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Evaluating the anti-hypoxic and anti-ischemic effects of some GABA-receptor mimetics in Brains of mice and rats

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Introduction: Cerebrovascular Accident (CVA) in which Cerebral hypoxia and Ischemia happen is one of the most important causes of disability and mortality in adults, however, it is not treated properly yet. Since the main reason of neural death in this disease is the release of excitatory substances like glutamate, inhibition of neurons with GABA receptor mimetics may reverse the excitotoxicity. In this study, we investigated the anti-hypoxic and anti-ischemic effects of diazepam and phenobarbital (GABA-A allosterics) and baclofen (GABA-B agonist) in comparison to phenytoin (sodium channel blocker and positive control) and normal saline (negative control).

Materials and Methods: The mentioned medicines were injected intra-peritoneally to mice in different doses before the hypoxia. For inducing hypoxia, we put mice individually in a sealed glass container in presence of soda lime and recorded their survival time. In order to create ischemic stress in rats for histopathological evaluation of the hippocampus, we used four-vessel occlusion method. 15 minutes after the ischemic period, 0.6-1cc normal saline, phenytoin 50mg/kg, diazepam 10mg/kg and phenobarbital 40mg/kg were then administered into the rats' peritoneums.

Results: There was a significant increase in the survival time of mice receiving 2mg/kg ($PV < 0.01$), 5mg/kg, 10mg/


kg, 15mg/kg ($PV < 0.001$) of diazepam, 40mg/kg ($PV < 0.01$) and 60mg/kg ($PV < 0.001$) of phenobarbital, and 10mg/kg, 20mg/kg, 30mg/kg and 40mg/kg of baclofen ($PV < 0.001$) compared to the negative control group (23.03 ± 0.78 minutes), while, the figure for phenytoin 100mg/kg (positive control) was 55.3 ± 3.21 minutes ($PV < 0.001$). Based on histopathologic examinations, diazepam had no noticeable anti-ischemic effect, however, the preventive effects of phenytoin and phenobarbital was prominent in comparison to the control group.

Conclusion: This study reveals that these compounds may be of great benefit in treating hypoxic-ischemic diseases of CNS.

Speaker Biography

Faezeh Nemati Karimooy has been graduated as an MD from Mashhad University of Medical Sciences, Iran. After graduation she immediately started to work as a GP and the Head of a general health center in Taybad city. Along with her GP career, she was engaged in neuroscience researches. She has also written a book in Persian- translation and completion- named "Sleep and Its Disorders" which is going to be published soon. As an MD, she is also interested in emergencies and collaborated in writing a book in Persian on procedures in emergency medicine.

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