

OVARY HORMONE DEFICIENCY EXACERBATED HIGH FAT AND HIGH SUGAR DIET - INDUCED OVERACTIVE BLADDER IN A RAT MODEL

Hypothesis / aims of study

The pathophysiology mechanism of menopause in the metabolic syndrome associated bladder dysfunction is still not clear. The major aims of the present study were to examine high-fat-high-sugar diet and surgical menopause - induced metabolic syndrome by elucidating the critical role of oxidative stress mediated by mitochondria and endoplasmic reticulum in overactive bladder.

Study design, materials and methods

Female *Sprague-Dawley* rats were fed with high-fat-high-sugar diet with/without ovariectomy surgery to mimic menopause and to induce metabolic syndrome. At six months after high-fat-high-sugar feeding, cystometrogram, physical indicator, urine and serum biochemistry parameters were measured. The terminal deoxynucleotidyl transferase nick-end labeling assay was performed to evaluate the distribution of apoptotic cells. Immunofluorescence studies and Western blots were carried out to examine the expressions of muscarinic and purinergic receptors, fibrosis-associated proteins, mitochondria stress markers, apoptosis-associated proteins and mitochondrial respiratory subunits enzymes.

Results

Bladder hyperactivity was induced accompanied by bladder interstitial fibrosis after 6 months of high-fat-high-sugar feeding, while surgical menopause exacerbated these bladder damages. In addition, surgical menopause enhanced the generation of oxidative stress mediated by mitochondria-dependent pathways, and consequently attributed to bladder apoptosis. Such oxidative stress-enhanced bladder cell apoptosis and urothelial barrier defects were potential factors that might play crucial role in bladder over-activity and interstitial fibrosis. Ovary hormone deficiency with high-fat-high-sugar feeding also induced bladder dysfunction via over-expression of muscarinic and purinergic receptors.

Interpretation of results

Surgical menopause and HFHS feeding - induced OAB symptoms and raising oxidative stress, resulted in bladder damage and interstitial fibrosis. Meanwhile, bladder tissues were accompanied by increases in the expressions of apoptosis-associated proteins (Bax, cytochrome c, caspase-3, and -9) which displayed the features of mitochondria-dependent apoptotic signals. Meanwhile, the expression levels of the subunits of mitochondria respiratory enzymes were significantly increased in bladder tissues. Moreover, ER stress markers and oxidative stress markers were also over-expressed. These results demonstrated that ovarian hormone deficiency exacerbated oxidative damage through mitochondrial- and ER-dependent pathways, and resulted in bladder apoptosis.

Concluding message

High-fat-high-sugar feeding enhanced the generation of oxidative stress mediated by mitochondria, while ovary hormone deficiency enhanced bladder apoptosis and interstitial fibrosis, exacerbated overactive bladder syndrome.

Disclosures

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