Current Management of Feline and Canine Diabetes

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By
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Current Management of Feline & Canine Diabetes Mellitus

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www.uq.edu.au/ccah

Goals of therapy

- To effectively manage diabetic dogs and cats, essential to know the goals of therapy for each animal
- Need to understand the likely pathogenesis in each animal
- Pathogenesis determines treatment goals
- Primary treatment goal either diabetic remission OR control of clinical signs and avoidance of hypoglycemia
Feline Diabetes

- Hyperglycemia results from:
  - Type 2 diabetes - in 85-95% of diabetic cats in Nth Am, Europe, Aust
  - Results from a combination of insulin resistance & beta cell failure

1° Treatment goal: Remission

"Other specific types" of diabetes 5-20%

- Results from diseases which cause insulin resistance: acromegaly, hyperadrenocorticism

1° Treatment goal for hyperA: Remission
Others: Control signs & avoid hypoG

Feline Diabetes - Type 2 pathogenesis

Insulin resistance (genotype, obesity, physical inactivity, drugs)

Increased insulin production

β damage → β cell failure

GLUCOSE TOXICITY

Hyperglycemia

Diabetes mellitus (Insulin dependent initially)

Glucose: 7-12 mmol/L (126-216 mg/dl)
Cat requires low CHO diet + ideal wt + exercise + oral hypoglycemics
Glucose Toxicity

- Glucose is toxic to B-cells above 180-220 mg/dL (10-12 mmol/L)
- Dose-dependent inhibition of insulin secretion
- Almost complete suppression of insulin secretion after 3-7 days of blood glucose at 480 mg/dL (27 mmol/L)
- Ketoacidosis occurs unless treated with insulin
- Glucose toxicity is initially reversible if glucose concs are normalized
- Progressive B-cell damage occurs with persistent hyperglycemia
- Later it causes irreversible beta cell damage!

What are goals of therapy?

- Ultimate and primary goal: Diabetic remission (non-insulin dependence)
- Control of signs of polyuria/polydipsia, and weight loss
- Avoidance of clinical hypoglycemia (seizures, coma, blindness)

What is Diabetic Remission?

- Normal blood glucose 3.5-6.7mmol/L, (60-120 mg/dL) without exogenous insulin or hypoglycemic agents
What insulin do I choose & how do I adjust dose?

Lente & NPH insulin last less 12hr

Comparison of Glargine, PZI and Lente Insulins in diabetic cats*.

Remission rates:
- Lente = 2 of 8 (25%)
- PZI = 3 (4) of 8 (37-50%)
- Glargine = 8 of 8 (100%)

*Most remissions within 4-6 wks

Comparison of glargine and lente insulin in diabetic cats

- 50 cats treated for median 16 weeks with lente
- If not in remission →
  - Changed to glargine & home monitoring
  - Remission rate 84% if changed < 6mths after diagnosis (34% after 6mths)


What does remission require?

- Functioning B-cells
  - Reverse glucose toxicity
- Good glycaemic control for 2-16+ weeks

Good Glycemic Control

- Long-acting insulin
  - glargine (Lantus) or detemir (Levemir)
- Low carbohydrate diet
  - < 15% ME carb
- Diligent monitoring of blood glucose & appropriate adjustment of dose
Indications For Using Glargine (or Detemir)

- All newly diagnosed diabetic cats
  - to increase chance of remission
- Poorly controlled or unstable diabetic cats
  - glargine’s long duration of action is likely to benefit these cats
- When SID dosing is desired or demanded
  - BUT better glycemic control and higher remission rates will be obtained with BID dosing
  - SID dosing only provides similar control and remission rates to lente BID (Weaver et al, 2006)

Starting cats on glargine

If BG > 360mg/dL → 0.5U/kg BID (20mmol/L)

If BG < 360mg/dL → 0.25U/kg BID

Use IDEAL body weight, not obese wt
- average total dose 1-3 U/cat BID
- 12hr curves for 3 days with blood glucose measured every 3-4hrs
- If not monitored for first 3 days, start with 1U/CAT BID

Starting cats on glargine

- ONLY increase dose in first week if minimal response
- Most cats require a reduction in dose in the first 3 days
- Home after 3 days and recheck blood glucose curve 7 days later
- Subsequent blood glucose curves every 5-7 days until remission or for 4 months of treatment, then less frequently
- Measure blood glucose every 3-6 hrs eg. 8am, 12pm, 4pm, 8pm, before bed
Adjusting dose: Pre-Insulin versus nadir glucose

