World Academy of Science, Engineering and Technology
International Journal of Biomedical and Biological Engineering
Vol:11, No:05, 2017

Contribution of NLRP3 Inflammasome to the Protective Effect of 5,14-HEDGE, A 20-HETE Mimetic, against LPS-Induced Septic Shock in Rats

Authors : Bahar Tunctan, Sefika Pinar Kucukkavruk, Meryem Temiz-Resitoglu, Demet Sinem Guden, Ayse Nihal Sari, Seyhan Sahan-Firat, Mahesh P. Paudyal, John R. Falck, Kafait U. Malik

Abstract : We hypothesized that 20-hydroxyeicosatetraenoic acid (20-HETE) mimetics such as N-(20-hydroxyeicosa-5[Z],14[Z]-dienoyl)glycine (5,14-HEDGE) may be beneficial for preventing mortality due to inflammation induced by lipopolysaccharide (LPS). This study aims to assess the effect of 5,14-HEDGE on the LPS-induced changes in nucleotide binding domain and leucine-rich repeat protein 3 (NLRP3)/apoptosis-associated speck-like protein containing a caspase activation and recruitment domain (ASC)/pro-caspase-1 inflammasome. Rats were injected with saline (4 ml/kg) or LPS (10 mg/kg) at time 0. Blood pressure and heart rate were measured using a tail-cuff device. 5,14-HEDGE (30 mg/kg) was administered to rats 1 h after injection of saline or LPS. The rats were sacrificed 4 h after saline or LPS injection and kidney, heart, thoracic aorta, and superior mesenteric artery were isolated for measurement of caspase-1/11 p20, NLRP3, ASC, and β-actin proteins as well as interleukin-1β (IL-1β) levels. Blood pressure decreased by 33 mmHg and heart rate increased by 63 bpm in the LPS-treated rats. In the LPS-treated rats, tissue protein expression of caspase-1/11 p20, NLRP3, and ASC in addition to IL-1β levels were increased. 5,14-HEDGE prevented the LPS-induced changes. Our findings suggest that inhibition of renal, cardiac, and vascular formation/activity of NLRP3/ASC/pro-caspase-1 inflammasome involved in the protective effect of 5,14-HEDGE on LPS-induced septic shock in rats. This work was financially supported by the Mersin University (2015-AP3-1343) and USPHS NIH (PO1 HL034300).

Keywords : 5,14-HEDGE, lipopolysaccharide, NLRP3, inflammasome, septic shock
Conference Title : ICI 2017 : International Conference on Inflammation
Conference Location : Amsterdam, Netherlands
Conference Dates : May 14-15, 2017