International Conference on Recent Innovations in Science, Agriculture, Engineering and Management
University College of Computer Applications Guru Kashi University, Bathinda, Punjab (India)
20th November 2017, www.conferenceworld.in ISBN: 978-93-86171-80-1

Palmitate induced lipotoxicity is associated with intracellular Ca^{2+} mediated ER Stress and CYP2E1-induced oxidative stress in human liver cells

Ashraf Ul Nissar[1,*,#], Love Sharma[1], Sheikh A Tasduq[1]

[1]*Academy of Scientific and Innovative Research (AcSIR), New Delhi, (India)*

[2]*PK-PD and Toxicology Division, CSIR-Indian Institute of Integrative Medicine, Canal Road, Jammu Tawi, Jammu and Kashmir, (India)*

#Present address: department of Biotechnology, University of Kashmir

ABSTRACT

Increased levels of free fatty acids, lipid droplet formation and lipoapoptosis in hepatocytes are hallmarks of Non Alcoholic Fatty Liver Disease. However the associated events that link the elevated serum fatty acids to cellular demise remains poorly understood. Our aim was to establish the missing link connecting lipid droplet formation, ER stress mediated lipogenesis and cellular demise that finally leads to the liver damage and progression of disease. Ethnically three different cell models (Hep3B: Black, Huh7: Japanese and HepG2: Caucasian) of lipid overloading were used. Cells were exposed to different concentrations of free fatty acid for varied time periods. Intracellular Ca^{2+} levels, factors involved in lipid import and export, ER stress, Oxidative stress, CYP2E1 levels, mitochondrial dysfunction and lipoapoptosis were investigated. Exposure of hepatocytes to saturated fatty acids (SFA) induced significant accumulation of lipids with concentration dependent decrease in cell viability , increased Caspase activation and apoptosis. SFA treatment induced expression of SREBP1 that was associated with increased CD36 protein levels and decreased Mttp levels, leading to increased influx and reduced efflux of fatty acids. Intracellular Ca^{2+} levels were increased and ER stress markers and members of PERK-eIF2α pathway were upregulated. The intracellular Ca^{2+} levels were associated with overexpression of CYP2E1, oxidative stress and loss of mitochondrial membrane potential. In Conclusion the study suggests that SFA induces intracellular Ca^{2+} release from ER that leads to lipogenesis, lipid droplet formation and triggers the series of events in hepatocytes leading to generation of oxidative stress, ER stress and mitochondrial dysfunctioning.

Key words: *NAFLD; ER Stress; Mitochondrial dysfunction; oxidative stress; SREBP1; CD36; Mttp; CYP 2E1*