ELEVATION OF PLASMA URIC ACID LEVELS IN URICASE KNOCKOUT MICE BY DIETARY SODIUM LOAD

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INTRODUCTION and OBJECTIVES

Familial Juvenile Hyperuricemic Nephropathy type 2 is caused by the defect of renin gene [1)], therefore, serum uric acid level is known to correlate with the renin-angiotensin system. As for changes in serum uric acid level by the dietary sodium load in humans, chronically high sodium intake is associated with increases in serum uric acid level [2)] (Fig.1). In addition, serum uric acid level is reduced by the Dietary Approaches to Stop Hypertension (DASH) diet. However, under DASH diet, higher sodium intake decreased serum uric acid level [3)] (Fig.2).

In this study, we investigated the change of uric acid dynamics and gene expression levels of uric acid transporters in uricase knockout (Uox-KO) mice by sodium citrate load.

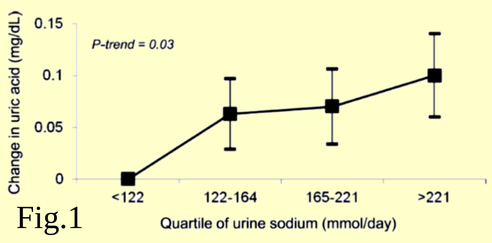


Fig.1

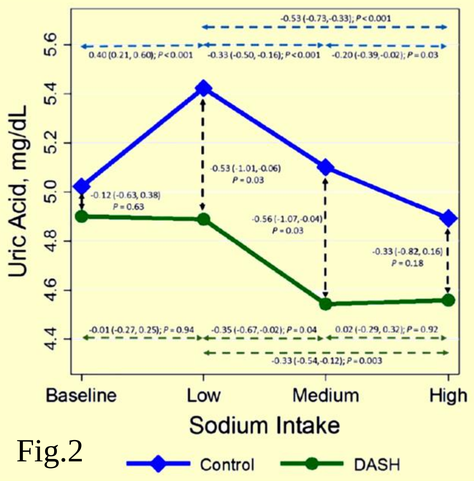
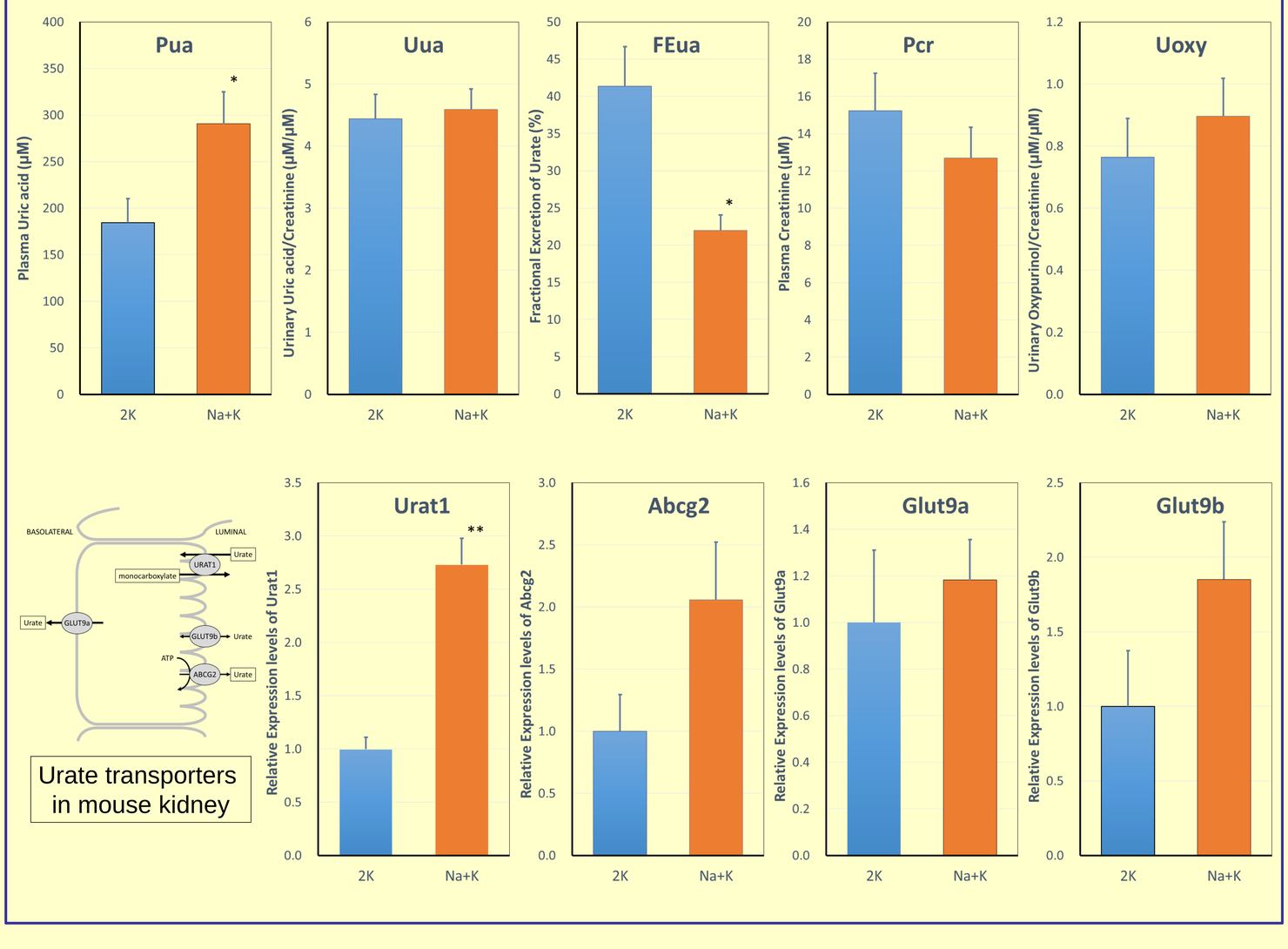


