Influence of hypotensive drugs on lipopolysaccharide (LPS)-induced serum concentrations of tumor necrosis factor alpha (TNF-α), interleukin (IL)-1β, IL-6 in spontaneously hypertensive rats (SHR)

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Abstract:
A growing body of evidence suggests that some drugs used in cardiovascular diseases may modulate the level of proinflammatory cytokines. Therefore, we have investigated whether propranolol, doxazosin, amiodipine and indapamide can influence lipopolysaccharide (LPS)-induced serum concentrations of tumor necrosis factor alpha (TNF-α), interleukin (IL)-1β and IL-6 in spontaneously hypertensive rats (SHR). The animals were divided into five groups as follows: SHR + MET (control rats receiving 1% solution of methylcellulose), SHR + PROP (rats receiving propranolol – 40 mg/kg), SHR + DOX (rats receiving doxazosin – 10 mg/kg), SHR + AML (rats receiving amiodipine – 25 mg/kg) and SHR + IND (rats receiving indapamide – 1.5 mg/kg). Solution of methylcellulose (1%) and hypotensive drugs were administered by a gavage once a day for 21 days. Arterial blood pressure was measured in conscious rats, using the tail-cuff method. Serum TNF-α, IL-1β and IL-6 concentrations were measured with enzyme-linked immunosorbent assay kits. Additionally, total cholesterol and high density lipoproteins (HDL) cholesterol were evaluated. Propranolol and amiodipine significantly decreased LPS-stimulated TNF-α level after 21 days of administration in SHR. Three-week administration of propranolol, amiodipine and indapamide lowered IL-1β serum concentration after LPS stimulation. Doxazosin caused a significant increase of the IL-6 serum concentration in SHR. The results were accompanied by a statistically significant decrease in systolic, diastolic and medium blood pressure after 21 days of administration for propranolol and amiodipine. Indapamide lowered diastolic and medium blood pressure while doxazosin only diastolic blood pressure after 21 days. Hypotensive drugs showed no effect on lipid level. The present data indicate that hypotensive drugs possess additional properties, beyond their most commonly known mechanism of action. The elucidation of interactions between hypotensive drugs and cytokines could be of great importance in cardiovascular diseases (e.g., atherosclerosis).

Key words:
propranolol, doxazosin, amiodipine, indapamide, proinflammatory cytokines, LPS, SHR