URINARY PGE_2 AND $PGF_{2\alpha}$ IN DIABETES INSIPIDUS BRATTLEBORO AND LONG EVANS RATS SUBMITTED TO POTASSIUM LOADING

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Summary

The measurement of the 24 hour urinary excretion of PGE_2 and $PGF_{2\alpha}$ in diabetes insipidus and Long Evans rats submitted to a potassium load demonstrates that urinary $PGF_{2\alpha}$ excretion is significantly increased and the ratio $PGE_2/PGF_{2\alpha}$ significantly decreased during high potassium intake. The results suggest that $PGF_{2\alpha}$ and/or the activity of the renal PGE_2-9-reductase enzyme (evaluated by the $PGE_2/PGF_{2\alpha}$ ratio) may play a role in potassium homeostasis without influence of the antidiuretic hormone.

Introduction

In normal animals manipulations of antidiuretic hormone and sodium balance may influence the urinary excretion of prostaglandins [1,2] which reflect their tubulo-interstitial synthesis [3]. Low potassium diets did not influence the urinary excretion of prostaglandins in rats [4]. However, the PGE_2 synthesis of renal interstitial cells in culture seems to be affected by changes in potassium concentration [5]. In order to further evaluate the influence of potassium on the renal production of prostaglandins we decided to study the effects of potassium load on urinary PGE_2 and urinary $PGF_{2\alpha}$ in diabetes insipidus Brattleboro rats (with endogenous antidiuretic hormone) and in Long Evans heterozygote rats.

Methods

Female diabetes insipidus rats weighing between 186 and 233g and age matched female Long Evans rats weighing between 259 and 318g were used in the present study (from Centraael Proefdierenbedrijf TNO, Zeist, Holland).

A standard diet (containing 0.35g sodium and 0.5g potassium per 100g) was given to the rats, maintained in individual metabolic cages for 11 days.

Ten diabetes insipidus rats and 10 Long Evans rats drank distilled water ad libitum. In five diabetes insipidus rats and five Long Evans rats potassium intake was increased for 20 days (8 days before the experimental period in metabolic cages and 11 days in metabolic cages). The potassium load was performed by adding potassium chloride (0.75g/L in the distilled water given to the diabetes insipidus rats and 6g/L in the water given to the Long Evans rats). Three separate 24 hour urine collections were obtained in the last three days of the experiments. Potassium was measured by flame photometry, PGE_2 and urinary $PGF_{2\alpha}$, measured by radioimmunoassay [6], were evaluated in each urine collection. Statistical analysis of results was performed by using the Student's 't' test for unpaired results. Results are given as mean ± SD.

Results (Table I)

Urine volumes were not affected by the potassium load, the small increase during the experimental period (149±3 versus 139±3ml/24hr in diabetes insipidus rats and 21±3 versus 18±1ml/24hr in Long Evans rats) being not significant. No changes in urine osmolality were found. A significant increase in

TABLE I. Urinary volume, urinary osmolality, urinary potassium excretion, urinary PGE_2 and $PGF_{2\alpha}$ excretion in diabetes insipidus Brattleboro and Long Evans heterozygote rats before and after potassium load

	Basal potassium intake		High potassium intake	
	Diabetes insipidus	Long Evans	Diabetes insipidus	Long Evans
Urinary volume (ml/min)	139±3	18±1	149±3	21±3
Urinary osmolality (mOsm/kg)	216±7	1399±72	195±5	1504±103
Urinary potassium (mEq/24hr)	3.5±0.10	3.1±0.1	4.9±0.5*	5.5±0.5*
Urinary PGE_2 (ng/24hr/100g)	58.2±6.5	107.6±14.9	51.6±7.3	88±32.1
Urinary $PGF_{2\alpha}$ (ng/24hr/100g)	22.3±2.2	26.1±2.7	57.3±4.4*	66.2±4.7*
$PGE_2/PGF_{2\alpha}$ ratio	2.7±0.6	4.4±0.6	0.9±0.1*	1.2±0.4*

* $p<0.01$

in urinary potassium ($p<0.01$) was obtained in diabetes insipidus rats, 5.5± 0.5 versus 3.1±0.1mEq/24hr, and in Long Evans rats 4.9±0.5 versus 3.5±0.1 mEq/24hr during the experimental periods. A non-significant decrease in urinary PGE_2 was found in the two groups during the potassium loading period, but a significant rise in urinary $PGF_{2\alpha}$ ($p<0.01$) was present in the two groups,

57.3±4.4 versus 22.3±2.2ng/24hr/100g body weight in diabetes insipidus rats, 66.2±4.7 versus 26.1±2.7ng/24hr/100g in Long Evans rats. The $PGE_2/PGF_{2\alpha}$ ratio was calculated for each experiment. A significant lower value of this ratio was found in the group submitted to the potassium loading.

Discussion

Few studies have been done concerning the relationship between potassium and renal prostaglandins. Potassium depletion is associated with an increased production of renal PGE_2 in dogs [7] and man [8], but not in rats [4]. A decrease in the synthesis of PGE_2 has been demonstrated in rabbit medullary interstitial cells in culture incubated in low potassium media [5]. In the present study urinary $PGF_{2\alpha}$ was significantly higher during potassium loading in diabetes insipidus and Long Evans rats. The urinary excretion of PGE_2 was mildly, but not significantly decreased. In consequence the $PGE_2/PGF_{2\alpha}$ ratio was found to be significantly decreased in the two groups of rats submitted to the high potassium load. These findings suggest that the renal medullary PGE_2-9-ketoreductase activity was raised during the high potassium intake, the $PGE_2/PGF_{2\alpha}$ ratio being an acceptable reflection of renal enzyme activity. Our results suggest that renal $PGF_{2\alpha}$ by itself and/or the PGE_2-9-ketoreductase activity, evaluated indirectly by the ratio, may have an important role in potassium homeostasis. Similar results were found in diabetes insipidus and Long Evans rats, suggesting that antidiuretic hormone does not play a major role in this adaptation.

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