U74389F

The purpose of a investigation was to compare the effects of treatment with glucocorticoid steroid methylprednisolone (MP) and the 21-aminosteroid U-74389G on the conduction of somatosensory evoked potentials (SEPs) during experimental spinal cord compression. Forty-five adult male Wistar rats were anesthetized and a laminectomy performed at the Th9-Th10 level. Animals with the same SEP patterns prior to and after laminectomy were randomly allocated to one of three groups (15 rats in each). A 14.8-g weight was applied to the dural surface of the spinal cord for 60 min. The SEPs were continually recorded during compression. The rats received a single intravenous bolus dose of three different agents two minutes after the start of compression. Animals in the first group received 0.5 ml of 0.9% NaCl, the second group received 30 mg/kg methylprednisolone and the third group received 3 mg/kg U-74389G. Following drug infusion the time period required for the SEPs to be completely suppressed was assessed. If the SEPs were not fully suppressed, the amplitude of the most stable and significant component of the SEPs was measured. The time taken to complete the SEPs suppression was significantly shorter in the control group ($p < 0.001$, Wilcoxon) than in the groups with either MP or U-74389G. However, the time taken to achieve full suppression was not significantly different between the MP and U-74389G groups. The proportional reduction of amplitude N1P1 was significantly different between the control and MP groups as well as between the control and U-74389G groups. The proportional reduction of amplitude N1P1 was not significant between the MP and the U-74389G groups. The present data indicate that both the glucocorticoid steroid MP and the 21-aminosteroid U-74389G protect spinal cord function to a similar extent during mild compression [1)].

U74389F, is beneficial for treatment of acute spinal cord trauma in rats, as it has been demonstrated that the bolus administration of the same compound one hour after injury facilitates the return of the spinal cord function as measured by electrophysiological recordings in this compression animal model of spinal cord trauma. Cortical somatosensory evoked potentials (CSSEPs) were recorded as an indicator of spinal cord function before and after a severe compression injury. Vital signs and the CSSEPs were monitored up to five hours post-injury. U-4389F treatment was given as a single injection (15 mg kg-1) one hour prior to the injury which was followed by a continuous infusion (3 mg kg-1h-1) during the procedure. The CSSEPs were abolished immediately after this injury both, in the untreated and treated animal groups. The majority of the treated animals (80%) demonstrated recovery of the CSSEPs within the second hour post-injury. The control group showed 40% recovery at this time period. At five hours post-injury, recovery rates were 47% and 87% for control and treated groups respectively. We conclude that the administration of the 21-Aminosteroid, U74389F, one hour prior to spinal cord injury facilitates the return of spinal cord function as measured by CSSEPs in a compression rat model of acute spinal cord trauma, supporting and verifying our previous experiences using the same compound as i.v. bolus injections one, two and three hours after the trauma, respectively [2)].

The aim of a study was to determine whether brain edema induced by a cryogenic injury can be influenced by the 21-aminosteroid U74389F. A cortical freezing lesion was applied to the right parietal region of Sprague-Dawley rats under ketamine-xylazine anesthesia. Systemic blood pressure was monitored in the peritraumatic period. Four different doses of U-74389F (A-D) were studied for their effect on post-traumatic brain swelling and edema. Respective control groups received only the solvent, citric acid buffer. (A) 3 mg/kg b.w.i.p. (total dose) 30 min before, 1 and 12 h; post trauma

(p.t.); (B) 9 mg/kg b.w.i.v. 30 min before, 1 and 12 h p.t.; (C) 25 mg/kg b.w.i.v. 30 min before, 1, 6, and 12 h p.t.; (D) 50 mg/kg b.w.i.v. 15 min before, 15 and 30 min as well as 1, 2, 6, and 12 h p.t. 24 h after trauma, brains were removed and hemispheric swelling and water content were determined from the difference between wet and dry weight. Application of the 21-aminosteroid U-74389F moderately reduced post-traumatic brain swelling in all treatment groups: (A) 5%, (B) 9%, (C) 12%, and (D) 14%. In parallel with this, the increase in water content of the traumatized hemisphere was marginally lowered by U-74389F in all groups; in (C) e.g. from 1.9 +/- 0.1% to 1.7 +/- 0.1%, p = 0.07. These two findings taken together indicate that the 21-aminosteroid U-74389F moderately reduces post-traumatic swelling and edema [3)].

1)
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