BRAINS OVER BRAWN: THE USE OF STEROIDS IN VETERINARY EMERGENCY AND CRITICAL CARE MEDICINE

KARL ALON, RVT
ECC/ICU TECHNICIAN VCA VETERINARY SPECIALISTS OF THE VALLEY

TYPES OF STEROIDS
• Corticosteroids ➔ glucocorticoids
• Mineralocorticoids
• Anabolic androgenic steroids (Anabolic)

BRIEF ADRENAL GLAND ANATOMY & PHYSIOLOGY
• Adrenal glands made of two main layers
  • Outer layer of the adrenal gland ➔ adrenal cortex
    • Cortex made up of 3 layers:
      • Zona glomerulosa (outer zone)
      • Production of mineralocorticoids
      • Zona fasciculata (middle zone)
      • Production of glucocorticoids
      • Zona reticularis (inner zone)
      • Production of gonadocorticoids
  • Inner portion of the adrenal gland ➔ adrenal medulla
    • Production of catecholamines

Steroid Types
• Corticosteroid
• Testosterone
• Aldosterone
• Progesterone
GLUCOCORTICOIDS

• Cortisol (hydrocortisone) most common endogenous glucocorticoid
  • Catabolic steroid
  • Breakdown proteins
• Exogenous glucocorticoids given for disease
  • More potent than cortisol (Prednisone, Dexamethasone, etc)
• 10% of circulating cortisol free
  • Remaining bound to plasma proteins
  • Corticosteroid-binding globulin (transcortin)
• All body cells contain glucocorticoid receptors
  • Profound systemic response

GLUCOCORTICOID EFFECTS ON METABOLISM

• Stimulates gluconeogenesis → liver
  • Lipids
  • Amino acids
• Stimulates amino acid production
  • Extrahepatic tissue
  • Substrates for gluconeogenesis
• Inhibits glucose uptake → muscle and adipose tissue
  • Promotes glucose conservation
• Promotes fat → adipose tissue
  • Lipolysis → fatty acids for energy production
  • Glycerol released → substrate gluconeogenesis

GLUCOCORTICOID EFFECTS ON INFLAMMATION

• Potent anti-inflammatory
  • Glucocorticoids reduce expression of
    • Cytokines
    • Chemokines
    • Adhesion molecules
    • Other inflammatory proteins
    • Prevent recruitment of inflammatory cells to sites of inflammation
• Bind glucocorticoid receptor (GR)
  • GR up-regulates expression anti-inflammatory proteins
  • Represses expression of pro-inflammatory cytokines
GLUCOCORTICOID EFFECTS ON IMMUNITY

- Glucocorticoids impede healing
  - Inhibit fibroblasts proliferation
- Suppress cells that promote immune response
  - Mediators (cytokines)
  - Proteins (adhesion proteins)
- Suppress immunity
  - Decrease circulating T-lymphocytes, monocytes, and eosinophils
  - Inhibit neutrophil, macrophage, and monocyte migration
  - Inhibit phagocytosis and chemotaxis
  - Decrease numbers of mast cells and histamine synthesis

MINERALOCORTICOIDS

- Produced in the cortex of adrenal glands
  - Just like glucocorticoids!
- Aldosterone is primary endogenous mineralocorticoid
- Glucocorticoids circulate approximately 100x more than mineralocorticoids
- Used in the maintenance of electrolytes in the body
  - Sodium (Na+) retention
  - Retention of sodium → retention of fluids
  - Passive potassium (K+) excretion

THE ANDROGEN GROUP-ANABOLIC STEROIDS

- Sex hormones
  - Testosterone
  - Estrogen
  - Progesterone
- Anabolic steroid
  - Build up of proteins
  - Often used in reproduction
  - Small and large animal
  - Can be used to treat incontinence in spayed females
  - Not used in Emergency and Critical Care Medicine
WHEN TO USE GLUCOCORTICOIDS

- Most commonly used for chronic disease processes
  - Asthma, chronic bronchitis, collapsing trachea
  - Immune Mediated processes
  - Addison's disease
  - Inflammatory bowel disease
  - Lymphoma
  - Allergies

- Rarely used in emergency and critical care setting for
  - Anaphylaxis → sometimes!
  - Brachycephalic Obstructive Airway Syndrome
  - Acute presentations of chronic diseases
  - CIRCI patients, refractory hypotension in septic shock

COMMON SIDE EFFECTS OF GLUCOCORTICOIDS

- Suppresses the immune system
  - Reduces ability to heal
  - Increases susceptibility to infection

- Increases risk of GI ulcers
  - Stomach and duodenum high risk

- Increases thirst (Polydipsia)
- Increases urination (Polyuria)
- Increases hunger (Polyphagia)
- Lethargy

