Abstract

Title: "Role of angiotensin converting enzyme inhibition in experimentally induced Alzheimer's disease"

Background: Reactive oxygen species (ROS) and renin-angiotensin system (RAS) are possible pathogenetic factors underlying Alzheimer's disease (AD) progression.

Aim: To evaluate the effects and protective mechanisms of a ROS scavenger, tempol, and a central RAS inhibitor, perindopril, against lipopolysaccharide (LPS)-induced AD.

Material and methods: Mice were allocated into a normal control group, an Alzheimer control group, a tempol treatment group, and two perindopril treatment groups, receiving test agents or vehicles for 7 consecutive days following a single i.p. dose of LPS. A behavioral study was conducted to evaluate spatial and non-spatial memory in mice. A biochemical study followed to explore the mechanisms of protection via the assessment of brain levels of Aβ and brain-derived neurotropic factor (BDNF) as Alzheimer markers, tumor necrosis factor-alpha (TNF-α), nitric oxide end products (NOx), neuronal nitric oxide synthase (nNOS) and inducible nitric oxide synthase (iNOS) as inflammatory markers, and superoxide dismutase (SOD), nitrotyrosine (NT), malondialdehyde (MDA) and glutathione reduced (GSH) as oxidative stress markers. Finally, histopathological examination of cerebral cortex, hippocampus and cerebellum sections was performed using routine and special stains.

Results: Tempol and perindopril improved spatial and non-spatial memory in mice, decreased brain Aβ deposition and BDNF depletion, decreased TNF-α, NOx, nNOS, iNOS, NT and MDA brain levels and increased brain

SOD and GSH contents, parallel to confirmatory histopathological evidences.

Conclusion: Protective potential of tempol and perindopril against experimental AD is attributed to suppression of brain Aβ deposition, conservation of BDNF, suppression of TNF-α production, and amelioration of oxidative and nitrosative stress.

Key words : Alzheimer's disease, β-amyloid, BDNF, Neuroinflammation, Oxidative stress, Lipopolysaccharide, Perindopril, Tempol.