Colchicines-induced neurotoxicity as an animal model of sporadic dementia of Alzheimer’s type

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Abstract:
Alzheimer’s disease (AD) is the most common type of dementia disorder of elderly affecting millions of people. The pathophysiology of the disease is complex and involves multiple pathways of neuronal damage. Sporadic dementia of Alzheimer’s type (SDAT) has been shown to be associated with microtubular dysfunction and is characterized by the appearance of specific cytoskeletal cellular abnormalities, including neurofibrillary tangles and senile plaques. Intracerebroventricular (icv) administration of colchicine, a microtubule-disrupting agent, causes cognitive dysfunction as evidenced by poor retention of memory in both Morris water maze and elevated plus-maze task paradigms that is associated with excessive free radical generation. Biochemical analysis revealed that icv colchicine injection significantly induced lipid peroxidation, increased nitrite and depleted reduced glutathione (GSH) and acetylcholinesterase (AChE) level in rat brains. Chronic treatment with rivastigmine (0.625 and 2.5 mg/kg, po) twice daily for a period of 25 days beginning 4 days prior to colchicine injection significantly improved the colchicine-induced cognitive impairment and reduced AChE level. The results of the present study clearly indicated that colchicines-induced cognitive impairment and oxidative stress in animals can be used as an animal model for drug screening for Alzheimer’s disease.

Keywords:
Colchicine, neurotoxicity, rivastigmine, Alzheimer’s disease