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高钾饮食对肾血管高血压大鼠血压、前列腺素、尿激肽释放酶的影响

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Effects of dietary K on blood pressure, prostaglandin, and kallikrein in renovascular hypertensive rats

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ABSTRACT The effects of dietary K (food and tap water both containing 1% KCl) on blood pressure and renal prostaglandin-kallikrein-kinin system were investigated in Wistar rats made hypertensive by constriction of left renal artery. Dietary K attenuated the development of hypertension and increased urine volume accompanied by increased excretion of K, but by uninfluenced excretion of Na. Dietary K also increased the urinary excretion of kallikrein, PGE_2 and aldosterone in Goldblatt hypertensive rats. There was no significant difference in the values of plasma Na between the two groups with and without dietary K. These results suggest that dietary K may attenuate the development of hypertension, increase urine volume via the mechanism of enhancing production of renal PGE_2 and kallikrein in hypertensive rats.

KEY WORDS dietary potassium: blood pressure: aldosterone: prostaglandins: kallikrein: renovascular hypertension: diuresis

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提要 放射免疫法(RIA)测定前列腺素 E_2(PGE_2)，分光光度法测定尿激肽释放酶，观察到高钾饮食可显

著抑制肾性高血压大鼠血压的升高，促使尿 PGE_2、激肽释放酶 24 h 排泄量增加。提示高钾饮食可通过促进高血压大鼠肾脏 PGE_2 和激肽释放酶生成增多而产生利尿、降压作用。

关键词 饮食钾；血压；醛固酮；前列腺素类；血管舒缓素；肾血管高血压；利尿

高钾饮食有抗高血压作用，流行病学发现钾摄入量与血压呈负相关[1]。高钾饮食通过利尿、排钠、抑制肾素分泌等作用阻滞两肾一夹型高血压大鼠血压的升高[2]。高钾饮食可对抗缩血管物质的血管收缩反应[3]。以往研究多侧重于高钾饮食可抑制肾素-血管紧张素-醛固酮(R-A-A)系统并产生降压作用，但高钾饮食的降压作用是否亦与前列腺素-激肽释放酶-激肽(P-K-K)系统有关，目前尚未见文献报道。本文就高钾饮食对两肾一夹型高血压大鼠 P-K-K 系统的影响及钾利尿机理进行实验性探讨。

MATERIALS AND METHODS

用♂Wistar 大鼠 53 只制作两肾一夹型高血压模型。体重 172±SD 20 g。戊巴比妥钠麻醉，腹中线切口，分离左肾动脉后放置银夹(内径 0.2 mm)，右肾不触及，术后 1 wk 将形成肾性高血压大鼠随机分为两组，一组为高钾饮食组，食物及饮水中均加 1% KCl，另一组为正常饮食组，饲以正常食物及饮水。另设假手术组，仅分离左肾动脉但不上银夹，接受正常食物及饮水，作为正常血压对照组。

用 CRS-3 型大鼠尾动脉血压计(上海高血压研究所监制)，每周测血压一次。各组大鼠在实验期间每周于代谢笼中收集 24 h 尿一次，记录尿量及当日饮水量。全部大鼠于 4 wk 末称重，乙醚轻度麻醉后，断头取血，进行各种测定。

用 RIA 测定大鼠尿 PGE_2[4]及尿醛固酮24 h 排泄量[5]；用分光光度法测定尿激肽释放酶 24 h 排泄量[6]；尿钠、钾用国产 630 型火焰光度计测定，血钠、钾、氯用 Beckman 公司生产的离子电极(E 4 A 型)测定。

PGE_2 药箱由中国医科院基础所提供，醛固酮药箱由上海内分泌研究所提供。

RESULTS

血压 实验期间正常饮食组大鼠收缩期血压逐渐升高，在 4 wk 末达到 26±4 kPa (+76.8%)。高钾饮食可明显抑制由肾动脉狭窄所引起收缩压的升高(±52.7%)，常压对照组血压无明显变化(Fig 1 A)。

