البحث الثالث

ACE2/ACE imbalance mediates bisphenol A-induced lung injury in Wistar rats: Results from captopril versus losartan histo-biochemical study

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Abstract

Bisphenol-A (BPA) is a synthetic chemical compound broadly used in the plastic and epoxy resin industries with a considerable potential for food contamination. Literary reports have suggested that the altered renin-angiotensin system (RAS) is a mechanism for lung injury and inflammation caused by variable agents. The current study sought to investigate the contribution of RAS to BPA- induced lung damage. Moreover, the study assessed whether angiotensin II and/or bradykinin pathways were involved. For this aim, the angiotensin-converting enzyme (ACE) inhibitor captopril (Cap), either alone or combined with bradykinin receptor antagonist icatibant (Icat), was attempted versus the angiotensin receptor blocker losartan (Los). An eight-week study was conducted on forty Wistar male albino rats randomly divided into five equal groups: control, BPA, BPA/Cap, BPA/Los, and BPA/Cap/Icat groups. Captopril (100 mg/mL) and losartan (200 mg/mL) were given orally in drinking water, but icatibant (Icat) was injected subcutaneously (250 μg/kg) during the last two weeks of captopril treatment. Biochemical analysis of bronchoalveolar lavage fluid (BALF) and lung tissues, polymerase chain reaction (PCR) assay for ACE, ACE2, and caspase- 3 genes expression, and histological and immunohistochemical studies were carried out to evaluate BPA-mediated pulmonary inflammation/apoptosis. BPA impaired the histological structure of the lungs, increased ACE, ACE2, and caspase-3 expressions at both gene/protein levels, and increased BALF inflammatory cytokines and lung oxidative markers. Inhibiting the ACE activity by captopril maintained the histological lung injury score, restored inflammation and the ACE2/ACE balance, and decreased apoptosis. Further improvement was obtained by the angiotensin II receptor (ATR1) blocker losartan. Icatibant (bradykinin B2 receptor blocker) didn't counteract the observed captopril effects. It was strongly suggested that RAS contributed to BPA- induced lung damage via alteration of ACE2 and ACE expression mediating angiotensin II gen- eration rather than bradykinin

Keywords: BPA lung injury Inflammation/apoptosis Altered renin-angiotensin system Rat immunohistochemistry