TOPIRAMATE PROTECTS APOE-DEFICIENT MICE FROM KIDNEY DAMAGE WITHOUT AFFECTING PLASMA LIPIDS

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Topiramate is an anticonvulsant drug also prescribed for migraine prophylaxis that acts through several mechanisms of action. Several studies indicate that topiramate induces weight loss and a moderate reduction of plasma lipids and glucose. Based on these favourable metabolic effects, aim of this study was to evaluate if topiramate could modulate atherosclerosis development and protect target organs of dysmetabolic conditions. Thirty apoE-deficient mice were divided into three groups and fed for 12 weeks a high fat diet (Control) or the same diet containing topiramate at 0.125% (T-low) and 0.250% (T-high). Body weight, water and food intake were monitored throughout the study. Plasma lipids and glucose levels were measured and a glucose tolerance test was performed. Atherosclerosis development was evaluated in the whole aorta and at the aortic sinus. Histological analysis of liver, kidney and adipose tissue was performed. Topiramate did not affect weight gain and food intake. Glucose tolerance and plasma lipids were not changed and, in turn, atherosclerosis development was not different among groups. Topiramate did not modify liver and adipose tissue histology. Conversely, in the kidneys, the treatment reduced the occurrence of glomerular lipidosis (on average, more than 11 glomeruli affected in Control vs 1 to 3 glomeruli affected in the treated groups) and tubular necrosis (30% in Control, 10% in T-low and 0% in T-high) and by decreasing foam cells accumulation and reducing the expression of inflammatory markers. Blood urea nitrogen levels were also reduced by treatment (-18% in T-low and -25% in T-high). Our results indicate that topiramate does not affect atherosclerosis development, but preserves kidney structure and function. The study suggests that topiramate could be investigated in drug repurposing studies for the treatment of glomerular lipidosis.