COMPANION ANIMAL
Research Award

Sustained release of locally delivered celecoxib provides pain relief for osteoarthritis in dogs: a prospective, randomized controlled clinical trial

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Introduction
Osteoarthritis (OA) is a common cause of pain and lameness in dogs. Non-steroidal anti-inflammatory drugs are effective against OA pain, but may be accompanied by side effects. Local administration via drug delivery platforms could offer a suitable treatment strategy for long-term OA management. The aim of this prospective, randomized controlled study was to investigate the efficacy of the intra-articular sustained release of celecoxib, in client-owned dogs with established OA.

Material and methods
Celecoxib release profiles and its anti-inflammatory properties were investigated in canine primary chondrocytes in monolayer culture for 28 days. Thirty dogs with clinical and radiological OA were included: 20 patients received celecoxib-loaded microspheres (70 mg/mL PEAMs, with 20wt% celecoxib), 10 received 70 mg/mL unloaded microspheres (placebo). Injection volume was adjusted to body weight: 15-30kg, 30-45kg and >45kg received 0.5, 1 and 1.5mL respectively, corresponding to 5.3mg, 10.6mg and 16mg. Weight-bearing was assessed by visual lameness scoring, kinetic gait analysis prior to, and 1 and 2 months after treatment; radiographs were scored for OA and synovial fluid was analysed after 2 months. Pain-related behaviour was scored by the owner via a questionnaire.

Results
In vitro, celecoxib release was shown for 28 days and suppressed prostaglandin E_2 (PGE_2), a biomarker of inflammation, during the entire culture period, without negatively influencing cellular homeostasis. Intra-articular administration of celecoxib-loaded microspheres improved lameness and pain-related behaviour. PGE_2 content in the synovial fluid of dogs treated with celecoxib-loaded microspheres was significantly lowered. Radiographic OA scores were not influenced by treatment.

Conclusions
Canine OA patients improved clinically after local application of celecoxib-PEAMs. These results provide a proof-of-concept for further translation of intra-articular administration of celecoxib-loaded microspheres from bench to (veterinary) bedside.