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Article

Loose-control of diabetes mellitus with protamine zinc insulin in cats: 185 cases (2005–2015)

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Abstract — This study evaluated the outcome of cats with diabetes mellitus treated with a loose-control approach using protamine zinc insulin and identified factors that influence the likelihood of remission and survival in these cats. A total of 185 client-owned domestic cats were followed until death, lost to follow-up, or the end of the 11-year study. These cats were treated primarily basing insulin dose adjustments on clinical response. Patient records were used to examine factors suspected of influencing success of diabetes management. The remission probability was 56.2%. Survival time ranged from 0 to 3808 days with a median of 1488 days. Recent pre-diabetic corticosteroid use, lower mean blood glucose concentration during treatment, and lower mean insulin dose significantly increased the likelihood of remission. A low-carbohydrate diet, occurrence of remission, lack of diabetic ketoacidosis at diagnosis, lower mean blood glucose value during treatment, and lower blood glucose value at diagnosis were significantly associated with increased survival time.

Résumé — Contrôle relâché du diabète sucré à l'aide de l'insuline au zinc de protamine chez les chats : 185 cas (2005–2015). Cette étude a évalué les résultats chez les chats atteints de diabète sucré traités à l'aide d'une approche de contrôle relâché ayant recours à l'insuline de zinc de protamine et a identifié les facteurs qui influencent la probabilité de rémission et de survie chez ces chats. Un total de 185 chats domestiques appartenant à des clients ont été suivis jusqu'à la mort, la perte de suivi ou à la fin de l'étude de 11 ans. Une approche de contrôle relâché et d'insuline au zinc de protamine a été utilisée, surtout sur la base des ajustements de la dose d'insuline en fonction de la réaction clinique. Les dossiers des patients ont été utilisés pour examiner les facteurs soupçonnés d'influencer le succès de la gestion du diabète. La probabilité de rémission était de 56,2 %. Le temps de survie s'échelonnait de 0 à 3808 jours avec une médiane de 1488 jours. L'usage récent de corticostéroïdes prédiabétiques, un taux de glycémie moyen inférieur durant le traitement et une dose d'insuline moyenne inférieure augmentaient significativement la probabilité de rémission. Une diète faible en glucides, l'occurrence de la rémission, l'absence de kétoacidose diabétique, une valeur moyenne inférieure de glycémie durant le traitement et une valeur inférieure de glycémie étaient significativement associées à des temps de survie accrus.

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This study received no external funding. Treatment expenses for each cat were borne by the cat's owner. No diets, drugs, including insulin products, or laboratory supplies were provided by their manufacturers at reduced price or for no charge to Alamo Feline Health Center.

The authors declare that there is no conflict of interest. One author (GDN) has given paid lectures endorsing protamine zinc insulins, of which he has used 3 commercial products made by 3 manufacturers for over 40 years.

Introduction

Following hyperthyroidism, diabetes mellitus (DM) is the second most common endocrine disease of domestic cats (1–3). The frequency has been reported at 43/10 000 (0.43%) in all cats and 159/10 000 (1.6%) in Burmese in a population of insured cats in the UK (4), 124/10 000 (1.2%) in teaching hospitals in the US (5), 50/10 000 (0.5%) in domestic shorthair cats, and 200/10 000 (2.0%) in Burmese in a private practice in Australia (1).

In 2004, Nelson (6) suggested increased emphasis on controlling clinical signs with decreased monitoring of blood glucose concentrations in affected cats. The most desirable outcome criteria for diabetic control were resolution of clinical signs, return to apparent health, normalization of body weight, and owner satisfaction (6). Maintaining a blood glucose range of 5.5 to 16.6 mmol/L (100 to 300 mg/dL) was suggested but was not considered paramount (6). Recently, the AHAA guidelines for managing DM in dogs and cats stated that the goal of successful management should be the control of clinical signs without the presence of hypoglycemia (7). The concept that managing clinical signs of diabetes supersedes using glucometer readings is the basis of the development of what the authors term the loose-control approach.

