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Sex differences in redox state, autophagy and lysosomal function

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Modifications of the normal redox state are connected with numerous diseases and conditions such as cardiovascular diseases, diabetes mellitus and its complications, liver diseases, and aging which are characterized by numerous sex differences. Evidences suggest that redox state might be different in males and females. Autophagy is crucial for the maintaining cellular homeostasis process whereby cytoplasmic components are delivered to lysosomes for degradation. Alteration in constitutive autophagy is implicated in many pathological conditions, including heart diseases, diabetes mellitus and its complications, and liver diseases. A cross-talk between ROS and autophagy has been described. The current study was conducted to investigate the influence of sex on lipid and protein oxidation and autophagic response in the heart, the liver and the kidney obtained from young adult healthy male and female rats.

7 week old Sprague-Dawley rats were used to obtain heart, liver and kidneys. Malondialdehyde (MDA), and carbonylated proteins were measured by spectrophotometric methods for redox state assessment. The autophagy biomarkers Beclin-1, and microtubule-associated protein 1 light chain 3 (LC3), the mammalian target of rapamycin (mTOR; checkpoint in autophagic process), and the lysosomal associated membrane protein (LAMP-1; biomarker of lysosomes) were evaluated by Western blotting. Immunofluorescence analysis was also performed for LC3 and LAMP-1 colocalization.

In the heart, Beclin-1, LC3-II/LC3-I were higher in males than in females suggesting that male heart have a major constitutive autophagy and this was linked with higher levels of carbonyl groups, indicating that protein oxidation could play a role. In the liver, it was found that LAMP-1 was higher in males and greatly colocalized with LC3 indicating a larger number of autophagolysosomes. None of the above parameters was significantly different in the kidneys of both sexes with the exception of MDA, which was significantly higher in females. These results suggest that the sex determinant affects the autophagy process and oxidation of proteins and lipids in an organ specific manner. It seems that the protein oxidation is more linked with constitutive autophagy, at least in cardiac ventricles, in comparison with lipid peroxidation.

Key words

Sex, protein carbonylation, autophagy, lysosomes.