack of owner compliance after the second scheduled visit at day 8.

Clinical signs

All owners had noted signs of polyuria and polydipsia. In 9 cases the owners reported that the dogs had polydipsia and polyuria for 1-4 weeks, in 3 cases for 5-12 weeks, and in one case for almost 6 months before diagnosis. In 2 cases the duration of signs was not reported. Nine owners had noted general fatigue. As reported above, the veterinarians were asked to examine the diabetic dog at days 8, 15, 30, 60, 90 and 180 to control the response to *Insulatard® Novolet®* treatment. The veterinarians followed this schedule quite well. Some added more control visits to the programme (recorded as non routine follow-ups).

Within 2 weeks, 3 of the 15 dogs had dropped out of the study. In 8 of the 12 remaining dogs the clinical signs ceased within this period. Within a month, another dog was euthanised and one had died. Seven of the 10 remaining dogs were clinically normal (Table 2).

At each follow-up an index of general behaviour (GB) from 1 (bad or worsened) to 4 (normal) was assigned by the veterinarian. This was based on daily recordings taken by the owner and on the dogs' presentation at consultation.

Eight dogs (nos. 1, 3, 5, 8 -11 and 14) were alive 6 months after inclusion. Three dogs (nos. 1, 8 and 10) were clinically normal with normal or close to normal glucose concentrations. Four dogs (nos. 3, 9, 11 and 14) were clinical normal but retained elevated glucose concentrations. One dog (no. 5) showed intermittent clinical signs related to elevated glucose concentrations. Three of these 8 dogs (nos. 1, 5 and 9) showed various degrees of cataract formation by the end of the observation period.

Four of the 8 intact bitches included in the study were not castrated as recommended. Two of the 4 intact bitches (nos. 2 and 13) died or were euthanised within a week after inclusion. The 2 other intact bitches (nos. 5 and 9) were still alive at the end of the study period, but both showed poor response to treatment, whereas the 4 castrated bitches (nos. 7, 8, 10 and 11) responded well.

Laboratory results

All the dogs had highly elevated pretreatment serum glucose levels ranging from 16.0 to 47.6 mmol/L with a mean of 23.6 mmol/L. Serum glucose levels were substantially lowered within 2 weeks in 3 of the remaining 12 dogs (nos. 7, 10 and 14) and in 4 of the remaining 10 dogs (nos. 7, 8, 10 and 11) 4 weeks after inclusion. Serum fructosamine measurements were performed on 13 dogs (nos. 1, 2, 4-14) before treatment was initiated. All 13 dogs showed elevated pretreatment serum fructosamine concentrations, $\bar{x}_{(13)} = 520\ \mu$mol/L, range 451-803 μmol/L (reference range 250-320 μmol/L). After 30 days, serum fructosamine concentrations returned to normal (<320 μmol/L) in 3 of the 10 remaining dogs (nos. 7, 8 and 11). These 3 dogs had also shown substantially reduced serum glucose within 2 weeks. In one dog (no. 1) moderately elevated serum fructosamine (320-500 μmol/L) persisted and in 5 dogs (nos. 3, 5, 9, 10 and 14) highly elevated concentrations (>500 μmol/L) persisted. For the remaining dog (no. 12) serum fructosamine was not measured at this time.

Comparison of serum glucose and serum fructosamine levels (Table 2) showed that a decline

Table 2. Relations of clinical condition, serum glucose, fructosamine and alkaline phosphatase levels.

