Dietary sodium content, renin-angiotensin system and cysts formation in ARPKD

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INTRODUCTION

Patients with ARPKD are advised to restrict their dietary sodium intake, as it is expected to reduce blood pressure and albuminuria. However, the contribution of dietary sodium intake to ARPKD development is not fully understood. Here we hypothesize that restriction of dietary sodium stimulates cyst formation via Renin-Angiotensin System (RAS) - mediated effects.

METHODS

To test our hypothesis, 6 weeks old PCK rats were switched to a normal (0.4%; NS), high salt (4%; HS), and sodium-deficient (0.01%; SD) NaCl diets for 8 weeks. Immunohistochemistry, GFR measurements and BUN measurements were employed here to test kidney injury following changes in dietary sodium. RAS metabolites were analyzed with an LC- MS/MS approach.

RESULTS

SD and HS diet groups revealed an increase of cystic area from 28.5% in NS group to 43.6% and 39.8% in SD and HS groups after 8 weeks of diet, respectively. However, cysts location was different between groups: SD diet caused extensive growth of small cysts in the cortical area, and augmented renal hypertrophy. Urinary output was significantly higher in the HS animals compared to both SD and NS groups; we found no difference in food intake or urinary creatinine in either group. Urinary chloride and sodium excretion was elevated in HS fed animals compared to NS and SD groups. GFR levels were found to be 0.40 ± 0.05, 0.65 ± 0.03, and 0.98 ± 0.11 μL/min/100g of body weight in SD, NS and HS fed rats, respectively. BUN was ~130 mg/dL in the SD group compared to < 20 mg/dL in NS and HS animals. Components of circulating RAS were significantly enhanced in animals fed a SD diet.

CONCLUSIONS

Both HS and SD diets significantly increased cystic area in PCK rats, although cyst formation and its effects on kidney function are different between these groups. RAS was enhanced in animals fed a SD diet, which could have contributed to cortical cyst development.

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