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Poster Presentation

Neuoprotective Effect of Cannabinoid CB1 Receptor Antagonists Rimonabant and AM251 on Hypoxic Mouse Model of Brain Oxidative Stress

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Abstract

Introduction: The hypoxic state, in which experimental animals were subjected to an atmosphere of 5% O2 and %95 N2, has been used to screen agents for possible cerebral protection by measuring their ability to prolong survival time in mice exposed to hypoxia. Researchers showed that rimonabant and AM251 allosteric potentiate all but the β1 subunit containing GABAA receptors at nM concentrations. We also showed the potentiating of GABA receptors prolonged the survival time of mice subjected to hypoxia and brain ischemia model. Oxidative stress is caused by excessive production of reactive oxygen species such as hydroxyl radical, superoxide anion radical and hydrogen peroxide. In this study we aimed to test potential protective effects of negative manipulation of cannabinoid receptors. **Materials and Methods:** Male mice weigh 25 to35 gram was separated into 4 groups of 10. The first group give 0.5 cc normal saline IP. Group2: 100 mg/kg phenytoin as standard neuroprotective agent. group3: 10 mg/kg Rimonabant and Group 4:1 mg/kg AM251 injected 30 minutes prior to hypoxia started. Hypoxic anoxia state was performed in closed glass box with N2 pumped and survival time measured by a chronometer. In all sessions the survival time from closing the door of box to stopping the animal breath was measured and recorded. The data were under appropriate statistical tests in SPSS and Prism 6 software. **Results:** In phenytoin group as a standard protective in hypoxic investigations, the survival time increased distinctly in all groups as expected. AM251 showed significant anti hypoxic effect than control group and comparable to phenytoin. Also Rimonabant have same increased in survival time in contrast to control. **Conclusion:** According to the result of this study, antagonizing the cannabinoid receptor, may have protective role in hypoxic trauma situation of nervous system. Although it is required to further investigation. We suggested to test these compound in ischemic situation with histological confirmations study.

Keywords: Hypoxia, Cannabinoid receptor، Neuroprotection

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