1. Changing dose - Glargine
   Increase by 0.5-1 U/injection:
   - If pre-insulin >180mg/dL (>10mmol/L)
   - Nadir (lowest) conc is > 144 mg/dL (> 8mmol/L)
   - Increase by ½-1 U depending how close to cut-off

2. Changing dose - SAME
   - If nadir glucose conc. 90-144 mg/dL (5-8mol/L) AND
   - Pre-insulin > 180 mg/dL (> 10 mmol/L)
   - After several weeks can aim for lower nadir (80-130 mg/dL; 4.6 – 7.4 mmol/l) or normal range

Blood glucose (mmol/L) normal range: 65-120 mg/dL (3.5-6.7 mmol/L)
3. Changing dose - Decrease 0.5-1U/injection

- If pre-insulin < 180 mg/dL (<10 mmol/L)
- OR
- If hypoglycemic < 70-80 mg/dL (<4-4.6 mmol/L)

Hypoglycemia

- If clinical signs of hypoglycemia evident, feed if mild or give glucose IV if severe, and reduce dose by 50%
- If biochemical hypoglycemia but no clinical signs, then just feed cat and reduce dose
- Most cats that have clinical hypoglycemia and have been regularly monitored are in remission within 2 weeks

How do I determine if the cat is in remission?

- Continue reducing dose until ½-1U/cat bid –½-1U/cat sid
- If pre-insulin is 86-180 mg/dL (10mmol/L) on ½ - 1U sid, withhold insulin and check for remission
- Do not be in a hurry to stop insulin - minimum of 2 weeks Tx

- Decision?
AAHA National Staff Meeting Web
Conferences: Current Management of Feline and Canine Diabetes On Thursday, March 12, 2009

**Glargine day 1**

- Graph showing blood glucose levels over time with 8 data points.
- Annotates: "No Increases in first 3 days" and "Dose reduced".

**Glargine day 3**

- Graph showing blood glucose levels over time with 8 data points.
- Annotates: "No Insulin" and "Same Dose".

**Glargine day 10**

- Graph showing blood glucose levels over time with 8 data points.
- Annotates: "Dose increased", "Dose reduced", and "Decrease dose".
Serial Blood Glucose Curves
Days 1-3, 10 (MeanSEM; n=6)

Blood glucose(mmol/L)

Blood Glucose (mg/dL)

Typical dose

- 1-3 units / cat bid ~ 5-6 U BID common (detemir dose tends to slightly lower)
- Range 1 U/cat sid to 10U/cat BID (except if acromegalic ~ 20+ U BID)
- If dose > 1.5 U/kg BID, rule out insulin resistance (measure IGFα etc)
- Usually, if get > 4 U/cat, dose can be (needs to be!) subsequently decreased
- Beware of stress hyperglycemia

Dietary Recommendations

- Recent studies indicate that high protein, low carbohydrate diets are best suited for management of diabetes in cats.
- Insulin dose can be reduced in most cats
- Insulin eliminated in more cats ~ 68% cats on 12% ME carbohydrate versus 41% on 26% ME carbs
- Protein similar 40% ME versus 37% ME (high carb)

Bennett, Greco et al 2005
Frank et al. 2002
Mazzaferro et al. 2003
Monitoring response to treatment

Monitoring response to treatment and adjustment of insulin dose

- Clinical information -
- LOOK AT CAT & TALK WITH OWNER
- Water drunk, changes in body weight, signs of hypoglycemia
- Blood glucose measurements - home monitoring if possible
- Urine glucose & ketones
- +/- Fructosamine

Monitoring glycemic control

- Does the dose need to go up or down?
- Glucose curve 1+/week - measure glucose q 3-6h for 12+ h glargine, detemir or PZI
  - Eg Preinsulin (8am), 12, 4pm, Preinsulin (8pm), (before bed)
  - q 2hr for 6-8h lente or NPH
- Use a glucose meter
  - 1 drop (< 0.6uL) of blood
  - Less stress to cat
  - Reduced cost
- Do not withhold food
  - feed the cat!

