THESIS TITLE : ROLES OF THE RENIN-ANGIOTENSIN SYSTEM ON RENAL FUNCTION IN GLUCOSE-FED RATS

AUTHOR : MISS THIDARAT KHONGNAKHA

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(Assistant Professor Dr. Paiboon Buranaruk)

ABSTRACT

High carbohydrate intake induces hypertension in the presence of the renin-angiotensin system overactivity, insulin resistance, and renal malfunction. This study tests the hypothesis that long-term high carbohydrate intake exacerbates renal function prior to a rise in arterial pressure via the renin-angiotensin system and insulin resistance. Three-week old male Spraque-Dawley rats were divided into 5 groups: group 1 untreated control (control, C) fed by a normal rat chow and tap water for 4 weeks (n=11), group 2 long-term high carbohydrate (long-term glucose feeding, LTG) fed by a normal rat chow and 5 % glucose in tap water for 4 weeks (n=6), group 3 control plus captopril (C+Cap) fed by a normal rat chow as the control and 48 hours after surgery being treated by captopril (400 mg/l in tap water) (n=7), group 4 long-term high carbohydrate plus captopril (LTG+Cap) fed by a normal rat chow and 5 % glucose in tap water as the LTG and 48 hours after sugery being treated by glucose and captopril in tap water (n=10), and group 5 short-term high carbohydrate (short-term glucose feeding, STG) fed by a normal rat chow as the control and 48 hours after surgery being fed by 5 % glucose in tap water (n=9). At 7-8 weeks of age, each rat was implanted with femoral arterial, venous, and

bladder catheters. Forty-eight hours later, arterial pressure was continuously recorded in a conscious restrained condition. Urine and blood samples were collected before, during, and after intravenous saline infusion (a mixture of 0.5 % inulin and 0.5 % PAH in isotonic saline, 5% of body weight, 0.5 ml/min) up to 90 minutes. After an overnight fasting, glucose tolerance tests were performed to estimate insulin resistance. At the end of the experiment, all rats were killed with ether, the heart and kidney weights were collected. The absolute body, heart, and kidney weights were not significantly different among the five groups, whereas the kidney to body weight ratio of the LTG was significantly higher than that of the control (0.89 ± 0.04 g vs. 0.80 ± 0.02 g; LTG vs. C, respectively; $P < 0.05$). Before (C 112.60 ± 2.72 mm Hg, LTG 113.85 ± 4.06 mm Hg, C+Cap 106.47 ± 1.34 mm Hg, LTG+Cap 107.86 ± 2.20 mm Hg, and STG 118.69 ± 2.43 mm Hg) and after saline load, mean arterial pressures of the 4 treated groups were not significantly different from the control. All groups displayed fasting and non-fasting blood glucose within the normal range (70-100 mg/dl) and well glucose tolerance. Basal water excretion, sodium excretion, potassium excretion, fractional water excretion (FE_{H2O}), fractional sodium excretion (FE_{Na}), fractional potassium excretion (FE_K), and the responses to an acute saline load of the rats fed by a normal rat chow and glucose in drinking water for 4 weeks (LTG) were significantly lower than those of the control (water excretion: 11.29 ± 2.42 μl/min/gKW vs. 27.75 ± 3.09 μl/min/gKW; Na^+ excretion: 1.13 ± 0.43 μEq/min/gKW vs. 3.80 ± 0.50 μEq/min/gKW; K^+ excretion: 0.58 ± 0.06 μEq/min/gKW vs. 1.12 ± 0.19 μEq/min/gKW; FE_{H2O}: 0.97 ± 0.20 % vs. 4.47 ± 0.61 %; FE_{Na}: 0.66 ± 0.27 % vs. 4.39 ± 0.70 %; FE_K: 12.55 ± 1.89 % vs. 47.83 ± 1010 %; LTG vs. C, respectively; $P < 0.05$). In contrast, their glomerular filtration rate (GFR) (LTG 1.37 ± 0.34 ml/min/gKW vs. C 0.71 ± 0.12 ml/min/gKW; $P < 0.05$) and filtration fraction (FF) (LTG 25.19 ± 5.71 % vs. C 10.18 ± 1.36 %; $P < 0.05$) were significantly higher than the control and other treated groups. These changes were not observed in the other treated groups and were returned to their normal control values when the renin-angiotensin system was inhibited by captopril in drinking water for 2 days. However, an effective renal blood flows and effective renal vascular resistances of all groups were not significantly different and remained close to their baseline values throughout the experiments. The present study indicates that the long-term high carbohydrate intake exacerbates the renal function before a rise in arterial pressure via the renin-angiotensin system, independent of insulin resistance.