DKA - SACCM

Key Points

- Prognosis is ~70% for dogs and cats getting discharged from hospital - 5-6 days is average
- BE is associated with outcome, presence of hyperadrenocorticism is associated with non survival
- Ketones are synthesized from fatty acids (after beta-oxidation turns them into acetyl-CoA)
- Aggressive fluid therapy, electrolyte correction, and insulin administration are needed and the mainstays of treatment
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Pathophysiology

- Fatty acids -> β-oxidation -> Acetyl-CoA
    - In presence of low insulin and high glucagon
- Insulin
    - Anabolic effects
        - conversion of glucose to glycogen
        - Storage of amino acids as proteins
        - Storage of fatty acids in adipose tissues
- Glucagon
    - Catabolic effects
        - Glycogenolysis
        - Proteolysis
        - Lipolysis
- Cortisol and Catecholamines also have catabolic effects
- Non-diabetics
    - Acetyl-CoA and pyruvate enter citric acid cycle to form ATP
        - Pyruvate cannot be formed from glucose appropriately in diabetics
            - Reduced citric acid cycle activity
- Ketone Bodies
    - Synthesized when INTRACELLULAR glucose concentrations cannot meet metabolic demands
        - Synthesized in the liver to
            - Acetoacetate*
                - β-hydroxybutyrate*
                - Acetone
            - * = anion of moderately strong acidity

- Acidosis is worsening by vomiting, dehydration, renal hypoperfusion

Risk Factors

- Diabetes (if you didn't know this, re-evaluate your life-choices)
  - Although most dogs and cats are newly diagnosed as diabetics when presenting for DKA
- Concurrent diseases
  - 70% of dogs, 90% of cats
    - Acute pancreatitis, UTI, hyperadrenocorticism are most common is dogs
    - Hepatic lipidosis, CKD, acute pancreatitis, bacterial or viral infections, neoplasia are most common in cats

Clin Path

- 50% of DKA dogs have non-regen anemia (not associated with hypophos), neutrophilia with left shift, or thrombocytosis
  - Also common in cats (minus the thrombocytosis)
    - Also have heinz bodies which are correlated with plasma β-hydroxybutyrate concentration
- Hyperglycemia
- ALT, AST, Cholesterol -> increased in ~50% of dogs
- ^ ALT, ^ cholesterol, Azotemia -> common in cats
- Electrolytes
  - +/- High SERUM potassium, but low INTRACELLULAR potassium
    - Hypokalemia exacerbated after therapy by fluids, insulin, correction of acidosis
  - Hypophosphatemia 2' to
    - Hyperglycemia, acidosis, hypoinsulinemia
    - Leads to hemolysis, seizures, weakness, myocardial depression, arrhythmias
  - Hypomagnesemia may occur in dogs and cats
    - Can contribute to hypokalemia
  - Hyponatremia (pseudohyponatremia), hypochloremia, hypocalcemia (ionized) in ~50% of dogs
- UA
  - 20% of dogs have aerobic bacterial growth on culture via cysto
  - May NOT have increased WBCs though due to immunosuppressive state of diabetes

Treatment

- IV fluids is the mainstay of treatment
  - Debate about normal saline vs balanced crystalloids
- Electrolyte supplementation
  - Potassium supplementation

        - At (or even sometimes above) KMax is needed (with ECG monitoring if above)
    - Phosphate supplementation
        - Potassium phosphate (remember to include in your calculations of KMax
            - Solutions containing 4.4mEq/ml of potassium and 3mM/ml of phosphate
                - (As far as I can find, 1mM Phos = 1 mEq Phos)
                - Administer 0.03 to 0.12 mM/kg/hr or phos component
                    - This means you will be administering K+ @ ~0.05-0.18 mEq/kg/hr
    - Magnesium supplementation
        - Mg Sulfate containing 4 mEq/ml
            - 0.5 - 1 mEq/kg/day
        - Mg toxicity -> vomiting, weakness, generalized flaccid muscle tone, mental dullness, bradycardia, respiratory depression, hypotension
- Insulin Therapy
    - Regular insulin
        - IM
            - Monitoring Q1h with Q1h injections
            - 0.2U/kg 1st dose
            - 0.1U/kg 2nd dose
            - Then if BG drops by:
                - More than 75mg/dl/hr = 0.05U/kg/hr
                - 50-75mg/dl/hr = 0.1U/kg/hr
                - Less than 50mg/dl/hr = 0.2U/kg/hr
        - IV as CRI
            - Monitoring Q2h
            - Administration set must be flushed with 50ml of mixture due to binding of insulin to the plastic tubing (see below for actual evidence that it should be 20ml)

Blood Glucose Concentration (mg/dl)	Fluid Composition	Rate of Administration (ml/hr)
>250	0.9% NaCl	10
200 to 250	0.45% NaCl + 2.5% dextrose	7
150 to 200	0.45% NaCl + 2.5% dextrose	5
100 to 150	0.45% NaCl + 5% dextrose	5
<100	0.45% NaCl + 5% dextrose	Stop fluid administration

* 2.2 U/kg of regular crystalline insulin added to 250 ml of 0.9 % NaCl solution. The administration set must be flushed with 50 ml of the mixture before administering the solution to the animal.

