LONG-LASTING ANTINOCICEPTIVE EFFECTS OF AMMONIUM GLYCYRRHIZINATE IN MICE

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Introduction: Chronic pain, considered to be pain lasting more than three months, is a common and often difficult to treat condition that can significantly impact upon function and quality of life. Although advances have been made in treatments for chronic pain, it remains inadequately controlled for many people and as a result there has been increased interest in integrative and alternative medicine strategies to help manage chronic pain. Licorice, the root of Glycyrrhiza glabra, is one of the oldest and most commonly used herbs in Chinese traditional medicine. Glycyrrhizin (GL), a major active constituent isolated from licorice, possesses a variety of pharmacological activities and, of note, antinociceptive effects were also reported for glycyrrhizic acid and derivatives. These effects, were observed short time after glycyrrhizinate (AG) or derivatives administration, but no data are reported on the effects induced by AG on pain in animal models 24-48h after the administration. The aim of the present investigation, was to evaluate the long-lasting effects induced by AG after a single administration using several pain models in mice.

Materials and methods: We evaluated the effects of AG in the following mouse model of pain after intraperitoneal (i.p.) administration: the writhing test, the formalin test and the zymosan-induced hyperalgesia and edema. Male mice were divided into three groups of 10 animals each: vehicle (10 ml/kg), AG (50 mg/kg,) and AG (150 mg/kg). Nociceptive threshold was measured 24h after the administration.

Results: In the writhing test, AG administered i.p. at the dose of 50 mg/kg 24hours before the test, light reduced writhes induced by acetic acid. Strong inhibition of the number of writhes was observed when AG was administered at the dose of 150 mg/kg. In the formalin test, the administration of AG at the dose of 50 or 150 mg/kg i.p. 24hours before formalin, did not change the nociceptive response induced by aldehyde in the early phase of the test. A significant reduction of the licking and biting activity induced by formalin, was instead observed in the late phase of the test 24h after AG administration. In the zymosan-induced hyperalgesia, AG administered at low dose (50 mg/kg, i.p) induced a light but not significant increase in pain threshold and edema. AG administered at the high dose (150 mg/kg, i.p.) was able to strongly increase nociceptive threshold and decrease edema volume from 1to 24-48h after the administration.

Discussion and conclusion: In the present study, we evaluated the potential long-lasting anti-nociceptive effects of glycyrrhizin using several animal models of pain. We found that glycyrrhizin caused significant long-lasting reduction of nociception and edema development, and this effect is most likely due to the inhibition of different aspects and mediators of inflammation, as already known for AG. Result of the present study, indicated that AG increase nociceptive threshold until 24h after a single administration in several animal models of pain, thus we cautiously suggest that AG might be developed as a therapeutic agent for the treatment of chronic painful conditions in humans.