POTENTIAL NEUROPROTECTIVE EFFECT OF NICOTINAMIDE, A PARP INHIBITOR AGAINST STREPTOZOTOCIN INDUCED EXPERIMENTAL DEMENTIA OF ALZHEIMER'S TYPE IN RATS

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Dysregulation in PARP activity has been considered to play important role in neurodegenerative processes associated with various CNS disorders. In the present study we have investigated the therapeutic potential of PARP inhibition by nicotinamide against streptozotocin (STZ) induced neurocognitive deficit and biochemical abnormalities in rats. Streptozotocin was administered intracerebroventrically (ICV 3mg/kg) bilaterally on day 1 and 3 in Wistar rats. Nicotinamide was administered (100 and 200 mg/kg/day p.o.) one week following 1st STZ infusion upto 21st day. Morris water maze and object recognition tasks were used to assess learning and memory. Terminally the level of oxidative stress, inflammatory cytokines and acetylcholinesterase (AChE) activity was measured in rat brain homogenate. Central ICV infusion of STZ produced significant learning and memory impairment and increased cerebral AChE activity in rats. Further significant increase in oxidative stress and pro-inflammatory cytokine levels was also observed in STZ infused rats. A PARP inhibitors, nicotinamide dose dependently attenuated STZ induced cognitive decline and other biochemical abnormalities observed following STZ infusion in rats. The observed neuroprotective effect of nicotinamide may be due to its antioxidant and anti-inflammatory activities. The findings from the current study clearly suggest PARP inhibition would be a novel strategy to curb cognitive decline associated with neurodegenerative disorders such as Alzheimer's disease.