Development and Characterization of the Monosodium Iodoacetate-Induced Osteoarthritis Model in Canines: Pharmacological Reversal of Pain Symptoms and Histopathological Findings

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Background
- The translation and relevance of pain in laboratory animals has been challenged due to the reliance on reflexive assessments as opposed to spontaneous or pain-suppressed behaviors.
- Despite the fact that they are the most commonly studied species in preclinical pain research, rodents - as prey animals - rapidly adapt to chronic pain conditions and rarely show overt signs of pain and distress.
- The monosodium iodoacetate (MIA) model of osteoarthritis (OA) pain has been studied extensively in rats, and is perhaps the most commonly used model for the assessment of novel therapeutics to treat OA-related pain.
- Common behavioral endpoints in the MIA model in rats include static or dynamic mechanical hyperalgesia, hind limb grip strength, and mechanical allodynia ipsilateral to the site of injection.

Materials & Methods
- All procedures were performed according to the Laboratory Animal Care and Use Committee prior to study start.
- Purpose-bred beagle dogs (Ridglin Farms, Mount Horeb, WI, USA), approximately 10 months of age were used in this study.
- OA induction: Under isoflurane anesthesia, each animal received an injection of 200 mg MIA in a 500 µL volume into the articular space of the right stifle on Day 0 and again on Day 1. Once deemed fit by veterinary staff, animals were exercised on a treadmill for 10-15 minutes 5 times per week.
- Veterinary assessment: Animals were assessed 1-2 times per week for signs of lameness, swelling, alterations in stance/weight bearing, and in response to palpation. Observations were noted as absent, mild, moderate, or severe.
- Functional assessment: Prior to MIA injection, animals were trained to perform two tasks – walk up and down a flight of stairs, and jump on to and off of a platform. The flight of stairs was composed of 9 stairs (4 up, 4 down, 1 on top) and each stair was approximately 15 cm in height. The platform was approximately 25 cm in height. All surfaces were covered in a non-slip rubber material.

Results
- Under isoflurane anesthesia, each animal received an injection of 200 mg MIA in a 500 µL volume into the articular space of the right stifle on Day 0 and again on Day 1. Once deemed fit by veterinary staff, animals were exercised on a treadmill for 10-15 minutes 5 times per week.
- In the immediate post-injection period, profound swelling with pain in the injected limb was evident in all animals and was successfully treated with buprenorphine (0.5 mg) per veterinary order.
- Intrathecally injected MIA produced a short-term joint inflammation in all animals, with resolution 4/6 animals 5 days after the second MIA injection, and with resolution in 1/6 animals within 11 days. One animal displayed intermittent clinical signs of inflammation for at least 33 days following the second MIA injection.
- Lameness was not observed in any animal beyond the initial 5 day period with the exception of a single observation for 1 animal on a single day (25 days after the second MIA injection, slight lameness while walking).
- Animals generally displayed normal behaviors in their home cages throughout the study.

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