ADRENAL GLAND REMODELING AND HORMONAL DYSREGULATION IN EXPERIMENTAL METABOLIC SYNDROME

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Abstract. The study assessed structural remodeling of the adrenal glands and its relationship with adrenal hormone levels in diet-induced metabolic syndrome (MS) in rats. A 10-week high-fat–high-fructose diet caused widening of the zona glomerulosa and zona fasciculata, narrowing of the zona reticularis, stromal fibrosis and capillary rarefaction, accompanied by increased cortisol and aldosterone and decreased DHEA-S. Morphometric indices correlated closely with hormonal and metabolic shifts.

Keywords: metabolic syndrome; adrenal cortex; remodeling; cortisol; aldosterone; DHEA-S; morphometry.

INTRODUCTION

Metabolic syndrome affects about a quarter of the world's adult population and is a major driver of type 2 diabetes and cardiovascular disease (Alberti et al., 2009; Saklayen, 2018). Its clinical similarity to hypercortisolism suggests that functional overactivity of the hypothalamic–pituitary–adrenal axis participates in its pathogenesis (Anagnostis et al., 2009), while obesity-related hyperaldosteronism contributes to hypertension and organ damage (Kargi & Iacobellis, 2014). However, data on how adrenal structure adapts to MS remain limited and contradictory (Swierczynska et al., 2015). The aim of the work was to characterise adrenal remodeling and hormonal dysregulation in experimental MS and to evaluate their interrelationship.

MATERIALS AND METHODS

Forty male Wistar rats were divided into a control group (n=10, standard chow) and an experimental group (n=30) fed a high-fat diet (60% fat, 20% protein, 20% carbohydrates) with 10% fructose solution for 10 weeks (Panchal et al., 2011). Body weight, systolic blood pressure, glucose and lipid profile were monitored. Serum cortisol, aldosterone and DHEA-S were determined by ELISA. Adrenal sections (4–5 μm) were stained with haematoxylin–eosin and Van Gieson; zone thickness, cell and nuclear diameters, nucleo-cytoplasmic ratio (NCR), capillary density and connective tissue fraction were measured in ImageJ (Schneider et al., 2012). Data were expressed as M±SD and compared with Student's t-test; Pearson's r was calculated; $p<0.05$ was considered significant. The experiments followed international bioethical principles.

RESULTS AND DISCUSSION

By the 10th week the experimental animals developed obesity (+23.7% body weight), hyperglycaemia (+58.3%), hypertriglyceridaemia (+97.9%), decreased HDL-

cholesterol and elevated systolic pressure (+20.3%), confirming the MS phenotype. Adrenal mass increased by 35.9% in absolute and by 9.9% in relative terms.

Remodeling of the cortex was zone-specific. Total cortical thickness increased by 15.8% owing to widening of the zona glomerulosa (+30.2%) and zona fasciculata (+21.1%), whereas the zona reticularis became 9.0% thinner. Fasciculata cells were hypertrophied (+22.8%) and overloaded with lipid vacuoles (58.6% vs 34.2% of cells), and the NCR decreased by 19.5%, indicating predominantly cytoplasmic enlargement. Reticularis cells were smaller, with nuclear pyknosis. Capsular thickening, an 85.4% increase in connective tissue fraction and an 18.0% decrease in capillary density reflected stromal and microvascular remodeling.

Hormonal changes paralleled the structural ones: cortisol rose by 72.0%, aldosterone by 55.8%, while DHEA-S fell by 26.2%. Zona fasciculata thickness correlated with cortisol (r=0.71), zona glomerulosa thickness with aldosterone (r=0.64) and systolic pressure (r=0.57), and zona reticularis thickness with DHEA-S (r=0.55); cortisol, in turn, correlated with glucose (r=0.62). These findings support the concept of functional hypercortisolism and obesity-associated hyperaldosteronism in MS and indicate that adrenal remodeling forms a self-sustaining loop that aggravates metabolic disturbances. As corticosterone is the main glucocorticoid in rats, its parallel measurement is advisable in further studies.

CONCLUSION AND RECOMMENDATIONS

Experimental MS induces zone-specific adrenal remodeling – hypertrophy of the zona glomerulosa and zona fasciculata, atrophy of the zona reticularis, fibrosis and capillary rarefaction – that is closely linked with increased cortisol and aldosterone and decreased DHEA-S. It is recommended to (1) use zone thickness, NCR, the proportion of vacuolized cells and the connective tissue fraction as morphological criteria of adrenal involvement in MS; (2) include adrenal hormone assessment in the evaluation of MS models and patients; (3) apply the model for testing corrective approaches – diet therapy, antioxidants and adaptogens – aimed at restoring adrenal balance.

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