Photos: Sara Ford; Rhett Marshall

Photo: Rhett Marshall

Photo: Sara Ford
Blood Glucose Measurements

- Beware of stress hyperglycemia!
  - Avoid struggling! → produces lactate → glucose
  - Struggling can increase blood glucose by 180 mg/dL (10mmol/L)
- Cats on glargine are less able to resist stress hyperglycemia
- Cephalic vein, local anesthetic cream & 29 g insulin syringe
- Try lancet on ear /foot pad instead of IV

Aim for high normal blood glucose (80-130 mg/dl; 4.6 – 7.4 mmol/l)

Meters calibrated for human blood read on average 35 mg/dL (2 mmol/L) (Bayer) and 25mg/dL (1.5 mmol/L) (Roche) lower compared to an automated serum analyzer.

Home monitoring

- Decreases stress-associated artefacts in blood glucose
- Provides more information to make a decision
- Better management - remission rate increased
- More convenient for owner
- More profitable
- Greater bond with owner
Monitoring – Urine Glucose

- Urine glucose is more useful for adjusting insulin dose with glargine or detemir than intermediate-acting insulins (but less useful for detecting remission)
- Once on correct dose of glargine or detemir, cats should no glucose or only a trace glucose present

Photo: Rhett Marshall

Monitoring control
Fructosamine: Normal cat < 400 umol/l;
Exemplary control < 400 umol/l
Obtain baseline value when well hydrated & not acidotic – FR can change by 100umol/l with no change in glucose
Fructosamine - Good control: < 400 glargine < 500 umol/l = lente,

Glucose 540 mg/dl; 30 mmol/L

Link & Rand, 1996
Monitoring control
Fructosamine

Use if:

- Conflicting evidence - eg. history of good clinical control but poor glycemic control when measured in hospital
- Inadequate or unreliable clinical information & blood glucose high
- Unable to measure blood glucose
- BUT water drunk better indicator of mean blood glucose

Link & Rand, 1996

Summary

- Glargine & detemir are safe and effective treatment for diabetic cats
- Glargine & detemir produce higher remission rates in newly diagnosed diabetic cats than lente and PZI insulin
- Home monitoring facilitates improved glycemic control
- Glargine or detemir, low carbohydrate diet and home monitoring are the optimal management strategies in diabetic cats
- See www.uq.edu.au/ccah for protocols

It’s time to talk about DOGS
**Causes of Canine Diabetes**

- Type 1 is most common form
- Results from immune-mediated destruction of pancreatic beta cells
  → Absolute insulin deficiency

1° Treatment goals:
Control signs & avoid hypoglycemia

**Pathogenesis of Canine Diabetes:**
Adult-onset form of Type 1

- Gradual beta cell destruction over months - years
- Slow, insidious onset of clinical signs
- Not associated with obesity
- Most dogs have absolute insulin deficiency
- 17% dogs have some residual beta cell function
- Progressive loss of beta cells over many months

Causes of Canine Diabetes: Other specific types

- Diseases which cause:
  - **Pancreatic destruction**
    - Pancreatitis causes approx. 25-30% of diabetes (> 80% of loss of B cells)
  - **1st Goal of treatment**: control signs
- **Chronic insulin resistance**
  - Hyperadrenocorticism – spontaneous or iatrogenic
  - **1st Goal of treatment**: remission if early
  - Acromegaly

Causes of Canine Diabetes

- Diestrus-associated
- Similar to human gestational
- In dog, hormone profile in diestrus same as pregnancy
- Canine mammary gland produces growth hormone = acromegaly
- **1st Goal of treatment**: remission (possible if recognised early)

Obesity and Canine Diabetes

- Marked obesity (40-50% above ideal weight)
  - halves insulin sensitivity
- Precipitates overt diabetes in dogs with B cell loss from:
  - Immune destruction (Type 1)
  - Pancreatitis
  - **Chronic insulin resistance** (estrus, steroids)
- BUT type 2 diabetes not convincingly documented in dogs
Management of Canine Diabetes

What insulin do I use?
Veterinary-use: 40U/mL mostly
- Lente (porcine = canine) Vetsulin/Caninsulin®
- [PZI (Protamine zinc)]
Human-use - 100 U/ml
- NPH (Isophane)
- Mixes - NPH & Regular
- Detemir, glargine

Use veterinary-use insulin unless clear advantage

Graph: L. Fleeman
What insulin do I use?
- **Lente** (Vetsulin/Caninsulin) in normal dogs
  - Duration: 10hr (Onset 0.6h)

What insulin do I use?
- **PZI** bovine in normal dogs
  - Duration: 19hr (Onset 3h)

What insulin do I use?
- **Glargine** (Lantus) in normal dogs
  - Duration: 13hr (Onset 2h)
What insulin do I use?

