Recuperation of experimental Alzheimer’s and vascular dementia by selective modulation of mineralocorticoid receptor and HIV-protease

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Introduction: Alzheimer’s disease and vascular dementia are the most common forms of dementia worldwide. My research lab is working in this area and in the recent time, we have worked on various models of Alzheimer’s disease and vascular dementia. Mineralocorticoid receptors and proteases (like HIV-protease) have variety of functions in almost all areas including CNS and CVS.

Objectives: The present study has been structured to investigate the role of eplerenone, a selective aldosterone antagonist and indinavir, a selective HIV-protease inhibitor in experimental Alzheimer’s disease and vascular dementia.

Methods: Alzheimer’s disease condition was induced in mice with the help of intracerebroventricular (i.c.v.) injection of streptozotocin (STZ). Whereas, vascular dementia was induced in rats by administration of deoxycorticosterone acetate subcutaneously (DOCA) and salt in drinking water. Morris Water Maze and elevated plus maze tests were used for assessment of learning and memory. Endothelial function was assessed using BIOPAC system. Oxidative stress (aortic superoxide anion, serum and brain thiobarbituric acid reactive species, glutathione), nitric oxide levels (serum nitrite/nitrate), inflammation (MPO) and acetylcholinesterase (AChE) activity were also measured.

Results: i.c.v.-STZ and DOCA-salt treated animals have shown impairment of learning, memory, along with higher levels of oxidative stress AChE activity and inflammation. DOCA-salt administration has also induced endothelial dysfunction in rats. Eplerenone and indinavir have significantly attenuated i.c.v.-STZ and DOCA-salt induced impairment of learning, memory, endothelial function and alterations in various biochemical parameters.

Conclusion: It may be concluded that i.c.v.-STZ and DOCA-salt have induced Alzheimer’s disease and vascular dementia respectively, which was attenuated by eplerenone and indinavir. Thus, modulators of mineralocorticoid receptors and HIV-protease may further be explored for their potential in Alzheimer’s disease and vascular dementia.

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