Characterization of Lumbar Facet Joint Osteoarthritis-Induced Back Pain and Therapeutic Drug Tests.

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INTRODUCTION: Degeneration of lumbar facet joints (FJs) has been implicated in lower back pain. MIA-induced cartilage degeneration and pathological alterations resemble OA-like structural modifications in rat knee joints which are correlated with behavioral changes. The main objective of this study is to establish links between FJ degeneration and the development of chronic back pain by examining the pathological lesions in cartilage and structural changes in subchondral bone in FJ upon intra-articular MIA administration. In addition, this study explores therapeutic modulation of chronic pain in a facet joint OA model by testing selective drugs for analgesic effects on back pain relief.

METHODS: We created an animal model for FJ degeneration by open surgery and intra-articular injection of monosodium iodoacetate (MIA) in FJs (L3/L4, L4/L5, L5/L6) of Sprague Dawley rats followed by behavioral pain tests. Animal behavioral tests: Vocalization threshold to the force (g) of an applied force gauge was measured by pressing the 0.5cm² device tip directly on the skin (digitalized algometer, Bioseb Co). The pressure was slowly increased at 100g/cm² per sec until an audible vocalization was heard. A cutoff pressure of 1000g/cm² was used to prevent tissue trauma. This pain test is clinically relevant as patients are tested by mechanical pressure on facet joint or disc to examine the degree of back pain. Histological, biochemical assessments and µCT imaging: Structural changes and proteoglycan (PG) loss and alterations of subchondral bone structure by MIA injection were measured. Drug treatments: Therapeutic modulation of chronic pain using pharmaceutical drugs was investigated by administration of morphine, pregabalin, celecoxib (selective inhibitor of COX-2) and ketorolac (inhibitor of COX-1 and -2). Quantitative RT-PCR and western blotting analyses were performed for examining mRNA and protein levels as previously described.

RESULTS:

CONCLUSION & DISCUSSION: (1) Intra-articular injection of MIA in to FJs causes OA-like joint degeneration with alteration of subchondral bone structure, which is correlated with behavioral chronic back pain responses assessed by pressure hyperalgesia. This animal model may prove to be a useful tool for studies on mechanisms of vertebral OA and for the development of new strategies that can prevent the pain-causing structural and functional changes that characterize FJ degeneration. (2) Pregabalin and Morphine are highly analgesic for FJ degeneration-caused chronic pain. Prominent anti-hyperalgesic effects were achieved by a single administration of the 10 mg/kg dose of pregabalin. The computed ED₅₀ at the time of peak effect (120 min after administration) was 5.39 mg/kg. (3) Modest effects are achieved with a selective COX-2 inhibitor and no response is observed with an NSAID. (4) These results suggest that chronic pain by FJ degeneration is a primarily a neuropathic syndrome rather than an inflammatory process, because gabapentoids are useful in patients with neuropathic pain (and in animal models of neuropathic pain). In contrast, the efficacy of NSAIDs in neuropathic pain patients is still unclear. These findings corroborate our recent report that chronic knee joint OA-like pain caused by intra-articular MIA injection may be linked to neuropathic pain pathways. (5) Because MIA injection produces rapid joint cartilage loss, the pain syndrome observed at 28 days post MIA should be considered an advanced stage of OA. Consequently, drugs widely used to treat patients with OA such as NSAIDs may be of limited use once joint destruction is complete.

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