WHEN NOT TO USE GLUCOCORTICOIDS

- Shock
- Sepsis
- Trauma
- Brain Injury
- CRASH study
- Rattlesnake envenomations
- Pancreatitis
- Diabetes
- Cardiac disease
- Pneumonia
- Heat stroke
- CPR
- Smoke inhalation
GLUCOCORTICOIDS IN ANAPHYLAXIS

- Anaphylaxis → Type 1 hypersensitivity reaction
  - Severe, potentially lethal reactions → tremendous histamine and leukotriene release
  - Mediators target blood vessels and smooth muscle
    - Profound vasodilation
    - Airway narrowing

ANAPHYLAXIS

- Treatment of choice typically Epinephrine
  - Increases cardiac output and vascular tone
- Crystalloids given IV
  - Maintain intravascular fluid volume
- Antihistamine (Diphenhydramine)
  - Decreases ongoing histamine release
- Glucocorticoids once cardiovascular collapse reversed
  - Glucocorticoids not extremely helpful during the crisis
    - Help to control ongoing anaphylaxis
      - Persistent mediator release (late phase reaction)

BRACHYCEPHALIC OBSTRUCTIVE AIRWAY SYNDROME

- Brachycephalic obstructive airway syndrome
  - Stenotic nares
  - Excessive pharyngeal tissues
  - Elongated soft palate
  - Tracheal hypoplasia
- Progress to
  - Laryngeal sacculae eversion
  - Laryngeal collapse
- Acute decompensation of a chronic condition characterized by
  - Hyperthermia
  - Upper airway obstruction
  - Accompanied by laryngeal and pharyngeal edema
BRACHYCEPHALIC OBSTRUCTIVE AIRWAY SYNDROME TREATMENT

- Oxygen support!
- Sedation
  - Butorphanol, acepromazine work well
- If rectal temperature > 106.5°F → actively cool
  - Cool until rectal temperature reaches 103.5°F → stop active cooling
- Depending on severity → intubation may be required → anesthesia necessary
- Anti-inflammatory dose of rapid acting glucocorticoid → helps reduce pharyngeal and laryngeal swelling

FELINE ALLERGIC AIRWAY DISEASE (ASTHMA)

- Hyperreactive airway response
  - Altered immunosensitivity of the respiratory tract
  - Diagnosed via history, physical exam, radiographs, signs/symptoms
- Oxygen support
- Anti-inflammatory dose of rapid acting glucocorticoid steroid
  - Injectable for crisis, oral or inhaled for chronic use
- Bronchodilators
  - Oral, inhaler, or injectable

IMMUNE-MEDIATED DISEASE

- Immune-Mediated disease → immune system out of control
  - Give immunosuppressive dose of steroids → prevents immune system from wreaking havoc
- Hundreds of immune-mediated diseases
  - Only a few seen through ECC
    - IMHA
    - ITP
IMMUNE-MEDIATED HEMOLYTIC ANEMIA

• Immune-mediated hemolytic anemia (IMHA)
  • Body's own immune system attacking and destroying red blood cells
  • Majority of patients require pRBC transfusion
  • Often need multiple during hospitalization
  • Oxygen therapy if anemia severe enough
  • No RBCs → no hemoglobin → no oxygen carrying capacity
  • Crystalloids to help maintain intravascular volume

IMMUNE-MEDIATED HEMOLYTIC ANEMIA

• Glucocorticoid steroids started → immunosuppressive dose
  • Commonly start injectable rapid acting steroid → move to oral when patient stabilized
  • Other immunosuppressants (i.e. Cyclosporine, Mycophenolate)
  • Antithrombotic therapy (i.e. Aspirin, Clopidogrel, Low molecular weight heparin)

IMMUNE-MEDIATED THROMBOCYTOPENIA

• Immune-Mediated Thrombocytopenia (ITP)
  • Immune system attacks and destroys the body's platelets
  • Patients at risk for spontaneous bleeding < 50k platelets
  • Transfusions
    • pRBC transfusion
    • For anemia, not thrombocytopenia
    • Platelet transfusions
      • Not readily available
      • Controversial
      • Destroyed by body
      • Questionable efficacy
  • Oxygen therapy
    • Anemia → no oxygen carrying capacity
IMMUNE-MEDIATED THROMBOCYTOPENIA

• Immunosuppressive dose injectable rapid acting glucocorticoids
  • Suppressive the immune system to prevent further destruction of platelets
  • Adjunct with immunosuppressive drugs (i.e. Cyclosporine, Mycophenolate)
• Vincristine
  • Chemotherapy drug
  • Stimulates platelet release from bone marrow

GLUCOCORTICOIDS IN ADDISONIAN CRISIS

• Addison’s Disease
  • Body doesn’t make enough glucocorticoid or mineralocorticoid steroids
  • Present cardiovascular collapse
    • Severe dehydration, vomiting, diarrhea, inappetence
  • Blood work for typical Addison’s
    • Elevated K+, decreased Na+
    • Often hypoglycemia
  • Atypical Addison’s
    • Similar presentation, normal electrolytes
    • Only deficient in glucocorticoid steroids

