

Title:

Effect of treatment with low doses of hydrocortisone on blood pressure and mortality in dogs with septic shock

Investigators:

This study is being conducted as a large multi-center study at university and referral hospitals across the country. The UGA investigators are:

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Study description:

Adrenal insufficiency occurs in some dogs with sepsis, and those with hypotension are more likely to have adrenal insufficiency than dogs with normal blood pressure. Septic shock carries a grave prognosis in the dog, and it is unknown whether supplemental steroid therapy would improve blood pressure and survival in this species as it does in humans.

This study aims to determine whether hydrocortisone improves blood pressure and survival in canine septic shock. For inclusion, dogs must be hospitalized in an ICU and have: 1) sepsis; and 2) low blood pressure unresponsive to fluids. Base line and ACTH-stimulated cortisol concentrations will be measured and clinicians blinded to test results. Dogs will be randomized by coin toss to receive either hydrocortisone or placebo. We will compare blood pressure and survival in dogs with adrenal insufficiency to those with adequate adrenal responsiveness across treatment groups. We hypothesize that dogs with adrenal insufficiency will have improved blood pressure and survival when treated with hydrocortisone, and that hydrocortisone therapy will have no benefit in dogs with adequate adrenal function.

Inclusion criteria: To be included, the dog must be hospitalized in the ICU and must meet the criteria for septic shock as defined by human and veterinary industry standards.¹⁴⁻¹⁷ Within a 24-hour period, dogs must have:

- i. A documented or highly suspected infection –**and**--
- ii. At least 2 of the following 4 criteria:
 1. hypo- or hyperthermia (rectal temperature <100°F or >103.0°F)
 2. tachycardia (HR > 120)
 3. PCO₂ < 32mmHg – **or** – tachypnea (respiratory rate >40 breaths per minute in a non-panting patient)
 4. leukopenia (total WBC <6,000 cells/uL), leukocytosis (total WBC >16,000 cells/uL), or >3% bands.
- iii. Hypotension refractory to fluid loading (systolic blood pressure <80mmHg or mean arterial pressure <60mmHg in the face of a central venous pressure measured via a jugular vein catheter of at least 4cmH₂O).

Exclusion criteria. Dogs will be excluded from the study if they have had glucocorticoid administration of > 1 week's duration any time in the 6 weeks prior to the study, or glucocorticoid administration at any time in the 7 days prior to study initiation. Dogs will also be excluded if they are being treated with ketoconazole, etomidate, or any other drug known to

affect the HPA axis; if they have known or suspected hyper- or hypoadrenocorticism; or if the primary clinician in charge of the dog refuses participation.

Duration of study:

The study will remain active until a total of 90 dogs have been recruited nationwide. The goal is to have the study completed within one year.

Potential benefits to veterinary medicine:

If this study confirms a benefit of treatment with hydrocortisone in dogs with septic shock and adrenal insufficiency, outcome may be significantly improved in this highly fatal syndrome. Dogs of all breeds will benefit if this study identifies such treatment benefit.