Dog No.		Follow-up visit no [1]							Comments:
		0	1	2	3	4	5	6	
1	GB:	1	3	–	3	4	4	4	Bilateral cataract at inclusion. Progressed to partial blindness during the trial. Insulin dose probably too low.
	SG:	20,0	23,3	–	20,3	21,7	14,4	14,6	
	SF:	466	472	–	474	511	406	436	
	ALP:	7224	6996	–	3876	2556	742	1178	
2	GB:	1	–	–	–	–	–	–	Euthanised for unknown reasons.
	SG:	22,1	–	–	–	–	–	–	
	SF:	480	–	–	–	–	–	–	
	ALP:	334	–	–	–	–	–	–	
3	GB:	1	4	4	4	4	4	4	Quick clinical normalisation. Moderately elevated SF reflects moderately elevated SG.
	SG:	28,8	24,2	21,1	21,3	6,8	18,8	20,7	
	SF:	–	546	620	531	450	406	521	
	ALP:	349	256	282	317	254	229	189	
4	GB:	4	4	4	1	–	–	–	Symptoms of incontinence. Euthanised. Necropsy: Endocardiosis and adrenal hyperplasia.
	SG:	23,8	23,4	23,3	–	–	–	–	
	SF:	467	521	628	–	–	–	–	
	ALP:	2436	2494	–	–	–	–	–	
5	GB:	1	3	3	4	4	4	2	Ovariohysterectomia was not performed and might have contributed to unstable periods reported during the trial.
	SG:	16,0	27,0	25,2	23,7	21,2	20,6	28,3	
	SF:	464	556	617	560	558	595	550	
	ALP:	440	697	609	764	735	896	727	
6	GB:	4	4	4	1	–	–	–	Initially good response. Euthanised due to severelly depressed clinical condition after being mistakenly treated with *Test Medium*® *Novolet*®[2]
	SG:	19,2	16,4	21,6	24,2	–	–	–	
	SF:	536	466	628	480	–	–	–	
	ALP:	150	174	76	956	–	–	–	
7	GB:	1	4	4	4	4	4	–	The decline in SG was followed by a decline in SF. The dog died of unexpected heart failure. Necropsy was not performed.
	SG:	20,2	5,7	5,5	–	2,0	5,1	–	
	SF:	451	463	343	251	186	225	–	
	ALP:	75	72	59	54	56	34	–	
8	GB:	1	4	–	4	4	4	4	The decline in SG was followed by a decline in SF. Minor incident of Hypoglycaemia.
	SG:	25,7	3,8	–	3,6	2,8	4,4	1,9	
	SF:	803	521	–	298	313	327	211	
	ALP:	227	217	76	147	58	82	47	
9	GB:	1	3	–	–	4	4	4	Intact bitch combined with extreme overweight might explain poor response to treatment.
	SG:	19,3	20,7	21,2	19,1	–	28,0	22,6	
	SF:	530	529	531	558	–	–	521	
	ALP:	153	195	236	277	–	318	308	
10	GB:	4	4	4	4	4	4	4	SF reflects a normalisation of the glycaemic condition.
	SG:	28,0	22,1	16,9	11,4	3,1	3,2	10,2	
	SF:	452	538	505	518	428	344	466	
	ALP:	503	492	416	238	162	182	193	
11	GB:	1	4	4	4	4	4	4	Almost immediate response. Treatment was interrupted after hypoglycaemic episodes, but reinstated after severe hyperglycaemia.
	SG:	24,1	6,1	–	1,8	40,8	25,8	19,3	
	SF:	619	405	–	254	517	280	318	
	ALP:	170	162	–	132	200	692	423	
12	GB:	4	4	4	4	1	–	–	Mild bilateral cataract at inclusion. Euthanised due to blindness. Insulin dose seemed inappropriate.
	SG:	47,6	30,9	23,8	29,2	21,3	–	–	
	SF:	552	560	488	–	624	–	–	
	ALP:	1616	560	387	611	555	–	–	
13	GB:	4	1	–	–	–	–	–	Although the glycaemic situation seemed to be under control, the dog died. Necropsy was not performed.
	SG:	18,7	8,8	–	–	–	–	–	
	SF:	433	460	–	–	–	–	–	
	ALP:	680	1115	–	–	–	–	–	
14	GB:	4	4	4	1	2	3	4	The reason for the appearent insulin resistence was not discovered.
	SG:	21,3	25,1	14,2	19,4	15,7	14,7	17,6	
	SF:	478	559	498	648	505	523	596	
	ALP:	690	611	605	666	706	592	466	
15	GB:	4	4	–	–	–	–	–	Drop-out due to lack of owner compliance.
	SG:	19,2	19,7	–	–	–	–	–	
	SF:	–	605	–	–	–	–	–	
	ALP:	114	95	–	–	–	–	–	

[1] 0: Day =; 1: Day 7 ± 1; 2: Day 15 ± 2; 3: Day 30 ± 3; 4: Day 60 ± 4; 5: Day 90 ± 5; 6: Day 180 ± 6.

[2] *Test Medium*® *NovoLet*®, Novo Nordisk A/S. For demonstration purposes only, does not contain insulin.

GB (Index of general behaviour): 1 = bad or worsened, 2 = no change, 3 = improved, 4 = normal.

