Veterinary Health Center
MANHATTAN, KANSAS
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Pilot study on analgesic efficacy of perioperative injectable methadone for dogs undergoing TPLO surgery

Study Purpose: This study aims to determine the effectiveness and occurrence of side effects of two different dosing treatments of injectable methadone (an opioid analgesic) in canines undergoing routine surgery for cranial cruciate ligament (CCL) rupture at the Veterinary Health Center (VHC). This is an injury similar to anterior cruciate ligament (ACL) rupture in people.

Brief Study Description: Cranial cruciate ligament rupture in dogs is one of the most common condition in dogs. Left untreated, this condition can lead to lameness and progressive osteoarthritis. Therefore, tibial plateau leveling osteotomy (TPLO) is one of the most common surgeries preferred from small animal surgery surgeons to treat this condition due to high owner satisfaction rates and good limb function.

The World Small Animal Veterinary Association classifies post-operative pain for orthopedic conditions as moderate to severe. Injectable opioid analgesic serve as a cornerstone of post-operative analgesia in patients undergoing orthopedic surgery. However, there is only one currently approved and marketed food and drug administration (FDA) approved injectable opioid for use in dogs, butorphanol, and it is only approved for relief of chronic nonproductive cough associated with conditions of the upper respiratory tract. As a result, all use of injectable opioids for post-operative analgesia in dogs is extra-label. Extra-label drug use is an FDA regulated activity in veterinary medicine. As a result, an FDA approved injectable opioid for analgesic use in dogs is desirable. Methadone is a safe and effective parenteral opioid already approved in some countries for perioperative pain management in dogs.

An initial step towards achieving FDA approval of injectable methadone for analgesia in dogs is proving that it is an effective analgesic at the tested dose and administration frequency as well as reporting side effects attributable to its administration. Using an orthopedic surgical procedure will allow for FDA approval for moderate to severe post-operative pain. As TPLO surgeries are one of the most commonly performed orthopedic procedures in companion canines and are relatively standardized, this procedure serves as an ideal model for assessment of post-operative analgesic efficacy.

Procedures: This is a blinded, randomized, prospective pilot study of the efficacy of perioperative injectable methadone in dogs undergoing TPLO surgery. The primary objective of this study is to evaluate the effectiveness of methadone for adequate pain control for at least 4 hours after each dose is given, and to determine if any additional (rescue) analgesia is needed. Patients will be closely monitored for up to eight hours after the last dose is administered. Another primary objective is the reporting of adverse events noted to potentially be associated

to methadone. Methadone has been shown to have high analgesic efficacy when administered by injection and to have minimal adverse cardiovascular or respiratory effects.

Timeline: Dogs that are deemed eligible to participate in the trial will be randomized to receive either low dose methadone (0.25 mg/kg) or high dose methadone (0.5 mg/kg), while on study. Neither you, nor your study veterinarian will know which dose your dog is receiving in order to not be biased when making assessments of patients while on study.

Study participation will begin just prior to TPLO surgery and will conclude 8 hours after the last dose is administered. Each participant will receive a minimum of two doses (low vs high) of methadone. The first dose will be administered just prior to surgery and the second dose will be given four hours after the first dose. Additionally, all dogs will receive an injectable dose of carprofen (4.4mg/kg), approximately four hours after the second dose of methadone is given.

All patients will be closely monitored, at scheduled intervals, for up to 8 hours after the last dose is administered. If needed, additional analgesics will be administered. In this case, dogs will be classified a treatment failures and will receive rescue intervention at the discretion of the anesthesiologist or the attending clinician.

Inclusion and Exclusion criteria: All dogs will be pre-screened to determine their eligibility to participate in the study. This includes e.g., an orthopedic examination and preoperative radiographs to further diagnose CCL insufficiency; and bloodwork prior to anesthesia and TPLO surgery. Furthermore, there are reasons your dog may not be eligible to participate in this trial. Some exclusions include the use of certain medications just prior to TPLO surgery and enrollment [e.g., use of carprofen or other analgesic within 48 hours; NSAID use (other than carprofen) within the previous 7 days; steroid use within previous two months; previously diagnosed and uncontrolled, or clinically suspected systemic or endocrine disease; aggressive or anxious temperament that might interfere with stance analysis and subjective pain scoring; neurologic disease; significant respiratory, cardiac, hepatic, or renal dysfunction].

Client Compensation: All dogs will be pre-screened to determine their eligibility to participate in the study. This includes e.g., an orthopedic examination to further diagnose CCL insufficiency; preoperative radiographs; and bloodwork prior to anesthesia and TPLO surgery. If your dog is deemed eligible to be enrolled, the study funds will cover the cost of the preoperative bloodwork (CBC and chemistry), two nights of daily care, and the study medication (methadone). Furthermore, there are no fees for participation in this study. No direct compensation is provided and the owner is responsible for e.g., preoperative radiographs; TPLO surgery and the associated anesthesia; and any additional testing or treatments, as recommended by the attending clinician.

Owner Responsibilities: You are responsible for disclosing full and true information to the study investigators regarding your pet's medical history, including current or previous diseases and all medications. Your dog's participation in this trial will end approximately 12 hours after his/her surgery. There are no follow up appointments required for this trial.

Contact Information: Please contact the Clinical Trials Coordinator at the Veterinary Health Center, for more information about this study.
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