Fifth research

Title

Bisphenol-A exposure alters liver, kidney, and pancreatic Klotho expression by HSP60- activated mTOR/autophagy pathway in male albino rats.

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ABSTRACT:

The effect of bisphenol-A (BPA) on Klotho protein (aging-suppressing protein) expression in different body organs has not been sufficiently addressed by literature studies. The study investigated the impact of BPA on Klotho expression in multiple organs including the liver, kidney, and pancreas and suggested the involved molecular pathways. Twenty-seven male Wistar albino rats were divided into 3 equal groups: control, low-dose BPA (4.5 μg/L), and high-dose BPA (8 μg/L) groups in drinking water for 45 consecutive days. Liver, kidney, and pancreatic specimens were prepared for a gene study of Klotho, HSP60, mTOR, and ULK1 mRNA expressions.

Also, the tissue specimens were measured for malondialdehyde (MDA), superoxide dismutase (SOD), and nitric oxide (NO) levels. Paraffin-embedded sections were also prepared and subjected to Hematoxylin and Eosin (H&E) staining and immunohistochemical detection of Klotho and HSP60. The results revealed an alteration in the MDA, SOD, NO tissue levels, disturbed gene expression profile, and apoptotic changes in the histological findings of the examined organs which were obvious ($p < 0.05$) in the high-dose group. The anti-aging Klotho gene/protein expression was reduced ($p < 0.05$) more in the high-dose BPA group than in the low dose. In contrast, HSP60 gene/protein expression was significantly increased

($p < 0.05$) more in the high dose. The increased mTOR gene expression was strongly correlated ($p < 0.05$) with the decreased autophagy related gene ULK1. It was concluded that BPA exposure contributed to cell stress and markedly reduced Klotho protein expression in liver, kidney, and pancreatic tissues, possibly by modulation of the HSP60-activated mTOR/autophagy signaling.

Keywords: Cell stress and senescence, endo crine disruptors, environmental pollution, Klotho and HSP60 immunohistochemistry, rat gene study of ULK1.