ACUTE TREATMENT OF OSTEOARTHRITIC KNEES WITH AN ENDOCANNABINOID HYDROLASE INHIBITOR AMELIORATES CHRONIC JOINT PAIN

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INTRODUCTION / AIM

The alleviation of osteoarthritis (OA) pain is inadequate in most patients and current drug therapies are associated with toxic side-effects. We have previously shown that joint inflammation and OA pain can be alleviated by promoting endocannabinoids in the arthritic joint. The primary limitation of endocannabinoids as a treatment strategy is that they are rapidly broken down by enzymes such as fatty acid amide hydrolase (FAAH). By using the FAAH inhibitor URB597 we have been able to reverse OA pain acutely. The aim of the present study was to determine whether early, acute administration of URB597 during the onset of OA could alter joint pain long-term.

METHODS

Experimental OA was induced in male C57Bl/6 mice (20-42g) by injecting sodium monooiodoacetate (0.3mg) into the right stifle joint. Animals were then treated with four injections of URB597 (0.3mg/kg i.p.) administered on four consecutive days (days 0-3). On day 14, central sensitization was assessed by applying von Frey hairs to the plantar surface of the ipsilateral hindpaw, while direct joint nociception was determined by hindlimb incapacitance. The effect of URB597 was compared to vehicle-treated animals.

RESULTS

OA mice demonstrated tactile allodynia but not a weight bearing deficit. The hypersensitivity of OA mice to von Frey hairs was inhibited by early treatment with URB597 (P<0.05; n=8-10). Hindlimb weight bearing was unaffected by URB597.

DISCUSSION / CONCLUSIONS

Early treatment of OA knees with URB597 attenuated late onset tactile allodynia. These data suggest that acute promotion of endocannabinoids in OA joints can attenuate the development of central sensitization thereby protecting the joint against future chronic pain.

OTHER AUTHORS

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