Many owners have difficulty assuming the responsibilities associated with traditional- or tight-control of DM due to financial, time, or physical constraints. The goal of tight-control of DM is to keep the blood glucose between 4.4 and 11.0 mmol/L (80 and 200 mg/dL) (8), and the aim of traditional-control is to keep the blood glucose between 5.5 and 16.6 mmol/L (100 and 300 mg/dL) (9). These goals may result in a high euthanasia rate in the primary care setting (10,11). Clients seen at a primary care hospital may differ from those who seek care at referral centers; it is suspected that in the primary care setting many owners are less motivated to regulate their diabetic cats, especially those that are difficult to regulate. Patients in the referral setting are often there due to difficulty in regulation which only adds to the overall bias. Published studies often originate from a referral population and, therefore, may have an inherent selection bias when measuring success of tight- or traditional-control (8,12).

One source of frustration for practitioners managing DM is the discord between a cat's clinical signs and its blood glucose levels (10,11,13). In 1 study, control of DM using clinical signs was termed "markedly better" than the control that blood glucose or fructosamine levels indicated (14). Control of DM as determined by owners based on their cat's observed clinical signs was 5 times better than the degree of control as determined by veterinarians attending to these cats based on the cat's blood tests (14). Most of those attending the American Board of Veterinary Practitioners Roundtable Discussion on Feline Diabetes expressed similar frustrations about the lack of correlation between clinical signs and blood values (10,11). Thus, emphasis on blood glucose levels independent of clinical signs can result in underestimation of the degree of diabetic control achieved and may lead to unwarranted insulin dose increases or euthanasia. In addition, those Board-certified feline practitioners felt their remission rates were much lower compared with those in published studies using the traditional control approach (10,11). They also reported that although home blood glucose testing was almost universally recommended, only about 25% of owners complied on a long-term basis, usually due to avoidance of the owner by the cat (11).

There are 2 schools of thought regarding the desired outcome of therapy for diabetic cats. One is that remission, defined as being euglycemic without insulin for more than 30 d, should be the goal since it appears to benefit both the cat and the owner long-term, and lack of remission is a poor outcome (8,15,16). The other is that prolonged quality of life should be the goal, and remission is a welcome side-effect (17,18).

Recently the American College of Physicians (ACP) released a paper detailing over-regulation in humans with Type-2 diabetes (19). The ACP recommended more focus on controlling hypoglycemic events by allowing for an overall higher blood sugar level. This contrasts with the American Diabetes Association which still recommends tight glycemic control in these patients [i.e., keeping blood glucose in the normal range (4.4 to 6.1 mmol/L; 80 to 110 mg/dL)] (19,20). This discrepancy and conflict in human medicine mirrors the controversy in the management of diabetes mellitus investigated in this manuscript.

Few publications have examined long-term survival in treated diabetic cats (21–23). The authors are unaware of any publications regarding long-term management of more than 50 diabetic cats in a primary care setting. Therefore, the objectives of the study herein were to evaluate the outcome of cats with diabetes mellitus treated without serial blood glucose curves and home testing, but with owner-observed changes in clinical signs (polyuria, polydipsia, polyphagia) and examination findings such as weight changes and hydration to identify factors associated with the likelihood of remission and survival in these cats, and to investigate the hypothesis that loose-control of diabetes mellitus is a viable clinical approach to management of this disease.

Materials and methods

A retrospective study was conducted using the following protocols. Multiple doctors treated the patients over the course of the study, but all adhered to the same protocols.

Loose-control method

Protamine zinc insulin (PZI) was used exclusively and given approximately q12h. Owners were discouraged from performing home glucose testing. Owners treated their cats with insulin and diet and were asked to monitor weight changes and the approximate levels of food consumption, water consumption, and urine output. The owners were instructed on the best ways to note changes in these behaviors (i.e., monitoring size of urine clumps in litter box and specific measurements of the amount of food and water provided to the cat). Dose changes were made by the veterinarian and were based on physical examination, clinical signs, and a single blood glucose determination at approximately 12 h post-insulin; glucose curves were not used. Cats were not managed by remote means of communication, i.e., by telephone, fax, or e-mail.

