PROTECTIVE EFFECT OF ALPHA-1 ADRENOCEPTOR ANTAGONIST ON N-METHYL-D-ASPARTATE–INDUCED EXCITOTOXICITY IN RAT HIPPOCAMPAL CA1 NEURONS

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Introduction & Objectives: Recently, it has been suggested that N-methyl-D-aspartate (NMDA) glutamate transmission has an essential role in the development of OAB after cerebral infarction (CI). We examined how 1α AR acts on neuronal activation in mammalian central nervous system neurons, to determine the protective effect of tamsulosin against NMDA-induced excitotoxicity in rat hippocampal CA1 neurons.

Material & Methods: Slices of hippocampi of Sprague-Dawley rats (postnatal day 7) were cultured, pre-treated with tamsulosin before NMDA treatment, and divided into 6 groups: the control group, 10−4 M NMDA-treated group, 10−7, 10−6, 10−5, and 10−4 M tamsulosin–pretreated group. NMDA-induced neuronal damage of the hippocampal CA1 region was visualized through the Propidium iodide (PI) staining. And, electrical recordings were performed.

Results: After 36 h of exposure to 10−4 M NMDA, PI uptake was markedly increased. The PI uptake in the groups pre-treated with tamsulosin at 10−7, 10−6, 10−5, and 10−4 M was decreased, respectively. In electrophysiological study on dissociated CA1 neurons, glutamate (10−5 M) was applied every 2 min. The magnitude of the glutamate-induced ion current was decreased at 2, 4, 6, 8, 10, and 12 min, respectively, after 10−5 M and 10−4 M tamsulosin application. Pre-treatment with 10−5 M tamsulosin slightly inhibited the glutamate-activated ion current; however, this inhibition was not statistically significant. Pre-treatment with 10−4 M tamsulosin reversibly inhibited glutamate-activated ion current.

Conclusions: The inhibitory effect of tamsulosin on NMDA-induced current may be a mechanism for the neuroprotective effect of 1α AR antagonist against glutamate toxicity in CI.