Effects of Different Doses of Some GABAergic Agents in Mouse Brain Under Hypoxic State: Possible Role in Neuro-Inflammation

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Abstract

Introduction: Pro-inflammatory chemokines and cytokines such as MCP-1 and IL6 can activate microglial cells that has found in some neuro-inflammatory disorders. Hypoxia activates cerebral endothelial cells to release these pro-inflammatory mediators. We aimed to investigate the anti-hypoxic effects of different doses of some GABAergic agents.

Materials and Methods: We randomly divided 150 mice into 3 drug groups (n=10) and tested them by three discrete experiments. We investigate the effects of phenobarbital, diazepam and baclofen in comparison with phenytoin as standard neuro-protective agent and normal saline as a control group. Mice in each group were undergone acute hypoxic conditions, including: 1. Closed empty chamber 2. Closed chamber with soda lime as CO2 absorbent 3. Closed chamber with the substitution of N2 with O2. The survival time (the interval time between closing the chamber cap to stop the rat’s breath) was measured. The data in each group were analyzed by prism 6.

Results: In diazepam treated groups, despite no effect seen at lower doses, a significant effect was observed at the dose of 10mg. In soda lime group phenobarbital was most effective at a dose of 40mg although it was less than phenytoin. In the other two phenobarbital groups highest effect was observed at the dose of 30mg. The most effective dose of baclofen was 20 mg in N2-hypoxic group, 30mg in the one without soda-lime and 40 mg in the group with soda-lime however it was not as effective as phenytoin in the last group.

Conclusion: With respect of the significant and direct correlation of survival time to the dose of diazepam, it is suggested to use this drug, to alleviate the Neuro-inflammatory complications as a result of hypoxia.

Keywords: Gaba receptors, Hypoxia, Neuroprotective

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