Rechecks consisted of weight determination, a report from the owner concerning the approximate levels of food consumption, water consumption, and urine output, and a single glucose

Table 1[a]. Recommendations for insulin dose changes based on clinical signs and a single blood glucose determination at approximately 12 hours post-insulin for cats receiving protamine zinc insulin (PZI).

9.9 mmol/L (< 180 mg/dL)	Stop insulin for 2 to 4 d then recheck the BG. If BG is normal, discontinue insulin until clinical signs return. If BG is elevated and clinical signs have returned, resume insulin at about 50% of the previous dose and recheck in 1 wk.
9.9 to 13.8 mmol/L (180 to 250 mg/dL)	Although the clinical signs will be well-controlled, decrease the dose by about 50% and recheck in 1 wk for potential further dosage adjustment.
13.8 to 22.1 mmol/L (250 to 300 mg/dL)	Clinical signs will be well-controlled. Decrease the dose by about 50% and recheck in 1 to 2 wk for potential further dosage adjustment.
16.6 to 22.1 mmol/L (300 to 400 mg/dL)	If clinical signs are controlled, continue present dose and recheck in 4 wk. If not, maintain current insulin dose and recheck in 1 to 2 wk. If clinical signs are still not well-controlled, increase the dose by about 33%.
22.1 to 27.6 mmol/L (400 to 500 mg/dL)	If clinical signs *are* well-controlled, do not change dose; however, consider fructosamine testing to determine the presence of stress hyperglycemia. If fructosamine is not determined or is normal, continue present dose and recheck in 4 wk.
22.1 to 27.6 mmol/L (400 to 500 mg/dL)	If clinical signs *are not* well-controlled, increase dose by about 33% and recheck in 1 to 2 wk. Be cautious with these cases. If the dose is increased by more than 33%, recheck in 1 wk. Beware of occurrence of hypoglycemia. Consider rechecking blood at 6 h post-insulin. If the cat is lethargic or has a poor appetite check blood pH and test for ketones in the urine or serum.
27.6 to 33.1 mmol/L (500 to 600 mg/dL)	Evaluate the cat's clinical signs for DKA and check for ketones in the urine or serum. If negative, continue the recommendations for the not well-controlled 22.1 to 27.6 mmol/L (400 to 500 mg/dL) group. Consider treatment for concurrent disease (e.g., dental disease, pancreatitis).

[a] This table reviews the technique for using the loose-control approach to manage diabetes mellitus in the cat. It is impossible to cover every individual situation that can occur clinically and these numbers should be used as general guidelines. The final decision regarding diabetic management should be at the discretion of the practitioner responsible for the case.
Clinical signs — polyuria, polydipsia, polyphagia, weight loss.
Well-controlled clinical signs — Resolution or decrease of polyuria, polydipsia, and/or polyphagia, and/or a weight increase.
BG — Blood glucose.
DKA — Diabetic ketoacidosis.

determination using a feline-specific glucometer (AlphaTRAK 2; Zoetis, Parsippany, New Jersey, USA). Rechecks were performed approximately every 7 to 14 d at about 12 h post-insulin during initial regulation, if the dose of insulin was changed, or if the clinical signs, including weight loss, were troubling to the veterinarian or owner. Once a reasonably stable dose was achieved, rechecks were performed approximately every 4 to 6 wk. A stable dose of insulin meant that no significant blood glucose changes resulting in insulin dosing changes occurred for 3 consecutive rechecks. For example, if the cat lived for 4 y with diabetes mellitus, one can estimate that it was seen ~35 times by the veterinarian. Cats in remission were checked every 6 mo or if the owner noted a return in the clinical signs.

