REPEATED TREATMENT WITH AM404 REDUCES MECHANICAL ALLODYNIA AND THERMAL HYPERALGESIA IN A MODEL OF NEUROPATHIC PAIN WITHOUT CENTRAL EFFECTS

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Cannabinoids have been shown to be effective in alleviating pain in several animal models (1). Among these, the rat sciatic nerve chronic constriction injury (CCI) (2) is one of the most frequently used to study the drug efficacy in neuropathic pain, characterized by thermal hyperalgesia and mechanical allodynia. In this study we report the effect of N-(hydroxyphenyl)-5Z,8Z,11Z,14Z,-eicosatetraenamide (AM404; 1, 3, and 10 mg/kg, sc), an anandamide transporter inhibitor, on plantar and von Frey tests on injured paw (3). Acute or repeated (chronic) treatments of AM404 resulted in an increase of withdrawal threshold in both tests evaluated at 7^{th} and 14^{th} after CCI. Furthermore, using CB1 and CB2 antagonists (SR141716A and SR144528, respectively), the involvement of cannabinergic system and the main role of CB1 receptor were demonstrated. Finally, we evaluated the effect of AM404 on the expression of induced inflammatory enzymes, which are involved in the development and maintenance of neuropathy. Chronic treatment with this drug reduced protein expression of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) in injured sciatic nerves.
Furthermore, AM404 failed to modify the motor coordination and the basal withdrawal of thermal and mechanical thresholds measured in controlateral paws.
Our results demostrated that AM404 reduces mechanical allodynia and thermal hyperalgesia , in a model of neuropathic pain, probably through the reduction of inflammatory enzymes without psychoactive effects.

References

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