SG = serum glucose (mmol/L), SF = serum fructosamine (μmol/L), ALP = alkaline phosphatase (U/L).

from the hyperglycaemic state was followed by a decline in serum fructosamine 1-2 weeks later. Dramatic rises in fructosamine seemed indicative of present or incipient deterioration in clinical condition (nos. 4, 6 and 14).

Before treatment was initiated, 5 of the included 15 dogs showed normal ALP activity in serum (<200 U/L), 4 dogs showed slightly increased activity (200-500 U/L), 3 dogs showed moderately increased activity (500-1000 U/L) and 3 dogs showed highly increased activity (>1000 U/L). The highest activity was measured in dog no. 1 (7224 U/L) (Table 2).

At the end of the study period 3 of 8 dogs showed normal ALP activity in serum (<200 U/L), 3 showed slightly increased activity (200-500 U/L), one showed moderately increased activity (500-1000 U/L) and one dog showed highly increased activity (>1000 U/L). The highest activity was measured in dog no. 1 (1178 U/L) (Table 2).

Initial dosages

Initially, the veterinarians ordered 2 daily doses of isophane insulin, the average dose was 0.33 IU/kg for large dogs (>15 kg b.w., n = 6), 0.23 IU/kg being the lowest and 0.42 IU/kg the largest starting dose used (Fig 1). For small dogs (<15 kg b.w., n = 8) the veterinarians ordered an average dose of 0.50 IU/kg, with a range of 0.22–0.67 IU/kg (Fig 1).

Final dosages

At the end of the study the average dose was 0.37 IU/kg for large dogs (>15 kg b.w., n = 2) with upper and lower values of 0.40 and 0.36 IU/kg respectively (Fig 1). For small dogs (<15 kg b.w., n = 5) the average dose was 0.49 IU/kg ranging between 0.21 and 0.80 IU/kg (Fig 1). For one dog (no. 14), information concerning insulin dose at the end of the study was not reported.

Injection technique

Correct use of the *Insulatard® Novolet®* prefilled syringes was easily learned by all owners, who were taught subcutaneous injection technique with *Test Medium Novolet®*. Most owners found the injection techniques quite easy and were very satisfied with the pen system.

A total of more than 3 500 injections were performed and recorded using *Insulatard® Novolet®* in this study. No injection troubles or mechanical problems were reported.

Diet and exercise

Thirteen owners chose to use a commercial diet as the main feed for their diabetic dog. One dog (no. 4) received mixed commercial and home made meals. For one dog (no. 2) the diet was not reported.

All owners carried out regular exercise of the diabetic dog.

Hypoglycaemia

Three episodes of hypoglycaemia were reported in 2 different dogs (no. 8 and no. 11). In one dog (no. 8) the episode was so slight that veterinary intervention was not required. In the other dog (no. 11) which showed transient hypoglycaemic signs for several days, insulin treatment was interrupted, but reinstated when after a month the dog gradually developed hyperglycaemia. The dog was well regulated at the end of the study.

Discussion

Based on the clinical findings and laboratory data all the 15 dogs included had diabetes mellitus. However, some dogs undoubtedly suffered from other serious unrecognised diseases at the time of inclusion, a fact that emphasises the importance of a thorough clinical examination before insulin treatment is initiated. The implemented procedures for diagnosis of the disease follow the recommendations in scien-

tific handbooks and publications on the subject (*Nelson* 1995). Blood samples were drawn at each follow-up and mailed to the Central Laboratory, NCVM. According to *Thoresen et al.* (1992) the analytes under test show satisfactory stability in serum or heparinized plasma for at least 3 days, and most of the samples arrived at the laboratory within one or 2 days.

Although ovariohysterectomy of bitches participating in the study was recommended, only 4 out of 8 bitches actually underwent surgery. The 4 bitches that remain intact were not satisfactory regulated. When in oestrus or dioestrus the female dog is very difficult to regulate. Castrating bitches seems advisable if satisfactory glycaemic regulation is wanted.