Ideally, rechecks occurred 12 h after the last insulin dose; this was the peak of the glucose curve (24). If this timing was not workable for the client, it was conducted approximately 6 h after the last insulin dose; this was the approximate time of the nadir when using PZI (24). A 6-hour recheck was not used routinely because the time of the nadir was less predictable on any given cat and on any given recheck. If a 6-hour recheck was used, the recommendations for dose changes listed in Table 1 did not apply. Dose adjustments were made considering the clinical signs and the blood glucose level. Insulin dose increased or decreased by 0.5- or 1-unit increments (Table 1).

The ideal blood glucose level at 12 h post-insulin for a cat with what was considered well-regulated diabetes mellitus was 16.6 to 19.3 mmol/L (300 to 350 mg/dL). However, a blood glucose level up to 22.1 mmol/L (400 mg/dL) was acceptable if the clinical signs were controlled. Some cats with good control of clinical signs, including stable weight, had blood glucose values of 22.1 to 27.6 mmol/L (400 to 500 mg/dL) and were also considered well-regulated. See Table 1 for insulin dose changes.

Some cats with blood glucose levels in the 27.7 to 33.3 mmol/L (500 to 600 mg/dL) range had mild to moderate clinical signs (PU/PD and polyphagia), but often had stable weights. This was not a level that consistently equated to ketosis or ketoacidosis which could be verified by checking for ketones and pH in urine or serum. It should be noted that these cats did not require hospitalization and were clinically doing well at the time of the recheck.

Data collection

A search of electronic medical records at Alamo Feline Health Center (AFHC) identified cats newly diagnosed with DM during the 11 y beginning January 1, 2005. Inclusion criteria were: i) a diagnosis of DM based on at least 2 clinical signs of polydipsia, polyuria, polyphagia, or weight loss; blood glucose ≥ 16.6 mmol/L (300 mg/dL); and the presence of glucosuria; ii) treatment exclusively with PZI twice per day (if treated), until death, remission, or lost to follow-up; iii) no clinical suspicion of or confirmed hyperadrenocorticism or acromegaly; and iv) the use of the loose-control approach as previously defined without being previously treated with an alternate approach to diabetic management.

Factors that have previously been deemed important in obtaining remission and survival, including diet, recent corticosteroid administration, mean blood glucose concentrations at diagnosis and over the course of treatment, and mean insulin dose during treatment (12,15,25) were assessed. Clinical signs of increasing weight and decreasing polyuria, polydipsia, and polyphagia, as well as the 12-hour post-insulin blood glucose value were used to assess the overall level of glycemic control in the individual cat. The insulin dose was adjusted based on these factors as opposed to placing significance on the number alone. A common exception was when the blood glucose was less than 13.9 mmol/L (250 mg/dL) at 12 h post-insulin; these cats had minimal PU/PD, polyphagia, and weight gain but were deemed over-regulated.

All cats were evaluated for the presence of diabetic neuropathy (diagnosed by rear leg weakness or a plantigrade stance) at the time of diagnosis. A diet determination was made. A low carbohydrate diet (LCD) was defined as one having < 18% metabolizable energy from carbohydrates on a dry matter basis. The diet form (canned or dry) was not noted. Diabetic ketoacidosis was diagnosed in cats that were clinically ill, had a blood glucose level > 31 mmol/L (550 mg/dL) +/− significant electrolyte abnormalities, had low serum pH, and ketones in the urine or serum (urine > 1.5 mmol/L). At the time of the study, serum pH could not be consistently measured so the clinicians used the presence of ketones in addition to the appropriate clinical signs (including lethargy, anorexia, vomiting, severe weight loss) to make the presumptive diagnosis of diabetic ketoacidosis. Biochemical hypoglycemia was differentiated from clinical hypoglycemia. Biological hypoglycemia was defined as a blood glucose < 3.7 mmol/L (75 mg/dL) [reference range: 4.2 to 8.4 mmol/L (75 to 150 mg/dL)]. Clinical hypoglycemia was defined as cats with a blood glucose < 3.7 mmol/L (75 mg/dL) and the presence of seizures and/or profound lethargy requiring treatment with IV dextrose; those cats typically had blood glucose levels < 2.8 mmol/L (50 mg/dL).

