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CHRONIC KIDNEY DISEASE. NUTRITION, INFLAMMATION AND OXIDATIVE STRESS

SP344 EFFECTS OF INOS INHIBITION IN HIGH FAT DIET-INDUCED OBESITY

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Introduction and Aims: Obesity is a worldwide problem caused by caloric excess promoting deleterious cellular responses in organs. Endothelial dysfunction, impaired vasodilation and insulin resistance are considered as key features of obesity. Interactions between metabolic and hemodynamic factors activate intracellular signalling pathways, leading to the production of oxidative stress, pro-inflammatory cytokines and fibrotic factors. Among vasoactive factors, nitric oxide (NO) has been determined as playing a critical role in the pathogenesis of metabolic diseases. The aim of this study is to investigate the involvement of inducible nitric oxide synthase (iNOS) in the development of progressive renal dysfunction leading to obesity-induced kidney disease as well as in liver and adipose tissue.
Methods: To do so, C57BL/6 male mice were randomized to a low fat diet (LFD) or a high fat diet (HFD) and treated with pharmacological agent, L-NIL (iNOS inhibitor; 0.1 % in drinking water), for 16 weeks.
Results: We have demonstrated that iNOS inhibition with L-NIL prevented several changes in mice fed a HFD: increase of body weight, fasting blood glucose level and plasma levels of triglyceride, non-esterified fatty acids and insulin. Interestingly, the increase in albuminuria and mesangial matrix expansion were not ameliorated with L-NIL, while there was a significant improvement in glycosuria and proteinuria. Moreover, the urinary hydrogen peroxide level, a stable product of ROS production, significantly higher in mice fed a HFD, was reduced with L-NIL. To evaluate the beneficial effect of L-NIL in the development of insulin resistance, liver and peri-renal white adipose tissue were also investigated. Histological analysis revealed an increasing size of adipocytes and an accumulation of lipid vacuoles into hepatocytes of mice fed a HFD along with increased liver triglyceride level which were significantly decreased with L-NIL treatment. However, inflammation, as attested by macrophage infiltration and enhanced MCP-1 level, was only prevented by L-NIL in the adipose tissue but not in the liver.
Conclusions: These results suggest that inhibition of iNOS leads to beneficial effects in kidney, especially in regard to tubular function. We also observed a favourable role of L-NIL administration in liver and adipose tissue of mice fed a HFD. However, further investigations are needed to better determine the role of iNOS in the targeted organs.