Role of Dolichol Kinase and GPT cascade in amyloid induced dementia of Alzheimer type

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Background: Alzheimer disease belonging to the class of neurodegenerative disorder which is characterized by the pathological accumulation of amyloid beta plaques and neurofibrillary tangles. About 4 percent people over age of 60 affected by AD Worldwide. The biosynthesis of lipid linked oligosaccharides takes place at the membrane of ER neurons and is characterized by the involvement of a special lipid carrier, dolichol. Dolichol kinase and GPT plays important role N glycosylation of APP. This study was done to investigate the effects of Dolichol kinase and GPT modulation in intracerebro ventricular Amyloid beta model in rat for improved memory cognition and function.

Methodology: Male Wistar rats (220 to 250 g), were divided into five different groups: normal control, Sham, ICV amyloid beta control, Mefloquine (25 mg/kg, orally, single dose) & ICV amyloid beta, Tunicamycin (0.02 mg/kg, sc for 26 days), Mefloquine per se (25 mg/kg, orally, single dose), Tunicamycin per se (0.02 mg/kg). ICV amyloid beta was administered using stereotaxic apparatus. Memory impairments for cognition and retention were estimated through various behavioural assessments using morris water maze, Y maze, balance beam, open field and photoactometer test. The biochemical estimations for oxidative stress like lipid peroxidation, glutathione, and acetylcholinesterase were made in rat brain homogenate. All observations were analyzed using GraphPad Prism version 5.

Results: Administration of amyloid beta through ICV route into the brain exhibited memory deficit as assessed on morris water maze, Y maze, balance beam, open field and photoactometer test. Administration of Mefloquine and Tunicamycin showed significant restoration of memory dysfunction. The brain tissue biochemical estimations showed significant decrease in TBARS, AChE and increase in glutathione level, on treatment with mefloquine in ICV amyloid beta treated rat.

Conclusion: The finding of the current study revealed that inhibition of Dolichol Kinase and GPT in ICV amyloid beta induced neuronal impairment plays pivotal role in improving memory in Alzheimer’s disease.