Introduction: Endotoxemia is one of the important causes of death in clinics which trigger septic shocks and multiple organ damage. The cholinergic anti-inflammatory pathway is a physiological neuroimmune mechanism that regulates innate immune function and controls inflammation. The functional activity of this pathway can be modulated through its neuronal (efferent vagal neurons and higher brain structures) and non-neuronal (alpha7 nicotinic cholinergic (α7nACh) receptors on cytokine-producing cells) cholinergic components.

Aim: The aim of the study is to investigate the anti-inflammatory role of the cholinergic pathway in endotoxemia induced multiple organ damage and the interaction between pathway and nitric oxide synthase (NOS) and cyclooxygenase (COX) systems.

Materials and Methods: Endotoxemia was induced in male and female Sprague-Dawley rats (250-300 g; n=8/group) by intraperitoneal (ip) administration of 10mg/kg Escherichia coli (LPS; serotype 0111:B4) following a 16 hour starvation period. Control group was received physiological saline solution (1ml/kg; ip). The treatment groups were injected either nicotine (1mg/kg; ip), or nicotine + aminoguanidin (AG; 8mg/kg, ip) or nicotine + nimesulide (NIM; 10mg/kg, ip) for 3 days before LPS administration. At the 24th hour after LPS induction, blood, liver and kidney samples were collected. Samples were stored at -70 °C for the measurement of malondialdehyde (MDA), glutathione (GSH) levels, and myeloperoxidase (MPO) activity.

Results: Tissue damage scores, serum ALT, AST, BUN, MDA and MPO levels and chemiluminescence levels increased, GSH levels decreased (p<0.05-0.001) in LPS group comparing to control group. Nicotine treatment ameliorated microscopic scores and biochemical parameters of inflammation in all tissues and serum (p<0.05-0.01). Nicotine+AG and Nicotine+NIM treatments attenuated all tissue and serum inflammation parameters which increased with LPS induction except kidney GSH levels. While Nicotine+NIM treatment reduced microscopic damage in kidney, Nicotine+AG treatement reduced only liver damage.

Conclusion: The stimulation of cholinergic anti-inflammatory pathway with nicotine had beneficial effects on endotoxemia model in rats. iNOS or COX-2 inhibition did not changed the nicotin effects. In some cases, iNOS and COX-2 inhibition contributed positive nicotinic effects.