Bicarbonate

- Controversial
    - American Diabetes Association recommends Bicarbd only is pH remains below 7.0 after 1 hour of fluid therapy
    - Risks include exacerbation of hypokalemia, increased ketone production, paradoxical cerebrospinal fluid acidosis, cerebral edema, worsening intracellular acidosis (due to increased production of CO2)
    - Retrospective study in dogs showed worse acidosis = poor survival and bicarb administration associated with poor survival (but could be just dogs with bad acidosis got bicarb)
    - Tx protocol
        - ½ - ⅓ of (0.3 x wt x Base Deficit) over a 20 minute interval every hour while monitoring venous pH
            - No studies to support this

Outcomes

- 70% overall survival to discharge
    - Hyperadrenocorticism is associated with worse outcomes
    - Worsening BE associated with worse outcomes
- 6 day median hosp time for dogs
- 5 days for cats
- 7% recurrence for dogs
- Up to 40% recurrence for cats

Questions

1. List 3 of the anabolic effects of insulin and 3 of the catabolic effects of glucagon

2. True/False: WBC count over 20/hpf in urine is >50% predictive of urinary tract infection in DKA

3. True/False: Despite dogs and cats presenting with DKA having a total body increase of potassium, aggressive potassium supplementation is often required early on in therapy

4. Of the 3 types of ketones, _____ and _____ are both synthesized from _____.

5. What are the recurrence rates of DKA for dogs and cats respectively
    a. 20%, 20%
    b. 20%, 60%
    c. 5%, 10%
    d. 7%, 40%

Answers

1. List 3 of the anabolic effects of insulin and 3 of the catabolic effects of glucagon
    a. Anabolic
        i. conversion of glucose to glycogen
        ii. Storage of amino acids as proteins
        iii. Storage of fatty acids in adipose tissues
    b.
        i. Glycogenolysis
        ii. Proteolysis
        iii. Lipolysis

2. True/**False**: WBC count over 20/hpf in urine is >50% predictive of urinary tract infection in DKA
    a. False - WBC is usually normal despite 20% of cases having UTIs

3. True/**False**: Despite dogs and cats presenting with DKA having a total body increase of potassium, aggressive potassium supplementation is often required early on in therapy.
    a. They have total body depletion of K, despite often having hyperkalemia

4. Of the 3 types of ketones, **acetone** and **b-hydroxybutyrate** are both synthesized from **acetoacetate**.

5. What are the recurrence rates of DKA for dogs and cats respectively
    a. 20%, 20%
    b. 20%, 60%
    c. 5%, 10%
    d. 7%, 40%

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"Waste not, want not": determining the optimal priming volume for intravenous insulin infusions.

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Abstract

BACKGROUND: Insulin adsorbs to plastics used for intravenous (IV) tubing. As a result, clinical IV insulin infusion procotols advise an initial priming volume of up to 50 mL, which may be wasteful-especially since most institutions use 100-mL IV solution bags. In this brief report, we sought to determine the optimal priming volume required for clinical IV insulin infusions.

METHODS: One hundred units of regular human insulin was dissolved into 100 mL of 0.9% NaCl. Employing a standard polypropylene infusion set, a priming infusion was started. At 10- mL intervals, from 0 to 50 mL, effluent was collected directly into glass vials. After dilution (1:10,000) using a proprietary buffer, insulin concentrations were then measured using a double antibody radioimmunoassay. Twenty individually prepared insulin bags were tested in this manner.

RESULTS: Insulin levels without prime were 15.8% [95% confidence interval (CI), 9.1-22.6%] lower than insulin levels following 50 mL of prime (designated as "maximal values"). After a priming volume of 10 mL, insulin adsorption losses fell to a marginally significant 6.6% (95% CI, 0.1-13.1%). Following 20 mL of prime, insulin concentrations were indistinguishable from maximal values (3.4% loss, 95% CI, -0.2% to 7.1%).

CONCLUSIONS: For standard IV insulin infusions, a priming volume of 20 mL is sufficient to minimize the effect of insulin adsorption losses to IV lines. Priming volumes exceeding 20 mL are wasteful, increase costs, and generate unnecessary work for nurses and pharmacists.