Statistical analysis

Data were analyzed to evaluate factors associated with the cat's likelihood of achieving remission. Diabetic remission was diagnosed in cats meeting the aforementioned diagnostic criteria and subsequently achieving normoglycemia [blood glucose: 4.2 to 8.4 mmol/L (75 to 150 mg/dL)] without insulin therapy for 28 or more days. Data were analyzed to evaluate factors that were associated with achieving remission using either a log-rank test or Cox proportional hazards regression, with results presented as predicted time-to-event probabilities, hazard ratios (HR), and 95% confidence intervals (95% CI) (Stata IC/13.1; StataCorp, College Station, Texas, USA). *P*-values < 0.05 were considered significant. All 185 cats included in the study were used in the calculation of any data parameters measured. No exclusions were made for cats euthanized either on the day of diagnosis or for other reasons in order to avoid unintentional bias when calculating the results.

Results

Diabetes mellitus, the second most common endocrine disease diagnosed at AFHC, was diagnosed in 112/10 000 (1.1%) of patients during this study. Of 185 neutered cats which met the criteria and were included in the study, 71% were male and 29% were female. The median age at diagnosis was 11 y (range: 4 to 19 y). The remission probability for all cats was 56.2% (95% CI: 47.4% to 65.3%). Median time to remission was 286 d. There was no significant difference in the remission proportion for males (55.5%) and females (57.6%) ($P = 0.59$). Median survival time (duration from diagnosis to death) was 1488 d, with a range of 0 to 3808 d.

Of the factors that were analyzed, 5 had a significant association with survival. Ninety-four cats died during the study and were used to calculate survival data. It was suspected that diabetes mellitus (either leading to euthanasia or by natural causes) was the cause of death in 37 of the 185 cats. Cats not fed an exclusively low-carbohydrate diet ($n = 99$) were 50% more likely to have died during the study compared with cats that ate an exclusively low-carbohydrate diet (HR = 0.51, 95% CI: 0.29 to 0.89, $P = 0.015$). Cats that experienced diabetic ketoacidosis (DKA) at any time during treatment had a rate of death more than twice that of cats that did not experience DKA (HR = 2.36, 95% CI: 1.10 to 5.04, $P = 0.023$). This includes cats euthanized after developing DKA. Achieving remission during the course of therapy was associated with a declining rate of death (HR = 0.29, 95% CI: 0.16 to 0.55, $P < 0.001$). As overall measured mean blood glucose values increased by 2.8 mmol/L (50 mg/dL), the rate of death increased (HR = 1.58, 95% CI: 1.36 to 1.83, $P < 0.001$). As mean blood glucose values at diagnosis increased by 2.8 mmol/L (50 mg/dL), the rate of death increased (HR = 1.20, 95% CI: 1.01 to 1.42, $P = 0.037$). There was no significant association between the rate of death and gender ($P = 0.43$), incidence of hypoglycemia ($P = 0.85$), steroid-associated diabetes ($P = 0.22$), diabetic neuropathy at diagnosis ($P = 0.70$), elevated feline pancreatic lipase immunoreactivity (*f*PLI) at diagnosis ($P = 0.91$), and mean insulin doses ($P = 0.54$).

Three factors significantly influenced remission: steroid-associated diabetes, lower mean blood glucose during treatment, and lower mean insulin dose. Cats with steroid-associated DM had a 3- to 4-fold greater remission rate than cats without steroid-associated DM (HR = 3.58, 95% CI: 2.22 to 5.78, $P < 0.001$). As mean blood glucose increased by 0.6 mmol/L (50 mg/dL), the rate of remission decreased by approximately half (HR = 0.49, 95% CI: 0.42 to 0.57, $P < 0.001$). As mean insulin increased by 1 unit, the rate of remission decreased by approximately half (HR = 0.46, 95% CI: 0.36 to 0.59, $P < 0.001$). The weighted mean insulin dose ranged from 0.0 to 8.1 units. There was no significant association between remission and blood glucose at diagnosis ($P = 0.086$), LCD ($P = 0.58$), gender ($P = 0.59$), occurrence of clinical hypoglycemia ($P = 0.091$), DKA ($P = 0.53$), diabetic neuropathy at diagnosis ($P = 0.25$), or an elevated *f*PLI at or near diagnosis ($P = 0.40$).

