Evaluation of isolated vascular response to 5HT1A, 5HT1B1D & 5HT2A receptors agonist & antagonist in chronic endotoxemic rats

Azam bakhtiarian, Razieh Afshar moghaddam
Department of pharmacology, School of medicine, Tehran University of medical sciences, Tehran, Iran.
Email: bakhtiar12@yahoo.com, razieh2744@yahoo.com

Abstract:

The main vascular abnormality seen in endotoxemia is impaired contractile responses to vasoactive agents. This study examines the aortic response to 5HT1A, 5HT1B1D & 5HT2A receptors agonist & antagonist in aortic rings of chronic endotoxemic rats. Chronic endotoxemia induced by intraperitoneal injection of 1 mg/kg lipopolysaccharide (Salmonella typhimurium) for 5 days. Control rats received intraperitoneal injection of saline (1 ml/kg) for 5 days. Rats divided into 3 groups. In first group, DOI hydrochloride used as an agonist & sarpogrelate hydrochloride as an antagonist of 5HT2A receptor. In second group, (R)-(+)-8-OH-DPAT hydrobromide used as an agonist & WAY100135 as an antagonist of 5HT1A receptor. In third group, Zolmitriptan used as an agonist & GR127935 hydrochloride hydrate as an antagonist of 5HT1B1D receptor. Thoracic aorta removed for pharmacological examination and placed in organ bath. Real time-PCR & histopathological study performed to investigate gene expression & tissue protein localization of receptors. Cumulative 8-OH-DPAT & zolmitriptan in separate experiments caused first-doses vasorelaxation in control group. The same treatments generated enhanced vasodilation during endotoxemia. The contractile response to DOI hydrochloride converted to relaxation response in endotoxin-treated group. PCR studies showed significantly enhanced expression of 5HT1A receptor gene in endotoxemic aorta while the expression of 5HT1B1D & 5HT2A receptor genes were diminished. Histopathological studies showed mild focal inflammation and damaged endothelium in endotoxemic aorta. In conclusion, data support the evidence for lipopolysaccharide-induced increase in endothelium-dependent relaxation & impaired vasoconstriction in aortic rings of endotoxemic rats.

Keywords: Endothelium, Vasodilation, Endotoxins, Aorta, Serotonin.