The participating veterinarians were free to adjust the insulin dose based on general recommendations given for small (<15 kg b.w.: 0.5-0.7 IU/kg) and large (>15 kg b.w.: 0.3-0.4 IU/kg) dogs (*Lorenzen* 1988, *Goeders et al.* 1987). Compared with the study conducted by *Lorenzen* (1990) the Norwegian dogs received initially on average less insulin per kg b.w., both for small (0.50 IU/kg compared to 0.61 IU/kg) and large (0.33 IU/kg compared to 0.48 IU/kg) dogs. By the end of the study the dosages were on average 0.49 IU/kg for small dogs and 0.37 IU/kg for large dogs. Comparable numbers from *Lorenzen* (1990) were respectively 0.64 IU/kg and 0.43 IU/kg and from *Lorenzen* (1992) 0.79 IU/kg and 0.44 IU/kg. These data indicate that the small dogs in the present study might have been dosed suboptimally, and that the possibility of hypoglycaemic episodes might have been overstressed.

According to a previous report (*Lorenzen* 1990), the urine glucose concentrations in diabetic dogs fluctuate considerably. The report concluded that knowledge of the regulation of the urinary excretion of glucose in the dog is too sparse to use this parameter as a main standard monitor of the accuracy of insulin dosage. Therefore, in the present study, serum fructosamine was introduced as a potentially more useful parameter to monitor the glycaemic status and the accuracy of insulin dosing. Serum fructosamine measurements provided a simple and easy way to diagnose persistent hyperglycaemia and monitor the success of treatment in diabetic patients. ALP seems also to be a useful prognostic indicator since the activity was well correlated to the glycaemic status. Compared with the study by *Lorenzen* (1992), using a similar dosing device from the same manufacturer, the results obtained in the present study showed a generally lower degree of glycaemic control with fewer dogs completing the study period and a higher incidence of complications. This might be explained by a lack of tradition and experience of treating diabetic dogs in Norway (*Thoresen & Grøndalen* 1995). With one exception each participating veterinarian in the present study treated only one dog. Most of the diabetic dogs in this study were the first diabetic dog treated extensively by the participating veterinarian. This is in large contrast to the Swedish study (*Lorenzen* 1990) where fewer and more experienced veterinarians participated treating several dogs each.

Regarding the over all results obtained the study was considered a reasonable success, and hopefully they might contribute to encourage veterinarians to gain further experience concerning diagnosing, monitoring and treating canine diabetes mellitus patients.

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Sammendrag

Diabetes mellitus hos hund: En utprøving av engangsinjektorer med isophane insulin og nytten av fruktosamin målinger i diagnostikk og oppfølging av lidelsen.

15 hunder fra hele Norge som nylig hadde fått diabetes mellitus ble inkludert i studien. Alle hundene ble fulgt opp av sine lokale veterinærer og innkalt til regelmessige kontroller hos disse i løpet av oppfølgingstiden på 6 måneder.

Alle 15 hundene viste innledningsvis markert hyperglykemi, $\bar{\times}_{(15)}$ = 23.6 mmol/L med en spredning på 16.0-47.6 mmol/L (referanse område: 3.6-6.6 mmol/L). Fruktosamin målinger ble foretatt på 13 hunder før behandling ble igangsatt. Alle disse 13 hundene viste forhøyede fruktosaminverdier, $\bar{\times}_{(13)}$ = 520 μmol/L med en spredning på 451-803 μmol/L (referanse område: 250-320 μmol/L).

Hos 8 av de 12 hundene som var i live etter 2 uker var den kliniske tilstanden normalisert. Etter en måneds behandling var den kliniske tilstanden normalisert hos 8 av 10 hunder og fruktosamin i serum var normalisert hos 3 hunder. En hund viste moderat forhøyet fruktosamin konsentrasjon, mens 5 hunder fremdeles viste markert forhøyede verdier. Hos en hund ble serum fruktosamin ikke undersøkt på dette tidspunktet. Seks hunder døde eller ble avlivet i løpet av oppfølgingstiden. En hund møtte ikke opp etter den første kontrollen. Tre moderate episoder med hypoglykemi ble rapportert. To hunder utviklet katarakt i løpet av oppfølgingsperioden. To hunder hadde katarakt ved inklusjon som utviklet seg videre.

Tilsammen utførte eierne til disse 15 hundene ca. 3 500 injeksjoner med *Insulatard® Novolet®*, 100 IU/mL uten at tekniske eller praktiske problemer ble rapportert.

Denne studien viser at engangsinjektorer med isophane insulin, *Insulatard® Novolet®*, og målinger av serum fruktosamin er velegnet i behandling, diagnostikk og oppfølging av diabetes mellitus hos hunder.

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