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Galantamine potentiates neuroprotective potential of Taurine in A β (1-42) induced animal model of Alzheimer's disease: The synergistic role of GABAA & α 7 nicotinic acetylcholine receptors

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Background: Taurine, 2-aminoethanesulfonic acid, acts as a neuromodulator, osmoregulator, prevent mitochondrial dysfunction, apoptosis and oxidative stress. Also prevent the neurotoxicity of beta amyloid peptide ((A) (1-42)) by binding on GABAA receptor. Galantamine, acetylcholinesterase inhibitors (AChEIs), is a novel treatment for AD and modulates nicotinic acetylcholine receptors (nAChRs). It also produces neuroprotection by inhibiting neuroinflammatory pathway (nAChR-Jak-NFkB) and the ROS pathway (iNOS/NOX). In this study, the combination of taurine and AChEIs (galantamine) is used as a therapeutic strategy to improve cognition in AD.

Objective: The objective of this study was to evaluate the neuropotentiating effect of galantamine on taurine in amyloid beta $((A\beta)(1-42))$ induced cognitive dysfunction in rats.

Materials & Methods: Intrahippocampal (i.h.) A β (1-42) (1 μ g/ μ l; 4 μ l/site) were administered, followed by drug treatment with taurine (25, 50 and 100 mg/kg), galantamine (2 mg/kg) and their combinations for a period of 21 days. Various neurobehavioral parameters followed by biochemical, acetylcholinesterase (AChEs) level, neuroinflammatory marker (TNF- α), mitochondrial respiratory enzyme complexe level (I-IV), neurotransmitters level and histopathological alterations were assessed.

Results: Administration of A β (1-42) significantly impaired cognitive performance in Morris water maze (MWM) test, causes oxidative stress, raised AChEs level, neuroinflammation, mitochondrial dysfunction alterations in histopathology and neurotransmitter levels as compared to sham treatment. Treatment with taurine (25, 50 and 100 mg/kg) and galantamine (2 mg/kg) alone improved cognitive performance as evidenced by reduced transfer latency and increased time spent in the target quadrant in MWM test, reduced AChEs activity, neuroinflammation, oxidative damage (reduced LPO, nitrite level and restored SOD, catalase and GSH levels), TNF- α level, restored mitochondrial respiratory enzyme complex (I, II, III, IV) activities, histopathological alterations and neurotransmitter levels as compared to A β (1-42) treated animals. Further, combinations of taurine (25 and 50 mg/kg) with galantamine (2 mg/kg) significantly modulate the neuroprotective potential of taurine.

Conclusion: The present study suggests the neuropotentiating effect of galantamine on taurine. This combination in multifaceted pattern improved A ((1-42) induced neurotoxicity as indicated by improving oxidative stress, mitochondrial functions, neuroinflammation, histopathological alterations and neurotransmitter levels.

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