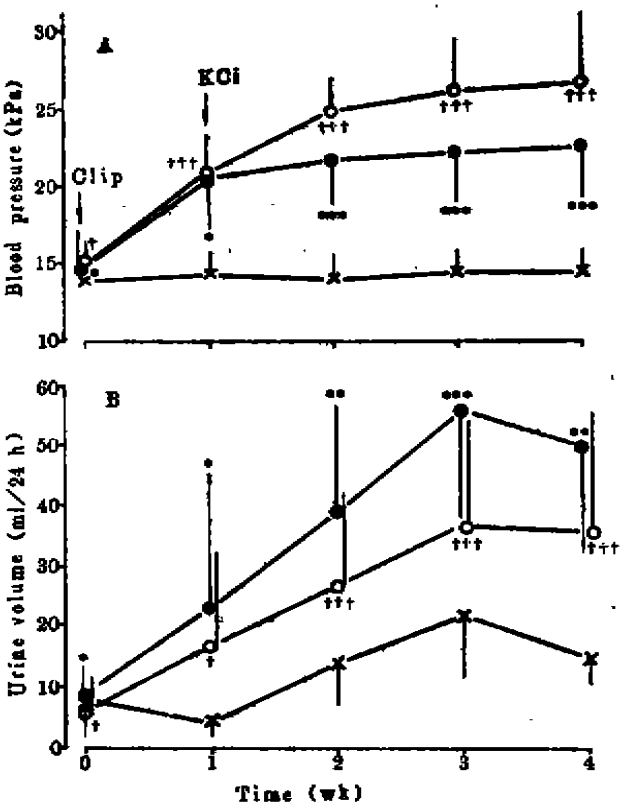

Fig 1. Effects of dietary K (food and tap water both containing 1% KCl) on systolic blood pressure (A) and urine volume (B) in renal hypertensive rats. $\bar{X}\pm SD$. $^{*}P>0.05$, $^{**}P<0.05$, $^{***}P<0.01$ treated with 1% KCl group (●, $n=21$) *vs* untreated group (○, $n=18$). $^{\dagger}P>0.05$, $^{\dagger\dagger\dagger}P<0.01$ untreated group *vs* sham-operated group (×, $n=15$).

饮水量、尿量、尿钠、钾排泄量 正常饮食组大鼠从手术后 1 wk 开始，其饮水量、尿量均逐渐增多，3 wk 达高峰。高钾饮食组增

Tab 1. Effects of dietary K on urinary excretions of Na and K (mmol/24 h) in renal hypertensive rats. $\bar{x}\pm SD$. $^{*}P>0.05$, $^{***}P<0.01$ treated with 1% KCl group *vs* untreated group. $^{\dagger}P>0.05$, $^{\dagger\dagger\dagger}P<0.01$ untreated group *vs* sham-operated group.

Groups	Untreated ($n=18$)		1% KCl ($n=21$)		Sham-operated ($n=15$)	
	Na	K	Na	K	Na	K
0 wk	3.0±2.0†	1.4±0.8†	3.8±1.5*	2.0±0.7*	3.0±2.1	1.4±0.8
1 wk	3.2±1.5†††	2.2±08†††	2.9±1.7*	2.1±0.7*	1.5±0.8	1.3±0.5
2 wk	6.8±3.0†††	2.7±1.0†	6.8±1.9*	10.0±3.4***	3.9±1.8	2.6±0.8
3 wk	9.8±2.4†	3.0±0.6†	11.0±3.0*	12.3±3.3***	8.6±3.2	2.7±0.8
4 wk	7.3±2.7†	2.6±0.7†	8.7±2.3*	11.9±3.3***	6.0±2.0	2.4±0.7

加更为明显，均有显著差异(Fig 1 B)。

在术后的 1-2 wk，正常饮食组大鼠尿钠 24 h 排泄量较常压对照组显著增多，3-4 wk 无显著差异。高钾饮食组大鼠尿钠排出量增加不明显，而尿钾排泄量明显增多(Tab 1)。