Ten cats (5.4%) became clinically hypoglycemic during treatment. The hypoglycemic incidence rate was 1 event per 9662 treatment days. Eighteen cats (9.7%) were diagnosed with DKA; 7 of those (3.8%) occurred during the course of treatment. Fifteen cats were diagnosed with diabetic neuropathy at the time of diagnosis; all signs resolved after weeks to months of treatment. Eighty-eight cats had urine cultures at the time of diagnosis; 7 (3.8%) had growth including 5 with *Escherichia coli,* 1 with *Enterococcus* spp. and 1 with *Proteus* spp. Ninety-four cats had *f*PLI values determined (median = 6.2 µg/L, range: 1.1 to 97.9 µg/L). Fifty-six percent were above the reference range (0 to 5.4 µg/L). Significant concurrent disease occurred in 137 (74.0%) cats at some point during treatment. The 3 most commonly diagnosed diseases were renal disease in 52 cats, pancreatitis in 15 cats, and small bowel lymphoma in 20 cats.

Discussion

The remission rate of 56.2% (95% CI) compares favorably with other studies (47.4%, 65.2%) (16,25), treatment approaches,

and insulin types used. The identified factors that favored remission were steroid-associated diabetes, lower mean blood glucose during treatment, and lower insulin dose during treatment. The identified factors that favored increased risk of shorter survival were not feeding a low carbohydrate diet, DKA at initial presentation, higher mean blood glucose values during treatment, lack of remission, and higher blood glucose levels at the time of diagnosis.

Based on the authors' clinical experience, for owners, a cat's quality of life is likely perceived as better if there are less frequent veterinary visits, lack of in-hospital blood glucose curves, no at-home blood collection, and reduced patient stress. The goal of the loose-control approach is to provide good quality of life for both the cat and the owner so treatment for a prolonged period is feasible; the success of this was shown by the fact that the median survival time was over 4 y and the maximum was over 10 y. In the authors' clinical experience, decreasing the amount of stress on the cat by reducing blood collection and hospitalization to obtain glucose curves while maintaining acceptable glycemic control favor prolonged maintenance of a good quality of life.

One possible drawback with the loose-control approach is the potential for glucotoxicity because overall mean blood glucose values remain higher than those found with tight- and traditional-control approaches. It is believed that prolonged hyperglycemia causes suppression of pancreatic beta-cells that can become permanent if not addressed (26–28). Endogenous adequate production of insulin is the basis for remission; thus, remission is more likely with adequate pancreatic function. Adequate control of hyperglycemia may partially reverse glucotoxicity in the pancreas (8,16,29–31). In this study, cats with lower mean blood glucose [each mean glucose increase of 2.8 mmol/L (50 mg/dL) decreased remission rate by 50%] were more likely to achieve remission, supporting the theory that glucotoxicity is preventable or reversible at lower blood glucose levels. Most cats in this study had their clinical signs well-controlled even though their 12-hour post-insulin blood glucose values were often between 19.5 and 24 mmol/L (350 and 450 mg/dL). Because the remission probability was acceptable, it is likely these levels were low enough to permit adequate recovery of beta-cell function in more than half of diabetic cats.

Few cats experienced clinical hypoglycemia; only 5.4% (10/185) of cats in the study experienced hypoglycemic episodes during treatment. Clinical hypoglycemia occurrence in this study was less than 10% of that reported by the participants of the ABVP Roundtable discussion on DM who did not use the loose-control approach (11). The nadir of PZI is approximately 6 h post-injection (8), and if hypoglycemia became a significant issue, the lowest blood glucose would occur at times when the owner was most likely at work or asleep. This could prove fatal for the cat because treatment need for clinical hypoglycemia is urgent. Possible explanations for the low incidence of clinical hypoglycemia include the loose-control approach favoring higher blood glucose levels thus avoiding clinical hypoglycemia and that cats are more tolerant to low blood glucose levels than were traditionally thought.

