The Effects of Progesterone Receptors’ Antagonist RU-486 on Brain Edema, Intracranial Pressure and Neurological Outcomes after Traumatic Brain Injury

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Abstract

In previous studies, the neuroprotective effect of progesterone in diffuse traumatic brain injury has been shown. This study used mifepristone (RU-486), a potent progesterone receptor antagonist, to evaluatethe hypothesis that the neuroprotective effect of progesterone in traumatic brain injury is mediated by the progesterone receptors. The ovariectomized rats were divided into 6 groups. Brain injury was induced by Marmarou’s method. Progesterone was injected 30 minutes after traumatic brain injury, and RU-486 was injected before traumatic brain injury and also before progesterone treatment. The brain water content (BWC) and Evans blue dye content (EBC) were measured 24 and 5 hours after traumatic brain injury, respectively. The neurologic outcomes and intracranial pressure (ICP) were assessed before, 4, and 24 hours after traumatic brain injury. BWC and EBC were less in progesterone -treated group comparison to vehicle group. RU-486 eliminated the effects of progesterone on brain edema and blood brain barrier permeability. ICP was increased significantly after trauma, and progesterone decreased intracranial pressure at 4 and 24 hours after traumatic brain injury in comparison to vehicle. This inhibitory effect was also eliminated by treatment with RU-486. RU-486 also inhibited the progesterone induced increase in neurologic outcomes following traumatic brain injury. The results suggest that a genomic pathway of progesterone receptor have probably a role in the neuroprotective function of progesterone following traumatic brain injury.

Keywords: Progesterone Receptors’ Antagonist, RU-486, Traumatic Brain Injury

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