- **First Choice:** Lente (porcine = canine) Vetsulin/Caninsulin®
- **If inadequate duration of action:**
  - PZI (Protamine zinc)
  - Detemir

How often do I give insulin?

- Duration of action of Vetsulin/Caninsulin in diabetic dogs = 13hr - BID best
- Likely better control with PZI, detemir or glargine if BID
- Frequency of clinical hypoglycemia is less when insulin given BID compared to SID

Adjust insulin dose based on:

1. Clinical information:
   - Water intake
   - Other clinical data (appetite, weight, physical activity, evidence of hypoglycemia)
2. Blood glucose curves
3. Urine glucose & ketones
Rules for adjusting insulin

1. Look at dog and talk to owner!!!
   - Is dog PU/PD or is water drunk <50-100ml/kg/24h (canned vs dry)
   - Is dog losing weight unintentionally or is underweight
   - Urine glucose > 2 +, OR ketones
   - Is dog alert all day? Is the dog active?
     Is there evidence of signs of hypoglycemia?

Increase dose—BE CONSERVATIVE

- If nadir glucose > 8 mmol/L (145 mg/dl) **AND**
- If lowest pre-insulin G > 10 mmol/L (180 mg/dl)
- Increase dose 20% rounded down to nearest unit **OR** by 1 unit if close to cut-off values

3. SAME dose -

- Nadir 5-8 mmol/L (90-145 mg/dl) **AND**
- Lowest pre-insulin G ≥10 mmol/L (180 mg/dl)
3. Decrease dose

- Nadir < 5 mmol/L (90 mg/dl) OR
- Lowest pre-insulin G < 10 mmol/L (180 mg/dl)
- Decrease by 20% rounded down OR
  1 U if close to cut-off values

If dog won't eat

- Dog MUST eat to make right interpretation of glucose concs.
  - Take pre-insulin blood glucose & get owner to feed away from clinic
  - If unsuccessful, omit pre-insulin glucose and have owner feed at home
  - Better still – teach the owner home monitoring of blood glucose
Home Monitoring of Blood Glucose

- At least 50% of owners are prepared to try
- Buccal mucosa most successful site & best tolerated of ear, buccal mucosa & abdomen

Photos: Linda Fleeman
Home Monitoring of Blood Glucose

- The best lancing device and the best site for blood collection vary with the individual dog & owner.

Photos: Sara Ford

Urine glucose

- Persistently 3-4+
  - OR
- Persistently negative glucosuria
- Evaluate serial blood glucose measurements to:
  - Determine if dose needs decreasing (ie. risk of hypoglycemia)
  - Determine if dose increase is needed or change in insulin type required
  - Be conservative with dose

DOGS DIE FROM HYPOGLYCEMIA
Remission rarely possible
**Goals of therapy:**

- Remission if indicated
- Otherwise control of clinical signs
- No clinical hypoglycemia
- Active dog
- Water intake < 60-100ml/kg/24h
- Stable, ideal body weight
- Negative urine ketones

**What do I feed?**

- Balanced, palatable high quality maintenance diet with moderate fiber - canned has lower carbs
- Keep food relatively constant - carbohydrate content determines insulin dose
- Can try increased fiber (beware of weight loss)
- Low carbohydrate (<10% ME) has similar effect to high fiber
- + Added carnitine

**Summary: Management of Canine Diabetes**

- Lente (or PZI insulin) BID
- Try PZI or detemir if too short duration of action
- Monitor carefully using clinical data (water intake, activity, weight, clinical hypoglycemia)
- Monitor glycemic control with blood glucose measurements (home monitoring provides more data) and urine glucose & ketones
- Feed premium maintenance diet
- Keep food type relatively constant
Questions?

www/uq.edu.au/ccah

Instructions for CE Certificate

1. Complete the evaluation by Monday, March 30, 2009. Please have only one person from your practice complete the evaluation.
   - To complete the evaluation, please go to the following website: http://www.keysurvey.com/survey/244770/2079/

2. After completing the evaluation, you will automatically be linked to the Continuing Education Certificate. The CE certificate can only be accessed after the evaluation is completed.

3. Download the CE Certificate (in pdf format) to your computer and print enough copies for your entire team.

Your input is very important! We take feedback seriously in order to provide you with the highest quality experience possible.

If you have any questions about completing the evaluation or accessing your CE certificate, please email us at webconference@aahanet.org or call 800/252-2242.

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