GLUCOCORTICOIDS IN ADDISONIAN CRISIS

• Often administration of fast, rapid acting steroid
  • Desamethasone Sodium-Phosphate often chosen
    • Warm after ACTH test needed for diagnosis
  • Desamethasone lacks mineralocorticoid activity, only replaces lacking glucocorticoids
  • Desoxycorticosterone pivolate (DOCP)
    • Typically given after emergency situation is resolved and diagnosis of typical addisonian
    • Replaces mineralocorticoids
    • Corrects electrolyte abnormalities
    • Given every 20-30 days based on response
• Crystalloids given IV
  • Maintain fluid balance ➔ replace losses ➔ treat dehydration
  • Can give dextrose ➔ hypoglycemia, if present
**CRITICAL ILLNESS-RELATED CORTICOSTEROID INSUFFICIENCY**

- What is CIRCI??
  - Critical Illness-Related Corticosteroid Insufficiency
  - Most commonly seen in patients with septic shock
  - Hypotension refractory to fluid therapy
- Severe stress response
  - Adrenal gland unable to keep up with need
  - Cells have a more impaired response to cortisol
  - Underlying pathophysiology of CIRCI unknown → likely a complex combination of altered hypothalamic, pituitary, adrenal, hormonal, enzymatic, and receptor function

**CRITICAL ILLNESS-RELATED CORTICOSTEROID INSUFFICIENCY**

- Well described in humans
  - Low doses of hydrocortisone improve blood pressure
  - Little clinical evidence in veterinary medicine
  - Guidelines for diagnosis are not well established

**TREATMENT OF CRITICAL ILLNESS-RELATED CORTICOSTEROID INSUFFICIENCY**

- Recommended treatment
  - Physiologic dose of steroids
    - Hydrocortisone typically chosen → most closely resembles cortisol
  - Again…only if refractory to vasopressors and fluids
    - If blood pressure responsive to fluids → NO steroids!
GLUCOCORTICOIDS IN THORACIC AND ABDOMINAL TRAUMA

• Contraindicated → fallen out of practice and standard of care medicine
  • Proven only to be effective if given directly before a trauma
  • Not helpful
• Due to effects on immune system → often makes healing and treatment of trauma worse
• Treat the trauma → wounds → fractures → internal injuries
• Absence of strong evidence of benefit

GLUCOCORTICOIDS IN TBI

• Contraindicated
  • Severe detrimental effects
• TBI → Traumatic Brain Injury
  • Steroids given to reduce brain swelling
• CRASH study
  • Patients given steroids → increased mortality
• Pathophysiology why?
  • Still uncertain → no evidence of severe infection or GI bleed
  • Hyperglycemia seen → poor prognostic indicator in TBI
  • Concern for unknown side effects of steroids on neuro status
• Absence of strong evidence of benefit

GLUCOCORTICOID USE IN CPR

• Contraindicated
  • Little to no benefit associated
• Immunosuppression
• GI ulcers
• Decreased renal perfusion
• Absence of strong evidence of benefit
GLUCOCORTICIDS USE IN LUNG INJURY

- Contraindicated in use for lung injury
  - Pneumonia, aspiration pneumonia, smoke inhalation, etc
- Immunosuppressive ➔ can greatly worsen infection
- Retards healing ➔ makes it extremely difficult for the body to heal
- Absence of strong evidence of benefit

GLUCOCORTICOID USE IN ENVENOMATION

- Contraindicated
- Suppresses the immune system ➔ makes it much harder for body to fight
- Absence of strong evidence of benefit
- Anti-venom only medicine proven to benefit outcome

PRESENTING TO ER FOR GLUCOCORTICOID USE

- Many pets are on glucocorticoid steroids for chronic diseases processes
- Owners may make mistakes with the prescribed medication
  - Due to the numerous side effects of glucocorticoids ➔ some may be emergent!
- Very important clients be educated on the medications
  - Example: Never stop giving glucocorticoids without a doctor’s permission
    - Taper dose ➔ prevents iatrogenic Addisonian crisis from abrupt withdrawal
    - Giving too much of a dose ➔ equally bad
- Hepatopathy
- Cushnoid symptoms
GLUCOCORTICOID INDUCED DIABETES

- Glucocorticoids cause hyperglycemia
  - Increased glycolysis
  - Increased gluconeogenesis
- Glucocorticoids suspected in metabolic changes
  - Pancreatic beta cell dysfunction (sensitivity to glucose and ability to release insulin)
  - Insulin resistance in other tissue
  - Glucose unable to enter the cell and be utilized for energy

CONCLUSION

- Glucocorticoid steroid have a place and time for their use in ECC medicine. However, they are not a cure all! They have pretty tremendous side effects, so they should be utilized with caution and only in circumstances where there is strong evidence that their benefit outweighs the risk.