If the cat was presented in DKA or had a notable comorbidity, such as renal failure or an abdominal mass, euthanasia was likely. If the owner was financially limited, time restrained, physically disabled (i.e., poor vision or digital arthritis), or simply did not wish to spend money or effort on the cat, euthanasia was usually performed, typically on the day of diagnosis. It is probable that few of these cats are examined at university or referral institutions. It is notable that the remission probability of 56.2% includes these cats and circumstances, since without them, the remission rate would likely change. There were 20 cats that were euthanized or died in the first 3 d, comprising 10.8% of the study group.

One interesting factor was the absence of association between an LCD and remission. Feeding an LCD reduces the need for the beta-cells to produce insulin and, therefore, is considered better for diabetic control (32). Diet was found to influence remission in other studies (22), and the finding in this study was not expected. However, a cat does not become diabetic due to diet alone; there are many factors involved in the development of diabetes (33), which could explain this lack of association. Lack of remission could also be due to owner compliance; owners may have been feeding other diets concurrently that were not reported to the veterinarian. Feeding an LCD could also have had other advantageous effects on the cat's well-being, which may have also increased survival time in this study. Cats that ate an LCD lived longer on average, suggesting LCD should be included as part of one's diabetic management protocol.

The blood glucose level at the time of diagnosis was significantly associated with decreased survival time but not remission. Cats with a lower mean insulin dose throughout treatment were more likely to go into remission. This may signify a higher level of function in the pancreatic beta-cells of these cats.

There was a reported association between cats receiving corticosteroids and the development of diabetes (8). This study found a significant increase in remission rates for cats that received corticosteroids during the 30 d before becoming diabetic. However, there was no association between survival time and cats receiving corticosteroids.

Compared to other control methods, the loose-control approach was less burdensome on the cat and the owner and produced an infrequent occurrence of hypoglycemia and DKA. It is notable that those 2 events are at opposite ends of diabetic control. Few cats experienced DKA; it occurred in only 3.8% (7/185) during the course of therapy. This is notable because even with blood glucose levels considerably higher than the tight traditional approaches, the incidence of DKA was lower than that of hypoglycemia. This could be interpreted to mean that cats tolerate hypoglycemia better than other species. Compared to traditional- and tight-control protocols, loose-control of feline diabetes has several advantages that may outweigh the possibility of glucose toxicity and may increase long-term therapy and quality of life for the patient and owner. Home blood collection, which may be poorly received and rejected by both owners and cats, was avoided. The veterinarian did not need to interpret owner-reported blood glucose values and make therapeutic recommendations without examining the cat; i.e., data received by telephone, fax, or e-mail. Expensive in-hospital glucose curves and routine fructosamine testing were avoided, and frustration over the discordance between blood glucose results and clinical signs did not occur.

There are some limitations to the loose-control approach, as with any disease-control protocol that relies heavily on owner involvement. Determinations of water and food intake and urine output are made by owners and are usually a subjective assessment, especially in a multi-cat household. Consistency of insulin administration, proper insulin dosing, and adherence to stated diets, and the reporting thereof, rely on owner dedication and honesty. In addition, all are often performed by more than 1 caregiver resulting in another possible reason for inconsistencies. These limitations, however, are also true regardless of the therapeutic approach taken. Long-term remission rate determinations in large numbers of diabetic cats in a primary care setting using traditional- and tight-control methods would be desirable so true comparisons can be made. The new looser recommendations for use in select human diabetics proposed by the American College of Physicians met with strong resistance from the American Diabetes Association (19). This type of peer-based resistance has also occurred with the proposed loose-control approach in felines when presented to other veterinarians. Evidence-based studies of alternative treatment protocols remain essential in a profession that desires to offer all cat owners, regardless of financial or other limitations, legitimate and accessible options for managing any feline disease.

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