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Juan Y[1], Lee Y[2], Lu M[3], Wu W[4], Jang M[4], Ho W[5], Chen S[6], Liu K[7], Chuang S[8]

1. *Kaohsiung Medical University; Kaohsiung Municipal Hsiao-Kang Hospital,* ***2.*** *Department of Urology, Chi-Shan Hospital, Department of Health, Executive Yuan,* ***3.*** *Graduate Institute of Marine Biotechnology, National Dong Hwa University,* ***4.*** *Department of Urology, Kaohsiung Municipal Hsiao-Kang Hospital,* ***5.*** *Department of Urology, Kaohsiung Medical University,* ***6.*** *Kaohsiung Municipal Hsiao-Kang Hospital,* ***7.*** *Department of Anatomy, College of Medicine, Kaohsiung Medical University,* ***8.*** *Translational Research Center, Cancer Center, Kaohsiung Medical University*

THE PROTECTIVE EFFECT OF EPIGALLOCATECHIN GALLATE ON OXIDATIVE STRESS TRIGGERED THROUGH MITOCHONDRIA AND ENDOPLASMIC RETICULUM IN A METABOLIC SYNDROME –INDUCED BLADDER OVERACTIVITY RAT MODEL

Hypothesis / aims of study

Long-term metabolic syndrome develops lower urinary tract symptoms. The pathophysiology mechanism underlying the metabolic syndrome associated with bladder dysfunction is still not clear. The major aim of our study is to elucidate metabolic syndrome-induced bladder dysfunction in association with oxidative stress triggered through mitochondria and endoplasmic reticulum (ER) in a metabolic syndrome –induced bladder overactivity rat model. The other aim of the present study is to elucidate the protective effect of epigallocatechin gallate (EGCG) on metabolic syndrome –induced bladder overactivity.

Study design, materials and methods

Female Sprague-Dawley rats are divided into control group, high fat high sugar (HFHS) diet group, HFHS diet with bilateral ovariectomy (OVX) (HFHS +OVX) group, HFHS diet with bilateral OVX and EGCG treatment (HFHS+OVX+EGCG) group, and HFHS diet with EGCG (HFHS+EGCG) group, respectively. Cystometry (CMG) and micturition frequency/volume studies were recorded for bladder voiding function. The terminal deoxynucleotidyl transferase dUTP nick-end labeling (TUNEL) assay was performed to evaluate the distribution of apoptotic cells. Western blot was carried out to examine the expressions of interstitial fibrosis markers, muscarinic receptors (M2 and M3), oxidative stress markers, endoplasmic reticulum stress markers (GRP78, CHOP, caspase-12), apoptosis-associated proteins, and the subunits of mitochondrial respiratory complexes. The antioxidant enzymes, including superoxide dismutase and catalase, were investigated by real-time PCR.

Results

The HFHS diet with OVX treated rats displayed bladder overactivity. Bladder contractility was considerably decreased in HFHS with OVX group in response to electric field, carbachol, and KCl stimulation as compared with those in the control group. Such bladder dysfunction was accompanied by a significant increase in oxidative stress markers, ER-associated oxidative stress proteins, apoptosis-associated proteins, and the subunits of mitochondrial respiratory complexes. Conversely, the mRNA expressions of antioxidant enzymes Mn-SOD, Cu/Zn-SOD and catalase were also decreased after long-term HFHS treatment with/without OVX. However, EGCG treatment can improve the extent of oxidative stress and lessen bladder hyperactivity.

Interpretation of results

These results demonstrated that HFHS-induced apoptosis was correlated with mitochondrial- and ER-dependent pathways. Ovariectomy could enhance HFHS -induced bladder overactivity. The assessment of mitochondrial function was acquired by the analysis of the expressions of the subunits of mitochondria respiratory enzyme complexes. Such HFHS-induced increase in the expressions of mitochondria respiratory enzyme complexes suggested that HFHS with OVX caused an enhancement in the generation of ROS. EGCG could eliminate HFHS-induced bladder overactivity through its antioxidant, antiapoptosis and antifibrosis effects.

Concluding message

HFHS combined with OVX enhanced the generation of oxidative stress mediated through mitochondria- and ER-dependent pathways, and consequently attributed to bladder apoptosis, whereas EGCG treatment could eliminate these oxidative stress and reverse bladder dysfunctions.

Disclosures

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