RESEARCH PROGRESS REPORT SUMMARY

Grant 02252: Investigating a Ketogenic Medium-Chain Triglyceride (MCT) Supplement for the Treatment of Drug-Resistant Canine Idiopathic Epilepsy and Its Behavioral Comorbidities

Principal Investigator: Holger Volk, DVM, PhD

Research Institution: Royal Veterinary College, University of London

Grant Amount: $107,697.06

Start Date: 5/1/2016 **End Date:** 9/30/2019

Progress Report: Mid-Year 3

Report Due: 4/30/2019 **Report Received:** 4/29/2019

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Original Project Description:

Canine epilepsy is a chronic neurological condition, often requiring lifelong medication with anti-epileptic drugs (AEDs). Despite appropriate treatment with available AEDs, seizure freedom may not always be achievable. Indeed, over two thirds of dogs with epilepsy continue to have seizures long-term and around 20-30% remain poorly controlled on standard AEDs. The hardest to treat dogs are termed 'refractory' or 'drug-resistant' patients. There is an urgent need to develop alternative treatments to improve the quality of life (QoL) of drug-resistant patients. The ketogenic diet, originally characterized as high in fat and low in carbohydrates, has been a successful treatment in children with epilepsy for several decades, decreasing seizure activity and even leading to seizure freedom in drug-resistant patients. Recent research has identified that a component of the ketogenic diet, a medium-chain fatty acid (MCT) called C10 has direct anti-seizure effects on the brain. The investigators will assess whether dietary supplementation with ACT oil containing C10 for dogs with drug-resistant epilepsy will reduce seizure frequency and/or severity. As epilepsy has multiple impacts on QoL beyond seizure frequency, the researchers will also investigate whether the MCT supplement alters the side effect profile of AEDs, improves behavioral problems associated with epilepsy (e.g. anxiety) and cognition, and improves the stress levels of the affected dog. If successful, MCT supplements could provide a new tool for canine epilepsy treatment.

Publications:

Packer, R. M. A., Volk, H. A., & Fowkes, R. C. (2017). Physiological reactivity to spontaneously occurring seizure activity in dogs with epilepsy and their carers. Physiology & Behavior, 177, 27–33. http://doi.org/https://doi.org/10.1016/j.physbeh.2017.04.008

Berk, B. A., Packer, R. M. A., Law, T. H., & Volk, H. A. (2018). Investigating owner use of dietary supplements in dogs with idiopathic epilepsy. Res Vet Sci, 119, 276–284. https://doi.org/10.1016/J.RVSC.2018.07.004

Presentations:

Berk BA, Packer RM, Law T, Volk HA. Investigating the use of dietary supplements in dogs with idopathic epilepsy. (Abstract) Annual ECVN/ESVN conference, Helsinki, Finland. Sept. 21-23, 2017

Report to Grant Sponsor from Investigator:

Canine epilepsy is a chronic neurological condition, often requiring lifelong medication with anti-epileptic drugs (AEDs). Despite appropriate treatment with available AEDs, seizure freedom may not always be achievable. There is an urgent need to develop alternative treatments to improve the quality of life (QoL) of drug-resistant patients, who may continue to experience unpleasant AED side- effects despite their lack of success. The project will investigate whether supplementing the diet of dogs with drug-resistant epilepsy with an MCT oil containing C10 will reduce seizure frequency and/or severity. As epilepsy has multiple impacts on QoL beyond seizure frequency, we will also investigate whether the MCT supplement alters the side effect profile of AEDs the patient is already receiving, improves any behavioral problems associated with epilepsy (e.g. anxiety), cognition and improves the stress levels of the affected dog and their owner. We have made good progress after we have identified oils which have a good palatability. We have received full ethical approval, have recruited staff on the trial, have standardized and established all the additional cognitive, behavioral, blood and gait tests in the lab currently have good case recruitment numbers. While previously there was some delay in recruitment we have now finished the recruitment with the last patient completing the trial in February 2018. We were able to show that by supplementing the diet with MCT oil, seizure frequency can be reduced significantly and multiple behaviors including cognition could be improved. We have identified interesting neurotransmitter changes in the urine showing that GABA might play a role in improving seizure control in dogs fed MCT. The untargeted metabonomics did not yield an interesting hit, but we have now just finished a targeted metabonomics run and are analyzing the results.