Fig.2

METHODS

390mg Na citrate + 463mg K citrate (Na+K group), or 893mg K citrate alone (2K group) was added to the 100g feed, which were mixed 27mg allopurinol.

After 1 week feeding with each of the feed to Uox-KO mice, the plasma levels of uric acid and creatinine, and the urinary excretion of uric acid and oxypurinol (metabolite of allopurinol) were measured by HPLC with C18 column. In addition, mRNA levels of uric acid transporter Urat1, Abcg2, and Glut9 were measured in the kidneys by qPCR.



RESULTS

Plasma uric acid levels of Na+K group mice are 290.7±34.4μM, which was significantly higher than those of 2K group mice, 184.5±25.7μM (Mean±SE, n=7, $p<0.05$).

From the fact that there was no significant difference in uric acid excretion in the urine, fractional excretion of urate (FEua) of Na+K group mice were significantly reduced to approximately one-half of the FEua of 2K group mice. In addition, there was no significant difference in the plasma creatinine levels or in the urinary excretion of oxypurinol between Na+K group mice and 2K group mice.

For gene expression levels of urate transporters, only the mRNA levels of Urat1 in Na+K group mice were significantly increased than those in 2K group mice (n=3, $p<0.01$).

CONCLUSIONS

Since there is no significant difference in the urinary excretion of uric acid and oxypurinol, or plasma creatinine level, the elevation of plasma uric acid level by sodium load is not due to the attenuation of the effect of allopurinol nor renal dysfunction. Since the FEua was decreased by sodium load, plasma uric acid level might be increased by the enhancement of uric acid reabsorption via Urat1, whose expression was increased by sodium load.

REFERENCES:

1) Zivna M, Hulkova H, Matignon M, Hodanova K, Vylet'al P, Kalbacova M, et al. Dominant renin gene mutations associated with early-onset hyperuricemia, anemia, and chronic kidney failure. Am J Hum Genet. 2009;85(2):204-13
2) Forman JP, Scheven L, de Jong PE, Bakker SJ, Curhan GC, Gansevoort RT. Association between sodium intake and change in uric acid, urine albumin excretion, and the risk of developing hypertension. Circulation. 2012;125(25):3108-16.
3) Juraschek SP, Gelber AC, Choi HK, Appel LJ, Miller ER, 3rd. Effects of the Dietary Approaches to Stop Hypertension (DASH) Diet and Sodium Intake on Serum Uric Acid. Arthritis Rheumatol. 2016;68(12):3002-9.

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