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INCREASED OXIDATIVE STRESS AND REDUCED ANTIOXIDANT ENZYME ACTIVITY CONTRIBUTE TO THE IMPAIRED EXCITATORY NEUROTRANSMISSION OF BLADDER IN INSULIN-RESISTANT OBESE ZUCKER RAT

Hypothesis / aims of study

Both metabolic syndrome (MS) and type II diabetes mellitus (IIDM) are known risk factors for lower urinary tract symptoms and detrusor overactivity, being the latter a well-known cause of urgency urinary incontinence in obese individuals. A recent study has suggested that a lower expression and diminished function of neuronal cannabinoid CB_1 and CB_2 receptors, as well as a lower nerve fiber density is involved in the impaired excitatory neurotransmission of the urinary bladder in the insulin-resistant obese Zucker rat (OZR), a MS experimental model similar to that produced in man (1). Antioxidants are agents that protect cells from the damage caused by unstable molecules known as free radicals or reactive oxygen species (ROS). Since increased oxidative stress can cause bladder nerve dysfunction, nerve fiber and mitochondrial injury and detrusor muscle cell damage (2), we investigate whether this pathophysiological mechanism is involved in the bladder motor dysfunction in OZR.

Study design, materials and methods

Bladder samples from OZR and their respective controls lean Zucker rat (LZR) were processed for western blot, spectrophotometry and/or fluorimetry for oxidative stress and antioxidant enzymatic activity measurement. Detrusor strips from OZR and LZR were also mounted in myographs for isometric force recordings induced by electrical field stimulation (EFS) on basal tension.

Results

EFS-elicited contraction was considerably lower in OZR bladder compared with that exhibited in LZR. In OZR bladder homogenates, an increased amount of ROS and of the thiobarbituric acid reactive substances (TBARS) and protein carbonyls levels were detected. In addition, superoxide dismutase (SOD), catalase (CAT), glutathione reductase (GR) and glutathione peroxidase (GPx) activities were found to be significantly lower (p=0.0001) in OZR in comparison with LZR controls. The glutathione/oxidized glutathione ratio (GSH/GSSG) decreased significantly, causing a more oxidized GSH redox status.

Interpretation of results

These results suggest that the decline in the antioxidant enzyme system reflects a reduction in the cellular defense to ROS and an increased susceptibility of the bladder tissue to oxidative damage in OZR, leading to impaired excitatory neurotransmission of detrusor muscle in these rats.

Concluding message

An increased oxidative stress and reduced antioxidant enzyme activity could contribute to the bladder motor dysfunction in OZR through an impaired ROS-related pathway.

References

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Disclosures

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