Anti-inflammatory and antinociceptive effectiveness of palmitoylethanolamide in a rat model of osteoarthritis: a comparison with nimesulide and acetaminophen

G. Donvito, F. Comelli and B. Costa

Dept. of Biotechnology and Bioscience, University of Milano-Bicocca, Milano, Italy

Osteoarthritis (OA) is the most prevalent joint disease that reduced quality of life. Acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs) are employed for pain relief associated with OA. However, their prolonged use induces serious side effects. So the identification of alternative drugs is crucial for the OA pathology. Previous studies by our research group have shown that the exogenous administration of palmitoylethanolamide (PEA), an endogenous lipid analogous of the endocannabinoid anandamide, possesses anti-inflammatory and antinociceptive properties. Aim of this study was to investigate the anti-inflammatory and antinociceptive efficacy of PEA also in the well known OA model induced by intrapatellar injection of MIA and to compare its effect with that evoked by nimesulide and acetaminophen. PEA 50 mg/kg, nimesulide 10 mg/kg and acetaminophen 300 mg/kg were orally administered for 21 consecutive days starting from the day after the pathology induction. As expected, rats developed a significant knee swelling, as index of inflammation. We observed that PEA was able to completely abolish knee swelling, as nimesulide and acetaminophen treatment. Additionally, as further index of inflammation, the day after MIA-injection, rats developed a significant decrease in thermal withdrawal latency. Treatment of MIA rats with PEA resulted in a significant relief of thermal hyperalgesia, as observed after nimesulide and acetaminophen administration. After MIA-injection, rats also developed mechanical allodynia, as a index of chronic pain. Treatment of MIA rats with PEA resulted in a significant, even if partial, relief of mechanical allodynia, as nimesulide and acetaminophen treatment. However, PEA anti-allodynic effectiveness was major than that elicited by nimesulide and acetaminophen. We also evaluated the motor functionality by a walking track analysis. In particular, according with the footprints, the SFI (sciatic functional index) value was calculated: a value approximately around zero indicates a normal locomotor function, while a value close to -100 indicates a significant impairment of locomotor function. As expected, intra-articular injection of MIA resulted in a significant increase of joint discomfort. PEA treatment completely restored locomotor functionality and this effect remained stable after one week of treatment, as nimesulide and acetaminophen treatment. However, only PEA treatment preserved such an effect at the end of the treatment. In addiction, we observed a mild/moderate cartilage damage after MIA injection (large chondral erosions and exposure of subchondral bone). Repeated PEA treatment preserved cartilage from damage, conversely to repeated nimesulide and acetaminophen treatment. OA patients show elevated levels of pro-inflammatory and pro-algogen mediators such as the tumor necrosis factor-alpha (TNF-α) and nerve growth factor (NGF) in their synovial fluid. Starting from these observations, we also determined the NGF and TNFα levels in the synovial fluid of MIA rats. Repeated administration of PEA restored the physiological NGF level, as nimesulide and acetaminophen administration. However, none of the three drugs has an effect on TNFα increasing. In conclusion, we demonstrated that the repeat administration of PEA reduced knee swelling, mechanical allodynia, thermal hyperalgesia, motor impairment and slowed the degradation of cartilage interposition in MIA-induced osteoarthritis model. PEA efficacy was superimposable and in some cases greater than that evoked by nimesulide and acetaminophen, two of the most drugs used for OA treatment, so suggesting a therapeutic use of PEA in clinic, without showing side effect.