INVESTIGATION OF NEUROINFLAMMATORY AND NEUROPROTECTIVE EFFECTS OF 6-PARADOL IN AMYLOID BETA INFUSED ALZHEIMER DISEASE RAT MODEL

SUMMARY

Alzheimer's disease (AD) is a progressive type of age related dementia in humans. It is considered that increase in oxidative stress due to microglia activation may cause progression of the disease. Studies have shown that 6-Paradol, one of the ginger metabolites, has positive effects on memory and reduces microglia activated-neuroinflammation. Therefore, the aim of the present study is to investigate the neuroprotective and anti-neuroinflammatory effects of 6-Paradol in amyloid beta ($A\beta_{1-42}$)-injected AD model in rats. In this study, 33 adult rats (12-month-old) were divided into 5 groups; healthy control (n=6, no treatment), Sham control (n=6, $A\beta_{1-42}$ solvent (5 µL) injected by intracerebral injection (i.c.v)), $A\beta_{1-42}$ (n=9, 5 µL $A\beta_{1-42}$ (i.c.v.) to the hippocampus), Positive control (n=6, 5 µL $A\beta_{1-42}$ (i.c.v.) and 21 days of donepezil (2mg/kg) treatment), 6-Paradol (n=6, 5 µL $A\beta_{1-42}$ (i.c.v.) and 2 weeks of 6-Paradol (5 mg/kg) treatment). Behavioral tests were performed after two weeks of treatment. Then, the rats were sacrificed and histological and molecular studies were performed. As a result, compared to the control group, it was observed that the rats in the $A\beta_{1-42}$-injected AD group had delay in learning and deficiency in memory performance which measured by Morris Water Maze and passive avoidance test. 6-Paradol had no effect on learning and memory performance of rats. According to the resuls obtained by hematoxylin and eosin, the histological structures of brain tissues of the control groups and pozitive drug group were similar each other which were healthy appearance. However, in sections belonging to $A\beta_{1-42}$ and 6-Paradol groups, it was observed that the nuclei of some neuronal cells were irregular and pycnotic. Also, there was vacuolization in brain tissue of the 6-Paradol group. According to Nissl staining, there was a significant decrease in the number of CA1 pyrimidal cells in the $A\beta_{1-42}$ group of hippocampus ($p<0.05$). An increase in cell count was observed in the treatment groups given Donepezil and 6-Paradol. In Congo-red staining, which shows the presence of amyloid plaques, there was no change in the groups with treatment. Protein expression studies performed with Western blotting showed that apoptosis increased in the $A\beta_{1-42}$ group and decreased significantly in the treatment groups. Also the expressions of fractalkine and fractalkine receptors, which are associated with microglia activation, were examined, and there was no significant change in the amount of fractalkine ligand among groups, there was a significant increase in its receptor in the $A\beta_{1-42}$ group and this increase was improved by 6-Paradol treatment. While the amount of AD indicator proteins (pTau and PSEN1) increased with $A\beta_{1-42}$, the concentrations of these proteins decreased to control levels by 6-Paradol treatment. No significant difference was observed among groups in the expression of BACE and Reelin proteins. In summary, the 6-Paradol teratment in AD model of rats shows an anti-inflammatory effect as it causes an improvement in microglia-related proteins.

Keywords: Alzheimer's Disease, 6-Paradol, Neuroprotective, Neuroinflammation