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   2022G021

2. Title
   Effect of Nicotine on Renal Glomerular Endothelial Cell Homeostasis by Aldosterone Natriuretic Peptide System

3. Period
   2022-2024

4. Summary

   We investigated the effects of aldosterone, a known aggravating factor in kidney disease, with a focus on the importance of glomerular endothelial cells. We used endothelial cell（EC）-specific guanylyl cyclase-A (GC-A) knockout (KO) mice for our analysis. Since smoking has been reported to impair endothelial cell function, but its detailed mechanism remains unclear, we also examined the effects of nicotine exposure on the kidney. Male EC GC-A KO mice and control mice were divided into four groups based on nicotine administration. All groups were subjected to uninephrectomy, high salt diet, and aldosterone (ALDO). After four weeks, the mice were sacrificed, and measurements were taken for blood pressure, body weight, urine volume, water intake, kidney weight, heart weight, serum urea nitrogen (UN) and creatinine (Cr). Additionally, we analyzed glomerular mRNA expression, conducted histological examinations of kidney tissues, and measured the urine albumin-tocreatinine ratio. As a result, there was no significant difference in body weight between ALDO EC GC-A KO mice and ALDO control mice. However, both mouse groups showed weight loss in the nicotine-administered groups. EC GC-A KO mice exhibited increased systolic blood pressure. Urine volume and water intake increased with ALDO but decreased in both mouse groups with nicotine administration. Gene expression analysis showed that glomerular *Serpine1* expression decreased in nicotine-treated control mice, while *Tgfb1, Ctgf, Fn1, Emr1, Ccl2, and Acta2* mRNA expression levels showed no significant differences among the four groups. Urinary albumin excretion tended to increase in nicotine-administered ALDO EC GC-A KO mice. On the other hand, glomerular enlargement, a marker of glomerular damage, was reduced in nicotine-administered ALDO EC GC-A KO mice. These findings suggest that nicotine may have a protective effect against kidney damage.