尿激肽释放酶、尿醛固酮、尿 PGE_2 排泄量 4 wk 末高钾饮食组大鼠尿醛固酮、尿 PGE_2、尿激肽释放酶 24 h 排泄量均较正常饮食组大鼠显著增高。正常饮食组大鼠尿醛固酮、尿 PGE_2 24 h 排泄量较常压对照组明显增多，而尿激肽释放酶排泄量却较常压对照组为低。在高钾饮食组和正常饮食组，其尿 PGE_2 24 h 排泄量均与尿量呈正相关(Tab 2)。

Tab 2. Effects of dietary K on plasma electrolytes (mmol/L) and urinary excretions of aldosterone, PGE_2, and kallikrein in renal hypertensive rats at the end of 4 th wk. $\bar{x}+SD$. $^{*}P>0.05$, $^{**}P<0.05$, $^{***}P<0.01$ treated with 1% KCl group *vs* untreated group. $^{\dagger}P>0.05$, $^{\dagger\dagger\dagger}P<0.01$ untreated group *vs* sham-operated.

Groups	Untreated ($n=18$)	1% KCl ($n=21$)	Sham-operated ($n=15$)
Na^+	142±4†††	144±6*	146±3
K^+	6.0±1.3†	7.3±2.4*	6.4±1.9
Cl^-	115±2†	116±2*	115±7
Aldosterone (μg/24 h)	0.43±0.18†††	1.30±1.00***	0.28±0.07
PGE_2 (ng/24h)	24±9†††	34±12***	14±4
Kallikrein (Eu/24 h)	10±6†††	16±10**	24±6

血浆钠、钾、氯值 4 wk 末，正常饮食组血浆钠值较常压对照组低，高钾饮食组与正常饮食组大鼠血浆钠值无显著差异。高钾组和正常饮食组，正常饮食组与常压对照组之间血浆钾、氯值亦均无显著差异(Tab 2)。

DISCUSSION

尿激肽释放酶和尿 PGE_2 排出的多少可代表肾内激肽释放酶和 PGE_2 生成的多少[7]。从本文实验结果可见，高钾饮食可促使肾内 PGE_2、激肽释放酶产生增多。尿量与 PGE_2 排泄量呈正相关，提示高钾饮食的利尿作用可能是高钾饮食促进肾内 PGE_2 和激肽产生增多的结果。

肾脏 PGE_2 具有利钠的效应，在本实验中虽然高钾饮食显著增加 24 h PGE_2 排泄量，但尿钠排泄量增加并不明显，其原因可能为钾刺激醛固酮生成增多，对抗了 PGE_2 的利钠效应[8]。

Croxatto 报告，静脉内注射肾脏半纯化肾素，对尿激肽释放酶排泄存在剂量依赖性抑制作用[9]，因此血浆肾素升高可能是两肾一夹型高血压大鼠尿激肽释放酶减少的原因。高钾饮食后，高血压大鼠尿激肽释放酶排泄量显著增加，其原因可能为高钾饮食抑制肾素分泌、减弱了肾素对尿激肽释放酶合成抑制作用的结果。

本实验结果提示，高钾饮食可能通过促进两肾一夹型高血压大鼠肾脏 PGE_2 和尿激肽释放酶生成增多的机理而产生利尿、降压作用。

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伊吗唑咀和达唑氧苯对培养血管内皮细胞 cAMP 含量和 PGI_2 生成的影响[1]

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Effects of imazodan and dazoxiben on cAMP levels and PGI_2 production in cultured bovine aortic endothelial cells

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ABSTRACT We have investigated the effects of imazodan, a potent inhibitor of phosphodiesterase III (PDE III) and dazoxiben, a selective inhibitor of thromboxane synthetase on cAMP levels and PGI_2 production in cultured bovine aortic endothelial cells by radioimmunoassay. When cultured endothelial cells were incubated with imazodan, intracellular levels of cAMP were increased in a dose-dependent manner. PGI_2 production induced by arachidonic acid (AA) was not affected by imazodan 0.1-10 μmol/L. But imazodan 100 μmol/L caused a 35% inhibition of PGI_2 production. In the presence of AA, dazoxiben could also elevate intracellular levels of cAMP. Furthermore, dazoxiben 1-10 μmol/L caused a marked increase in PGI_2 production, but

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