Hyperkalemia in Greyhounds under General Anesthesia

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Proposal:

Hyperkalemia is a term used to describe an elevation in potassium within the blood. The majority of the body's potassium is found within mammalian cells and is essential for maintaining cell volume and supporting cell growth (DiBartola & De Marais,2011). The remainder of potassium lies within the space outside of cells (extracellular fluid) and is responsible for many functions including, maintaining the electrical stability of the cardiac muscle cells (DiBartola & De Marais, 2011; El-Sherif & Turrito, 2011). When this tightly regulated gradient is altered, life-threatening cardiac arrhythmias can occur secondary to hyperkalemia. In humans, severe hyperkalemia is one of the most common electrolyte disorders leading to significant cardiac arrhythmias and possibly cardiopulmonary arrest (Alfonzo et. al, 2006).

There are several known causes of hyperkalemia including renal causes (such as urinary tract obstruction or oliguric renal failure), dietary factors (potassium-rich foods), drugs (such as ACE inhibitors), endocrine disorders (Addison's, insulin deficiency), hematologic disorders (blood transfusion, hemolysis), and massive cell death (tumor lysis syndrome, rhabdomyolysis) (Alfonzo et. al, 2011). There have been increasing reports of dogs developing acute hyperkalemia while under general anesthesia with the underlying cause yet to be established (Pye & Ward, 2023; Tisotti et. al 2023). Of domestic species, there appears to be a possible predisposition for Greyhounds developing unanticipated hyperkalemia (Jones et. al, 2019; Pye & Ward, 2023). In an abstract presented at the Association of Veterinary Anesthetists hyperkalemic events occurred in 36 out of 95 (38%) anesthetized Greyhounds at a hospital in Colorado (Jones & Mama, 2018). Prolonged periods of time under general anesthesia appears to be a possible contributing factor in some of the case reports (Jones & Mama, 2018; Pye & Ward, 2023; Tisotti et. al 2023). Importantly, a variety of anesthetic drug protocols have been utilized in these patients and it has also been documented that hyperkalemia may develop during one anesthetic event but not another for the same patient (personal communication Dr. Stacey Jones).

With more awareness in the veterinary community of the occurrence of hyperkalemia in greyhounds during general anesthesia, many veterinarians have instituted diligent monitoring and treatment when potassium levels begin to rise. This has allowed early identification before the potassium reaches life threatening levels and administration of medications to restore normokalemia. Intervention then facilitates continuation of the anesthetic procedure and improves safety of the patients. These life saving discoveries still leave us with questions such as why do greyhounds seem predisposed to

hyperkalemia compared to other canine breeds and are there underlying trigger(s) that cause hyperkalemia to develop during anesthesia?

It is important to consider a possible familial/genetic component in Greyhounds as it is understood that the Greyhound breed possesses distinct physiologic adaptations due to their selection as racing sighthounds (Lopez et. al, 2013). Greyhounds are reported to have naturally higher concentrations of red blood cells (hematocrit), glomerular filtration rate (an assessment of kidney function), and lower levels of serum potassium compared to other breeds (Lopez et. al, 2013). Certain diseases with a genetic cause have been documented in greyhounds (Karamatic et al 2022, Karlsson et al 2013).

As there may be a breed and geographic correlation to development of high potassium in greyhounds, our aim is to sequence the genome of three greyhound dogs from distinct geographical locations across the United States who experienced documented hyperkalemia during an anesthetic procedure and compare these genomes with the very large database of canine genome in the genetics labs here at the University of Minnesota campus to look for a potential mutation. This is an investigative study, if there are differences noted in the genomes of the affected dogs, more in depth work can be done with the ultimate goal of potentially developing a screening test. This test would identify which greyhounds might be susceptible to this life threatening problem resulting in educating owners, veterinarians, and improving anesthetic safety of these dogs. Funding will be primarily be to perform the whole genome sequencing on these samples.

IACUC approval for this study has been completed. Owners of the greyhounds will be contacted and informed of this study and we will obtain signed permission to collect a blood sample (5 ml) from their dog. The blood samples will be mailed to the University of Minnesota veterinary school (no special handling required) and will be analyzed in Dr. Steve Friedenberg's lab undergoing whole genome sequencing. The blood samples will be saved for potential later use.

Dissemination and publication of the results will occur in a peer reviewed veterinary journal, state and national veterinary conferences including ACVAA, and the greater greyhound community through social media and owner education.

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