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High citrate diet delays progression of renal insufficiency in the ClC-5 knockout mouse model of Dent's disease.

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BACKGROUND: Dent's disease, an X-linked renal tubular disorder, is characterized by low-molecular-weight proteinuria, hypercalciuria, nephrocalcinosis, nephrolithiasis, and progressive renal failure. Dent's disease results from mutations of the voltage-gated chloride channel CLC-5. METHODS: We studied the effect of zero and high citrate diet on renal function of ClC-5 knockout mice and wild-type mice. The mice were placed in metabolic cages from which the urine was collected. Mice were sacrificed to obtain serum and tissues for analysis. RESULTS: ClC-5 knockout mice fed zero or high citrate diet had significantly increased urinary calcium excretion compared with wild-type mice fed the same diets. Nine-month-old ClC-5 knockout mice on a zero citrate diet had significantly decreased glomerular filtration rate (GFR), whereas 9-month-old ClC-5 knockout mice on a high citrate diet had normal renal function. ClC-5 knockout mice fed a zero citrate diet had significantly increased tubular atrophy, interstitial fibrosis, cystic changes, and nephrocalcinosis compared to ClC-5 knockout mice fed a high citrate diet. Transforming growth factor-beta1 (TGF-beta1) was significantly increased in 9-month-old ClC-5 knockout mice on zero citrate diet compared to 9-month-old wild-type mice on the same diet. CONCLUSION: High citrate diet preserved renal function and delayed progression of renal disease in ClC-5 knockout mice even in the apparent absence of stone formation. We conclude from this that long-term control of hypercalciuria is an important factor in preventing renal failure in these mice.

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